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V BABASHOV, MSC,[1] S PALIMAKA, MBIOTECH,[1] G BLACKHOUSE, MSC, MBA,[1,2] DJ O'REILLY, PHD, MSC[1,2]

1. Programs for Assessment of Technology in Health (PATH) Research Institute, St. Joseph's Healthcare, Hamilton, ON, Canada
2. Department of Clinical Epidemiology and Biostatistics, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

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ABSTRACT

Background

Uterine fibroids, or leiomyomas, are the most common benign tumours in women of childbearing age. Some women experience symptoms (e.g., heavy bleeding) that require aggressive forms of treatment such as uterine artery embolization (UAE), myomectomy, magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU), and even hysterectomy. It is important to note that hysterectomy is not appropriate for women who desire future childbearing.

Objectives

The objective of this analysis was to evaluate the cost-effectiveness and budgetary impact of implementing MRgHIFU as a treatment option for symptomatic uterine fibroids in premenopausal women for whom drugs have been ineffective.

Review Methods

We performed an original cost-effectiveness analysis to assess the long-term costs and effects of MRgHIFU compared with hysterectomy, myomectomy, and UAE as a strategy for treating symptomatic uterine fibroids in premenopausal women aged 40 to 51 years. We explored a number of scenarios, e.g., comparing MRgHIFU with uterine-preserving procedures only, considering MRgHIFU-eligible patients only, and eliminating UAE as a treatment option. In addition, we performed a one-year budget impact analysis, using data from Ontario administrative sources. Four scenarios were explored in the budgetary impact analysis:

- MRgHIFU funded at 2 centres
- MRgHIFU funded at 2 centres and replacing only uterine-preserving procedures
- MRgHIFU funded at 6 centres
- MRgHIFU funded at 6 centres and replacing only uterine-preserving procedures

Analyses were conducted from the Ontario public payer perspective.

Results

The base case determined that the uterine artery embolization (UAE) treatment strategy was the cost-effective option at commonly accepted willingness-to-pay values. Compared with hysterectomy, UAE was calculated as having an incremental cost-effectiveness ratio (ICER) of $46,480 per quality-adjusted life-year (QALY) gained. The MRgHIFU strategy was extendedly dominated by a combination of UAE and hysterectomy, and myomectomy was strictly dominated by MRgHIFU and UAE. In the scenario where only MRgHIFU-eligible patients were considered, MRgHIFU was the cost-effective option for a willingness-to-pay threshold of $50,000. In the scenario where only MRgHIFU-eligible patients were considered and where UAE was eliminated as a treatment option (due to its low historic utilization in Ontario), MRgHIFU was cost-effective with an incremental cost of $39,250 per additional QALY.

The budgetary impact of funding MRgHIFU for treatment of symptomatic uterine fibroids was estimated at $1.38 million in savings when funded to replace all types of procedures at 2 centres, and $1.14 million when funded to replace only uterine-preserving procedures at 2 centres. The potential savings increase to $4.15 million when MRgHIFU is funded at 6 centres to treat all women eligible for the procedure. Potential savings at 6 centres decrease slightly, to $3.42 million, when MRgHIFU is funded to replace uterine-preserving procedures only.

Conclusions

Our findings suggest that MRgHIFU may be a cost-effective strategy at commonly accepted willingness-to-pay thresholds, after examining the uncertainty in model parameters and several likely scenarios. In terms of budget impact, the implementation of MRgHIFU could potentially result in one-year savings of $1.38 million and $4.15 million in the scenarios where MRgHIFU is implemented in 2 or 6 centres, respectively. From a patient perspective, it is important to consider that MRgHIFU is the least invasive of all fibroid treatment options for women who have not responded to pharmaceuticals; it is the only one that is completely noninvasive. Also important, from a societal point of view, is the potential benefit from faster recovery times. Despite these benefits, implementation of MRgHIFU beyond the 2 centres which currently offer the treatment faces logistical challenges (for example, competing demands for use of existing equipment), as well as financial challenges, with hospitals needing to fundraise to purchase new equipment.

PLAIN LANGUAGE SUMMARY

Uterine fibroids are the most common benign tumours in women of childbearing age. There are often no symptoms, but when symptoms do occur they can include heavy bleeding and anemia. Fibroid symptoms can have a broad impact on a woman's health and lifestyle, and fibroids can also cause fertility problems.

Hysterectomy is one common treatment for fibroids. It means removing the uterus, so it is clearly inappropriate for women who want to bear children in future. Treatments that do not require removal of the uterus include myomectomy, uterine artery embolization (UAE), and magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU). Of these, MRgHIFU is not currently available in Ontario. At present, a clinical trial on MRgHIFU is being held at 2 research institutes in the province.

Health Quality Ontario was asked to investigate the use of MRgHIFU and the economic impact it might have on the health care system. This included writing a clinical analysis (a companion report to this one) to look at MRgHIFU's effectiveness and safety, compared with other treatments. It found MRgHIFU to be a promising technology, with comparable effectiveness and minimal adverse effects.

For this economic analysis, we compared the long-term costs and QALYs of MRgHIFU to those of the currently available treatments: hysterectomy, myomectomy, and UAE. (QALY stands for quality-adjusted life-year. It is calculated by taking the number of years a person is expected to gain as the result of a treatment, and adjusting it based on the quality of life they are expected to have, with a value of "1" representing one year of life lived at perfect health and a value of "0" representing death.)

We started with a base case (a basic scenario we could then vary to look at other possibilities) which assumed that 35% of patients were eligible for MRgHIFU. In the base case and other scenarios, we looked at ICERs. (ICER stands for incremental cost-effectiveness ratio. When 2 interventions are being compared, the ICER is the difference in their costs divided by the difference in their outcomes. In other words, it is the extra cost per extra unit of effect—the effect, in this case, being the QALY gained.)

In our base case, comparing UAE versus hysterectomy resulted in an ICER of $46,480 per QALY gained. Myomectomy was strictly dominated by both MRgHIFU and UAE (meaning it was less effective and more costly than either), and MRgHIFU was extendedly dominated by a combination of UAE and hysterectomy (meaning it was less effective and more costly than a program that would combine both). We then conducted sensitivity analyses by manipulating key variables. In one resulting scenario, we found MRgHIFU to be cost-effective in 20% of cases at a willingness-to-pay threshold of $50,000 (i.e., if the government was willing to pay $50,000 for the equivalent of one year of perfect health for patients). In another scenario, we assumed that 100% of patients (instead of 35%) were eligible for MRgHIFU. This made MRgHIFU the cost-effective option at the $50,000 threshold. We then used the same scenario but eliminated UAE as a treatment option, due to its historically low rate of use in Ontario. This made MRgHIFU cost-effective, when compared with hysterectomy, with an ICER of $39,250 per QALY gained.

We estimate that the Ministry of Health and Long-Term Care spends about $35.5 million a year on the treatments that are now available for symptomatic uterine fibroids. After our examination of several likely scenarios, we believe that MRgHIFU may be a cost-effective strategy at willingness-to-pay thresholds that are commonly accepted. It could potentially result in 1-year

savings of about $1.38 million if implemented in 2 centres, or about $4.15 million if implemented in 6 centres. Logistical challenges would arise—for example, competing demands for the use of existing equipment. So would financial challenges, with hospitals needing to fundraise to buy new equipment. However, MRgHIFU is the least invasive of all fibroid treatment options for women who have not responded to pharmaceuticals; it is the only one that is completely noninvasive. This is an important consideration for women. Also important, from a societal point of view, is the potential benefit from faster recovery times.

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LIST OF ABBREVIATIONS

AUB	Abnormal uterine bleeding
CCI	Canadian Classification of Health Interventions
CEAC	Cost-effectiveness acceptability curve
CIHI	Canadian Institute for Health Information
DAD	Discharge Abstract Database
ICD-10	International Classification of Diseases (10th revision)
ICER	Incremental cost-effectiveness ratio
ICES	Institute for Clinical Evaluative Sciences
MRI	Magnetic resonance imaging
MRgHIFU	Magnetic resonance-guided high-intensity focused ultrasound
OCCI	Ontario Case Costing Initiative
OHIP	Ontario Health Insurance Plan
OHTAC	Ontario Health Technology Advisory Committee
OSB	Ontario Schedule of Benefits
QALY	Quality-adjusted life-year
SDS database	Same Day Surgery database
SOGC	Society of Obstetricians and Gynaecologists of Canada
UAE	Uterine artery embolization
WTP	Willingness to pay

BACKGROUND

The Programs for the Assessment of Technology in Health (PATH) Research Institute was commissioned by Health Quality Ontario to evaluate the cost-effectiveness and predict the long-term costs and effects of magnetic resonance-guided high-intensity focused ultrasound for symptomatic uterine fibroids. Published economic evaluations are reviewed, and the structure and inputs of the economic model used to estimate cost-effectiveness are summarized. The results of the economic analyses are presented for magnetic resonance-guided high-intensity focused ultrasound versus uterine artery embolization, myomectomy, and hysterectomy, and the budget impact of implementing each intervention is estimated.

Health Quality Ontario conducts full evidence-based analyses, including economic analyses, of health technologies being considered for use in Ontario. These analyses are then presented to the Ontario Health Technology Advisory Committee, whose mandate it is to examine proposed health technologies in the context of available evidence and existing clinical practice, and to provide advice and recommendations to Ontario health care practitioners, the broader health care system, and the Ontario Ministry of Health and Long-Term Care.

DISCLAIMER: Health Quality Ontario uses a standardized costing method for its economic analyses. The main cost categories and associated methods of retrieval from the province's perspective are described below.

Hospital costs: Ontario Case Costing Initiative cost data are used for in-hospital stay, emergency department visit, and day procedure costs for the designated International Classification of Diseases diagnosis codes and Canadian Classification of Health Interventions procedure codes. Adjustments may be required to reflect accuracy in the estimated costs of the diagnoses and procedures under consideration. Due to difficulties in estimating indirect costs in hospitals associated with a particular diagnosis or procedure, Health Quality Ontario normally defaults to a consideration of direct treatment costs only.

Non-hospital costs: These include physician services costs obtained from the Ontario Schedule of Physician Benefits, laboratory fees from the Ontario Schedule of Laboratory Fees, drug costs from the Ontario Drug Benefit Formulary, and device costs from the perspective of local health care institutions whenever possible, or from the device manufacturer.

Discounting: For cost-effectiveness analyses, a discount rate of 5% is applied (to both costs and effects/QALYs), as recommended by economic guidelines.

Downstream costs: All reported downstream costs are based on assumptions of population trends (i.e., incidence, prevalence, and mortality rates), time horizon, resource utilization, patient compliance, health care patterns, market trends (i.e., rates of intervention uptake or trends in current programs in place in the province), and estimates of funding and prices. These may or may not be realized by the Ontario health care system or individual institutions and are often based on evidence from the medical literature, standard listing references, and educated hypotheses from expert panels. In cases where a deviation from this standard is used, an explanation is offered as to the reasons, the assumptions, and the revised approach.

The economic analysis represents *an estimate only*, based on the assumptions and costing methods explicitly stated above. These estimates will change if different assumptions and costing methods are applied to the analysis.

NOTE: Numbers may be rounded to the nearest decimal point, as they may be reported from an Excel spreadsheet.

Objectives of Analysis

The objectives of this analysis were to determine the long-term cost-effectiveness and one-year budgetary impact of magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU) for treatment of symptomatic uterine fibroids, from the perspective of the Ontario Ministry of Health and Long-Term Care.

Clinical Need and Target Population

Description of Disease/Condition

Uterine fibroids, or leiomyomas, are the most common benign tumours in women of childbearing age. (1) These myometrial tumours, composed of smooth muscle cells and collagenous fibrous tissue, develop near or within the wall of the uterus. (2) Although benign, they are often accompanied by severe symptoms including pelvic pain, prolonged periods with heavy bleeding, bladder pressure, and adverse reproductive outcomes. (3-5)

Medications such as nonsteroidal anti-inflammatory drugs and/or hormonal therapy can be used to manage symptoms related to uterine fibroids, but some women need more aggressive forms of treatment. Historically, the most common of these treatments has been hysterectomy. More recently, a number of uterine-preserving techniques have been developed to avoid removal of the uterus and to preserve the woman's childbearing ability. These alternative technologies include uterine artery embolization (UAE), myomectomy, and magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU), each with its distinct advantages and disadvantages. (6)

Prevalence and Incidence

A recent study of white and African-American women in the USA estimates that by age 50 almost 70% of the former and more than 80% of the latter will have uterine fibroids that are detectable by ultrasound. In many cases these will not be symptomatic. However, in their thirties and forties, up to 35% of these white women and 50% of these African-American women will experience symptoms. (7)

Ontario Context

Thousands of women are treated for symptomatic uterine fibroids in Ontario every year. According to administrative data sources, these fibroids have been one of the leading indications for hysterectomy in the province, with over 5,300 hysterectomies being performed annually to treat this condition in women of all ages. (See Budget Impact Analysis, page 34, for details.)

At present, MRgHIFU is being used in a research context, with a dual-site centre collaboration between Sunnybrook Research Institute and Thunder Bay Regional Research Institute. The MRgHIFU system used at these centres was approved by the U.S. Food and Drug Administration in 2004, (8) with Health Canada approval granted in 2013. (9) These centres have been working to develop and pioneer new treatments using MR-guided focused ultrasound for a range of medical conditions, with treatment of uterine fibroids chosen as the first clinical trial.

The Council of Academic Hospitals of Ontario estimates that MRgHIFU for the treatment of uterine fibroids could save Ontario's health care system over $35 million per year, and Canada's health care system over $90 million per year, given the reduced risks of MRgHIFU and the rapid recovery time relative to surgical procedures. (10) Although details of the costing and estimates of number of procedures are not reported, the potential for cost savings is supported through the primary analysis presented later in this report.

