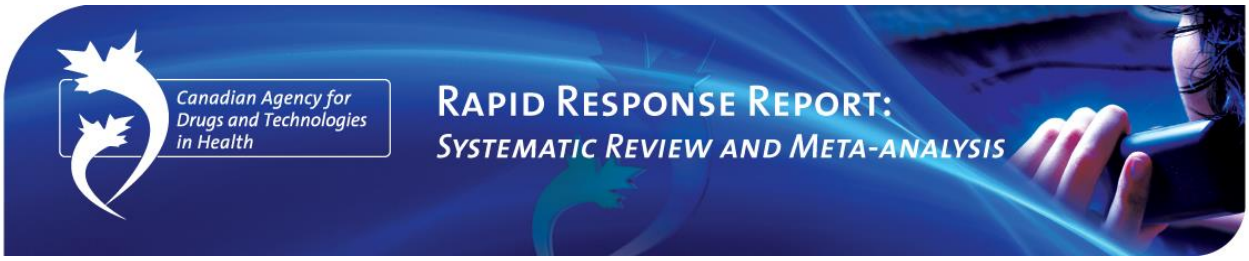


TITLE: Uterine-Preserving Interventions for the Management of Symptomatic Uterine Fibroids: A Systematic Review of Clinical and Cost-Effectiveness

DATE: August 2015

EXECUTIVE SUMMARY

To be completed once draft is final

CONTEXT AND POLICY ISSUES

Uterine fibroids (or leiomyoma) are the most common pelvic tumours and the most common benign tumours in women. Why fibroids develop and grow isn't fully understood, but hormones are known to play a role.[3] Age is a risk factor for their development; the prevalence of fibroids increases with age until menopause. As a result, fibroids are usually diagnosed late in a woman's reproductive period and are present in up to 40% of women after the age of 40. Ethnicity is another risk factor for uterine fibroids. African-American women have a higher incidence of fibroids - 60% by age 35 and more than 80% by age 50, compared to Caucasian women whose incidence of fibroids was 40% by age 35 and almost 70% by age 50.[1]

Approximately 25% of fibroids are symptomatic. Symptoms may include abnormal uterine bleeding, pelvic pressure and pain, infertility, and recurrent pregnancy loss. As a result, uterine fibroids may lead to a significant reduction in a woman's quality of life.[2-4]

Asymptomatic fibroids may be discovered on routine pelvic examination and can be verified with an ultrasound. According to clinical practice guidelines developed by the Society of Obstetricians and Gynaecologists of Canada, treatment of fibroids must be individualized and the following factors should be considered: symptomatology, size and location of fibroids, age, desire for future pregnancy or preservation of the uterus, the availability of therapy, and the experience of the therapist.[5]

Removal of the uterus (hysterectomy) can be the ultimate solution for many women with fibroids. In fact, in the US and Canada, fibroids are responsible for the majority of hysterectomies.[6] Approximately 30% of the hysterectomies performed in Canada are for uterine fibroids,[7] and a similar percentage (33%) were reported for fibroid treatment in a British study.[1] However, many patients seek alternatives to hysterectomy, to preserve fertility and potentially avoid invasive surgery. Alternatives include myomectomy (surgical removal of the fibroid), uterine artery embolization (disruption of the blood supply to the fibroid with small particles), myolysis (disruption of the blood supply to the fibroid with an electrical current or other methods), and endometrial ablation (destruction of the uterine lining). Various methods are used in these approaches.[1,7-13] Drug therapy with selective progesterone receptor modulators or gonadotropin-releasing hormone (GnRH) agonists have also been shown to reduce fibroid-related abnormal uterine bleeding and bulk symptoms such as pelvic pressure; however, they are usually used in the short-term or as pre-surgical treatment of fibroids.[5,7] Compared to hysterectomy, these interventions are less invasive and the uterus is preserved. Each technology carries a specific safety and effectiveness profile; therefore, the best candidates for one technology may not be for another. In addition, the technologies all vary significantly in cost. Not all technologies are readily available across Canada, such as magnetic resonance-guided focused ultrasound, and this lack of accessibility may limit their use.. The choice of intervention is also influenced by patient preference.

This study systematically reviews the clinical and cost-effectiveness of interventions for symptomatic uterine fibroids that preserve the uterus and are available in Canada. This will help to identify the optimal fibroid management options for clinical practice. The optimal strategy may differ depending on the patient or the characteristics of the fibroid and these will be considered in the review by using subgroup analysis when data are available.

RESEARCH QUESTIONS

1. What is the clinical effectiveness and safety of uterine-preserving interventions for the treatment of symptomatic uterine fibroids?
2. What is the cost-effectiveness of uterine-preserving interventions for the treatment of symptomatic uterine fibroids?

KEY FINDINGS

The findings were inconsistent across the included clinical studies. Compared with conventional hysterectomy, uterine-preserving interventions for the treatment of symptomatic uterine fibroids are associated with fewer complications, shorter hospital stay and more patient satisfaction, however patients treated with hysterectomy reported better health-related quality of life. Symptoms of abnormal uterine bleeding and pelvic pressure were reduced after uterine artery embolization, uterine artery occlusion, myomectomy, or radiofrequency thermal ablation.

Data on reproductive outcomes were reported, but should be interpreted with caution due to the small study population and insufficient power of the studies.

Findings from a Canadian economic evaluation demonstrated that magnetic resonance-guided focused ultrasound was only more cost-effective than embolization when it was assumed that all patients were eligible for this treatment. When focused ultrasound was not available, embolization was more cost-effective than hysterectomy.

METHODS

Literature Search Strategy

A peer-reviewed literature search was conducted using the following bibliographic databases: MEDLINE, PubMed, Embase, The Cochrane Library, and the University of York Centre for Reviews and Dissemination (CRD) databases. Grey literature (literature that is not commercially published) was identified by searching relevant sections of the *Grey Matters* checklist (https://www.cadth.ca/resources/finding-evidence/grey-matters-practical-search-tool-evidence-based-medicine). Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, controlled clinical trials, cohort studies, and economic studies and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English- or French-language documents. Conference abstracts were excluded from the search results. The search for randomized controlled trials, controlled clinical trials, cohort studies, and economic studies was not limited by publication year. The search for health technology assessments, systematic reviews, meta-analyses, and guidelines was limited to documents published since January 1, 2005. Regular alerts were established to update all searches until project completion. The search strategy is presented in Appendix 1.

Selection Criteria and Methods

Two reviewers independently screened the titles and abstracts of all citations retrieved from the literature search and, based on the selection criteria, ordered the full text of any articles that appear to meet those criteria. The reviewers then independently reviewed the full text of the selected articles, applied the selection criteria to them, and compared the independently chosen

included/excluded studies. Disagreements were resolved through discussion until consensus was reached. Duplicate publications of the same trial were excluded unless they provided additional outcome information of interest.

Table 1: Selection Criteria	
Population	Women with symptomatic uterine fibroids Possible subgroups: • age • size of uterus or fibroid(s), number of fibroids, location of fibroids • types of symptoms (e.g., heavy menstrual bleeding, pain, pressure) • previous treatment for uterine fibroids • anemia • body mass index
Intervention	Uterine-preserving interventions to eliminate or specifically alleviate fibroid-related health problems: • myomectomy (laparotomy, laparoscopy, or hysteroscopy) • myolysis (ultrasound, laser, cryotherapy, radiofrequency, or other methods) • uterine artery embolization • endometrial ablation (electrosurgery, heat, laser, radiofrequency, or other methods) • magnetic resonance-guided focused ultrasound ablation • uterine artery occlusion • uterine artery ligation
Comparator	• Other uterine-preserving interventions such as those previously listed • Watchful waiting and monitoring • Placebo • Drug therapy (selective progesterone receptor modulators, GnRH agonists) • Hysterectomy
Outcomes	Clinical effectiveness: • change in abnormal uterine bleeding • change in pelvic pressure (pain, bladder pressure, painful sexual intercourse, urinary frequency, incontinence, nocturia, or constipation) • change in fibroid size • health-related quality of life • pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery) • relapse/re-intervention rate • length of hospital stay

	• patient satisfaction Cost-effectiveness: • incremental cost-effectiveness ratio • quality-adjusted life-year • incremental net monetary benefit • incremental net health benefit Safety: • Adverse events (operation complications, pregnancy complications, etc.)
Study Designs	• Randomized controlled trials and non-randomized studies with a control group • Economic evaluations

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, or if they were duplicate publications of the same study. Studies of infertile women who are asymptomatic were excluded. Studies evaluating the effectiveness of combination therapy were excluded. Economic studies were excluded if they reported cost data only. Economic studies conducted in developing countries were excluded due to the differences between healthcare systems and the challenge in generalizing the study results to the Canada context.

Data Extraction Strategy

A data extraction form for the clinical effectiveness review was designed a priori to document and tabulate relevant study characteristics. Data were extracted by one reviewer, and were verified by the second reviewer for accuracy and completeness. Any disagreements were resolved through discussion until consensus is reached.

Critical Appraisal of Individual Studies

The validated Downs and Black checklist[14] was used to assess the study quality of randomized controlled trials and non-randomized studies based on the quality of reporting, external validity, and risk of bias. The quality of the economic evaluations was assessed using the Drummond checklist.[15] Numeric scores were not calculated, instead the strengths and limitations of the included studies were described narratively.

Data Analysis Methods

Meta-analyses were not possible due to the variability in study characteristics, such as the instruments used for symptom assessment, and outcome measures with diverse definitions. Instead, a narrative synthesis and summary of findings were presented. In the included clinical studies, there were no data on any of the pre-defined subgroups; therefore subgroup analyses were not performed.

RESULTS

Quantity of Research Available

The process of study selection is outlined in the PRISMA flowchart (Appendix 2). The literature search yielded 1,189 citations. Upon screening titles and abstracts, 1,055 citations were excluded and 134 potentially relevant articles were retrieved for full-text review. Three potentially relevant reports were retrieved from grey literature or hand searching and one additional potentially relevant reference was identified via literature alerts.[16] Of the 137 potentially relevant reports, 42 were selected as being relevant to the research questions and 95 were excluded. Of the 42 reports, 34 (on 25 unique studies) addressed the clinical research questions with respect to the clinical effectiveness and safety of uterine-preserving interventions, and eight (on seven unique studies) addressed the economic research questions about the cost-effectiveness of these interventions.

Included clinical studies are listed in Appendix 23, while articles not eligible for this review are listed in Appendix 3**: INCLUDED STUDIES FOR CLINICAL EVIDENCE**

Ambat S, Mittal S, Srivastava DN, Misra R, Dadhwal V, Ghosh B. Uterine artery embolization versus laparoscopic occlusion of uterine vessels for management of symptomatic uterine fibroids. Int J Gynaecol Obstet. 2009 May;105(2):162-5.

