

# Magnetic Resonance–Guided High-Intensity Focused Ultrasound (MRgHIFU) for Treatment of Symptomatic Uterine Fibroids: OHTAC Recommendation

ONTARIO HEALTH TECHNOLOGY ADVISORY COMMITTEE

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Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with advisory panels, clinical experts, developers of health technologies, scientific collaborators, and field evaluation partners to provide evidence about the effectiveness and cost-effectiveness of health interventions in Ontario.

To conduct its systematic reviews of health interventions, the Evidence Development and Standards branch examines the available scientific literature, making every effort to consider all relevant national and international research. If there is insufficient evidence on the safety, effectiveness, and/or cost-effectiveness of a health intervention, HQO may request that its scientific collaborators conduct economic evaluations and field evaluations related to the reviews. Field evaluation partners are research institutes focused on multicentred clinical trials and economic evaluation, as well as institutes engaged in evaluating the safety and usability of health technologies.

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Once finalized and approved by the Board of Directors of Health Quality Ontario, the research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding OHTAC recommendations and associated reports are also published on the HQO website. Visit <http://www.hqontario.ca> for more information.

When sufficient data are available, OHTAC tracks the ongoing use of select interventions it has previously reviewed, compiling data by time period and region. The results are published in the Ontario Health Technology Maps Project Report.

## TABLE OF CONTENTS

<b>BACKGROUND.....</b>	<b>5</b>
<b>FINDINGS OF THE EVIDENCE-BASED ANALYSES .....</b>	<b>6</b>
<b>CONCLUSIONS.....</b>	<b>7</b>
<b>DECISION DETERMINANTS.....</b>	<b>8</b>
<b>OHTAC RECOMMENDATIONS .....</b>	<b>9</b>
Appendix 1: Decision Determinants .....	10
<b>REFERENCES .....</b>	<b>12</b>

## BACKGROUND

Magnetic resonance–guided high-intensity focused ultrasound (MRgHIFU) is a new, non-invasive treatment for symptomatic uterine leiomyomas (fibroids). It has been offered as a uterine-preserving treatment option for women who seek alternatives to hysterectomy for their fibroid symptoms. A common occurrence, uterine fibroids are benign but can have a broad impact on a woman's overall health and lifestyle, and continue to be the main indication for hysterectomy. Fibroids can also adversely impact fertility. The current societal trend of delaying childbearing to a later age, when fibroids commonly occur, brings an increasing need for treatment options that preserve not only the uterus but also fertility. Overall, uterine fibroids represent a public health burden that is costly to women, their families, employers, and the health care system.

The Evidence Development and Standards branch at Health Quality Ontario conducted an evidence-based analysis (1) to answer the following research questions:

- What are the patient eligibility criteria, technical success, safety, effectiveness, and durability of magnetic resonance–guided high-intensity focused ultrasound (MRgHIFU) for treatment of symptomatic uterine fibroids?
- What is the comparative safety and effectiveness of MRgHIFU in the treatment of symptomatic uterine fibroids, versus other uterine-preserving procedures and versus hysterectomy?

Our systematic search of studies published between 2000 and 2014 identified 2 systematic reviews, 2 randomized controlled trials (RCTs), 45 cohort studies, and 19 case reports. In all, this involved investigators from 29 institutes in 12 countries reporting on their clinical results regarding MRgHIFU treatment of symptomatic uterine fibroids.

In addition, Health Quality Ontario commissioned the Programs for Assessment of Technology in Health (PATH) Research Institute to review the economic literature and conduct a primary economic evaluation (2) to answer a related research question:

- What is the cost-effectiveness of MRgHIFU and the 1-year budgetary impact of using MRgHIFU, compared with current interventions, for the treatment of symptomatic uterine fibroids in women who have been unresponsive to pharmacotherapy, from the perspective of the Ontario Ministry of Health and Long-Term Care?

Their systematic search for economic studies published between 2000 and 2014 identified 3 relevant cost-effectiveness studies. These were then used to inform the structure of an original cost-utility model with Ontario-specific costs and treatment pathways. Also, to inform the budget-impact analysis, data were collected from the Institute for Clinical Evaluative Sciences to determine the number of uterine fibroid treatments performed in Ontario each year.