Health Quality Ontario has produced a clinical evidence-based analysis on MRgHIFU for symptomatic uterine fibroids, i.e., one that examines its safety and effectiveness as a treatment. It accompanies this economic analysis and provides additional context. (11)

Interventions Under Evaluation

We conducted evaluations for MRgHIFU compared with uterine artery embolization (UAE), myomectomy, and hysterectomy. Each procedure is described below. Another intervention, thermal balloon endometrial ablation (TBEA) is also described below because it can be used to treat symptomatic uterine fibroids. However, for reasons which will be explained, it was not included in the cost-effectiveness model.

MRgHIFU

MRgHIFU is a completely noninvasive thermal ablation technology that combines 2 technologies—magnetic resonance (MR) imaging and high-intensity focused ultrasound (HIFU). The MR and thermal mapping system are used to visualize the patient's anatomy, map the volume of tissue to be treated, monitor the tissue temperature during the ablation process, and evaluate the treatment results. Ultrasound guidance has been used with HIFU treatments too, but MR guidance is seen as being key in the guiding and controlling of HIFU delivery, to ensure that the treatment is safe and effective. HIFU has been investigated for a wide range of solid benign and malignant tumour indications such as breast, prostate, liver, kidney, pancreas, brain, and painful bone metastases. (12) Since the 1950s there has been a gradual increase in clinical indications for HIFU; prostate cancer and uterine fibroids are currently the principal indications in clinical trials and commercial treatments. (12)

Prior to the MRgHIFU procedure, patients are examined clinically. Physical and pelvic imaging or screening MR exams are performed the day before, to determine eligibility and for treatment planning. Generally, fibroids ranging from smaller (2 to 3 cm) to larger (e.g., 10 cm) can be treated with this procedure, with the fibroids' location also playing a role in eligibility. The procedure can take up to 3 hours, not including patient preparation or set-up of the HIFU table. This time period is considered adequate to treat a single fibroid of about 7 to 8 cm; a larger fibroid or multiple fibroids may require subsequent procedures. The 3-hour time limit was initially established due to concerns about deep vein thrombosis from prolonged immobilization. (13)

During the procedure, the focused ultrasound waves must raise temperatures to more than 50°C to kill the tissue. (14) Typically, multiple short sonications are delivered (60 to 90 in total, each about 20 seconds long with 1,000 to 3,000 J of energy), with continual thermal feedback provided. There are 90-second pauses between sonications to limit thermal damage to non-target areas. (15) After the procedure, the patient must wait several hours before discharge. It is important to note that of the treatment options considered for this report, MRgHIFU represents the least invasive as the entire procedure is performed without making a single incision.

Uterine Artery Embolization

Uterine artery embolization (UAE) is a relatively new option for the treatment of uterine fibroids for patients who do not wish to undergo surgery. It is performed by an interventional radiologist, who introduces a catheter through the femoral artery into the internal iliac and uterine arteries. An embolizing agent is then injected to block the uterine arteries and cut off the fibroids' blood supply. This causes the fibroids to become avascular and shrink. (16, 17)

UAE has been used in Canada for decades for a number of indications, including postpartum hemorrhage, bleeding after Caesarean section, and bleeding after gynecological surgery. (18) It was extended to the treatment of uterine fibroids following studies by Ravina et al in 1995. (19)

Since then, many thousands of these procedures have been performed, with increasing public awareness of UAE's availability for fibroid treatment.

Myomectomy

Myomectomy is a uterine-preserving alternative to hysterectomy, suitable if a patient desires future pregnancies or wishes to retain her uterus for other reasons. Types of myomectomy include abdominal (also called laparotomy), laparoscopic, and hysteroscopic. Abdominal is the route most often taken for multiple fibroids or a significantly enlarged uterus. Where fibroids impinge on the uterine cavity, hysteroscopic myomectomy or hysterectomy is required, while smaller fibroids can be removed via laparoscopic myomectomy. Overall, myomectomy is a much less common operation than hysterectomy. (16)

In abdominal myomectomy, the surgeon makes an open abdominal incision to access the uterus and remove the fibroids. In laparoscopic myomectomy, a minimally invasive procedure, the surgeon accesses and removes fibroids through several small abdominal incisions. The fibroid is cut into small pieces and removed through these small incisions in the abdominal wall or, rarely, through an incision in the vagina. Hysteroscopic myomectomy is a procedure to treat large fibroids. The surgeon accesses and removes fibroids using instruments inserted into the uterus through the vagina or cervix. A clear liquid, usually a sterile salt solution, is inserted into the uterus to expand the cavity, and a resectoscope (a small, lighted instrument) is used to cut tissue via electricity or laser beam. With the resectoscope, the surgeon shaves pieces from the fibroid until it aligns with the surface of the uterine cavity. (20)

Hysterectomy

Hysterectomy has historically been the most frequently performed surgical procedure in gynecology generally, and for uterine fibroids specifically. It involves the partial or complete removal of the uterus, and sometimes other organs, to completely eliminate symptoms. The decision to proceed to a hysterectomy rests with the woman, who should be fully educated about the risks and expected benefits.

Several types of hysterectomy are available for women, including complete or total, partial or subtotal, and radical hysterectomy. A complete or total hysterectomy involves the removal of the uterus and cervix, but not the ovaries or fallopian tubes. This is the most common type of hysterectomy performed in Ontario. A partial or subtotal hysterectomy removes only the upper part of the uterus and does not involve the cervix or other organs. Finally, a radical hysterectomy involves the removal of the uterus, the cervix, the upper part of the vagina, supporting tissues, and usually the pelvic lymph nodes. This operation is typically performed to treat cancer. (21)

Hysterectomy, like myomectomy, may be performed through a number of methods. Vaginal hysterectomy, where the uterus is removed through the vagina, causes less pain and results in a faster recovery of day-to-day activities than abdominal hysterectomy. Laparoscopic hysterectomy may be used in combination with a vaginal hysterectomy. This allows the uterus to be detached from inside the body by small instruments passed through small cuts in the abdomen, while the physician observes the pelvic organs through a camera attached to a telescope. After the uterus is detached, it is removed through a small cut at the top of the vagina. In abdominal hysterectomy, the uterus is removed through a 15 to 20 cm-long cut in the abdomen, either a midline or bikini cut. This procedure is associated with a longer hospital stay and recovery time because of its relative invasiveness. (21)

Robot-assisted laparoscopic hysterectomy is a recently developed method to overcome some of the limitations of laparoscopic surgery. It enables surgeons to more easily perform procedures that are often complex, through improved visualization, more accurate control of instruments, and increased ease of use. (22)

Thermal Balloon Endometrial Ablation (TBEA)

TBEA is a tool to control abnormal uterine bleeding, and can be used to treat uterine fibroid symptoms. TBEA relies on the transfer of heat from heated liquid within a balloon that is inserted into the uterus. It does not require a hysteroscope for direct visualization of the uterus and can be performed under local anesthesia. TBEA is not appropriate for patients with long or irregularly shaped uterine cavities, as the balloon must be in direct contact with the uterine wall to cause ablation. (23)

The Ontario Health Technology Advisory Committee (OHTAC) has previously reported on TBEA for the treatment of abnormal uterine bleeding (AUB), (24) which is defined as an increase in frequency of menstruation, duration of flow, or amount of blood lost, and which may be a symptom of uterine fibroids. The treatment of AUB that is secondary to fibroids differs from the treatment of AUB for unknown causes. In the United States, the American College of Obstetricians and Gynecologists recommend endometrial ablation only for submucosal myomata. (25) Similarly, the Practice Committee of the American Society for Reproductive Medicine states that endometrial ablation is effective for managing menorrhagia (in the absence of fibroids). (26)

The Society of Obstetricians and Gynaecologists of Canada (SOGC) guidelines recommend endometrial ablation for management of AUB with unknown underlying causes, but do not include it in the recommended pathway for AUB secondary to uterine fibroids. Endometrial ablation is available as a treatment option, but is most often used for dysfunctional endometrium, and sometimes but rarely for submucosal fibroids, which constitute a small minority of symptomatic fibroid cases. In keeping with the SOGC guidelines and after consulting with a number of practising gynecologists in Ontario, we excluded endometrial ablation from the cost-effectiveness model.

ECONOMIC ANALYSIS

Research Questions

What is the cost-effectiveness and one-year budgetary impact of using MRgHIFU compared with current interventions for the treatment of symptomatic uterine fibroids, in cases where drugs have been ineffective, from the perspective of the Ontario Ministry of Health and Long-Term Care?

Economic Literature Review

Research Methods

Literature Search

Search Strategy
An economic literature search was performed on March 27, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, The Cochrane Library (HTA database and NHSEED), HEED, and PubMed (for non-MEDLINE records), for studies published from January 1, 2000, to March 26, 2014. (Appendix 1 provides search strategy details.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2000, and March 26, 2014
- full economic evaluations: cost-utility analyses, cost-effectiveness analyses, cost-benefit analyses
- economic evaluations reporting incremental cost-effectiveness ratios (ICERs) (i.e., cost per quality-adjusted life-year [QALY]/life-years gained)
- studies comparing MRgHIFU with other non-pharmacological treatment options for treatment of symptomatic uterine fibroids

Exclusion Criteria

- pediatric populations
- foreign-language publications
- narrative reviews
- abstracts, posters, reviews, letters/editorials, unpublished studies

Results of Economic Literature Review

The database search yielded 89 citations published between January 1, 2000, and March 26, 2014 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

From a total of 89 abstracts, 4 full-text articles were retrieved and 3 were identified as potentially relevant. Table 1 summarizes the results of the cost-effectiveness studies that are considered applicable to patients in Ontario.

O'Sullivan et al conducted a cost-effectiveness analysis of MRgHIFU versus hysterectomy, myomectomy, UAE, and pharmacotherapy in the treatment of symptomatic uterine fibroids among premenopausal women in the United States. (27) Their decision analytic model, populated with data from secondary sources, predicted long-term costs and effects of MRgHIFU treatment over a lifetime horizon for women with a mean starting age of 40 years. Patient eligibility rates for MRgHIFU were assumed to be 35% in the base-case scenario. The authors estimated the quality-adjusted life-years (QALYs) to be 17.39, 17.36, 17.31, 17.18, and 16.70 for UAE, MRgHIFU, myomectomy, hysterectomy, and pharmacotherapy, respectively. Lifetime discounted costs were estimated at $28,892, $27,285, $35,057, $19,799, and $9,207 for UAE, MRgHIFU, myomectomy, hysterectomy, and pharmacotherapy, respectively. Myomectomy was dominated by both UAE and MRgHIFU as it was more costly and less effective (lower QALYs) than these 2 interventions. The incremental cost per QALY gained was estimated at $21,800 for moving from pharmacotherapy to hysterectomy and $41,400 for moving from hysterectomy to MRgHIFU. The cost per QALY for moving from MRgHIFU to UAE was $52,200. Based on the authors' base-case analysis, MRgHIFU would be considered the cost-effective strategy if decision-makers' maximum willingness to pay for a QALY was between $41,400 and $52,200. If willingness to pay for a QALY was greater than $52,200, then UAE would be considered the cost-effective strategy. Sensitivity analysis considered the scenario with the eligibility rate for MRgHIFU increased to 50%: the incremental cost-effectiveness ratio (ICER) for MRgHIFU relative to hysterectomy became $38,700 per QALY gained, and the ICER for UAE relative to MRgHIFU became $64,300. Overall, model outcomes were sensitive to changes in rates of fibroid recurrence, cost of procedures, MRgHIFU eligibility rates, and assumptions regarding quality of life following hysterectomy. The study concluded that MRgHIFU was as effective as other treatment options and was in the range of currently accepted willingness-to-pay thresholds for cost-effectiveness.

According to our appraisal, the authors used transparent and robust methods to build the economic model, despite the use of data from secondary sources (i.e., published and unpublished studies, administrative databases).

Zowall et al conducted a cost-effectiveness analysis of MRgHIFU as an initial therapy compared with current clinical practice including hysterectomy, myomectomy, and UAE from a health system perspective in the United Kingdom, for the treatment of symptomatic uterine fibroids among women aged 39 to 56 years. (28) In the base-case scenario, the current practice strategy was assumed to comprise a mix of UAE (25%), myomectomy (25%), and hysterectomy (50%). The authors determined that MRgHIFU resulted in lower cost and higher QALYs than current clinical practice, with average cost savings of £295 per patient ($495 CAD) and effectiveness of 0.0107 QALYs gained per woman. MRgHIFU treatment was dominant in 86% of the scenarios analyzed. The cost per QALY was sensitive to patient age, cost of MRgHIFU treatment relative to current treatment options, and ratio of nonperfused volume to total volume of fibroids. The study concluded that MRgHIFU is likely to be cost-effective, and, had productivity losses been taken into account, that initial treatment with MRgHIFU would have resulted in greater cost savings per woman.

Our appraisal concluded that the authors of this study used valid methods in their cost-utility analysis despite a paucity of data on several input parameters and on the model assumptions.

In the most recent of the 3 studies (published just this year), Cain-Nielsen et al investigated the cost-effectiveness of uterine-preserving procedures for the treatment of symptomatic uterine fibroids in the American health care setting. Both a third-party payer perspective and a societal perspective were taken in the analysis. (29) Costs were reported as $15,459 for myomectomy, $15,274 for MRgHIFU, and $18,653 for UAE. Over a 5-year time horizon, QALYs were estimated to be 3.957, 3.953, and 3.943 for myomectomy, MRgHIFU, and UAE procedures, respectively. When a societal perspective was taken by incorporating productivity costs, treatment costs were estimated at $21,232, $22,599, and $22,819 for MRgHIFU, myomectomy, and UAE, respectively. Probabilistic sensitivity analysis confirmed that myomectomy was cost-effective at all examined levels of willingness-to-pay thresholds. The study concluded that the 3 uterine-preserving therapies were of similar effectiveness and could all be deemed cost-effective over a 5-year time horizon.