Brochner AC, Mygil B, Elle B, Toft P. Inflammatory response in patients undergoing uterine artery embolization as compared to patients undergoing conventional hysterectomy. Acta Radiol. 2009 Dec;50(10):1193-7.

Broder MS, Goodwin S, Chen G, Tang LJ, Costantino MM, Nguyen MH, et al. Comparison of long-term outcomes of myomectomy and uterine artery embolization. Obstet Gynecol. 2002 Nov;100(5 Pt 1):864-8.

Cunningham E, Barreda L, Ngo M, Terasaki K, Munro MG. Uterine artery embolization versus occlusion for uterine leiomyomas: a pilot randomized clinical trial. J Minim Invasive Gynecol. 2008 May;15(3):301-7.

The EMMY study:

Hehenkamp WJ, Volkers NA, Birnie E, Reekers JA, Ankum WM. Symptomatic uterine fibroids: treatment with uterine artery embolization or hysterectomy--results from the randomized clinical Embolisation versus Hysterectomy (EMMY) Trial. Radiology [Internet]. 2008 Mar [cited 2015 May 28];246(3):823-32. Available from: http://pubs.rsna.org/doi/pdf/10.1148/radiol.2463070260

Hehenkamp WJ, Volkers NA, Donderwinkel PF, de Blok S, Birnie E, Ankum WM, et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): peri- and postprocedural results from a randomized controlled trial. Am J Obstet Gynecol. 2005 Nov;193(5):1618-29.

Volkers NA, Hehenkamp WJ, Birnie E, Ankum WM, Reekers JA. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2

years' outcome from the randomized EMMY trial. Am J Obstet Gynecol. 2007 Jun;196(6):519-21.

Hehenkamp WJ, Volkers NA, Birnie E, Reekers JA, Ankum WM. Pain and return to daily activities after uterine artery embolization and hysterectomy in the treatment of symptomatic uterine fibroids: results from the randomized EMMY trial. Cardiovasc Intervent Radiol. 2006 Mar;29(2):179-87.

Hehenkamp WJ, Volkers NA, Bartholomeus W, de Blok S, Birnie E, Reekers JA, et al. Sexuality and body image after uterine artery embolization and hysterectomy in the treatment of uterine fibroids: a randomized comparison. Cardiovasc Intervent Radiol [Internet]. 2007 Sep [cited 2015 May 28];30(5):866-75. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2039794

van der Kooij SM, Hehenkamp WJ, Volkers NA, Birnie E, Ankum WM, Reekers JA. Uterine artery embolization vs hysterectomy in the treatment of symptomatic uterine fibroids: 5-year outcome from the randomized EMMY trial. Am J Obstet Gynecol. 2010 Aug;203(2):105-13.

Goodwin SC, Bradley LD, Lipman JC, Stewart EA, Nosher JL, Sterling KM, et al. Uterine artery embolization versus myomectomy: a multicenter comparative study. Fertil Steril. 2006 Jan;85(1):14-21.

Hahn et al.

Hahn M, Brucker S, Kraemer D, Wallwiener M, Taran FA, Wallwiener CW, et al. Radiofrequency volumetric thermal ablation of fibroids and laparoscopic myomectomy: long-term follow-up from a randomized trial. Geburtshilfe Frauenheilkd [Internet]. 2015 May [cited 2015 Jul 2];75(5):442-9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4461677

Brucker SY, Hahn M, Kraemer D, Taran FA, Isaacson KB, Kramer B. Laparoscopic radiofrequency volumetric thermal ablation of fibroids versus laparoscopic myomectomy. Int J Gynaecol Obstet [Internet]. 2014 Jun [cited 2015 May 28];125(3):261-5. Available from: http://www.sciencedirect.com/science/article/pii/S0020729214001040

Hald et al.

Hald K, Noreng HJ, Istre O, Klow NE. Uterine artery embolization versus laparoscopic occlusion of uterine arteries for leiomyomas: long-term results of a randomized comparative trial. J Vasc Interv Radiol. 2009 Oct;20(10):1303-10.

Hald K, Kløw NE, Qvigstad E, Istre O. Laparoscopic occlusion compared with embolization of uterine vessels: a randomized controlled trial. Obstet Gynecol. 2007 Jan;109(1):20-7.

Helal A, Mashaly A, Amer T. Uterine artery occlusion for treatment of symptomatic uterine myomas. J Soc Laparoendosc Surg [Internet]. 2010 Jul [cited 2015 May 28];14(3):386-90. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3041036

Holub Z, Mara M, Eim J. Laparoscopic uterine artery occlusion versus uterine fibroid embolization. Int J Gynaecol Obstet. 2007;96(1):44-5.

HOPEFUL

Hirst A, Dutton S, Wu O, Briggs A, Edwards C, Waldenmaier L, et al. A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study. Health Technol Assess [Internet]. 2008 Mar;12(5):1-248. Available from: http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0006/64671/FullReport-hta12050.pdf

Dutton S, Hirst A, McPherson K, Nicholson T, Maresh M. A UK multicentre retrospective cohort study comparing hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids (HOPEFUL study): main results on medium-term safety and efficacy. BJOG. 2007 Nov;114(11):1340-51.

Ikink ME, Nijenhuis RJ, Verkooijen HM, Voogt MJ, Reuwer PJ, Smeets AJ, et al. Volumetric MR-guided high-intensity focused ultrasound versus uterine artery embolisation for treatment of symptomatic uterine fibroids: comparison of symptom improvement and reintervention rates. Eur Radiol. 2014 Oct;24(10):2649-57.

Iverson RE Jr, Chelmow D, Strohbehn K, Waldman L, Evantash EG. Relative morbidity of abdominal hysterectomy and myomectomy for management of uterine leiomyomas. Obstet Gynecol. 1996 Sep;88(3):415-9.

Manyonda IT, Bratby M, Horst JS, Banu N, Gorti M, Belli AM. Uterine artery embolization versus myomectomy: impact on quality of life--results of the FUME (Fibroids of the Uterus: Myomectomy versus Embolization) Trial. Cardiovasc Intervent Radiol. 2012 Jun;35(3):530-6.

Mara M, Kubinova K, Maskova J, Horak P, Belsan T, Kuzel D. Uterine artery embolization versus laparoscopic uterine artery occlusion: the outcomes of a prospective, nonrandomized clinical trial. Cardiovasc Intervent Radiol. 2012 Oct;35(5):1041-52.

Mara et al.

Mara M, Maskova J, Fucikova Z, Kuzel D, Belsan T, Sosna O. Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. Cardiovasc Intervent Radiol [Internet]. 2008 Jan [cited 2015 May 28];31(1):73-85. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2700241

Mara M, Fucikova Z, Maskova J, Kuzel D, Haakova L. Uterine fibroid embolization versus myomectomy in women wishing to preserve fertility: preliminary results of a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2006 Jun 1;126(2):226-33.

Narayan A, Lee AS, Kuo GP, Powe N, Kim HS. Uterine artery embolization versus abdominal myomectomy: a long-term clinical outcome comparison. J Vasc Interv Radiol [Internet]. 2010 Jul [cited 2015 May 28];21(7):1011-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2900435

Odejinmi F, Maclaran K, Agarwal N. Laparoscopic treatment of uterine fibroids: a comparison of peri-operative outcomes in laparoscopic hysterectomy and myomectomy. Arch Gynecol Obstet. 2015 Mar;291(3):579-84.

Pinto I, Chimeno P, Romo A, Paul L, Haya J, de la Cal MA, et al. Uterine fibroids: uterine artery embolization versus abdominal hysterectomy for treatment--a prospective, randomized, and controlled clinical trial. Radiology [Internet]. 2003 Feb [cited 2015 May 28];226(2):425-31. Available from: http://pubs.rsna.org/doi/pdf/10.1148/radiol.2262011716

Razavi MK, Hwang G, Jahed A, Modanlou S, Chen B. Abdominal myomectomy versus uterine fibroid embolization in the treatment of symptomatic uterine leiomyomas. AJR Am J Roentgenol [Internet]. 2003 Jun [cited 2015 May 28];180(6):1571-5. Available from: http://www.ajronline.org/doi/pdf/10.2214/ajr.180.6.1801571

Ruuskanen A, Hippelainen M, Sipola P, Manninen H. Uterine artery embolisation versus hysterectomy for leiomyomas: primary and 2-year follow-up results of a randomised prospective clinical trial. Eur Radiol. 2010 Oct;20(10):2524-32.

Sawin SW, Pilevsky ND, Berlin JA, Barnhart KT. Comparability of perioperative morbidity between abdominal myomectomy and hysterectomy for women with uterine leiomyomas. Am J Obstet Gynecol. 2000 Dec;183(6):1448-55.

Siskin GP, Shlansky-Goldberg RD, Goodwin SC, Sterling K, Lipman JC, Nosher JL, et al. A prospective multicenter comparative study between myomectomy and uterine artery embolization with polyvinyl alcohol microspheres: long-term clinical outcomes in patients with symptomatic uterine fibroids. J Vasc Interv Radiol. 2006 Aug;17(8):1287-95.

Spies JB, Bradley LD, Guido R, Maxwell GL, Levine BA, Coyne K. Outcomes from leiomyoma therapies: comparison with normal controls. Obstet Gynecol. 2010 Sep;116(3):641-52.

Spies JB, Cooper JM, Worthington-Kirsch R, Lipman JC, Mills BB, Benenati JF. Outcome of uterine embolization and hysterectomy for leiomyomas: results of a multicenter study. Am J Obstet Gynecol. 2004;191(1):22-31.

CLINICAL REVIEW

Study Characteristics

This systematic review identified 25 unique clinical studies (reported in 34 publications) assessing the treatment effects of various uterine-preserving interventions in women with symptomatic uterine fibroids. These interventions were either compared with the conventional surgical intervention (hysterectomy), or with other less invasive interventions. The interventions included in this review are: myomectomy, uterine artery embolization (UAE), uterine artery occlusion (UAO), magnetic resonance-guided focused ultrasound (MRgFU), and radiofrequency volumetric thermal ablation (RFVTA). The following comparisons were identified from the literature:

- UAE versus hysterectomy versus myomectomy: one non-RCT[17]
- Myomectomy versus hysterectomy: three non-RCTs[18-20]
- UAE versus hysterectomy: three RCTs[21-23] and three non-RCTs[24-26]
- UAE versus myomectomy: seven studies[27-33]
- UAE versus UAO: four RCTs[34-37] and two non-RCTs[38,39]
- UAE versus MRgFU: one non-RCT[40]
- Myomectomy versus RFVTA: one RCT[41]

Individual clinical study details are presented in tables in Appendix 6: Clinical Evidence – Study Characteristics (study characteristics) and Appendix 7: Clinical Evidence – Study Results (study results).