## FINDINGS OF THE EVIDENCE-BASED ANALYSES

### Clinical Analysis

Multiple clinical and technical factors resulted in highly variable eligibility rates for MRgHIFU, ranging from 14% to 74%. In clinical cohort studies involving 1,594 patients, 26 major complications (1.6%) were reported, MRgHIFU treatment resulted in statistically and clinically significant reductions in fibroid-related symptoms in clinical cohort studies from sites in 9 countries. However, few studies involved follow-up of longer than a year. Retreatment rates following MRgHIFU were higher in the earlier clinical studies involving regulatory required restricted fibroid ablation, than in the later studies, which involved more complete ablation; emergent interventions, however, were rare. Although a desire for fertility was a study exclusion criteria, full-term pregnancies did occur following HIFU suggesting that HIFU may also have a role in fertility preservation. There were no randomized trials comparing MRgHIFU with other methods of imaging guidance, other minimally invasive treatments, or surgeries for symptomatic uterine fibroids.

### Economic Analysis

The economic analysis conducted by PATH for Health Quality Ontario included a cost-utility analysis to estimate the long-term incremental costs and benefits of myomectomy, hysterectomy, uterine artery embolization (UAE), and MRgHIFU for treatment of symptomatic uterine fibroids in premenopausal women. In the base case, UAE was cost-effective when compared with hysterectomy; MRgHIFU was extendedly dominated by a combination of UAE and hysterectomy (i.e., MRgHIFU is less effective and more costly than a program which provides both UAE and hysterectomy); and myomectomy was strictly dominated by MRgHIFU and UAE. In scenarios where MRgHIFU-eligible patients only were considered, and where UAE was eliminated as a treatment option for this patient population (due to its historically low rate of use in Ontario), MRgHIFU became the cost-effective option at commonly accepted willingness-to-pay thresholds (i.e., \$50,000 to \$100,000 per year of life in perfect health).

The budget impact of implementing MRgHIFU was explored for a number of scenarios. The analysis found that the implementation of MRgHIFU could potentially result in 1-year savings of approximately \$1.3 million if implemented at 2 centres, and \$4.1 million if implemented at 6 centres (the estimated number of sites required to treat all eligible patients).

## CONCLUSIONS

### Clinical Analysis

For women with symptomatic uterine fibroids who are unresponsive to medical therapy (i.e., pharmacotherapy) and seek alternatives to hysterectomy, MRgHIFU is a safe and effective non-invasive uterine-preserving treatment from which they can rapidly recover. Treatment durability, for which there is more limited information, depends on the delivery of adequate thermal energy to ablate fibroid tissue. This is greatly influenced by patient and/or technical factors.

There are several limitations with MRgHIFU technology. These include restricted eligibility criteria and the need for an MR scanner that is compatible with the specific brand of HIFU equipment being used. This may mean the purchase of a dedicated scanner for MRgHIFU, or, if an existing scanner is used, loss of MR opportunity time for other patients due to the lengthy procedure time for MRgHIFU. In Ontario, there is also limited access as few centres have: interventional radiologists with technical competence in the procedure, multidisciplinary team approaches to fibroid management, or organized referral patterns for this condition. There is also a lack of comparative evidence on MRgHIFU versus other uterine-preserving treatments such as UAE and myomectomy, limiting the ability to make informed decisions between these treatment options. The main deciding factor between these interventions may well depend on patient factors, given the restrictive criteria for MRgHIFU.

### Economic Analysis

After examining several likely scenarios to address uncertainty in model parameters, it was found that MRgHIFU may be a cost-effective strategy for treating symptomatic uterine fibroids in premenopausal women, at commonly accepted willingness-to-pay thresholds.

The budgetary impact analysis found that the implementation of MRgHIFU in 2 or 6 Ontario centres could potentially result in 1-year savings of approximately \$1.3 million or \$4.1 million, respectively.

## DECISION DETERMINANTS

OHTAC has developed a decision-making framework that consists of 7 guiding principles for decision making and a decision determinants tool. When making a decision, OHTAC considers 4 explicit main criteria: overall clinical benefit, consistency with expected societal and ethical values, value for money, and feasibility of adoption into the health system. For more information on the decision-making framework, please refer to the *Decision Determinants Guidance Document* available at: <http://www.hqontario.ca/evidence/evidence-process/evidence-review-process/decision-making-framework>.

Based on the decision determinants criteria, particularly the criteria of clinical benefit and societal and ethical values, OHTAC weighted in favour of recommending that MRgHIFU be available as a treatment option for symptomatic uterine fibroids, particularly as a treatment alternative to hysterectomy.

Appendix 1 provides a summary of the decision determinants for this recommendation.