According to our appraisal, the authors used transparent and robust methods to build the economic model, despite the use of data from secondary sources (i.e., published and unpublished studies, administrative databases).

The results of the literature review suggest that MRgHIFU may potentially be cost-effective compared with current treatment options. We therefore developed a primary cost-effectiveness model relevant to the Ontario context.

Table 1: Results of Economic Literature Review on MRgHIFU and Other Interventions for Symptomatic Uterine Fibroids—Summary

Name, Year, Country	Study Design and Perspective	Population	Interventions	Time Horizon (Mean Starting Age)	Results		
					Health Outcomes	Costs	Cost-Effectiveness
Cain-Nielsen et al, 2014 (29) United States	Cost-utility analysis Decision model Payer perspective	Premenopausal women with symptomatic uterine fibroids, who want to preserve their uteri	MRgHIFU Myomectomy UAE	5 years (pre-menopausal)		*USD (2014)*	*ICER (i.e.., Cost/QALY)*
					3.953 QALY (MRgHIFU)	$15,274 (MRgHIFU)	$46,250[a]
					3.957 QALY (Myomectomy)	$15,459 (Myomectomy)	*Reference*
					3.943 QALY (UAE)	$18,653	Myomectomy is dominant
O'Sullivan et al, 2009 (27) United States	Cost-utility analysis Decision model Societal perspective	Premenopausal women with symptomatic uterine fibroids	Pharmacotherapy Hysterectomy MRgHIFU UAE Myomectomy	Lifetime (40 years)		*USD (2005)*	*ICER (i.e.., Cost/QALY)*
					16.699 QALY (Pharmacotherapy)	$9,207 (Pharmacotherapy)	-
					17.183 QALY (Hysterectomy)	$19,799 (Hysterectomy)	$21,800
					17.364 QALY (MRgHIFU)	$27,285 (MRgHIFU)	$41,400
					17.394 QALY (UAE)	$28,892 (UAE)	$54,200
					17.305 QALY (Myomectomy)	$35,057 (Myomectomy) Discount rate: 3.0%	Myomectomy is dominated by MRgHIFU and UAE
Zowall et al, 2008 (28) United Kingdom	Cost-utility analysis Decision model NHS perspective	Premenopausal women with symptomatic uterine fibroids	MRgHIFU Current practice	17 years (39 years)		*GBP (2005)*	*ICER (e.g., Cost/QALY)*
					10,793.874 QALY (MRgHIFU)	£3,101,644 £3,396,913	MRgHIFU is dominant
					10,783.216 QALY (Current practice)	Discount rate: 3.5%	

Abbreviations: GBP, British pound; QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; NHS, National Health Service (United Kingdom); QALY, quality-adjusted life-year; UAE, uterine artery embolization; USD, United States dollar.

[a]MRgHIFU is less expensive and less effective than reference (in this case, myomectomy), which inverts the decision rule; MRgHIFU is cost-effective for willingness-to-pay thresholds above $46,250.

Cost-Effectiveness Analysis

Although the published economic evaluations that we identified in our literature review addressed the intervention of interest, none of them took a Canadian perspective. In response to this limitation, we conducted a primary economic evaluation in the Ontario context with Ontario-specific unit costs and care pathways.

Research Methods

Type of Analysis

A cost-utility analysis was chosen to estimate the long-term incremental costs and effects (i.e., cost per QALY) of non-pharmacological therapeutic interventions for treatment of symptomatic uterine fibroids. Our decision model included health states defined by presence/absence of symptoms and treatment received, with transitions across health states occurring at 6-month intervals. Each health state was associated with an assigned utility and cost. The Markov model that we used incorporated half-cycle corrections.

Interventions Evaluated

We considered 3 current clinical interventions in the base case—myomectomy, hysterectomy, and UAE—as comparators to MRgHIFU for treatment of symptomatic uterine fibroids. Three separate scenario analyses were performed:

- MRgHIFU compared with other uterine-preserving interventions only (myomectomy and UAE), with a general cohort of patients as a starting population
- MRgHIFU compared with all other interventions, with MRgHIFU-eligible patients as a starting population
- MRgHIFU compared with all other interventions but with UAE removed as a treatment option, with MRgHIFU-eligible patients as a starting population

Perspective

We conducted this economic analysis from the perspective of the Ontario Ministry of Health and Long-Term Care.

Discounting and Time Horizon

All costs and QALYs were discounted at an annual discount rate of 5% in accordance with Canadian guidelines. (30) Women started in the model at age 40 and continued until they reached menopause (i.e., aged 51 years).

All costs are reported in 2014 Canadian dollars.

Target Population

Patients initiated in the model were assumed to be premenopausal women with symptomatic fibroids for whom pharmacotherapy had not been effective, and who had a mean age of 40 years, in accordance with previously published cost-effectiveness studies.

Variability and Uncertainty

To assess variability and uncertainty, we used a probabilistic model and one-way sensitivity analyses. All input variables were varied in one-way analyses. Model parameter uncertainty was

assessed using probabilistic sensitivity analysis by assigning distributions around the point estimate.

Parameter uncertainty was evaluated using probabilistic sensitivity analysis and expressed as cost-effectiveness acceptability curves (CEACs) based upon 1,000 second-order Monte Carlo simulations. Beta distributions were used for parameters whose values are constrained between zero and one. These include probability parameters, base-line utility variables, and applied disutilities. Log-normal distributions were used for pre-, peri-, and post-procedure costs. Based on assumptions, no distributions were applied to certain variables (i.e., discount rate, background mortality, probability of procedure-related death for MRgHIFU, probability of recurrence of symptoms for hysterectomy, probability of success of hysterectomy, and utility of the death health state). Results were presented in the form of CEACs showing the probability that the intervention would be cost-effective by various willingness-to-pay values.

In addition to the one-way and probabilistic sensitivity analyses, we explored 3 more scenarios. The first scenario looked only at uterine-preserving procedures by considering a treatment pathway where hysterectomy is not offered as a first-line option. The second scenario considered a starting population in which all patients are eligible for the MRgHIFU procedure. The third scenario considered the situation where all patients are MRgHIFU-eligible, and UAE has been removed as a treatment option due to its low level of utilization in Ontario (see Budget Impact Analysis, page 34, and, for further details, the clinical evidence-based analysis that accompanies this report.) (11)

Model Structure

Figure 1 shows the Markov decision-analytic model that was used to evaluate the long-term costs and outcomes of each therapeutic option. Health states of the Markov model were defined according to the treatment received and whether or not symptoms were resolved. The model was run until women with uterine fibroids reached menopause, using 6-month health state transitions. Parameters informing the branch probabilities were obtained from published literature.

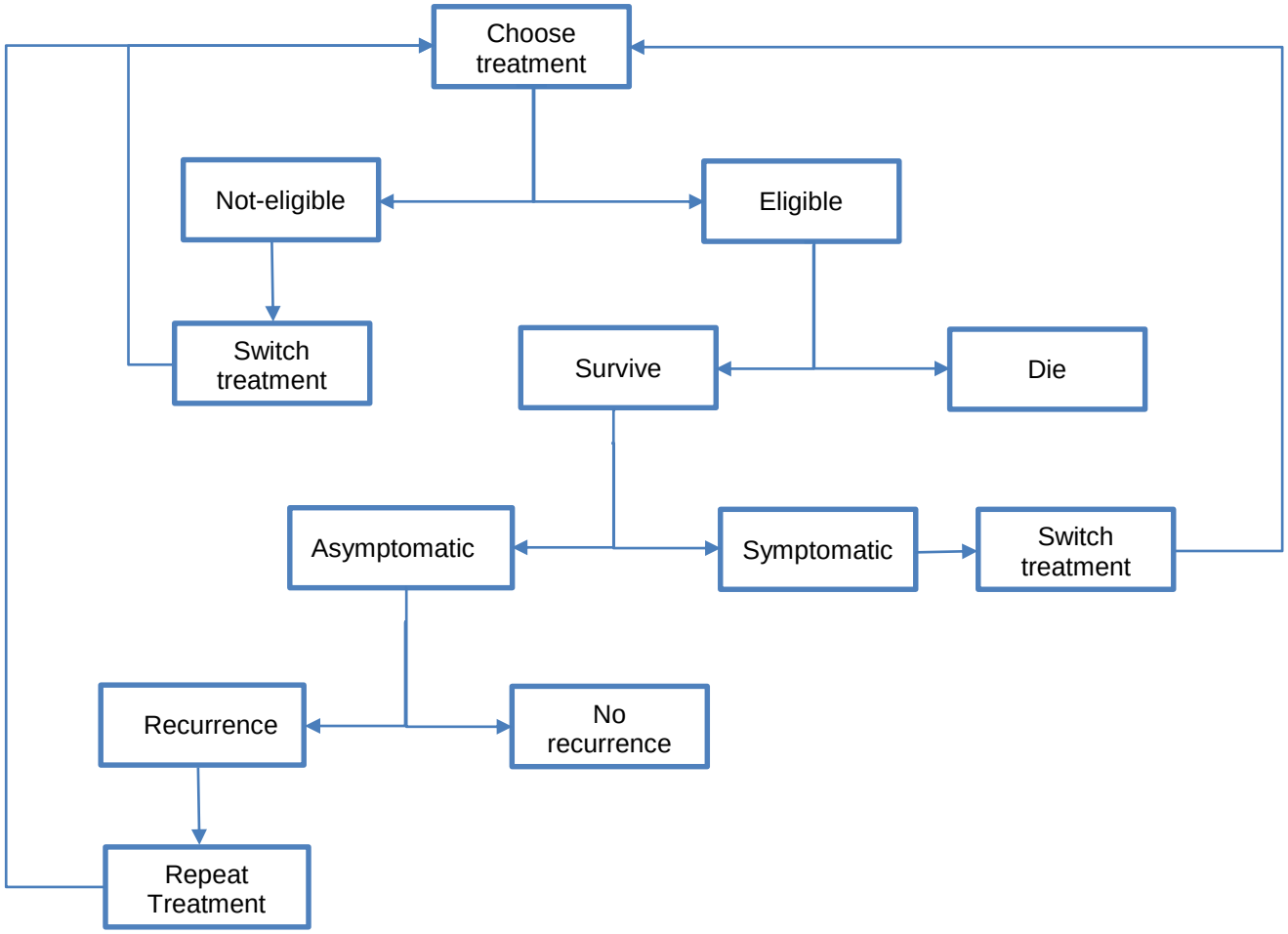


Figure 1: Model Structure

The mean age for patients entering the cost-effectiveness model was assumed to be 40 years and it was further assumed that Ontario women reach menopause at the age of 51 years.

In the model, women were allocated to hysterectomy, myomectomy, UAE, or MRgHIFU as a first-line treatment according to the eligibility rate of each intervention, as some women would not be eligible for some treatments due to the size or location of their fibroids. To assess eligibility for the chosen treatment procedure, all patients undergo diagnostic tests. Those who received UAE or MRgHIFU treatment as a first-line procedure had been required to undergo an additional magnetic resonance imaging test. Those patients who were ineligible for UAE or MRgHIFU were assumed to receive the least invasive of the remaining treatment options (with the level of invasiveness increasing from MRgHIFU to UAE to myomectomy to hysterectomy). All women with symptomatic uterine fibroids were assumed to be eligible for myomectomy and hysterectomy. (The proportion of patients eligible for each treatment strategy is outlined as the first variable in Table 3.)

Patients are at risk of procedure-related death following treatment, and not all patients will achieve symptom resolution. Successfully treated patients may later (up until menopause) experience a symptom recurrence. It was assumed that all patients experiencing symptom recurrence were re-treated with the same first-line procedure. On the other hand, patients for

whom the first-line treatment failed were assumed to receive second-line treatment with the next least invasive alternative treatment (i.e., if women undergoing MRgHIFU did not have adequate symptom relief in the first cycle, they underwent UAE in the next 6-month cycle). Women could receive a maximum of 3 rounds of treatment due to treatment failure or symptom recurrence. Those requiring third-line treatment were assumed to undergo hysterectomy, which completely removes the fibroids. Table 2 outlines the treatment patterns pertaining to the assumptions around first-, second-, and third-line treatment strategies. Both the model structure and assumptions were validated through the expert opinion of several Ontario-based gynecologists and interventional radiologists.

Table 2: Treatment Strategies for Symptomatic Uterine Fibroids

Treatment Strategy[a]	First Line	Second Line		Third Line	
		Recurrence	Failure	Recurrence	Failure
1	MRgHIFU	MRgHIFU	UAE	Hysterectomy	N/A
2	UAE	UAE	Myomectomy	Hysterectomy	N/A
3	Myomectomy	Myomectomy	Hysterectomy	Hysterectomy	N/A
4	Hysterectomy	N/A	N/A	N/A	N/A

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; N/A, not applicable; UAE, uterine artery embolization.
[a]In the case of hysterectomy, no further treatment strategy is considered, as underlying cause of bleeding is assumed to be eliminated.

Model Input Parameters

A number of different input parameters were used to populate the model. These include not only variables used to model the natural history of the disease, but also variables used to modify the natural history model to account for treatment effects and costs of the interventions being evaluated.

Model Input Parameters: Natural History

We extracted model input parameters for natural history and treatment effects from the published literature (see Table 3). These parameters include proportion of women eligible for treatment, probability of symptom relief, probability of symptom recurrence, probability of major complication, and probability of procedure-related death.