UAE versus hysterectomy versus myomectomy

In one American study,[17] the clinical effect of UAE, hysterectomy and myomectomy on health-related quality of life was compared to each other as well as with normal control (no history of uterine fibroid but had regular menstrual cycles). Results from this study (UAE versus hysterectomy; myomectomy versus hysterectomy; UAE versus myomectomy) are presented under the respective comparisons.

Myomectomy versus Hysterectomy

The four non-RCTs included one prospective cohort study[17] and three retrospective cohort studies,[18-20] with the span of publication dates ranging from 1996 to 2015. Three were conducted in the United States[17,19,20] and one in the United Kingdom.[18] The number of study participants ranged from 167 to 400 across the studies. Patient baseline characteristics varied between the comparison groups. Compared with women in the myomectomy group, those in the hysterectomy group were older, had larger uterus size, complained about abnormal uterine bleeding more often and had more previous pregnancies. In the prospective study, different types of hysterectomy and myomectomy were performed abdominally or vaginally via open surgery or endoscopy. Hysterectomy and myomectomy were performed abdominally in the retrospective studies. The key outcome measures were health-related quality of life in the prospective study, and perioperative complications in the three retrospective studies.

UAE versus Hysterectomy

The seven studies included in this category were conducted in Europe[21-25] and the United States.[17,26] The number of study participants ranged from 40 to 1108 across the studies. Two of them reported long-term outcomes: the EMMY study[22] presented data up to five years after the

primary intervention, while patients in the HOPEFUL study[25] were followed over five years. Over 1,000 patients were recruited in the HOPEFUL study; however, subgroup analysis was not conducted due to the insufficient power in the small subgroups if data were analyzed separately. Various routes of access were used in hysterectomy, but the majority of this surgery was performed abdominally. In the RCTs,[21-23] patients' baseline characteristics were comparable between treatment groups with respect to age, fibroid size, presenting symptoms and pervious fibroid therapy. Intramural fibroids were commonly presented in both groups. In the non-RCTs (three prospective studies[17,24,26] and one retrospective study[25]), patients in the two treatment groups had similar age and uterus/fibroid size, but the hysterectomy patients had higher previous pregnancy rate than the UAE patients. Improvement in fibroid-related symptoms and change in health-related quality of life were the main outcome measures in these studies.

UAE versus Myomectomy

Of the eight studies identified for this comparison, two were RCTs[27,28] and six were prospective[17,30,31] or retrospective[29,32,33] cohort studies. They were conducted in Europe[27,28] or the United States.[17,29-33] The number of study participants ranged from 81 to 375 across the studies. Myomectomy was performed via different routes. Patients' baseline characteristics were generally imbalanced between the two treatment groups. Women who had UAE tended to be older,[17,29-33] had larger uteri,[17,30,31] and abnormal uterine bleeding was usually the main complaint in this group.[27,29-32] Patients who had myomectomy were more likely to report pelvic pressure symptoms.[31-33] Improvement in fibroid-related symptoms and change in health-related quality of life were the main outcome measures in these studies.

UAE versus UAO

Six studies (four RCTs[34-37] and two prospective cohort studies[38,39]) were included for this comparison. They were conducted in Egypt,[34] India,[35] the United States[36] and Europe.[37] Three RCTs[35-37] enrolled a smaller number of participants, ranging from 14 to 58. Comparisons of patient baseline characteristics between UAE and UAO were inconclusive due to the small patient population. In one study enrolling 200 participants,[38] patients treated with UAE had larger fibroid size than those treated with UAO at baseline. Improvement in menstrual blood loss and post-procedural complications were the main outcome measures in these studies.

UAE versus MRgFU

In one prospective cohort study,[40] the effect of UAE on fibroid-related symptom relief was compared with MRgFU in 119 Dutch women with symptomatic fibroids. Patients treated with MRgFU were older, had larger fibroids, and were more likely to complain about bulky symptoms such as pelvic pain, while heavy uterine bleeding was more common in the UAE group.

Myomectomy versus RFVTA

One RCT[41] evaluated the treatment effect of myomectomy relative to radiofrequency volumetric thermal ablation on fibroid-related symptom relief and procedure-related complications in 50 German patients. Both myomectomy and RFVTA were performed via laparoscopy. Compared to the myomectomy group, patients in the RFVTA group were older and had more complaint about heavy menstrual bleeding but less pelvic discomfort/pain. Intramural and subserosal fibroids accounted for over 95% of the total number of treated fibroids.

No evidence was found on the treatment effect of myolysis or uterine artery ligation, which were identified as interventions of interest in the research protocol.

Critical Appraisal of Individual Studies

The objectives of the included studies were clearly described in all studies. Conflict of interest and funding source were declared in the majority of the studies.[17,18,21,22,24-28,30,31,33,36,38,40,41] A description of the investigating interventions was provided in all studies.

Of the 25 clinical studies, 15 were non-RCTs.[17-20,24-26,29-33,38-40] Patients in each treatment group were recruited over the same period of time in six studies.[24,30-33,38] It was unclear whether the patients were recruited over the same period of time in seven studies.[17-19,26,29,39,40] In two studies, participants were enrolled at different period of time.[20,25] If patients are not enrolled and treated over similar time periods in each group, it is possible that any differences seen are due to other changes between time period (e.g. changes in standard of care, hospital practices, etc.) and not necessarily wholly due to the intervention itself. The treatment plan in these studies was developed according to the patient's health status, severity of disease, reproductive history, standard of care in the specific study site, or patient preference. In general, patient baseline characteristics (such as age, parity, size/number/location of the fibroids, severity of symptom and previous fibroid management) in these non-RCTs were not comparable between the comparison groups. For instance when comparing myomectomy with hysterectomy, women in the myomectomy group tended to be younger and had fewer previous pregnancies; however, patients who had hysterectomy were older, had larger uterine fibroids, and menorrhagia was more common in this group. The interpretation of the study findings is challenging when patient baseline characteristics are imbalanced between treatment groups, because the treatment decisions were influenced by a variety of factors such as participant's clinical characteristics, desire for future pregnancy, preference, availability of a certain intervention, or the clinician's experience. For instance, women with larger fibroids may suffer from more severe symptoms and requests more aggressive treatment (such as hysterectomy), and subsequently report better quality of life after the intervention; while women with smaller fibroids may prefer myomectomy to preserve the uterus, however the regrowth of the fibroids can lead to further treatment in the future and negatively affect their quality of life. In addition, while the inclusion of a control group may increase the strength of the conclusions, these observational studies suffer from a risk of bias due to uncontrolled confounders. Even though some non-RCTs indicated that potential confounders had been identified a priori and appropriate statistical methods were employed to adjust for the confounding effects, it is unclear whether all the relevant confounders have been recognized. It is challenging to draw conclusions based on these imbalanced baseline characteristics and uncertainty.

Many of the included studies recruited a small number of patients. A description of the sample size calculation or power calculation was often absent from the published reports, especially for non-randomized studies. Therefore it is questionable whether these studies have sufficient power to detect clinically and statistically meaningful differences (if they exist) between the treatment groups.

All but two[36,41] of the included RCTs were open-label due to the nature of the procedures. This could have an impact on patient-reported outcomes such as health-related quality of life, change in symptoms, or treatment-related adverse events. Randomization was carried out using computer-generated random number in most of the RCTs, except for three studies comparing UAE with UAO or hysterectomy,[21,34,36] where sealed envelopes were used in treatment

assignment but no further details were provided to determine the appropriateness of the randomization process. Loss of follow-up was reported in most studies, except for one RCT[35] and three non-RCTs.[18,26,32] This was unlikely to be a concern because of the low rate (< 5%), except for one RCT enrolling 14 patients in which four were lost-to-follow-up.[36] Methods of missing data imputation were described in two studies.[25,29]

With respect to the external validity of the clinical evidence, some studies were published in 1990s, when the technologies, equipment and practice patterns were likely different from the current practice.[1] In addition, due to the inadequate reporting of the patient and disease characteristics, it was often not clear whether the populations studied reflected the larger populations from which they were drawn and to whom study results are intended to apply.

A summary of the strengths and limitations of the individual studies is presented in Appendix 5: Clinical Evidence – Critical Appraisal of Studies.

Data Analyses and Synthesis

Findings from the individual studies are presented in Appendix 6: Clinical Evidence – Study Characteristics and Appendix 7: Clinical Evidence – Study Results. Meta-analyses and subgroup analyses were not possible due to the variability in study characteristics, such as the instruments used for symptom assessment, and outcome measures with diverse definitions.

Myomectomy versus hysterectomy

Change in symptoms / Health-related quality of life
One non-RCT[17] reported changes in symptom severity and health-related quality of life. The results suggested that one year after the procedure, compared to myomectomy, patients treated with hysterectomy reported statistically significant improvement in the Symptom severity subscale and HRQL total subscale of the UFS-QOL ($P < 0.01$).

Complications
Four studies reported on this outcome.[17-20] Conflicting results were found across the trials for blood loss: in one study published in 2005,[18] hysterectomy via laparoscopy was associated with significantly less blood loss during the procedure than myomectomy via laparoscopy (215.1 mL vs. 316.2 mL, $P < 0.0001$), however in another study published in 2000,[19] it was related to statistically significantly more blood loss than myomectomy (483.6 mL vs. 226.7 mL, $P = 0.00001$).

Length of hospital stay
Three studies reported on this outcome.[17-19] Inconsistent results were reported: hysterectomy was related to shorter hospital stay than myomectomy in two studies (1.81 days vs. 2.12 days in a 2015 study, $P=0.0003$; 1.9 days vs. 2.1 days in a 2010 study, P value was not reported),[17,18] but related to longer hospital stay in the third (4.42 days vs. 3.96 days in a 2000 study, $P=0.048$).[19]

UAE versus hysterectomy

Change in symptoms
Six studies reported on this outcome.[17,21,23,25,26,42] Findings from one RCT with 6-month data suggested that cessation of bleeding occurred in 86% of the patients (cessation of menorrhagia

and metrorrhagia in 56%, reduction in menorrhagia and/or metrorrhagia in 14% and amenorrhea in 17%) in the UAE group.[23] Two other RCTs[21,43] indicated that two years after UAE, approximately two thirds of the patients (62% to 67%) reported substantial improvement in menorrhagia. There was no information provided for the scales that were used in bleeding assessment. Five years after UAE, 76% of the women who had an intact uterus were no longer experiencing menorrhagia. Data from non-RCT[26] up to one year post-procedure supported the results from RCTs, showing similar improvement in bleeding in women underwent UAE. In addition, UAE and hysterectomy both eased pelvic pressure. The between-group difference was statistically significant in one RCT[21] ($P = 0.029$. At baseline, 74% of the UAE patients reported pelvic pressure symptoms and 95% of them reported symptom relief at year-2 follow up, compared with 87% of the hysterectomy patients reporting pelvic symptom at baseline but 69% of them reporting symptom relief at year-2 follow-up), but not in another[42] ($P = 0.71$. Similar percentages of patients reported pelvic symptoms at baseline between treatment groups).