## OHTAC RECOMMENDATION

- Based on the current available evidence, OHTAC recommends that magnetic resonance–guided high-intensity focused ultrasound (MRgHIFU) be considered as one option in the treatment of symptomatic uterine fibroids in women who are unresponsive to medical therapy.

## Appendix 1: Decision Determinants

**Table A1: Decision Determinants for MRgHIFU Treatment of Uterine Fibroids**

Decision Criteria	Subcriteria	Decision Determinants Considerations
<b>Overall clinical benefit</b> How likely is the health technology/intervention to result in high, moderate, or low overall benefit?	<b>Effectiveness</b> How effective is the health technology/intervention likely to be (taking into account any variability)?  <b>Safety</b> How safe is the health technology/intervention likely to be?  <b>Burden of illness</b> What is the likely size of the burden of illness pertaining to this health technology/intervention?  <b>Need</b> How large is the need for this health technology/intervention?	<p>MRgHIFU is an effective uterine-preserving treatment for fibroid-related symptoms. All cohort studies report statistical and clinical improvements in fibroid-related symptoms.</p> <p>HIFU is guided by real time continuous MR monitoring for the degree and location of tissue thermal heating and the technology has multiple technical safety safeguards. Although abdominal skin burns can occur, major adverse events rarely occur.</p> <p>Uterine fibroids are the most common pelvic tumour in women of reproductive age and can cause significant morbidity. In a study of white and black pre-menopausal women aged 35 to 39 years, 10% to 15% of the former and 30% to 40% of the latter had clinically significant fibroids, increasing to 35% of white and 50% of black women in their late forties. In 2012 in Ontario, 22,912 women came to medical attention for uterine fibroids—40% were managed surgically.</p> <p>Women of reproductive age, particularly those who have delayed childbearing to later ages, need safe and effective uterine- and fertility-preserving treatment alternatives to surgery.</p>
<b>Consistency with expected societal and ethical values<sup>a</sup></b> How likely is adoption of the health technology/intervention to be congruent with societal and ethical values?	<b>Societal values</b> How likely is the adoption of the health technology/intervention to be congruent with expected societal values?  <b>Ethical values</b> How likely is the adoption of the health technology/intervention to be congruent with expected ethical values?	<p>Many women choose to avoid hysterectomy for uterine fibroid treatment because of the considerable morbidities associated with major abdominal surgery, as well as the prolonged hospitalization and recovery period and related work absences. Also, women have reported in surveys that uterine-preserving and potentially fertility-sparing treatment options are particularly important to them. For younger women who have not completed their families, hysterectomy terminates any future reproductive options. Also, if oophorectomy is simultaneously performed, it places women in immediate menopause, often years before this would naturally occur.</p> <p>This treatment may avoid potential ethical issues associated with restricting women's reproductive choices and/or exposing them to greater present and future risks from unnecessary surgery.</p>
<b>Value for money</b> How efficient is the health technology likely to be?	<b>Economic evaluation</b> How efficient is the health technology/intervention likely to be?	<p>In the base case of the primary economic analysis, MRgHIFU was extendedly dominated by a combination of UAE and hysterectomy (i.e., MRgHIFU is less effective and more costly than a program which provides both UAE and hysterectomy).</p> <p>In scenarios where MRgHIFU-eligible patients only were considered, and where UAE was eliminated as a treatment option, MRgHIFU became a cost-effective option at commonly accepted willingness-to-pay thresholds.</p>

Decision Criteria	Subcriteria	Decision Determinants Considerations
<b>Feasibility of adoption into health system</b> How feasible is it to adopt the health technology/intervention into the Ontario health care system?	<b>Economic feasibility</b> How economically feasible is the health technology/intervention? <hr/> <b>Organizational feasibility</b> How organizationally feasible is it to implement the health technology/intervention?	In scenarios where MRgHIFU is implemented in 2 or 6 Ontario centres, it could potentially result in 1-year savings of \$1.3 million or \$4.1 million, respectively. It is important to note this does not incorporate the capital purchase of equipment. The advantages of an effective non-invasive outpatient-based treatment with discharge within hours and a rapid recovery are significant. However, they are offset by a lengthy HIFU procedure time requiring constant guidance by a compatible MR scanner.

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

<sup>a</sup>The anticipated or assumed common ethical and societal values held in regard to the target condition, target population, and/or treatment options. Unless there is evidence from scientific sources to corroborate the true nature of the ethical and societal values, the expected values are considered.

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