Table 3: Natural History Model Parameters Used in the Economic Model

Model Parameter	Base-Case Value	Sensitivity Analysis Range	Reference
Treatment Eligibility			
Proportion eligible for treatment			
Hysterectomy	1.0000	Fixed	(27)
Myomectomy	1.0000	Fixed	(27)
UAE	0.9000	0.8–1	(27)
MRgHIFU	0.3500	0.25–0.45	(27)
Treatment Efficacy[a]			
Probability of symptom relief			
Hysterectomy	1.0000	Fixed	(27)
Myomectomy	0.7990[b]	0.65–0.95	(31, 32)
UAE	0.8520[b]	0.6–1	(27, 31-33)
MRgHIFU	0.8940[b]	0.75–1	(27, 34, 35)
Probability of symptom recurrence in 6-month period			
Hysterectomy	0	Fixed	(27)
Myomectomy	0.0500	+/- 20%	(27)
UAE	0.0300	+/- 20%	(27)
MRgHIFU	0.0600	+/- 20%	(27)
Treatment Safety[a]			
Probability of major complications[c]			
Hysterectomy	0.0200	+/- 20%	(27)
Myomectomy	0.0210[b]	+/- 20%	(27, 31, 36)
UAE	0.0340[b]	+/- 20%	(27, 31, 33)
MRgHIFU	0.0130[b]	+/- 20%	(27, 35, 37)
Probability of procedure-related death			
Hysterectomy	0.0020	+/- 20%	(27)
Myomectomy	0.0020	+/- 20%	(27)
UAE	0.0015	+/- 20%	(27)
MRgHIFU	0		(27)

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

[a]Efficacy and safety with second- and third-line treatment are assumed to be the same as for the corresponding first-line treatment.

[b]Weighted average (weighted by number of subjects in each study).

[c]Major complications include infection, hemorrhage requiring infusion, unintended major surgery, life-threatening event, and rehospitalization for hysterectomy, (38) febrile morbidity for myomectomy, (39) pulmonary embolus for UAE, (40) and deep vein thrombosis for MRgHIFU. (35)

Model Input Parameters: Intervention Costs

We used various sources to estimate the cost of treatment alternatives. Professional fees were obtained from the Ontario Schedule of Benefits for Physician Services, (41) direct medical costs including hospital services were determined through the Ontario Case Costing Initiative database, (42) lab fees were obtained from the Ontario Schedule of Benefits for Laboratory Services, (43) and costs related to the maintenance and operation of MRgHIFU were obtained from clinical experts and the manufacturer.

The pre-, peri-, and post-procedure costs for all treatment alternatives are presented in Table 4 (see Appendix 2, Table A1 for a detailed breakdown of these costs). Medical resources used prior to, during, and post-procedure were determined through consultation and an online survey with Ontario-based physicians. All women with symptomatic uterine fibroids were assumed to have 1 gynecologist consultation, 1 interventional radiologist or surgeon consultation, an ultrasound, a complete blood count, and a creatinine test. In addition, women undergoing a surgical procedure were assumed to incur an anesthesiologist consultation fee. Patients undergoing MRgHIFU and UAE also received a diagnostic MRI scan to confirm eligibility for the procedure and for pre-procedure planning purposes. Successfully treated women were assumed to receive 1 interventional radiologist or gynecologist visit and 1 ultrasound in the first 6 months post-treatment.

Table 4: Average Cost of Procedures in Six-Month Cycle Used in the Economic Model

Resource	MRgHIFU	UAE	Myomectomy	Hysterectomy
Pre-procedure	$862.91	$862.91	$472.16	$472.16
Peri-procedure	$3,498.59	$4,269.55	$6,050.71	$6,479.72
Post-procedure[a]	$152.58	$152,58	$91.83	$91.83
Total cost per 6-month cycle	$4,514.08	$5,285.04	$6,614.70	$7,043.71

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.
[a]Post-procedure cost included in table represents half of the annual cost provided in Appendix 2, Table 1.

Model Input Parameters: Intervention Utilities

Using the results from our systematic literature review on cost-effectiveness studies, we extracted health state utility values for each health state of interest and disutilities associated with major complications, hysterectomy recovery, and post-hysterectomy symptom-free health state (see Table 5). We varied all utility values in sensitivity analysis according to ranges found in plausible ranges identified in the literature. (27)

Table 5: Utilities of Programs/Technologies Used in the Economic Model

Health State/Utility Decrement	Utility Value	SA Range	Reference
Symptomatic fibroids	0.67	0.50–0.78	(27)
Symptomatic relief	0.76	0.60–0.90	(27)
Death	0.00		Assumption
Utility decrement during recovery from hysterectomy	-0.20	0–0.4	(27)
Utility reduction associated with major complications	-0.20	0–0.4	(27)
Utility reduction post-hysterectomy	-0.015	0–0.025	(27)

Abbreviation: SA, sensitivity analysis.

Results of Cost-Effectiveness Analysis

Base Case Analysis

Table 6 presents the expected costs and expected QALYs and ICERs for each strategy considered in the analysis. As shown, initial hysterectomy had the lowest expected lifetime costs ($8,486), followed by MRgHIFU ($10,995), UAE ($11,321), and myomectomy ($13,399). At the same time, hysterectomy resulted in the fewest number of expected QALYs (6.221),

while UAE returned the highest number (6.282). MRgHIFU returned 6.275 QALYs, and myomectomy returned 6.229. With hysterectomy acting as reference (rather than as a comparator) in the base case analysis, myomectomy is strictly dominated (higher costs, lower QALYs) by all other strategies under consideration.

Table 6: Base Case Expected Costs, QALYs, and ICERS for Each Treatment Strategy for Symptomatic Uterine Fibroids

Treatment Strategy	Total		Incremental		ICER
	Costs	QALYs	Costs	QALYs	$/QALY
Hysterectomy	$8,485.48	6.221	Reference	Reference	Reference
Myomectomy	$13,399.09	6.229	$4,913.61	0.008	Dominated[a]
MRgHIFU	$10,995.29	6.275	$2,509.82	0.054	Dominated[b]
UAE	$11,320.76	6.282	$2,835.28	0.061	$46,480.07

Abbreviations: ICER, incremental cost-effectiveness ratio; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; QALY, quality-adjusted life-year; UAE, uterine artery embolization.
[a]Myomectomy is strictly dominated by MRgHIFU and UAE; [b]MRgHIFU is extendedly dominated by a combination of hysterectomy and UAE.

Using the principle of extended dominance, where each intervention is compared with the next-most-effective alternative by calculating the incremental cost-effectiveness ratio (ICER), MRgHIFU is extendedly dominated by UAE. Extended dominance rules out any intervention that has an ICER which is greater than that of a more effective intervention. This is difficult to see in Figure 2, which shows the cost-effectiveness efficiency frontier, because the ICERs are different by only a small amount—$46,496 per QALY for MRgHIFU versus UAE, compared with $46,480 per QALY for UAE versus hysterectomy, meaning the cost-effective strategy in this case is UAE (as an additional $16 must be paid to gain a QALY when using MRgHIFU). The efficiency frontier is thus made up of 2 treatment strategies: hysterectomy and UAE. The incremental cost per QALY of UAE compared with hysterectomy is estimated to be $46,480. Therefore, based on this analysis, if a decision-maker's willingness to pay for a QALY is less than $46,480, hysterectomy would be considered the cost-effective strategy. If willingness to pay for a QALY is $46,480 or greater, UAE would be the cost-effective strategy. Since MRgHIFU and myomectomy are dominated by the other treatment strategies, they would not be considered cost-effective at any willingness-to-pay value.

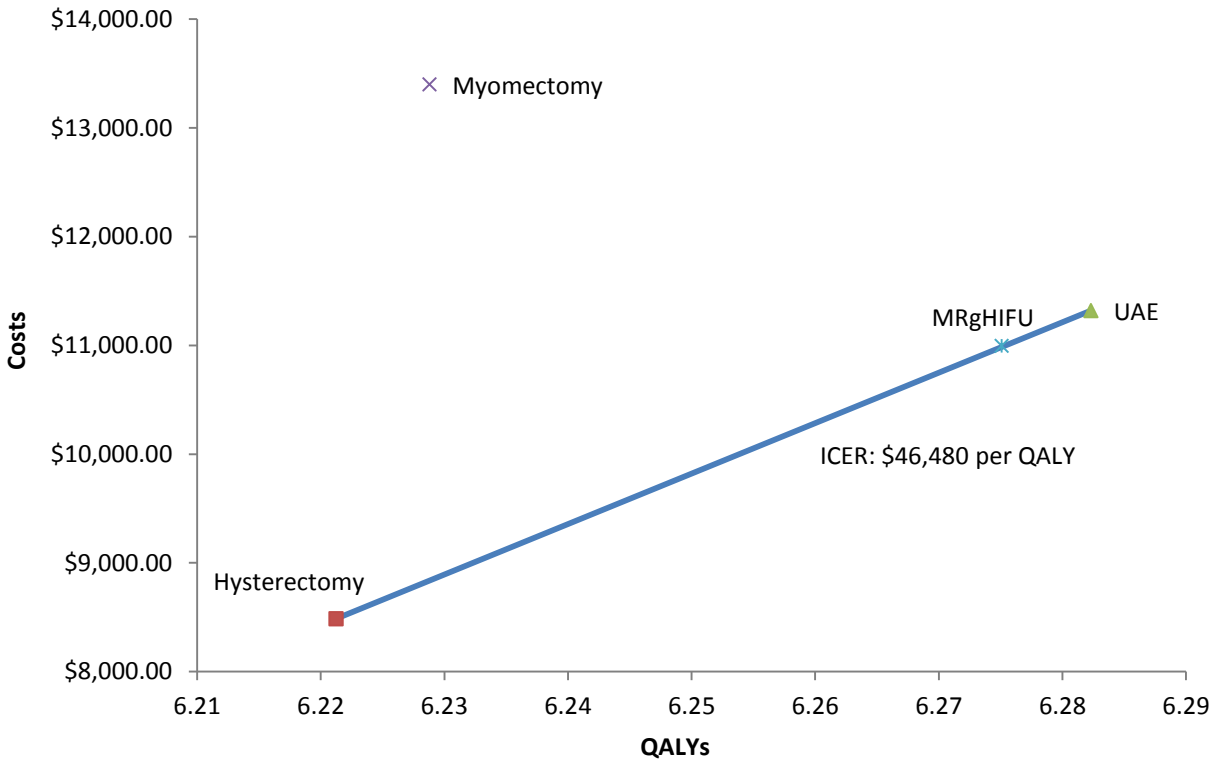


Figure 2: Cost-Effectiveness Efficiency Frontier for Treatment Strategies for Symptomatic Uterine Fibroids

Abbreviations: ICER, incremental cost-effectiveness ratio; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; QALY, quality-adjusted life-year; UAE, uterine artery embolization.

Scenario Analyses

Scenario 1—Hysterectomy Eliminated as a First-Line Option

Table 7 presents expected costs, QALYs, and ICERs for uterine-preserving strategies. As in the base-case results, myomectomy is strictly dominated (higher costs, lower QALYs) by MRgHIFU and UAE. The incremental cost per QALY of UAE compared with MRgHIFU is estimated to be $46,495.

Table 7: Scenario Analysis—Expected Costs, QALYs, and ICERS With Uterine-Preserving Treatment Options Only

Treatment Strategy	Total		Incremental		ICER
	Costs	QALYs	Costs	QALYs	$/QALY
Myomectomy	$13,399.09	6.229	Dominated	Dominated	Dominated[a]
MRgHIFU	$10,995.29	6.275	Reference	Reference	Reference
UAE	$11,320.76	6.282	$325.46	0.007	$46,495.29

Abbreviations: ICER, incremental cost-effectiveness ratio; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; QALY, quality-adjusted life-year; UAE, uterine artery embolization.
[a]Myomectomy is strictly dominated by MRgHIFU and UAE.

Scenario 2—MRgHIFU-Eligible Population

Table 8 presents expected costs, QALYs, and ICERs for all strategies for a population in which all patients are eligible for MRgHIFU treatment. As in the base-case results, myomectomy is strictly dominated (higher costs, lower QALYs) by MRgHIFU and UAE. In this scenario, MRgHIFU is no longer extendedly dominated, and its incremental cost compared with hysterectomy is $32,757 per QALY. The incremental cost of UAE as compared with MRgHIFU is $70,239 per QALY. This makes MRgHIFU the cost-effective option at a commonly cited willingness-to-pay value of $50,000, with UAE being the cost-effective option at a willingness-to-pay value of $100,000.

Table 8: Scenario Analysis—Expected Costs, QALYs, and ICERs With MRgHIFU-Eligible Population Only

Treatment Strategy	Total		Incremental		ICER
	Costs	QALYs	Costs	QALYs	$/QALY
Hysterectomy	$8,485.48	6.221	Reference	Reference	Reference
Myomectomy	$13,399.09	6.229	$4,913.52	0.008	Dominated[a]
MRgHIFU	$10,123.27	6.271	$1,637,79	0.050	$32,756.86
UAE	$11,106.62	6.285	$2,621.14	0.064	$70,239.29[b]

Abbreviations: ICER, incremental cost-effectiveness ratio; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; QALY, quality-adjusted life-year; UAE, uterine artery embolization.
[a] Myomectomy is strictly dominated by MRgHIFU and UAE.
[b]ICER value of UAE as compared with MRgHIFU.