Health-related quality of life

Three studies reported on this outcome.[17,26,42] Various instruments were used to examine patients' general health status and disease-specific quality of life. Two-year and five-year data in the EMMY study[22,44] indicated that there were no statistically significant differences between UAE and hysterectomy in improving quality of life outcomes measured by generic questionnaires such as *SF-36*, *HUI-3*, *EuroQol-5D* and disease-specific instruments such as the *Defecation Distress Inventory (DDI)* and *Incontinence Impact Questionnaire (IIQ)*, although these scores were improved significantly from baseline in both groups ($P < 0.05$), except for the DDI score, in that the improvement from baseline was only observed in patients underwent UAE, but not in those underwent hysterectomy. Data from one non-RCT[17] suggested that treatment with hysterectomy was associated with significantly greater improvement in the HRQOL total score in UFS-QOL.

Complications

Six studies reported on this outcome.[17,21,23,25,26,42] The risk of peri-operative complication was lower in the UAE group, where patients had statistically and clinically significantly less blood loss (436.1 mL with hysterectomy vs. 30.9 mL with UAE) and reported less severe pain compared to those in the hysterectomy group.

Re-intervention

Six studies reported on this outcome.[17,21,23-25,42] There was no statistically significant difference in the need for further interventions between the two groups, according to the data up to five years.

Patient satisfaction

Six studies reported on this outcome.[21,23-26,42] Findings from RCTs and non-RCTs suggested that the vast majority of the patients satisfied with the treatment they were assigned. The between-group differences were statistically significant in some studies.

Length of hospital stay

Five studies reported on this outcome.[17,23,24,26,42] Treatment with UAE was related to shorter hospital stay compared to hysterectomy ($P < 0.001$ was reported in one RCT and one non-RCT; *P*-values were not reported in the other studies).

UAE versus myomectomy

Change in symptoms

Seven studies reported on this outcome.[27-33] Symptom relief from baseline was observed in both UAE and myomectomy groups one year after the procedure. Statistically significant between-group differences in improving symptoms of bleeding (favoring UAE) and pelvic pressure (favoring myomectomy) were reported in one non-RCT, when patients were followed approximately 14 months after the primary procedure.[32] Improvement in fibroid-related symptoms from baseline was also observed in both treatment groups in the other six studies; however the between-group differences were either not statistically significant, or a P-value for the statistical comparison was not reported.

Health-related quality of life

Four studies reported on this outcome.[17,27,30,31] Patients' quality of life improved significantly from baseline in both groups. At the end of the studies (up to one year follow up), a statistically significant difference was not detected between UAE and myomectomy, except that in one non-RCT, more patients in the UAE group showed at least a 5-point increase in the UFQoL questionnaire (a 5-point increase was considered clinically meaningful in this study).[31]

Complications

Seven studies reported on this outcome.[17,27-32] Higher risks of procedure-related complications were observed in patients in the myomectomy group compared with those in the UAE group. Common procedure-related complications included injury of organs in the abdominal cavity, unplanned conversion from laparoscopic myomectomy to open surgery, infection, excessive pain, blood loss, or transfusion. The between-group difference was considered statistically significant in some studies,[29-32] but not all.

Reproductive outcomes

Three studies reported on this outcome.[28,30,31] The Mara 2008 study[28] enrolled patients who planned pregnancy. In this study, among the patients who tried to conceive, those in the myomectomy group had higher pregnancy rate and higher delivery rate, compared to the UAE group. No pregnancy was observed at year-1 follow up in one non-RCT,[30] and two unplanned pregnancies were reported in the UAE group at year-2 follow up in another study.[31]

Length of hospital stay

Seven studies reported on this outcome.[17,27-32] Patients in the UAE group had significantly shorter hospital stay compared to the myomectomy group, a statistically significan (< 0.05) *P*-value was reported in five of these studies.[27-30,32]

UAE versus UAO

Change in symptoms

Five studies reported on this outcome.[34-38] Reduction in abnormal uterine bleeding or reduction in pelvic pressure was observed between three months to one year after the procedure in both groups. There were no statistically significant differences found between UAE and UAO.

Complications

Four studies reported on this outcome.[35-38] Post-procedural pain was inconsistently reported in three studies with the number of patients ranging from 14 to 58; therefore no conclusion can be drawn with respect to the pain outcome. In one non-RCT, treatment with UAE was related to

significantly higher complication rates than treatment with UAO. The complications observed in the UAE group included fever, spasm of uterine artery, sloughing of myoma, hematoma of the procedure site, deep venous thrombosis, allergic reaction, decreased ovarian reserve and decreased libido.

Reproductive outcomes

Two studies reported on this outcome.[38,39] One non-RCT[38] indicated that no statistically significant difference was detected between UAE and UAO with respect to the number of pregnancies/deliveries, mean gestational week of the newborn, and risk of preterm delivery. Results from another non-RCT[39] showed that the UAE group was associated with more abortions and more Caesarean-sections compared with the UAO group.

Re-intervention

Two studies reported on this outcome.[37,38] The risk of re-intervention was similar between UAE and UAO in one study,[37] but significantly higher in the UAE group in another[38])39% in the UAE group versus 15% in the UAO group, *P* = 0.001).

Length of hospital stay

Four studies reported on this outcome.[35-38] Most of the studies reported equivalent length of hospital stay between UAO and UAE, except that in one RCT,[37] the average length of hospital stay was 57 hours for patients treated with UAE comparing to 46 hours for patients in the UAO group (*P* = 0.001).

UAE versus MRgFU (one study[40])

Change in symptoms

Patients in the UAE group reported significantly greater improvement in symptom severity score in the UFS-QOL three months after the procedure, compared with those in the MRgFU group (*P* < 0.001).

Health-related quality of life

Patients in the UAE group had a greater improvement in quality of life (measured by the HRQOL total score in the UFS-QOL) three months after the procedure, compared with those in the MRgFU group (*P* < 0.001).

Complications

There were no adverse events reported in the MRgFU group, while 13 adverse events were reported in the UAE group: two endometritis, two premature ovarian failure and related amenorrhea, one infected hematoma at the procedure site, one vulvar abscess due to non-target embolization and seven painful spontaneous expulsion of the treated uterine fibroid 6 to 12 weeks after UAE.

Re-interventions

The risk of requiring re-intervention one year after the primary procedure was higher in patients treated with MRgFU, compared with those treated with UAE (35% vs. 4.5%, *P* = 0.002). Reasons for the re-interventions were not specified.

Myomectomy versus RFVTA (one study[41])

Change in symptoms
Patients in the myomectomy group reported a greater reduction in bleeding compared with RFVTA one year after the treatment, but the between-group difference was not statistically significant. Meanwhile, there was no statistically significant difference in improvement in pelvic pressure between the two groups.

Health-related quality of life
There was no statistically significant difference in EQ-5D score between the two treatment groups.

Complications
Patients in the myomectomy group had greater blood loss during the procedure compared with those in the RFVTA group (51 mL vs. 16 mL, $P < 0.001$). It was unclear whether the between-group difference was clinically important given the small volume of blood.

Re-intervention
Patients in the myomectomy group did not require further interventions, while three additional interventions were required in the RFVTA group: two hysterectomies (one patient had hypermenorrhea shortly after the ablation, and hysterectomy was eventually performed to treat the uterine perforation resulting from dilation and curettage for hypermenorrhea; the second hysterectomy was performed due to a suspension of smooth muscle tumor of uncertain malignant potential from biopsy) and one myomectomy according to patient's preference (asymptomatic but had a desire of pregnancy).

Patient satisfaction
More patients in the myomectomy group reported being "very satisfied" than those in the RFVTA group (86.5% vs. 42.9%, P=0.004).
Length of hospital stay
The length of hospital stay was significantly longer in the myomectomy group than the RFVTA group (29.9 hours vs. 10.0 hours respectively, $P < 0.001$).

ECONOMIC REVIEW

Study Characteristics

Data from seven unique economic evaluations presented in eight publications were identified for inclusion.[2,45-51]

All economic evaluations were cost-utility analyses. Four evaluations were performed in the United States with an American societal perspective,[2,46,47,51] two in the United Kingdom from a public payer perspective,[48-50] and one evaluation was performed in Canada with an Ontario public payer perspective.[45] The studies examined the cost-effectiveness of UAE,[2,45-51] MRgFU,[2,45-47,49] myomectomy,[2,45,46,49] hysterectomy,[2,45,47-51] and pain management with pharmacotherapy[2] for the treatment of symptomatic uterine fibroids in premenopausal women. The majority of economic models had an 11 year time horizon ending at assumed age of menopause (51 or 55),[45,47,48,50,51] though the range of included time horizons was five years[46] to a lifetime horizon.[2]

Model inputs included patient eligibility for each treatment modality, probabilities of symptom relief and recurrence, probability of complications, and intervention costs. Of the majority of

economic evaluations that included patient eligibility for each procedure in the model, eligibility was set at 100% for hysterectomy and myomectomy, 90% for UAE, and 35% for MRgFU.[2,45-47] These probability estimates were mainly taken from reports in the clinical literature. One evaluation conducted in the UK that lacked data from the literature regarding the distribution of patients to various first-line treatments assumed for the base case that 25% received UAE, 25% received myomectomy, and 50% received hysterectomy.[49] Cost inputs for the economic models included physician and other staff costs,[2,45,47-51] direct medical costs including hospital services,[2,45-51] laboratory and/or screening costs,[2,45-47] productivity costs,[2,46-48,50,51] and costs related to equipment maintenance and operation.[2,45,49]

In general, patients with symptom recurrence would be re-treated with the same intervention,[2,45,47] while patients who experienced treatment failure would proceed to treatment with a more invasive modality.[2,45-47,49,51] The number of rounds of re-treatment specified in the models were variable. In the Canadian study, patients received up to three rounds of treatment for symptom recurrence or treatment failure, and third-line treatment was always hysterectomy.[45] However, in other evaluations, patients were treated until symptoms resolved or they reached menopause.[2,47] Complete symptom resolution was assumed after hysterectomy,[47,48,50,51] and symptom recurrence was assumed not to occur after menopause.[2,45]

Critical Appraisal of Individual Studies

In general, the authors of the economic evaluations used valid and well reported methods to conduct their analyses. All studies clearly presented their research questions, choice of economic evaluation and perspective, interventions and alternatives, as well as primary outcomes.[2,45-49,51] All evaluations stated their sources for model parameter estimates; however, several did not provide details of the study characteristics and results (when the estimates were derived from a single study)[2,11,46,47,51] or methods of synthesizing results from multiple studies to produce a single model parameter estimate.[2,11,47,50] All studies used QALYs to value benefits, but the details of patients from whom utilities were collected were not always clearly described.[2,47,49,51] For studies that assessed costs associated with lost productivity,[2,46-48,50,51] all but one[51] reported these costs separately from other results. Methods for the estimation of costs were generally described, but only one evaluation clearly reported the quantities of resource use separate from unit costs.[45]

All studies provided details of the model used for the analysis, and overall, the key parameters supporting these models were reasonable. Two studies did not include myomectomy as a first-line treatment option for uterine fibroids, though the authors acknowledged that myomectomy was a surgical alternative to hysterectomy, and it was a treatment option for UAE failure in the model.[47,48,50] All economic evaluations stated the time horizons and discount rates applied in the analyses, but the time horizon was limited to five years in one study.[46] All other evaluations had a time horizon of at least 11 years, and given that premenopausal patients, especially younger patients, may experience symptom recurrence beyond five years from initial treatment, this model may have missed relevant long-term health care costs. The authors discussed this limitation of their model but justified their choice by commenting that at the time of publication there were no clinical data beyond five years of follow-up.

One publication provided distribution details for the economic model parameters.[46] Most studies used appropriate approaches for the sensitivity analyses; however, sensitivity analyses were not performed for parameter estimates derived from a single study in one economic evaluation,[47] or for a number of relevant variables without explanation in another.[48,50] Incremental analysis was

also inconsistently reported for this latter study.[48,50] Overall, results and conclusions of the economic analyses were presented clearly and with relevant caveats.

Strengths and limitations of the included economic evaluations are provided in Appendix 10: Economic Evidence – Critical Appraisal of Studies.

Results

The majority of included economic evaluations indicated that MRgFU is the most cost-effective option for the treatment of symptomatic uterine fibroids in the evaluated base case[2,47,49] or in certain scenarios.[45,46] Two economic evaluations conducted from an American societal perspective at a decision threshold of $50,000/QALY showed that MRgFU was more cost-effective than UAE and hysterectomy,[47] or UAE, hysterectomy, and myomectomy.[2] MRgFU was also dominant compared with UAE, myomectomy, and hysterectomy in one economic evaluation from a UK public payer perspective.[49] MRgFU remained the dominant strategy in several scenario analyses that adjusted the distribution of patients to each treatment modality, recurrence rates, utilities, complication rates, and hospital costs. Another economic evaluation indicated that, from an American societal perspective and a willingness-to-pay of $50,000/QALY, MRgFU was more cost-effective than myomectomy when productivity costs were considered, and more cost-effective than UAE in either scenario.[46]
However, the Canadian economic evaluation[45] demonstrated that MRgFU was only more cost-effective than UAE in a scenario analysis when all patients were assumed to be eligible for MRgFU. For the base case when patient eligibility for MRgFU was set at 35%, UAE was more cost-effective than MRgFU, hysterectomy, and myomectomy at a willingness-to-pay of $46,480/QALY or greater. MRgFU and myomectomy were dominated by the other treatment strategies in the base case, and therefore would not be considered cost-effective at any decision threshold. A 35% eligibility rate for MRgFU in the base case was based on estimates derived from the clinical literature and was a common value to all economic models that evaluated this parameter; therefore, this is likely the more realistic scenario than assuming 100% eligibility for MRgFU and suggests that it would not be cost-effective in current clinical practice in Canada. Probabilistic sensitivity analyses demonstrated that UAE was most often the most cost-effective option compared with hysterectomy, MRgFU, and myomectomy, at a willingness-to-pay threshold of at least $46,000/QALY; MRgFU was the most cost-effective option in 20% of cases when willingness-to-pay was $50,000/QALY.

Of the economic evaluations that did not include MRgFU in the analysis, UAE was more cost-effective than hysterectomy for the treatment of symptomatic uterine fibroids from an American societal perspective[51] and a UK public payer perspective.[48,50] The UK study noted that UAE is only more cost-effective than hysterectomy within the first year of treatment, as UAE incurred additional procedure costs and fewer QALYs over time than hysterectomy.[48]

Three of the economic evaluations examining focused ultrasound were sponsored by the manufacturers.[2,49,52]

Details of the economic evaluations are presented in the tables in Appendix 8**: Economic Evidence – Study Characteristics** and Appendix 9: Economic Evidence – Study Results.

DISCUSSION

Summary of Evidence

Twenty-five randomized or non-randomized controlled studies in women with symptomatic uterine fibroids met the inclusion criteria of this review. The uterine-preserving interventions examined in these studies were: myomectomy, UAE, UAO, MRgFU and RFVTA. They were either compared with the conventional treatment for symptomatic uterine fibroids (hysterectomy), or compared with another minimally-invasive intervention. UAE was investigated in 21 studies (versus hysterectomy in six studies, versus myomectomy in seven studies, versus UAO in six studies, versus MRgFU in one study, and versus hysterectomy/myomectomy in one study), myomectomy in 12 studies (versus hysterectomy in three studies, versus UAE in seven studies, versus RFVTA in one study, and versus hysterectomy/UAE in one study), UAO in six studies (all versus UAE), MRgFU (versus UAE) in one study, and RFVTA (versus myomectomy) in one study.

In general, small sample sizes in most of the studies limited the quality of the evidence. Interpretation of study results was challenging due to the imbalanced patient baseline characteristics between treatment groups, particularly in non-randomized controlled trials, as well as the insufficient power of the study to detect meaningful differences in study outcomes. Meta-analysis of the outcome measures was not performed due to the heterogeneity of data reporting.

In summary:

- UAE reduced abnormal uterine bleeding (superior to myomectomy), improved bulk symptoms such as pelvic pain and pressure, improved patient's quality of life, was associated with a lower risk of peri-procedural complications such as blood loss (compared with hysterectomy and myomectomy), resulted in shorter hospital stay (compared with hysterectomy and myomectomy) and higher patient satisfaction (compared with hysterectomy and myomectomy). However, UAE was associated with a higher risk of re-intervention (than UAO).
- Myomectomy was associated with improved symptoms from pelvic pressure, reduced menorrhagia, improved quality of life, and was associated with higher pregnancy rate (data were from a study comparing myomectomy and UAE, although UAE was not recommended for women who desire future pregnancy).
- UAO reduced the abnormal uterine bleeding, improved bulk symptoms from pelvic pressure, and was associated with a lower risk of complications (compared with UAE).
- RFVTA improved abnormal uterine bleeding, improved patient's quality of life, was related to a lower risk of complications such as blood loss during the procedure (versus myomectomy) and shorter hospital stay (than myomectomy) however RFVTA was also related to more re-interventions in the future (than myomectomy) due to fibroid recurrence or insufficient symptom control.
- MRgFU was associated with lower risk of overall complications (compared with UAE) but may also be related to higher risk of re-intervention.

Patients undergoing conventional hysterectomy reported better health-related quality of life (both generic and disease-specific, compared with UAE or myomectomy) when symptoms of menorrhagia and pelvic pressure were relieved, but it was accompanied with higher procedure-related complications and longer hospital stay.

When UAE was compared with hysterectomy, patients in the latter group tended to have more severe symptoms prior to the procedure. During the follow-up, hysterectomy was found to be superior to UAE and other less invasive interventions (i.e. myomectomy) in improving patient's quality of life. This is not surprising, since hysterectomy ultimately eliminates fibroid-related symptoms, especially heavy uterine bleeding, and subsequently enhances patient's well-being. Minimally-invasive interventions such as UAE, RFVTA and MRgFU however, were associated with fewer peri-operative and post-operative complications, shorter hospital stay and therefore more patient satisfaction, compared with surgical interventions. On the other hand, they are related to more fibroid recurrence and more re-interventions correspondingly, which will negatively impact economics and patient satisfaction eventually. The included clinical studies generally had short study durations, therefore were not be able to examine the long-term effect of an intervention on patient satisfaction.

Although UAE has been recognized as an alternative to surgery in women who are not desiring future fertility,[5] and this has been reflected in the SOGC practice guidelines,[53] data on reproductive outcomes were available in a few included studies and suggested that women treated with UAE had less favorable outcomes than myomectomy, with respect to the rates of becoming pregnant and delivery. The data were derived from a subgroup of patients who desired to conceive in those studies, therefore should be considered with caution.
Several systematic reviews and meta-analyses have been published in recent years.[52,54-56] The results are generally consistent with the current review. In the systematic review conducted by Panagiotopoulou et al. published in 2013, two RCTs comparing UAE and myomectomy and three RCTs comparing UAE and UAO were included.[52] Results from indirect analysis showed that myomectomy and UAE were related to higher patient satisfaction than UAO. UAE and UAO were also associated with higher re-intervention rate compared with myomectomy. Comparable complication rates were observed among these three interventions. All five trials have been included in the current review. In a Cochrane review published in 2012,[55] seven RCTs (UAE was compared with abdominal hysterectomy in three, UAE was compared with myomectomy in two, and UAE was compared with hysterectomy or myomectomy in two) with 793 patients were included. Results of this review suggested that there were no statistically significant differences in patient satisfaction between UAE and surgery within two years following the procedure. Findings at five year follow-up were also inconclusive. In addition, UAE was associated with more future interventions compared with myomectomy and hysterectomy. Data from a selected subgroup in a small study suggested that myomectomy could be related to better fertility outcomes than UAE. One of the included studies was excluded in our review because patients underwent myomectomy combined with hysterectomy in this study and there were no separate results reported for each surgery. The systematic review conducted by van der Kooij et al. evaluated the treatment effect of UAE versus surgery (myomectomy or hysterectomy) on symptomatic fibroids.[56] Data from four RCTs enrolling 515 patients suggested that UAE was related to less blood loss and shorter hospital stay in the short term. The longer-term data (up to five years after the procedure) indicated comparable health-related quality of life between interventions of interest but higher re-intervention rates were reported in the UAE patients. Three RCTs in this review are also included in our review, but the REST study in the van der Kooij review was excluded because myomectomy and hysterectomy were mixed in one of the treatment arms. One systematic review conducted by Pron et al. investigated the effectiveness of MRgFU with other minimally invasive uterine-preserving interventions and surgeries in patients with uterine fibroids.[54] Two systematic reviews, two RCTs (examining ultrasound-guided focused ultrasound), 45 cohort study reports and 19 case reports were included. Findings from this review suggested that MRgFU reduced fibroid-related symptoms but had high re-treatment rate compared with ablation. There was no RCT evidence for MRgFU identified in

this review. Although there is a lack of comparative data, the authors suggested MRgFU may be a non-invasive alternative to hysterectomy for women who fail medical therapy.