Scenario 3—MRgHIFU-Eligible Population with UAE Eliminated as a Treatment Option

Table 9 presents expected costs, QALYs, and ICERs for a population in which all patients are eligible for MRgHIFU treatment in a scenario where UAE is not available. As in the base-case results, myomectomy is strictly dominated (higher costs, lower QALYS) by MRgHIFU and hysterectomy. In this scenario, the incremental cost per QALY of MRgHIFU compared with hysterectomy is estimated to be $39,254.

Table 9: Scenario Analysis—MRgHIFU-Eligible Population Only, With UAE Eliminated as a Treatment Option

Treatment Strategy	Total		Incremental		ICER
	Costs	QALYs	Costs	QALYs	$/QALY
Hysterectomy	$8,485.48	6.221	Reference	Reference	Reference
Myomectomy	$13,399.09	6.229	$4,913.61	0.008	Dominated[a]
MRgHIFU	$10,291.16	6.267	$1,805.68	0.046	$39,253.98

Abbreviations: ICER, incremental cost-effectiveness ratio; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; QALY, quality-adjusted life-year.
[a]Myomectomy is strictly dominated by hysterectomy and MRgHIFU.

One-Way Sensitivity Analyses

We tested the model outcomes for robustness at different willingness-to-pay thresholds, varying all the inputs over plausible ranges as identified in the studies that were included in the cost-effectiveness analysis by O'Sullivan et al. (27) In most scenarios, the UAE strategy was cost-effective when decision-makers' willingness-to-pay threshold was below $50,000 per QALY; it was cost-effective in almost all scenarios where the threshold was $100,000 per QALY. MRgHIFU was a cost-effective strategy at $50,000 per QALY when, *ceteris paribus*, utility of symptomatic fibroids was 0.78, utility for symptomatic relief was 0.6, cost for MRgHIFU was $2,798, recurrence rate following MRgHIFU treatment was 0.048, and when the recurrence rate following myomectomy was 0.04 or the proportion of patients eligible for MRgHIFU was 45%. See Table 10.

Table 10: One-Way Sensitivity Analyses—Cost-Effective Strategies Based on Willingness-to-Pay Thresholds

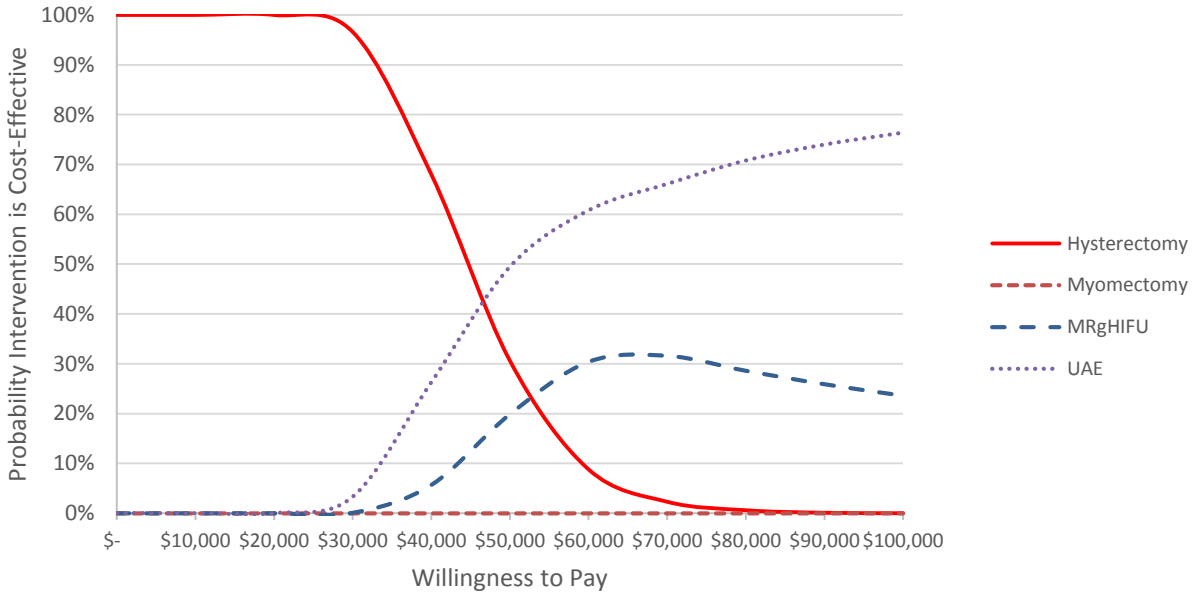
Parameters	Values	Cost-Effective Strategy Based on WTP	
		$50,000/QALY	$100,000/QALY
Utility of symptomatic fibroid (base-case)	0.6700	UAE	UAE
Low	0.5000	Hysterectomy	Hysterectomy
High	0.7800	MRgHIFU	UAE
Utility of symptomatic relief (base-case)	0.7600	UAE	UAE
Low	0.6000	MRgHIFU	UAE
High	0.9000	Hysterectomy	Hysterectomy
Disutility for post hysterectomy (base-case)	0.0150	UAE	UAE
Low	0.0120	Hysterectomy	UAE
High	0.0180	UAE	UAE
Cost of hysterectomy procedure (base-case)	$6,479.72	UAE	UAE
Low	$5,183.78	Hysterectomy	UAE
High	$7,775.66	UAE	UAE
Cost of UAE procedure (base-case)	$4,269.55	UAE	UAE
Low	$3,415.64	UAE	UAE
High	$5,123.46	Hysterectomy	UAE
Cost of MRgHIFU procedure (base-case)	$3,498.59	UAE	UAE
Low	$2,798.87	MRgHIFU	UAE
High	$4,198.31	UAE	UAE
Probability of recurrence, UAE (base-case)	0.0300	UAE	UAE
Low	0.0240	UAE	UAE
High	0.0360	Hysterectomy	MRgHIFU
Cost of monitoring for UAE & MRgHIFU (base-case)	$152.58	UAE	UAE
Low	$122.06	UAE	UAE
High	$183.09	Hysterectomy	UAE
Probability for recurrence, MRgHIFU (base-case)	0.0600	UAE	UAE
Low	0.0480	MRgHIFU	MRgHIFU
High	0.0720	UAE	UAE
Cost of screening for UAE & MRgHIFU (base-case)	$862.91	UAE	UAE
Low	$690.33	UAE	UAE
High	$1,035.49	UAE	UAE
Disutility during hysterectomy recovery (base-case)	0.2000	UAE	UAE
Low	0.1600	UAE	UAE
High	0.2400	UAE	UAE
Probability for recurrence, myomectomy (base-case)	0.0500	UAE	UAE
Low	0.0400	MRgHIFU	UAE
High	0.0600	UAE	UAE
Cost of monitoring for hysterectomy & myomectomy (base-case)	$91.83	UAE	UAE

Parameters	Values	Cost-Effective Strategy Based on WTP	
		$50,000/QALY	$100,000/QALY
Low	$73.46	Hysterectomy	UAE
High	$110.19	UAE	UAE
Cost of myomectomy procedure (base-case)	$6,050.71	UAE	UAE
Low	$4,840.57	UAE	UAE
High	$7,260.85	Hysterectomy	UAE
Probability for procedure related death, hysterectomy (base-case)	0.0020	UAE	UAE
Low	0.0016	UAE	UAE
High	0.0024	UAE	UAE
Probability for procedure related death, UAE (base-case)	0.0015	UAE	UAE
Low	0.0012	UAE	UAE
High	0.0018	UAE	UAE
Discount Rate (base-case)	0.050	UAE	UAE
Low	0	UAE	UAE
High	0.0300	UAE	UAE
Cost of screening for hysterectomy & myomectomy (base-case)	$472.16	UAE	UAE
Low	$377.73	UAE	UAE
High	$566.59	UAE	UAE
Probability for complications, UAE (base-case)	0.0340	UAE	UAE
Low	0.0272	UAE	UAE
High	0.0408	UAE	UAE
Probability for complications, myomectomy (base-case)	0.0210	UAE	UAE
Low	0.0168	UAE	UAE
High	0.0252	UAE	UAE
Probability for complications, hysterectomy (base-case)	0.0200	UAE	UAE
Low	0.0160	UAE	UAE
High	0.0240	UAE	UAE
Probability for complications MRgHIFU (base-case)	0.0130	UAE	UAE
Low	0.0104	UAE	UAE
High	0.0156	UAE	UAE
Portion eligible for MRgHIFU	0.3500	UAE	UAE
Low	0.2500	UAE	UAE
High	0.4500	MRgHIFU	UAE
Proportion Eligible for UAE	0.9000	UAE	UAE
Low	0.8000	Hysterectomy	UAE

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; QALY, quality-adjusted life-year; UAE, uterine artery embolization; WTP, willingness to pay.

Probabilistic Sensitivity Analysis

Figure 3 shows the probability that each procedure is cost-effective at varying willingness-to-pay values. From the figure, it is clear that hysterectomy dominates as the cost-effective option until the willingness to pay exceeds about $46,000, at which point UAE is the most cost-effective option in the majority of cases. MRgHIFU is the cost-effective option in about 20% and 23% of the model iterations at the willingness-to-pay values of $50,000 and $100,000, respectively. MRgHIFU is the most cost-effective option in about 32% of cases where the willingness to pay is $70,000, which represents the highest point on the MRgHIFU cost-effectiveness acceptability curve (CEAC).



Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

Figure 3: Cost-Effectiveness Acceptability Curves for All Treatment Options

Budget Impact Analysis

We conducted a budget impact analysis as well, also from the perspective of the Ontario Ministry of Health and Long-Term Care. The goal was to determine the estimated one-year cost burden (based on 2012/2013 administrative data) of implementing MRgHIFU to replace currently used uterine fibroid treatments under a number of different scenarios. All costs are reported in 2014 Canadian dollars.

Methods

The first step was to estimate the current annual utilization and costs of non-pharmacological management of uterine fibroids (i.e., hysterectomy, UAE, and myomectomy) for Ontario women aged 40 to 51 years for 2012/2013, using administrative data collected from the Institute for Clinical Evaluative Sciences (ICES). We then compared these values to those which would result from the following scenario: the 2 centres in Ontario that are currently funded to provide MRgHIFU (Sunnybrook Research Institute and Thunder Bay Regional Research Institute) each treat 312 patients a year using MRgHIFU, for a total of 624 patients per year (an estimate based on expert consultation). We then subtracted the difference from the total number of procedures (all types) done in Ontario in 2012/2013 to treat uterine fibroids, and then adjusted the remaining number according to how often each procedure is performed, proportionally, under current utilization patterns. Finally, the total annual costs for each scenario were calculated, and then the 2012/2013 costs were subtracted from the costs of the scenario where MRgHIFU is provided at the 2 centres.

We estimated the expected budgetary impact of implementing MRgHIFU for the following 3 scenarios:

- MRgHIFU replaced only the uterine-preserving procedures (UAE and myomectomy) in the 2 existing MRgHIFU centres (n = 624) while the number of hysterectomies being performed remained unchanged.
- It was assumed that all eligible patients would be able to receive MRgHIFU treatment. Maintaining the 312 treatments per year at a specialized facility and assuming 35% of patients with symptomatic uterine fibroids are eligible for the MRgHIFU procedure, 6 centres would need to be funded if MRgHIFU was to replace a proportion of each of the other 3 types of procedures.
- MRgHIFU replaced only the uterine-preserving procedures at this maximum number of centres required to meet the demand (i.e., 6 centres).

Under each scenario, the budgetary impact was calculated by multiplying the number of times each procedure was performed by the annual cost, as described below.

Sensitivity Analysis

Uncertainty in input parameter values due to model assumptions was addressed through several one-way sensitivity analyses over reasonably expected ranges. The variables we examined for each scenario included the cost of myomectomy, due to uncertainty in costs as captured through the Ontario Case Costing Initiative (OCCI); peri-procedure cost of MRgHIFU; the number of MRgHIFU treatments performed at each centre; and the number of additional centres funded for MRgHIFU.

Resource Utilization

The current annual number of UAE, myomectomy, and hysterectomy procedures performed in Ontario was determined from data captured through the Discharge Abstract Database (DAD) and Same Day Surgery (SDS) database from the Canadian Institute for Health Information (CIHI) and Ontario Health Insurance Plan (OHIP) databases for women aged 40 to 51 years. All women aged 40 to 51 years in Ontario with a diagnosis of uterine fibroids were included in the cohort. Individuals were excluded if they did not have a valid health insurance number, were not a resident of Ontario, if their gender was not recorded as female, or if they had an invalid date of birth or admission/discharge date.

Hysterectomies were collected from the DAD and SDS databases, i.e., whenever a hysterectomy procedure was recorded with the accompanying diagnosis of uterine fibroid (International Classification of Diseases (10th revision) [ICD-10] D25^). Myomectomy procedures were identified through the OHIP database using the Ontario Schedule of Benefits (OSB) fee code S764 to better capture procedures performed for uterine fibroids, because of broad Canadian Classification of Health Intervention (CCI) codes that incorporate a number of procedures. UAE procedures were captured from CIHI (DAD/SDS) (using the codes identified in Table A2) and diagnosis of uterine fibroids (ICD-10 D25^).

Table 11 summarizes the number of procedures per year from 2003 to 2012 for UAE, myomectomy, and hysterectomy, as captured through the DAD and SDS databases (described above). (Note that the number of procedures is presumed to exceed the number of patients treated: a patient with uterine fibroids might undergo more than 1 myomectomy or UAE procedure, though only 1 hysterectomy.) The number of hysterectomies decreases slightly from 2003 to 2012, with an increase in myomectomy procedures. The number of UAE procedures remains relatively constant at around 300, making up a small proportion (6%) of total procedures over the time period captured.