Tissue morcellation - division of solid tissue (such as a tumor) into pieces, which can then be removed – may facilitate a minimally invasive surgical approach and is associated with decreased perioperative risks. However recently, there have been concerns raised with the use of power morcellation during myomectomy or hysterectomy, mainly due to the potential seeding or spreading of undiscovered malignancy in the uterus.[57] We did not identify any relevant evidence on this issue. Guidance from the SOGC recommends that techniques that minimize specimen disruption and intra-abdominal spread should be considered; assessment for potential malignancy should be performed in women presenting with uterine fibroids; uterine morcellation should not be used in women with established or suspected cancer and a total abdominal hysterectomy should be performed instead; and appropriate training and experience are required in morcellation technique.[58]

Limitations

Inconsistent and conflicting results were commonly reported in the included clinical studies with respect to the effectiveness and safety of uterine-preserving interventions. This is partly explained by the small sample size and incomparable patient baseline characteristics. For instance, compared with patients in the myomectomy group, those in the UAE group were older, had more previous pregnancies, had poorer baseline quality of life, with larger fibroid size and more severe symptoms.

In the included studies, clinical outcomes were measured and reported in different manners, and various instruments were adopted in measuring the changes in symptoms before and after treatment. Quantitative synthesis was not performed in this review due to the significant heterogeneity across the studies.

Uterine-preserving interventions can be performed using a variety of methods. For instance, the type of hysterectomy and route of access were not standardized and were often left to the discretion of the attending gynecologist in the studies. Likewise, myomectomy was carried out via the abdominal route using laparoscopy or open (laparotomy) incision, or via the vaginal route using hysteroscopy. Study results were reported for patients receiving any types of surgical interventions. There were no separate results for the aforementioned subgroups of patients. Therefore we are not able to examine the clinical benefits and risks from a specific type of intervention.

Another challenge is the difficulty in comparing approaches that are fibroid location-specific. For example, a submucosal uterine fibroid may be better managed by hysteroscopic myomectomy[1,5] which is a day procedure with minimal recovery or pain versus a large serosal fibroid managed by abdominal or laparoscopic myomectomy.[1] Although both are examples of myomectomy the outcomes can vary significantly.[7] The comparators also vary because a simple intra-uterine fibroid, e.g. 2 cm in diameter, will not likely be managed with UAE so there is no comparison possible here.

Limited evidence was available for long term clinical effectiveness and safety for the uterine-preserving interventions for women with symptomatic uterine fibroids. Evidence on the benefits and risks of myolysis was not identified through the literature search.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Evidence from 25 studies on the clinical effectiveness and safety of uterine-preserving interventions were reviewed for women with symptomatic uterine fibroids. Study findings suggested that:
1) uterine artery embolization was superior to myomectomy in reducing abnormal uterine bleeding, while there were no statistically significant differences between uterine artery embolization and uterine artery occlusion, or between myomectomy and radiofrequency thermal ablation in reducing heavy uterine bleeding. However, myomectomy was more effective in reducing symptoms from pelvic pressure than embolization.

2) Conventional hysterectomy was associated with better health-related quality of life compared with uterine artery embolization and myomectomy; while embolization, radiofrequency thermal ablation and myomectomy seem to have a similar effect on patient's quality of life.

3) Magnetic resonance-guided focused ultrasound and uterine artery occlusion were related to lower risk of overall complications compared to embolization; while embolization and radiofrequency thermal ablation were associated with lower risk of complications than myomectomy.

4) Patients treated with myomectomy had better reproductive outcomes than those treated with embolization.

5) The rate of re-intervention was higher with radiofrequency thermal ablation or magnetic resonance-guided focused ultrasound compared with myomectomy or embolization.

6) Patients treated with embolization were more satisfied with the treatment than those treated with surgical interventions.

7) Embolization or radiofrequency thermal ablation was associated with shorter hospital stay than surgical interventions, while patients with embolization had similar length of hospital stay as those with artery occlusion.

The quality of these studies was low due to the small sample size and study design. Inconsistent results were observed across the included studies. Therefore, results should be interpreted with caution, especially for the outcomes that were only examined in a subgroup of study participants, for example, the reproductive outcomes that were evaluated in patients who wished to conceive.

Evidence from the economic evaluations indicated that focused ultrasound is the most cost-effective option for the treatment of symptomatic uterine fibroids, compared with embolization, hysterectomy and myomectomy. Three of the economic evaluations examining focused ultrasound were sponsored by the manufacturers of the technologies being examined. A Canadian economic evaluation demonstrated that focused ultrasound was only more cost-effective than embolization when all patients were assumed to be eligible for this treatment. When focused ultrasound was not available, embolization was more cost-effective than hysterectomy.

The uterine size, symptom severity, patient preference, fertility desire, and available facilities may influence the selection of appropriate uterine-preserving interventions for symptomatic uterine fibroid(s).

REFERENCES

1. Khan AT, Shehmar M, Gupta JK. Uterine fibroids: current perspectives. Int J Womens Health [Internet]. 2014 [cited 2015 Jul 16];6:95-114. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3914832
2. O'Sullivan AK, Thompson D, Chu P, Lee DW, Stewart EA, Weinstein MC. Cost-effectiveness of magnetic resonance guided focused ultrasound for the treatment of uterine fibroids. Int J Technol Assess Health Care [Internet]. 2009 Jan [cited 2015 Jul 16];25(1):14-25. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2811401
3. Gupta JK, Sinha A, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database Syst Rev. 2012;5:CD005073.
4. American Association of Gynecologic Laparoscopists (AAGL): Advancing Minimally Invasive Gynecology Worldwide. AAGL practice report: practice guidelines for the diagnosis and management of submucous leiomyomas. J Minim Invasive Gynecol. 2012 Mar;19(2):152-71.
5. Vilos GA, Allaire C, Laberge PY, Leyland N, Special C, Vilos AG, et al. The management of uterine leiomyomas. J Obstet Gynaecol Can. 2015 Feb;37(2):157-81.
6. Viswanathan M, Hartmann K, McKoy N, Stuart G, Rankins N, Thieda P, et al. Management of uterine fibroids: an update of the evidence. Evid Rep Technol Assess (Full Rep) [Internet]. 2007 Jul [cited 2015 Jul 16];(154):1-122. Available from: http://archive.ahrq.gov/downloads/pub/evidence/pdf/uterupdate/uterup.pdf
7. Singh SS, Belland L. Contemporary management of uterine fibroids: focus on emerging medical treatments. Curr Med Res Opin. 2015 Jan;31(1):1-12.
8. Lefebvre G, Vilos G, Allaire C, Jeffrey J, Arneja J, Birch C, et al. The management of uterine leiomyomas. J Obstet Gynaecol Can. 2003 May;25(5):396-418.
9. Common Drug Review. Clinical review report: ulipristal acetate (Fibristal) (5 mg tablets) [Internet]. Ottawa: CADTH; 2013 Dec. [cited 2015 Jul 16]. Available from: http://www.cadth.ca/media/cdr/clinical/SR0326_Fibristal_CL_Report_e.pdf
10. Common Drug Review. CDEC final recommendation: ulipristal acetate (Fibristal - Actavis Specialty Pharmaceuticals). Indication: uterine fibroids [Internet]. Ottawa: CADTH; 2013 Nov 15. [cited 2015 Jul 16]. Available from: http://www.cadth.ca/media/cdr/complete/complete_SR0326_Fibristal_19-Nov-13_e.pdf
11. Rabinovici J, David M, Fukunishi H, Morita Y, Gostout BS, Stewart EA, et al. Pregnancy outcome after magnetic resonance-guided focused ultrasound surgery (MRgFUS) for conservative treatment of uterine fibroids. Fertil Steril. 2010 Jan;93(1):199-209.
12. Berman JM, Guido RS, Chudnoff SG. Radiofrequency volumetric thermal ablation of fibroids: analysis of 3-year outcomes. Obstet Gynecol. 2014 May;123 Suppl 1:121S-2S.
13. [Pr]Fibristal™ ulipristal acetate, tablet, 5 mg [product monograph]. Salt Lake City (UT): Watson Laboratories, Inc.; 2013 Jun 19.
14. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health [Internet]. 1998 Jun [cited 2015 Jul 16];52(6):377-84. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf

15. Shemilt I, Mugford M, Byford S, Drummond M, Eisenstein E, Knapp M, et al. Incorporating economics evidence, figure 15.5a: Drummond checklist [Internet]. In: Higgins JP, Green S, editors. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. The Cochrane Collaboration; 2011 Mar. Chapter 15 [cited 2015 Jul 16]. Available from: http://handbook.cochrane.org/chapter_15/figure_15_5_a_drummond_checklist_drummond_1996.htm.

16. Hahn M, Brucker S, Kraemer D, Wallwiener M, Taran FA, Wallwiener CW, et al. Radiofrequency volumetric thermal ablation of fibroids and laparoscopic myomectomy: long-term follow-up from a randomized trial. Geburtshilfe Frauenheilkd [Internet]. 2015 May [cited 2015 Jul 2];75(5):442-9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4461677

17. Spies JB, Bradley LD, Guido R, Maxwell GL, Levine BA, Coyne K. Outcomes from leiomyoma therapies: comparison with normal controls. Obstet Gynecol. 2010 Sep;116(3):641-52.

18. Odejinmi F, Maclaran K, Agarwal N. Laparoscopic treatment of uterine fibroids: a comparison of peri-operative outcomes in laparoscopic hysterectomy and myomectomy. Arch Gynecol Obstet. 2015 Mar;291(3):579-84.

19. Sawin SW, Pilevsky ND, Berlin JA, Barnhart KT. Comparability of perioperative morbidity between abdominal myomectomy and hysterectomy for women with uterine leiomyomas. Am J Obstet Gynecol. 2000 Dec;183(6):1448-55.

20. Iverson RE Jr, Chelmow D, Strohbehn K, Waldman L, Evantash EG. Relative morbidity of abdominal hysterectomy and myomectomy for management of uterine leiomyomas. Obstet Gynecol. 1996 Sep;88(3):415-9.

21. Ruuskanen A, Hippelainen M, Sipola P, Manninen H. Uterine artery embolisation versus hysterectomy for leiomyomas: primary and 2-year follow-up results of a randomised prospective clinical trial. Eur Radiol. 2010 Oct;20(10):2524-32.

22. Hehenkamp WJ, Volkers NA, Birnie E, Reekers JA, Ankum WM. Symptomatic uterine fibroids: treatment with uterine artery embolization or hysterectomy--results from the randomized clinical Embolisation versus Hysterectomy (EMMY) Trial. Radiology [Internet]. 2008 Mar [cited 2015 May 28];246(3):823-32. Available from: http://pubs.rsna.org/doi/pdf/10.1148/radiol.2463070260

23. Pinto I, Chimeno P, Romo A, Paul L, Haya J, de la Cal MA, et al. Uterine fibroids: uterine artery embolization versus abdominal hysterectomy for treatment--a prospective, randomized, and controlled clinical trial. Radiology [Internet]. 2003 Feb [cited 2015 May 28];226(2):425-31. Available from: http://pubs.rsna.org/doi/pdf/10.1148/radiol.2262011716

24. Brochner AC, Mygil B, Elle B, Toft P. Inflammatory response in patients undergoing uterine artery embolization as compared to patients undergoing conventional hysterectomy. Acta Radiol. 2009 Dec;50(10):1193-7.

25. Dutton S, Hirst A, McPherson K, Nicholson T, Maresh M. A UK multicentre retrospective cohort study comparing hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids (HOPEFUL study): main results on medium-term safety and efficacy. BJOG. 2007 Nov;114(11):1340-51.

26. Spies JB, Cooper JM, Worthington-Kirsch R, Lipman JC, Mills BB, Benenati JF. Outcome of uterine embolization and hysterectomy for leiomyomas: results of a multicenter study. Am J Obstet Gynecol. 2004;191(1):22-31.
27. Manyonda IT, Bratby M, Horst JS, Banu N, Gorti M, Belli AM. Uterine artery embolization versus myomectomy: impact on quality of life--results of the FUME (Fibroids of the Uterus: Myomectomy versus Embolization) Trial. Cardiovasc Intervent Radiol. 2012 Jun;35(3):530-6.
28. Mara M, Maskova J, Fucikova Z, Kuzel D, Belsan T, Sosna O. Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. Cardiovasc Intervent Radiol [Internet]. 2008 Jan [cited 2015 May 28];31(1):73-85. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2700241
29. Narayan A, Lee AS, Kuo GP, Powe N, Kim HS. Uterine artery embolization versus abdominal myomectomy: a long-term clinical outcome comparison. J Vasc Interv Radiol [Internet]. 2010 Jul [cited 2015 May 28];21(7):1011-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2900435
30. Goodwin SC, Bradley LD, Lipman JC, Stewart EA, Nosher JL, Sterling KM, et al. Uterine artery embolization versus myomectomy: a multicenter comparative study. Fertil Steril. 2006 Jan;85(1):14-21.
31. Siskin GP, Shlansky-Goldberg RD, Goodwin SC, Sterling K, Lipman JC, Nosher JL, et al. A prospective multicenter comparative study between myomectomy and uterine artery embolization with polyvinyl alcohol microspheres: long-term clinical outcomes in patients with symptomatic uterine fibroids. J Vasc Interv Radiol. 2006 Aug;17(8):1287-95.
32. Razavi MK, Hwang G, Jahed A, Modanlou S, Chen B. Abdominal myomectomy versus uterine fibroid embolization in the treatment of symptomatic uterine leiomyomas. AJR Am J Roentgenol [Internet]. 2003 Jun [cited 2015 May 28];180(6):1571-5. Available from: http://www.ajronline.org/doi/pdf/10.2214/ajr.180.6.1801571
33. Broder MS, Goodwin S, Chen G, Tang LJ, Costantino MM, Nguyen MH, et al. Comparison of long-term outcomes of myomectomy and uterine artery embolization. Obstet Gynecol. 2002 Nov;100(5 Pt 1):864-8.
34. Helal A, Mashaly A, Amer T. Uterine artery occlusion for treatment of symptomatic uterine myomas. J Soc Laparoendosc Surg [Internet]. 2010 Jul [cited 2015 May 28];14(3):386-90. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3041036
35. Ambat S, Mittal S, Srivastava DN, Misra R, Dadhwal V, Ghosh B. Uterine artery embolization versus laparoscopic occlusion of uterine vessels for management of symptomatic uterine fibroids. Int J Gynaecol Obstet. 2009 May;105(2):162-5.
36. Cunningham E, Barreda L, Ngo M, Terasaki K, Munro MG. Uterine artery embolization versus occlusion for uterine leiomyomas: a pilot randomized clinical trial. J Minim Invasive Gynecol. 2008 May;15(3):301-7.
37. Hald K, Kløw NE, Qvigstad E, Istre O. Laparoscopic occlusion compared with embolization of uterine vessels: a randomized controlled trial. Obstet Gynecol. 2007 Jan;109(1):20-7.
38. Mara M, Kubinova K, Maskova J, Horak P, Belsan T, Kuzel D. Uterine artery embolization versus laparoscopic uterine artery occlusion: the outcomes of a

prospective, nonrandomized clinical trial. Cardiovasc Intervent Radiol. 2012 Oct;35(5):1041-52.

39. Holub Z, Mara M, Eim J. Laparoscopic uterine artery occlusion versus uterine fibroid embolization. Int J Gynaecol Obstet. 2007;96(1):44-5.

40. Ikink ME, Nijenhuis RJ, Verkooijen HM, Voogt MJ, Reuwer PJ, Smeets AJ, et al. Volumetric MR-guided high-intensity focused ultrasound versus uterine artery embolisation for treatment of symptomatic uterine fibroids: comparison of symptom improvement and reintervention rates. Eur Radiol. 2014 Oct;24(10):2649-57.

41. Brucker SY, Hahn M, Kraemer D, Taran FA, Isaacson KB, Kramer B. Laparoscopic radiofrequency volumetric thermal ablation of fibroids versus laparoscopic myomectomy. Int J Gynaecol Obstet [Internet]. 2014 Jun [cited 2015 May 28];125(3):261-5. Available from: http://www.sciencedirect.com/science/article/pii/S0020729214001040

42. Hehenkamp WJ, Volkers NA, Donderwinkel PF, de Blok S, Birnie E, Ankum WM, et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): peri- and postprocedural results from a randomized controlled trial. Am J Obstet Gynecol. 2005 Nov;193(5):1618-29.

43. Volkers NA, Hehenkamp WJ, Birnie E, Ankum WM, Reekers JA. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2 years' outcome from the randomized EMMY trial. Am J Obstet Gynecol. 2007 Jun;196(6):519-21.

44. van der Kooij SM, Hehenkamp WJ, Volkers NA, Birnie E, Ankum WM, Reekers JA. Uterine artery embolization vs hysterectomy in the treatment of symptomatic uterine fibroids: 5-year outcome from the randomized EMMY trial. Am J Obstet Gynecol. 2010 Aug;203(2):105-13.

45. Babashov V, Palimaka S, Blackhouse G, O'Reilly D. Magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU) for treatment of symptomatic uterine fibroids: an economic analysis. Ontario Health Technol Assess Series [Internet]. 2015 [cited 2015 May 28];15(5):1-61. Available from: http://www.hqontario.ca/Portals/0/Documents/eds/ohtas/economic-analysis-mrghifu-1503-en.pdf

46. Cain-Nielsen AH, Moriarty JP, Stewart EA, Borah BJ. Cost-effectiveness of uterine-preserving procedures for the treatment of uterine fibroid symptoms in the USA. J Comp Eff Res [Internet]. 2014 Sep [cited 2015 May 28];3(5):503-14. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4213230

47. Kong CY, Meng L, Omer ZB, Swan JS, Srouji S, Gazelle GS, et al. MRI-guided focused ultrasound surgery for uterine fibroid treatment: a cost-effectiveness analysis. AJR Am J Roentgenol [Internet]. 2014 Aug [cited 2015 Jun 2];203(2):361-71. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4321860/pdf/nihms659916.pdf

48. Hirst A, Dutton S, Wu O, Briggs A, Edwards C, Waldenmaier L, et al. A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study. Health Technol Assess [Internet]. 2008 Mar [cited 2015 May 28];12(5):1-248. Available from: http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0006/64671/FullReport-hta12050.pdf

49. Zowall H, Cairns JA, Brewer C, Lamping DL, Gedroyc WM, Regan L. Cost-effectiveness of magnetic resonance-guided focused ultrasound surgery for treatment of uterine fibroids. BJOG [Internet]. 2008 Apr [cited 2015 Jun 2];115(5):653-62. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2344162/pdf/bjo0115-0653.pdf

50. Wu O, Briggs A, Dutton S, Hirst A, Maresh M, Nicholson A, et al. Uterine artery embolisation or hysterectomy for the treatment of symptomatic uterine fibroids: a cost-utility analysis of the HOPEFUL study. BJOG. 2007 Nov;114(11):1352-62.

51. Beinfeld MT, Bosch JL, Isaacson KB, Gazelle GS. Cost-effectiveness of uterine artery embolization and hysterectomy for uterine fibroids. Radiology [Internet]. 2004 Jan [cited 2015 May 28];230(1):207-13. Available from: http://pubs.rsna.org/doi/pdf/10.1148/radiol.2301021482

52. Panagiotopoulou N, Nethra S, Karavolos S, Ahmad G, Karabis A, Burls A. Uterine-sparing minimally invasive interventions in women with uterine fibroids: a systematic review and indirect treatment comparison meta-analysis. Acta Obstet Gynecol Scand. 2014 Sep;93(9):858-67.

53. Carranza-Mamane B, Havelock J, Hemmings R. The management of uterine fibroids in women with otherwise unexplained infertility. J Obstet Gynaecol Can [Internet]. 2015 Mar [cited 2015 Aug 27];(321):277-85. Available from: http://sogc.org/wp-content/uploads/2015/03/gui321CPG1503E.pdf

54. Pron G. Magnetic resonance-guided high-intensity focused ultrasound (MRgHIFU) treatment of symptomatic uterine fibroids: an evidence-based analysis. Ontario Health Technol Assess Series [Internet]. 2015 [cited 2015 May 28];15(4):1-86. Available from: http://www.hqontario.ca/Portals/0/Documents/eds/ohtas/eba-mrghifu-1503-en.pdf

55. Gupta JK, Sinha A, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database Syst Rev. 2014;12:CD005073.

56. van der Kooij SM, Bipat S, Hehenkamp WJ, Ankum WM, Reekers JA. Uterine artery embolization versus surgery in the treatment of symptomatic fibroids: a systematic review and metaanalysis. Am J Obstet Gynecol. 2011 Oct;205(4):317-8.