Table 11: Annual Number of Procedures (Hysterectomy, Myomectomy, and UAE) for Treatment of Symptomatic Uterine Fibroids in Women Aged 40 to 51 Years

Year	Hysterectomy	Myomectomy	UAE	Total
2003	3,922	1,113	272	5,306
2004	3,883	1,257	342	5,481
2005	3,715	1,282	290	5,287
2006	3,454	1,364	355	5,173
2007	3,387	1,377	327	5,091
2008	3,385	1,593	306	5,284
2009	3,348	1,526	308	5,182
2010	3,213	1,596	309	5,117
2011	3,128	1,569	371	5,059
2012	3,142	1,677	336	5,155

Abbreviation: UAE, uterine artery embolization.

Unit Costs

Unit costs were derived from a number of sources and are presented in Table 12. Pre-procedure costs include diagnostic tests, consultation with experts, and additional magnetic resonance imaging (MRI) for MRgHIFU and UAE procedures. Peri-procedure costs include applicable professional fees and direct and indirect costs, obtained through the OCCI database.

Peri-procedure costs for MRgHIFU were estimated based on maintenance and operating costs and disposal supply costs, obtained through consultation with clinical experts and an MRgHIFU manufacturer. Post-procedure costs include follow-up with experts and ultrasound imaging. A complete breakdown of costs can be found in Appendix 2, Table A1 (with supporting information presented in Tables A2 to A8).

Table 12: Average Annual Unit Cost for All Uterine Fibroid Procedures

Resource	MRgHIFU	UAE	Myomectomy	Hysterectomy
Pre-Procedure	$862.91	$862.91	$472.16	$472.16
Peri-Procedure	$3,498.59	$4,269.55	$6,050.71	$6,479.72
Post-Procedure	$305.15	$305.15	$183.65	$183.65
Total Average Annual Cost	$4,666.65	$5,437.61	$6,706.52	$7,135.54

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

Results

Based on the utilization data from ICES, and assigning the unit costs for each procedure, it was determined that the total current one-year costs associated with the treatment of symptomatic uterine fibroids are approximately $35.5 million (see Table 13**Error! Reference source not ound.**).

MRgHIFU Replacing a Proportion of All Procedures (Two Centres)

Also explored was the budgetary impact of funding MRgHIFU at the 2 research centres currently equipped to provide it. From the perspective of the ministry, assuming an estimated 312 procedures to be performed per year at each centre (n = 624), estimated savings of $1.38 million could be realized within the first year (Table 13) if the 2 centres replaced a proportion of all other procedures with MRgHIFU.

Table 13: Estimated Budget Impact for MRgHIFU Replacing a Proportion of UAE, Myomectomy, and Hysterectomy in Two Currently Existing MRgHIFU Centres

Parameter	MRgHIFU	UAE	Myomectomy	Hysterectomy
Cost per procedure	$4,667	$5,438	$6,707	$7,136
Volume of procedures in 2012/2013	0	336	1,677623	3,142
Volume of procedures with the 2 currently funded MRgHIFU-equipped centres replacing a proportion of all procedures with MRgHIFU	624	295	1,474	2,762
Cost with the 2 MRgHIFU-equipped centres replacing a proportion of all procedures with MRgHIFU	$34,107,836			
Expenditure in 2012/2013	$35,491,984			
Budgetary Impact	($1,384,475)			

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

MRgHIFU Replacing a Proportion of Uterine-Preserving Procedures Only (Two Centres)

The total budgetary impact for the first year if MRgHIFU replaced a proportion of UAE and myomectomy procedures (n = 624) in the 2 research centres would be an estimated savings of $1.14 million, as shown in Table 14.

Table 14: Estimated Budget Impact for MRgHIFU Replacing a Proportion of UAE and Myomectomy in Two Currently Existing MRgHIFU Centres

Parameter	MRgHIFU	UAE	Myomectomy	Hysterectomy
Cost per procedure	$4,667	$5,438	$6,707	$7,136
Volume of procedures in 2012/2013	0	336	1,677	3,142
Volume of procedures with the 2 MRgHIFU-equipped centres replacing a proportion of uterine-preserving procedures with MRgHIFU	624	232	1,157	3,142
Cost with the 2 MRgHIFU-equipped centres replacing a proportion of uterine-preserving procedures with MRgHIFU	$34,351,209			
Expenditure in 2012/2013	$35,491,984			
Budgetary impact	($1,140,775)			

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

MRgHIFU Replacing a Proportion of All Procedures (Six Centres)

If 6 centres were to use MRgHIFU to replace a proportion of UAE, myomectomy, and hysterectomy procedures to treat symptomatic uterine fibroids, the total budgetary impact for the first year would be an estimated savings of $4.15 million, as shown in Table 15.

Table 15: Estimated Budget Impact for MRgHIFU Replacing a Proportion of UAE, Myomectomy, and Hysterectomy in Six Centres

Parameter	MRgHIFU	UAE	Myomectomy	Hysterectomy
Cost per procedure	$4,667	$5,438	$6,707	$7,136
Volume of procedures in 2012/2013	0	336	1,677	3,142
Volume of procedures with 6 centres replacing a proportion of all procedures with MRgHIFU	1,872	214	1,068	2,001
Cost with the 6 centres replacing a proportion of all procedures with MRgHIFU	$31,338,559			
Expenditure in 2012/2013	$35,491,984			
Budgetary impact	($4,153,425)			

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

MRgHIFU Replacing a Proportion of Uterine-Preserving Procedures Only (Six Centres)

The total budgetary impact for the first year associated with MRgHIFU replacing UAE and myomectomy in 6 centres would be an estimated savings of $3.42 million, as presented in Table 16.

Table 16: Estimated Budget Impact for MRgHIFU Replacing a Proportion of UAE and Myomectomy in Six Centres

Parameter	MRgHIFU	UAE	Myomectomy	Hysterectomy
Cost per procedure	$4,667	$5,438	$6,707	$7,136
Volume of procedures in 2012/2013	0	336	1,677	3,142
Volume of procedures with 6 centres replacing a proportion of uterine-preserving procedures with MRgHIFU	1,872	23	117	3,142
Cost with the 6 centres replacing a proportion of uterine-preserving procedures with MRgHIFU	$32,069,660			
Expenditure in 2012/2013	$35,491,984			
Budgetary Impact	($3,422,324)			

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

Sensitivity Analyses

The budgetary impact was sensitive to peri-procedure cost of myomectomy, peri-procedure cost of MRgHIFU, number of MRgHIFU procedures performed per week at each centre, and number of additional centres funded.

Table 17 shows the budgetary impact for MRgHIFU replacing a proportion of all 3 types of uterine fibroid treatment procedures in the 2 funded centres. Additional expenditures resulted only when the number of MRgHIFU procedures per week per centre was reduced to 3; all other scenarios resulted in cost savings. As the number of MRgHIFU procedures performed per week at each centre increased, the amount of savings increased substantially.

Table 17: Sensitivity Analysis—MRgHIFU Funded at Two Currently Existing Centres (Replacing a Proportion of All Procedures)

Parameter	Base Case Value	Sensitivity Analysis Value	Current Expenditure	Expenditure With MRgHIFU Funded	Budget Impact (Compared With Current Expenditure)
Base case results			$35,491,984	$34,107,509	($1,138,475)
Peri-procedure direct/indirect costs of myomectomy	$5,094				
		$6,000[a]	$37,011,256	$35,442,866	($1,568,390)
		$6,500	$37,849,706	$36,179,818	($1,669,888)
		$7,400	$39,358,916	$37,506,331	($1,852,585)
		$8,400	$41,035,816	$38,980,234	($2,055,581)
Peri-procedure cost of MRgHIFU	$3,499				
		-15%	$35,491,984	$33,780,041	($1,711,943)
		+15%	$35,491,984	$34,434,977	($1,057,007)
		+50%[b]	$35,491,984	$35,199,069	($292,915)
Number of MRgHIFU procedures per week	6				
		3	$35,491,984	$35,499,747	$7,763
		4	$35,491,984	$35,035,667	($456,317)
		5	$35,491,984	$34,571,588	($920,396)
		8	$35,491,984	$33,179,351	($2,312,633)
		10	$35,491,984	$32,251,192	($3,240,792)
Number of additional centres with MRgHIFU	0				
		1	$35,491,984	$33,415,272	($2,076,712)
		2	$35,491,984	$32,723,034	($2,768,950)
		3	$35,491,984	$32,030,797	($3,461,187)
		4	$35,491,984	$31,489,431	($4,002,553)

Abbreviation: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound.
[a]Maximum costs for myomectomy as captured through OCCI (codes 1RM87CAGX, 1RM87BAGX, 1RM87DAAG, and 1RM87LAAK), details in Appendix 2, Table A8.
[b]This value chosen to demonstrate the break-even point in terms of direct costs for MRgHIFU.

The analysis of MRgHIFU replacing a proportion of uterine-preserving procedures only (UAE and myomectomy) in 2 funded centres revealed that the budget was sensitive to the same variables with the same trends as was the previous scenario. However, overall savings were lower because hysterectomy—not replaced in this scenario—is the procedure with the highest unit cost. See Table 18.

Table 18: Sensitivity Analysis—MRgHIFU Funded at Two Currently Existing Centres (Replacing a Proportion of Uterine-Preserving Procedures Only)

Parameter	Base Case Value	Sensitivity Analysis Value	Current Expenditure	Expenditure With MRgHIFU Funded	Budget Impact (Compared With Current Expenditure)
Base case results			$35,491,984	$34,351,209	($1,140,775)
Peri-procedure direct/indirect costs of myomectomy	$5,094				
		$6,000[a]	$37,011,256	$35,399,459	($1,611,797)
		$6,500	$37,849,706	$35,977,963	($1,871,742)
		$7,400	$39,358,916	$37,019,271	($2,339,645)
		$8,400	$41,035,816	$38,176,279	($2,859,536)
Peri-procedure cost of MRgHIFU	$3,499				
		-15%	$35,491,984	$34,023,741	($1,468,243)
		+15%	$35,491,984	$34,678,677	($813,307)
		+50%[b]	$35,491,984	$35,442,769	($49,215)
Number of MRgHIFU procedures per week	6				
		3	$35,491,984	$35,621,597	$129,613
		4	$35,491,984	$35,198,134	($293,850)
		5	$35,491,984	$34,774,672	($717,312)
		8	$35,491,984	$33,504,284	($1,987,700)
		10	$35,491,984	$35,491,984	($2,834,625)
Number of additional centres with MRgHIFU	0				
		1	$35,491,984	$33,780,822	($1,711,162)
		2	$35,491,984	$33,210,434	($2,281,550)
		3	$35,491,984	$32,640,047	($2,851,937)
		4	$35,491,984	$32,069,660	($3,422,325)

Abbreviation: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound.
[a]Maximum costs for myomectomy as captured through OCCI (codes 1RM87CAGX, 1RM87BAGX, 1RM87DAAG, and 1RM87LAAK), details in Appendix 2, Table A8.
[b]This value chosen to demonstrate the break-even point in terms of direct costs for MRgHIFU.

With MRgHIFU replacing a proportion of all types of procedures (UAE, myomectomy, and hysterectomy) in 6 funded centres, the budgetary impact was sensitive to the following variables: number of procedures performed per week and peri-procedure costs. Additional expenditures were expected only when the number of procedures per centre per week was reduced to 3. See Table 19.

Table 19: Sensitivity Analysis—MRgHIFU Funded at Six Centres (Replacing a Proportion of All Procedures)

Parameter	Base Case Value	Sensitivity Analysis Value	Current Expenditure	Expenditure With MRgHIFU Funded	Budget Impact (Compared With Current Expenditure)
Base case results			$35,491,984	$31,338,559	($4,153,425)
Peri-procedure direct/indirect costs of myomectomy	$5,094				
		$6,000[a]	$37,011,256	$32,306,086	($4,705,169)
		$6,500	$37,849,706	$32,840,042	($5,009,664)
		$7,400	$39,358,916	$33,801,161	($5,557,754)
		$8,400	$41,035,816	$34,869,072	($6,166,743)
Peri-procedure cost of MRgHIFU	$3,499				
		-15%	$35,491,984	$30,365,155	($5,135,829)
		+15%	$35,491,984	$32,320,963	($3,171,021)
		+50%[b]	$35,491,984	$34,613,239	($878,745)
Number of MRgHIFU procedures per week	6				
		3	$35,491,984	$35,538,559	$46,575
		4	$35,491,984	$32,754,084	($2,737,900)
		5	$35,491,984	$29,969,609	($5,522,375)
		8[c]	$35,491,984	$21,616,184	($13,875,800)
		10[c]	$35,491,984	$16,047,234	($19,444,750)

Abbreviation: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound.

[a]Maximum costs for myomectomy as captured through OCCI (codes 1RM87CAGX, 1RM87BAGX, 1RM87DAAG, and 1RM87LAAK, respectively), details in Appendix 2, Table A8.

[b]This value chosen to demonstrate the break-even point in terms of direct costs for MRgHIFU.

[c]For greater than 6 procedures per week at 6 centres, it is assumed that more than 35% of patients are eligible for MRgHIFU procedure (48% and 61% for 8 procedures per week and 10 procedures per week, respectively).

Table 20 shows the budgetary impact of MRgHIFU replacing a proportion of uterine-preserving procedures only (UAE and myomectomy) in 6 funded centres. The budget was sensitive to the number of procedures per week and peri-procedure costs. The same trends were observed here as in the scenario involving all 3 treatments, but with overall lower values since hysterectomy, not replaced in this scenario, is the procedure with the highest unit cost. Additional expenditures were expected only when the number of procedures per week was reduced to 3.

Table 20: Sensitivity Analysis—MRgHIFU Funded at Six Centres (Replacing a Proportion of Uterine-Preserving Procedures Only)

Parameter	Base Case Value	Sensitivity Analysis Value	Current Expenditure	Expenditure With MRgHIFU Funded	Budget Impact (Compared With Current Expenditure)
Base case results			$35,491,984	$32,069,660	($3,422,325)
Peri-procedure direct/indirect costs of myomectomy	$5,094				
		$6,000[a]	$37,011,256	$32,175,866	($4,835,390)
		$6,500	$37,849,706	$32,234,479	($5,615,227)
		$7,400	$39,358,916	$32,339,982	($7,018,934)
		$8,400	$41,035,816	$32,457,207	($8,578,608)
Peri-procedure cost of MRgHIFU	$3,499				
		-15%	$35,491,984	$31,087,256	($4,404,729)
		+15%	$35,491,984	$33,052,064	($2,439,921)
		+50%[b]	$35,491,984	$35,344,340	($147,645)
Number of MRgHIFU procedures per week	6				
		3	$35,491,984	$35,880,822	$388,838
		4	$35,491,984	$34,610,434	($881,550)
		5	$35,491,984	$33,340,047	($2,151,937)
		8[c]	N/A	N/A	N/A
		10[c]	N/A	N/A	N/A

Abbreviation: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound.

[a]Maximum costs for myomectomy as captured through OCCI (codes 1RM87CAGX, 1RM87BAGX, 1RM87DAAG, and 1RM87LAAK), details in Appendix 2, Table A8.

[b]This value chosen to demonstrate the break-even point in terms of direct costs for MRgHIFU.

[c]Insufficient number of uterine-preserving procedures performed to operate more than 8 procedures a week at 6 MRgHIFU centres.

DISCUSSION

The Ontario-wide implementation of MRgHIFU for the treatment of uterine fibroids would face a number of challenges. Currently, Sunnybrook Research Institute and Thunder Bay Regional Research Institute are the only centres in the province with the appropriately trained staff and necessary equipment to perform the MRgHIFU procedure. The equipment consists of a HIFU system (ultrasound-equipped table, computer, disposables, etc.) to perform the procedure and an MRI scanner to help guide it. The procedure can occur up to 2 times per day; current estimates from Sunnybrook are a maximum of 2 procedures per day, 3 times per week over all indications (bone palliation, uterine fibroids, and neurological procedures). MRgHIFU implementation is probably most feasible at larger centres—those with the specialized staff and either the necessary equipment or the capital available to invest in it. In most cases, it is impractical to repurpose existing scanners (i.e., those used for diagnostic procedures) for MRgHIFU because of the long duration (e.g., 3 to 4 hours) of each MRgHIFU procedure. It is also important to note that the few HIFU systems available are each designed to be compatible with only one brand of MRI scanner, further limiting the potential to use existing MRI scanners to perform MRgHIFU.

A capital investment may be required from public fundraising efforts to enable a centre to implement MRgHIFU—and this may be a barrier. Smaller centres with shorter wait times for diagnostic MRI scans may have the capacity to use their existing scanners for MRgHIFU procedures without compromising their level of service. However, these centres would likely lack the funds required to purchase and maintain a HIFU system and provide the necessary training and support for staff. Larger centres may be better poised to train and support staff, but their higher patient load for diagnostic MRI may necessitate the purchase of a dedicated MRI scanner for MRgHIFU treatments, further increasing the financial commitment to MRgHIFU and resulting in the expansion of interventional radiology units. The Ministry of Health and Long-Term Care would fund the maintenance and operating costs of the MRI scanners and HIFU systems, with the capital purchases made with funds raised by the hospital or centre. However, despite this, the higher investment costs push the resultant ICER upwards for MRgHIFU relative to hysterectomy from the hospital perspective. From a value-for-money perspective, this may eliminate MRgHIFU as a viable treatment option.

The adoption of MRgHIFU as a treatment for uterine fibroids would face strategic challenges too, as we learned through consultation with Ontario physicians who treat uterine fibroids. Minimally invasive treatments for fibroids, specifically UAE, are capped at a maximum number of procedures per year, which leads to wait times approaching a year at some facilities. These caps are in place so that interventional radiologists can provide services to oncology patients and others whose indications take greater priority. This drives women with symptomatic fibroids to seek more invasive surgical options as a way to eliminate their symptoms in a more acceptable timeframe. The resulting underuse of minimally invasive fibroid procedures will continue unless these procedures receive additional funding from the province.

LIMITATIONS

Limitations of Cost-Effectiveness Analysis Results

The cost-effectiveness model has some limitations. Uncertainty around model input parameters is often unavoidable. Our utility estimates were derived from a single study and differed significantly from similar estimates in other relevant published studies. Additionally, several of the utility estimates reported in other studies (27, 29) were based on either unpublished clinical trial data or assumptions. We addressed these uncertainties through sensitivity analysis around utility input values used in the cost-effectiveness model. Another potential limitation is the assumption that patients in the post-discharge state would not experience complications incurring significant costs. This assumption was relaxed through the application of disutilities associated with post-procedure complications.

In the base-case model, we performed a number of scenario analyses to overcome limitations related to comparators and the relevant patient population. First, we considered a scenario that included only uterine-preserving procedures as first-line treatment options. This let us examine the implications of a patient population wishing to retain their uteri for various reasons, including potential childbirth. Our second scenario considered only MRgHIFU-eligible patients, in order to demonstrate cost-effectiveness in the subpopulation with fibroids of a size and location amenable to MRgHIFU. Finally, we considered a scenario in which UAE was eliminated as a treatment option for MRgHIFU-eligible patients. The use of UAE in the population of interest has been historically low (5% to 6% of all uterine fibroid procedures from 2003 to 2012) based on administrative data. So the scenario in which it is not modelled is important, given that many women are either unable to obtain UAE treatment or choose surgical procedures.

Limitations of Budget Impact Analysis Results

One key limitation concerns the difficulty in estimating the peri-procedure cost of myomectomy using the OCCI database. The code used for myomectomy is also used for a number of other procedures, including bisection (uterus), dilation and curettage (uterus), excision (congenital septum of uterus), excision (endometrial tissue-aberrant), fibroidectomy, fundectomy (uterine), hysterectomy (partial/subtotal, supra cervical, supra vaginal). We addressed this uncertainty in unit cost for myomectomy through sensitivity analyses for the 4 scenarios.

A further limitation involves the nature of the OCCI database that we used to estimate the budgetary impact of different scenarios of implementing MRgHIFU across the province. Inter-facility coding variation is possible in this database, and can result in inaccurate estimates of number of procedures. More importantly, the non-random availability of the data means they may not be representative of all facilities within the province; these data are collected on a voluntary basis and do not encompass all facilities. We explored the impact of this limitation on peri-procedure cost estimates and the weighting of invasive versus noninvasive procedures indirectly, through sensitivity analyses around cost and uptake.

Also to be considered is the lack of data on MRgHIFU-eligibility or size and location of fibroids in patients referred for UAE, myomectomy, and hysterectomy procedures. This lack of data informs assumptions that were used in the budgetary impact analysis. In the model, MRgHIFU procedures are captured from other procedures according to their current utilization. Thus, for a scenario in which MRgHIFU replaces a proportion of all procedures, the majority would replace hysterectomy due to it having the highest current utilization in Ontario. In scenarios where MRgHIFU replaces a proportion of uterine-preserving procedures only, we took the procedures

proportionally from UAE and myomectomy. Both scenarios are bound by the assumption that only 35% of patients are eligible for MRgHIFU, but, in the case of MRgHIFU replacing uterine-preserving procedures only, an implicit assumption is made: that all patients obtaining these procedures are MRgHIFU eligible. To mitigate these limitations, we conducted sensitivity analyses around the number of procedures, showing that there is an expected additional expenditure of $389,000 when 6 centres are funded for uterine-preserving procedures, assuming only 3 procedures a week per centre.

The lack of a professional fee code for MRgHIFU under the Ontario Schedule of Benefits may also constitute a limitation. However, we addressed this limitation through sensitivity analyses around the peri-procedure cost in each budgetary impact scenario. While funding and billing pathways may also differ, we combined professional and direct and indirect costs and explored them together to give a more accurate cost from the ministry's perspective.

CONCLUSIONS

In the base case, UAE treatment strategy versus hysterectomy resulted in an ICER of $46,480 per QALY gained. The MRgHIFU strategy was extendedly dominated by a combination of UAE and hysterectomy (with a minimal difference in cost and QALYs) and myomectomy was strictly dominated by MRgHIFU and UAE. Through examination of model parameter uncertainty, MRgHIFU was found to be cost-effective in 20% of cases at a willingness-to-pay threshold of $50,000. In the scenario where only MRgHIFU-eligible patients are considered, MRgHIFU becomes the most cost-effective option for a willingness-to-pay threshold of $50,000. In the scenario where only MRgHIFU-eligible patients are considered and where UAE is eliminated as a treatment option (due to its low historic utilization in Ontario), MRgHIFU becomes cost-effective with an incremental cost of $39,250 per additional QALY. These results suggest that MRgHIFU may be cost-effective under certain circumstances.

We estimated that the current use of procedures used to treat symptomatic uterine fibroids (UAE, myomectomy, and hysterectomy) costs the Ministry of Health and Long-Term Care approximately $35.5 million a year. We then estimated that the province would realize a savings of $1.38 million if MRgHIFU was funded at the 2 currently existing centres only, and $4.15 million if the number of centres was expanded to 6. These estimates are for one-year treatment costs and do not consider changes in downstream treatment costs.

The implementation would involve many challenges, such as the high capital investment needed to purchase HIFU systems and in some cases dedicated MRI scanners; and, in cases where existing MRI scanners would be used, the opportunity cost of performing 3- to 4-hour procedures using scanners that are already in high demand. However, the benefit of giving women a completely noninvasive treatment option is an important consideration, as is, from a societal perspective, the potential benefit from faster recovery times.

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Editorial Staff
Sue MacLeod, BA

Medical Information Services
Kaitryn Campbell, BA(H), BEd, MLIS
Corinne Holubowich, BEd, MLIS

ICES Analyst
Lauren Webster, MPH

Advisory Experts

Advisors	Representation	Affiliation
Dr. Elizabeth David	Interventional Radiologist	Sunnybrook Research Institute
Dr. Dheeraj Rajan	Head and Associate Professor Division of Vascular and Interventional Radiology Department of Medical Imaging	University Health Network University of Toronto
Dr. Grace Liu	Obstetrician/Gynaecologist	Sunnybrook Research Institute
Dr. Elaine Herer	Deputy Chief of Obs/Gyn	Sunnybrook Research Institute
Ex-Officio Members		
Dr. Les Levin	Vice-President, Evidence Development and Standards	Health Quality Ontario, 2011–2014

APPENDICES

Appendix 1: Literature Search Strategy

Database:
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present; Embase 1974 to 2014 Mar 26

Line #	Searches	Results
1	exp Leiomyoma/	30570
2	Myoma/	3215
3	Uterus/	100240
4	Myometrium/	16164
5	or/3-4	112506
6	and/2,5	587
7	Uterine Myomectomy/ use prmz	93
8	Myomectomy/ use oemezd	3282
9	Uterus Myoma/ use oemezd	9557
10	(((uterine or uterus) adj2 fibro*) or fibromyoma* or (fibroid adj2 tumo?r*) or angioleiomyoma* or angiomyoma* or elastomyofibroma* or hemangioleiomyoma* or hemangiomyoma* or leimyoma* or leiomyoma* or leyomyoma* or myofibroma* or myofibromatosis or myoma*).ti,ab.	39350
11	or/1,6-10	52360
12	exp High-Intensity Focused Ultrasound Ablation/ use prmz	868
13	exp High Intensity Focused Ultrasound/ use oemezd	2530
14	"Magnetic Resonance Guided Focused Ultrasound Surgery"/ use oemezd	24
15	Magnetic Resonance Imaging, Interventional/ use prmz	756
16	Interventional Magnetic Resonance Imaging/ use oemezd	762
17	Ultrasonic Therapy/ use prmz	7921
18	Ultrasonography, Interventional/ use prmz	14045
19	Ultrasound/ use oemezd	101481
20	Ultrasound Surgery/ use oemezd	176
21	Ultrasound Therapy/ use oemezd	6975
22	((MR or MRI or magnetic resonance imag* or magnetic resonance*) adj2 (guide* or ultrasound* or ultrasonograph*)).ti,ab.	17975
23	(ExAblate or Sonalleve or high intensity focused ultrasound* or HIFU* or focused ultrasound* or MRgFUS).ti,ab,dv.	6513
24	or/12-23	150489

25	*Economics/ use prmz	10325
26	*Economics, Medical/ use prmz	5228
27	*Economics, Pharmaceutical/ use prmz	1309
28	exp "Costs and Cost Analysis"/ use prmz	178538
29	exp Models, Economic/ use prmz	9952
30	Markov Chains/ use prmz	9486
31	Monte Carlo Method/ use prmz	19444
32	Quality-Adjusted Life Years/ use prmz	6785
33	*Economic Aspect/ use oemezd	13758
34	Health Economics/ use oemezd	33351
35	exp Health Care Cost/ use oemezd	201352
36	exp Economic Evaluation/ use oemezd	208131
37	exp Pharmacoeconomics/ use oemezd	164776
38	(econom* or cost or costly or costing or costed or price or prices or pricing or priced or discount or discounts or discounted or discounting or expenditure or expenditures or budget* or afford* or pharmacoeconomic* or pharmaco-economic*).ti,ab.	1148139
39	(cost* adj1 (util* or effective* or efficac* or benefit* or consequence* or analy* or minimi* or saving* or breakdown or lowering or estimate* or variable* or allocation or control or illness or sharing or life or lives or affordabl* or instrument* or technolog* or day* or fee or fees or charge or charges)).ti,ab.	240152
40	(decision adj1 (tree* or analy* or model*)).ti,ab.	23232
41	((value or values or valuation) adj2 (money or monetary or life or lives or costs)).ti,ab.	7984
42	(qoly or qolys or hrqol or qaly or qalys or qale or qales).ti,ab.	30957
43	(sensitivity analys*s or "willingness to pay" or quality-adjusted life year* or quality adjusted life year* or quality-adjusted life expectanc* or quality adjusted life expectanc*).ti,ab.	48148
44	(unit-cost or unit-costs or markov).ti,ab.	29847
45	or/25-44	1629817
46	11 and 24 and 45	103
47	limit 46 to english language	98
48	limit 47 to yr="2000 -Current"	95
49	remove duplicates from 48	72

Appendix 2: Additional Tables

Table A1: Resource Utilization Costs for Each Procedure (in 2014 Canadian Dollars) for Treatment of Symptomatic Uterine Fibroids

Resource Item	MRgHIFU	UAE	Myomectomy	Hysterectomy	Data Source and Comments
Pre-Procedure					
Obs/Gyn Consultation	$101.70	$101.70	$101.70	$101.70	OSB A205 – Consultation Obstetrics and Gynaecology
Special Surgical Consultation	-	-	$160.00	$160.00	OSB C935 – Special Surgical Consultation- Obstetrics and Gynaecology
Interventional Radiologist Consultation	$223.20	$223.20	-	-	OSB A365 – Special Interventional radiological consultation
Anesthesiologist Consultation	-	-	$106.80	$106.80	OSB A015 – Anaesthesia consultation
Diagnostic Tests					
Ultrasound					
Professional Fee	$81.95	$81.95	$81.95	$81.95	OSB J162 – Diagnostic ultrasound (pelvis, complete technical and professional)
Lab Tests (e.g., blood count, pregnancy test, luteinising hormone level)	$21.71	$21.71	$21.71	$21.71	L393-CBC and L065-Cretaine
MRI					
Professional Fee	$73.35	$73.35			OSB X461
Direct Cost	$361.00	$361.00			CCI 3.KT.30.^^, 3.KT.40.^^ (ambulatory)
Total Pre-Procedure Costs	***$862.91***	***$862.91***	***$472.16***	***$472.16***	
Peri-Procedure					
Direct Costs	-	$3,184.00	$5,094.00	$5,517.00	Obtained via CCI codes listed in Table A2
Surgical Assistant	-	-	$236.71[a]	$205.50[a]	Based on $12.04 fee for surgical assistant from OSB, see Table A4
Anesthesiologist	-	-	$336.10[a]	$294.23[a]	Based on $15.01 anesthetist fee from OSB, see Table A5
Professional Fee	$400	$1,085.55	$383.90	$463.00	Hysterectomy: OSB S757; Myomectomy: OSB S764; UAE: See Table A6
Physician Cost					
Operating Costs	$2,243.59				See Table A7 for operating costs (divided by estimated number of annual procedures; 312 from expert consultation)
Supplies per Procedure[b]	$855				
Total Peri-Procedure Costs	***$3,498.59***	***$4,269.55***	***$6,050.71***	***$6,479.72***	
Post-Procedure					
Physician Visits	$223.20	$223.20	$101.70	$101.70	Assumes 1 visit with specialist (interventional radiologist or surgeon), and 1 ultrasound
Ultrasound	$81.95	$81.95	$81.95	$81.95	

Total Post-Procedure Costs	***$305.15***	***$305.15***	***$183.65***	***$183.65***

Abbreviations: CCI, Canadian Classification of Health Interventions; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; MRI, magnetic resonance imaging; Obs/Gyn, obstetrics and gynaecology; OSB, Ontario Schedule of Benefits; UAE, uterine artery embolization.

[a]Professional fees for hysterectomy and myomectomy are weighted according to number of invasive and noninvasive procedures performed, as captured by the OCCI database. See subsequent text for explanation.

[b]Cost of supplies for a single procedure are approximately $855 (according to manufacturer), including: $250 treatment kit, $150 sedation medication, $75 Foley catheter, $80 gadolinium contrast agent, $50 general supplies (linens, gown, snacks, slippers, etc.).

The direct and indirect medical costs related to UAE, myomectomy, and hysterectomy were obtained from OCCI, using the CCI codes identified through CIHI's Canadian Classification of Health Interventions coding system. (44) These codes were confirmed through expert consultation and are listed in Table A2, which shows the codes for current uterine fibroid treatment options. Diagnosis codes were also identified in order to limit the search to procedures with indications relevant to treatment of uterine fibroids. These codes are further classified into "invasive" and "less invasive" procedures for purposes of costing, as shown in Table A3.

Table A2: CCI Codes Used to Estimate Costs in the Economic Model

Procedure	CCI Code[a]
Hysterectomy	1.RM.89.AA; 1.RM.89.CA; 1.RM.89.DA; 1.RM.89.LA
Myomectomy[b]	1.RM.87.BAAG; 1.RM.87.BAAK; 1.RM.87.BAGX; 1.RM.87.CAAK; 1.RM.87.CAGX; 1.RM.87.DAAG; 1.RM.87.DAAK; 1.RM.87.DAGX; 1.RM.87.LAAK
UAE	1.RM.13.GQC2; 1.RM.13.GQGE; 1.RM.13.GQWO

Abbreviations: CCI, Canadian Classification of Health Interventions; UAE, uterine artery embolization.

[a]Each search was performed using diagnosis codes D250, D251, D252, D259, D282, N938, and N939 to limit search to procedures with main responsible diagnosis related to uterine fibroids.

[b]Note that 1.RM.87.codes include a number of procedures: bisection (uterus), dilation and curettage (uterus), endometrectomy (with dilation), excision (congenital septum of uterus), excision (endometrial tissue-aberrant), fibroidectomy, fundectomy (uterine), hysterectomy (partial/subtotal, supra cervical, supra vaginal), and myomectomy. This creates uncertainty in costs surrounding myomectomy, which is explored through a sensitivity analysis.

Table A3 shows the weighting of costs for "invasive" and "less invasive" myomectomies and hysterectomies in order to obtain an overall estimate of costs. Using the OCCI database, we weighted the costs according to the type of procedure. For hysterectomy, 73.3% of procedures are "invasive"; that is, open (i.e., laparotomy). For myomectomy, 75.6% of procedures are "invasive" (i.e., laparotomy).

Table A3: Number of Procedures and Proportion of Invasive/Less-Invasive Myomectomies and Hysterectomies

Procedure	CCI Code	Classification	# Procedures[a]
Hysterectomy	1.RM.89.AA	Combination laparoscopic/vaginal	122 Less-invasive
	1.RM.89.CA	Vaginal	121 Less-invasive
	1.RM.89.DA	Laparoscopic	118 Less-invasive
	1.RM.89.LA	Open	991 Invasive
Myomectomy	1RM87BAAG	Hysteroscopic	FOI
	1RM87BAAK	Hysteroscopic	FOI
	1RM87BAGX	Hysteroscopic	26 Less-invasive
	1RM87CAAE	Vaginal	11 Less-invasive
	1RM87CAAF	Vaginal	FOI
	1RM87CAAK	Vaginal	FOI
	1RM87CAGX	Vaginal	12 Less-invasive
	1RM87DAAG	Laparoscopic	18 Less-invasive
	1RM87DAAK	Laparoscopic	FOI
	1RM87DAGX	Laparoscopic	129 Less-invasive
	1RM87LAAK	Open	FOI
	1RM87LAGX	Open	607 Invasive

Abbreviations: CCI, Canadian Classification of Health Interventions; FOI, freedom of information.
[a]Number of procedures not available in some cases, as noted, because, in accordance with the Freedom of Information and Protection of Privacy Act (FIPPA), the Ontario Case Costing Initiative database will not release diagnosis or procedure codes when there are 5 or fewer cases.

Table A4: Surgical Assistant Costs for Invasive/Less-Invasive Hysterectomies and Myomectomies

Procedure	Surgery Length, minutes	No. of 15-Minute Periods	No. of Time Units	No. of Basic Units	Total No. of Units	Total Billing
Invasive hysterectomy	101.3 (45)	7	10	6	16	$192.64
Less-invasive hysterectomy	127.7 (45)	9	14	6	20	$240.80
Invasive myomectomy	92.5 (46, 47)	7	10	6	16	$192.64
Less-invasive myomectomy	189.7 (46, 47)	13	25	6	31	$373.24

Abbreviation: No., number.

Table A5: Anesthesiologist Costs for Invasive/Less-Invasive Hysterectomies and Myomectomies

Procedure	Surgery Length, minutes	No. of 15-Minute Periods	No. of Time Units	No. of Basic Units	Total No. of Units	Total Billing[a]
Invasive hysterectomy	101.3 (45)	7	11	7	18	$270.18
Less-invasive hysterectomy	127.7 (45)	9	17	7	24	$360.24
Invasive myomectomy	92.5 (46, 47)	7	11	7	18	$270.18
Less-invasive myomectomy	189.7 (46, 47)	13	29	7	36	$540.36

Abbreviation: No., number.
[a]Based on $15.05 fee per time unit, from Ontario Schedule of Benefits.

The Ontario Schedule of Benefits professional fees for UAE were confirmed by a number of experts and are presented in Table A6. The fees include charges associated with the angiography suite as well as the embolization procedure itself.

Table A6: Breakdown of OHIP Professional Fees for Uterine Artery Embolization

OHIP Fee Code	Cost
OSB X181 – Angiogram by catheterization (non-selective)	$90.55
OSB X182 – Angiogram by catheterization (selective—per vessel, to a maximum of 4)	$116.75 × 4
OSB X165 – Photographic subtraction	$11.35
OSB J021 – Angiography—insertion of catheter	$121.40
OSB J022 – Selective catheterization	$60.15 × 4
OSB J040 – Embolization first vessel	$105.30 + $49.35 (for second vessel)
Total Cost	**$1,085.55**

Abbreviations: OHIP, Ontario Health Insurance Plan; OSB, Ontario Schedule of Benefits.

The peri-procedure cost of MRgHIFU was estimated through consultation with experts and MRgHIFU device manufacturers. The operating costs, for which the province is financially responsible, are presented in Table A7. Combining maintenance costs on the MRI scanner magnet, HIFU system, and staff to maintain the equipment, the total annual operating cost was estimated at $700,000. This was combined with the additional cost of disposables per procedure and interventional radiologist involvement in the treatment (as broken down in Table A1). This value was then divided by an annual caseload of 312, as estimated by clinical experts, to derive an average peri-procedure cost.

Table A7: Breakdown of Operating Costs Associated With MRgHIFU Treatment

Strategy	Cost	Notes
Maintenance of the magnet	$200,000	Expert consultation
Maintenance of the FUS system	$100,000	Expert consultation
MRI technician salary plus benefits	$125,000	Expert consultation
Physicist salary plus benefits	$137,500	Expert consultation
Nurse salary plus benefits	$137,500	Expert consultation
Total direct costs	**$700,000**	

Abbreviations: FUS, focused ultrasound; MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; MRI, magnetic resonance imaging.

Table A8 provides the total and maximum costs for CCI codes related to myomectomy (codes without a sufficient number of procedures were excluded as no costing information was reported). The total costs were weighted according to number of procedures (as shown in Table A3) in order to derive an estimate of total peri-procedure costs (in addition to relevant professional fees). The maximum costs are used as new total cost estimates for sensitivity analyses. As the CCI code for myomectomy includes a number of other procedures, some of them less expensive, the estimate used in the base case may represent an under-estimation of the cost of myomectomy and was thus explored in sensitivity analyses.

Table A8: Total and Maximum Cost for All CCI Codes Related to Myomectomy

CCI Code	Total Cost	Maximum Cost
1RM87BAGX	$3,929	$6,511
1RM87CAGX	$3,132	$5,951
1RM87DAAG	$4,432	$7,392
1RM87DAGX	$4,905	$8,405
1RM87LAGX	$5,250	$24,308[a]

Abbreviation: CCI, Canadian Classification of Health Interventions.

[a]This value was excluded from sensitivity analyses due to it likely being an outlier, representing an extreme case and not representative of average values.

Table A9: Comparison of Procedural Treatments for Symptomatic Uterine Fibroids

Treatment Factor	MRgHIFU	UAE	Myomectomy	Hysterectomy
Hospital stay	Outpatient procedure, no hospital stay; recovery time 1–2 hours (48)	Outpatient procedure, usually no hospital stay, (49, 50) recovery time of 4–6 (51, 52) hours	0–2 days (laparoscopic) (46) 1–3 days (abdominal) (46)	0–2 days (laparoscopic) 1–5 days (full abdominal) (53)
Return to normal activity	1–2 days (37)	10–14 days (54, 55)	2.9 +/- 1.8 weeks (laparoscopic) 3.7 +/- 2.9 weeks (abdominal) (56)	2–5 weeks (37, 54)
Future fertility	Insufficient data. Study of 54 pregnancies in 51 women showed 64% had vaginal delivery and 36% had caesarean delivery after MRgHIFU (57)	Not recommended. 12% risk of placental abnormalities. (58) Risk of ovarian failure, amenorrhea reported in < 15% (58)	Yes, although risks shown in pregnancy post-procedure (59)	Not possible

Abbreviations: MRgHIFU, magnetic resonance-guided high-intensity focused ultrasound; UAE, uterine artery embolization.

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Health Quality Ontario
130 Bloor Street West, 10th Floor
Toronto, Ontario
M5S 1N5
Tel: 416-323-6868
Toll Free: 1-866-623-6868
Fax: 416-323-9261
Email: EvidenceInfo@hqontario.ca
www.hqontario.ca

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