57. FDA warns against using laparoscopic power morcellators to treat uterine fibroids [Internet]. Silver Spring (MD): Food and Drug Administration; 2014 Nov 24. [cited 2015 Aug 27]. Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm424435.htm

58. Singh SS, Scott S, Bougie O, Leyland N. Technical update on tissue morcellation during gynaecologic surgery: its uses, complications, and risks of unsuspected malignancy. J Obstet Gynaecol Can [Internet]. 2015 Jan [cited 2015 Aug 28];317(1):68-78. Available from: http://www.jogc.com/abstracts/201501_SOGCClinicalPracticeGuidelines_1.pdf

59. Hehenkamp WJ, Volkers NA, Birnie E, Reekers JA, Ankum WM. Pain and return to daily activities after uterine artery embolization and hysterectomy in the treatment of symptomatic uterine fibroids: results from the randomized EMMY trial. Cardiovasc Intervent Radiol. 2006 Mar;29(2):179-87.

60. Hehenkamp WJ, Volkers NA, Bartholomeus W, de Blok S, Birnie E, Reekers JA, et al. Sexuality and body image after uterine artery embolization and hysterectomy in the treatment of uterine fibroids: a randomized comparison. Cardiovasc Intervent Radiol [Internet]. 2007 Sep [cited 2015 May 28];30(5):866-75. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2039794

61. Mara M, Fucikova Z, Maskova J, Kuzel D, Haakova L. Uterine fibroid embolization versus myomectomy in women wishing to preserve fertility: preliminary results of a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2006 Jun 1;126(2):226-33.

62. Hald K, Noreng HJ, Istre O, Klow NE. Uterine artery embolization versus laparoscopic occlusion of uterine arteries for leiomyomas: long-term results of a randomized comparative trial. J Vasc Interv Radiol. 2009 Oct;20(10):1303-10.

63. Moss JG, Cooper KG, Khaund A, Murray LS, Murray GD, Wu O, et al. Randomised comparison of uterine artery embolisation (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. BJOG. 2011 Jul;118(8):936-44.

64. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. BMJ [Internet]. 1996 Aug 3 [cited 2015 Aug 6];313(7052):275-83. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2351717

APPENDIX 1: LITERATURE SEARCH STRATEGY

OVERVIEW	
Interface:	Ovid
Databases:	Embase 1974 to present MEDLINE Daily and MEDLINE 1946 to present MEDLINE In-Process & Other Non-Indexed Citations **Note:** Subject headings have been customized for each database. Duplicates between databases were removed in Ovid.
Date of Search:	May 7, 2015
Alerts:	Bi-weekly search updates began May 21, 2015 and ran until Month, Day, Year.
Study Types:	Health technology assessments; systematic reviews; meta-analyses; randomized controlled trials; controlled clinical trials; cohort studies; economic studies; and guidelines
Limits:	Publication date limits: • Randomized controlled trials, controlled clinical trials, cohort studies and economic studies -- no date limits • Health technology assessments, systematic reviews, meta-analyses and guidelines -- 2005-present Language limit: English or French Conference abstracts: excluded Humans

SYNTAX GUIDE	
/	At the end of a phrase, searches the phrase as a subject heading
.sh	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
?	Truncation symbol for one or no characters only
adj#	Adjacency within # number of words (in any order)
.ti	Title
.ab	Abstract
.kw	Author keyword
.hw	Heading word; usually includes subject headings and controlled vocabulary
.pt	Publication type
.rn	CAS registry number
.yr	Publication year

.la	Language
pmez	Ovid database code; MEDLINE In-Process & Other Non-Indexed Citations, MEDLINE Daily and Ovid MEDLINE 1946 to Present
oemezd	Ovid database code; Embase 1974 to present, updated daily

CLINICAL DATABASE SEARCH

Multi-database Strategy	
Line #	**Search Strategy**
1	exp leiomyoma/
2	exp myoma/ and (uterus/ or myometrium/)
3	(fibroma* and (uter* or myometr*)).ti,ab,kw,hw.
4	(fibroid* or fibromyoma* or fibroleiomyoma* or leiomyoma* or angiomyoma* or leiomyomatosis or angioleiomyoma* or elastomyofibroma* or hemangioleiomyoma* or hemangiomyoma* or leimyoma* or leiomyoma* or leyomyoma* or myofibroma* or myoma* or (smooth muscle adj2 tumo?r*)).ti,ab,kw.
5	or/1-4
6	uterine artery embolization/ or embolization, therapeutic/
7	(emboliz* or embolis* or embolotherapy or UAE).ti,ab,kw.
8	endometrial ablation techniques/
9	((endometrial or endometrium) adj3 (ablat* or resect*)).ti,ab,kw.
10	(myolysis or cryomyolysis).ti,ab,kw.
11	(MRgFU or MRIgFUS or iMRI or MR-HIFU or MRHIFU).ti,ab,kw.
12	((MR or MRI or magnetic resonance) adj4 (ultrasound or ultrason* or ultra-sound or ultra-son* or sonograph* or "U/S")).ti,ab,kw.
13	(HIFU or USgHIFU or (high intensity adj3 (ultrasound or ultrason* or ultra-sound or ultra-son*))).ti,ab,kw.
14	High-Intensity Focused Ultrasound Ablation/
15	(PMWA or RFVTA or USgRFA or TBA or ablat*).ti,ab,kw.
16	Magnetic Resonance Imaging, Interventional/
17	exp Ultrasonic Therapy/
18	((ultrasound or ultrason* or ultra-sound or ultra-son* or sonograph*) adj2 therap*).ti,ab,kw.
19	exp Ultrasonography, Interventional/
20	(interventional adj2 (ultrasound or ultrason* or ultra-sound or ultra-son* or sonograph*)).ti,ab,kw.
21	or/6-20
22	5 and 21
23	uterine myomectomy/
24	(myomatectom* or myomotom* or myomectom* or fibroidectom*).ti,ab,kw.
25	or/23-24

26	22 or 25
27	26 use pmez
28	exp leiomyoma/
29	exp myoma/ and (uterus/ or myometrium/)
30	uterus myoma/
31	(fibroma* and (uter* or myometr*)).ti,ab,kw,hw.
32	(fibroid* or fibromyoma* or fibroleiomyoma* or leiomyoma* or angiomyoma* or leiomyomatosis or angioleiomyoma* or elastomyofibroma* or hemangioleiomyoma* or hemangiomyoma* or leimyoma* or leiomyoma* or leyomyoma* or myofibroma* or myoma* or (smooth muscle adj2 tumo?r*)).ti,ab,kw.
33	or/28-32
34	uterine artery embolization/
35	(emboliz* or embolis* or embolotherapy or UAE).ti,ab,kw.
36	endometrium ablation/
37	((endometrial or endometrium) adj3 (ablat* or resect*)).ti,ab,kw.
38	(myolysis or cryomyolysis).ti,ab,kw.
39	high intensity focused ultrasound/ or high intensity focused ultrasound device/ or ultrasound therapy/ or ultrasound surgery/
40	interventional magnetic resonance imaging/
41	radiofrequency ablation/
42	(MRgFU or MRIgFUS or iMRI or MR-HIFU or MRHIFU).ti,ab,kw.
43	((MR or MRI or magnetic resonance) adj4 (ultrasound or ultrason* or ultra-sound or ultra-son* or sonograph* or "U/S")).ti,ab,kw.
44	(HIFU or USgHIFU or (high intensity adj3 (ultrasound or ultrason* or ultra-sound or ultra-son*))).ti,ab,kw.
45	(PMWA or RFVTA or USgRFA or TBA or ablat*).ti,ab,kw.
46	((ultrasound or ultrason* or ultra-sound or ultra-son* or sonograph*) adj2 therap*).ti,ab,kw.
47	(interventional adj2 (ultrasound or ultrason* or ultra-sound or ultra-son* or sonograph*)).ti,ab,kw.
48	or/34-47
49	33 and 48
50	myomectomy/
51	(myomatectom* or myomotom* or myomectom* or fibroidectom*).ti,ab,kw.
52	or/50-51
53	49 or 52
54	53 not conference abstract.pt.
55	54 use oemezd
56	27 or 55
57	limit 56 to english language
58	56 and french.la.

59	or/57-58
60	(Randomized Controlled Trial or Controlled Clinical Trial).pt.
61	Randomized Controlled Trial/
62	Randomized Controlled Trials as Topic/
63	"Randomized Controlled Trial (topic)"/
64	Controlled Clinical Trial/
65	Controlled Clinical Trials as Topic/
66	"Controlled Clinical Trial (topic)"/
67	Randomization/
68	Random Allocation/
69	Double-Blind Method/
70	Double Blind Procedure/
71	Double-Blind Studies/
72	Single-Blind Method/
73	Single Blind Procedure/
74	Single-Blind Studies/
75	Placebos/
76	Placebo/
77	Control Groups/
78	Control Group/
79	(random* or sham or placebo*).ti,ab,hw.
80	((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,hw.
81	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,hw.
82	(control* adj3 (study or studies or trial*)).ti,ab.
83	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw.
84	allocated.ti,ab,hw.
85	((open label or open-label) adj5 (study or studies or trial*)).ti,ab,hw.
86	cohort.ti,ab,hw.
87	or/60-86
88	59 and 87
89	exp animals/
90	exp animal experimentation/ or exp animal experiment/
91	exp models animal/
92	nonhuman/
93	exp vertebrate/ or exp vertebrates/
94	or/89-93
95	exp humans/
96	exp human experimentation/ or exp human experiment/
97	or/95-96
98	94 not 97

99	88 not 98
100	meta-analysis.pt.
101	meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/
102	((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab.
103	((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab.
104	((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab.
105	(data synthes* or data extraction* or data abstraction*).ti,ab.
106	(handsearch* or hand search*).ti,ab.
107	(mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab.
108	(met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab.
109	(meta regression* or metaregression*).ti,ab.
110	(meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
111	(medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.
112	(cochrane or (health adj2 technology assessment) or evidence report).jw.
113	(comparative adj3 (efficacy or effectiveness)).ti,ab.
114	(outcomes research or relative effectiveness).ti,ab.
115	((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab.
116	or/100-115
117	59 and 116
118	limit 117 to yr="2005 -Current"
119	(guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.
120	(guideline* or standards or consensus* or recommendat*).ti.
121	(practice parameter* or position statement* or policy statement* or CPG or CPGs or best practice*).ti.
122	(care adj2 (path or paths or pathway or pathways or map or maps or plan or plans or standard)).ti.
123	((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti.
124	(algorithm* and (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti.
125	(algorithm* and (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti.
126	or/119-125
127	59 and 126

128	limit 127 to yr="2005 -Current"
129	99 or 118 or 128
130	remove duplicates from 129

OTHER DATABASES	
PubMed	Same MeSH, keywords and limits used as per MEDLINE search, with appropriate syntax used. PubMed is searched for citations not found in MEDLINE.
Cochrane Library	Same MeSH, keywords and limits used as per MEDLINE search, excluding study types and human restrictions. Syntax adjusted for Cochrane Library databases.
Trial registries (Clinicaltrials.gov)	Same keywords and limits used as per MEDLINE search. Search limited to completed trials.

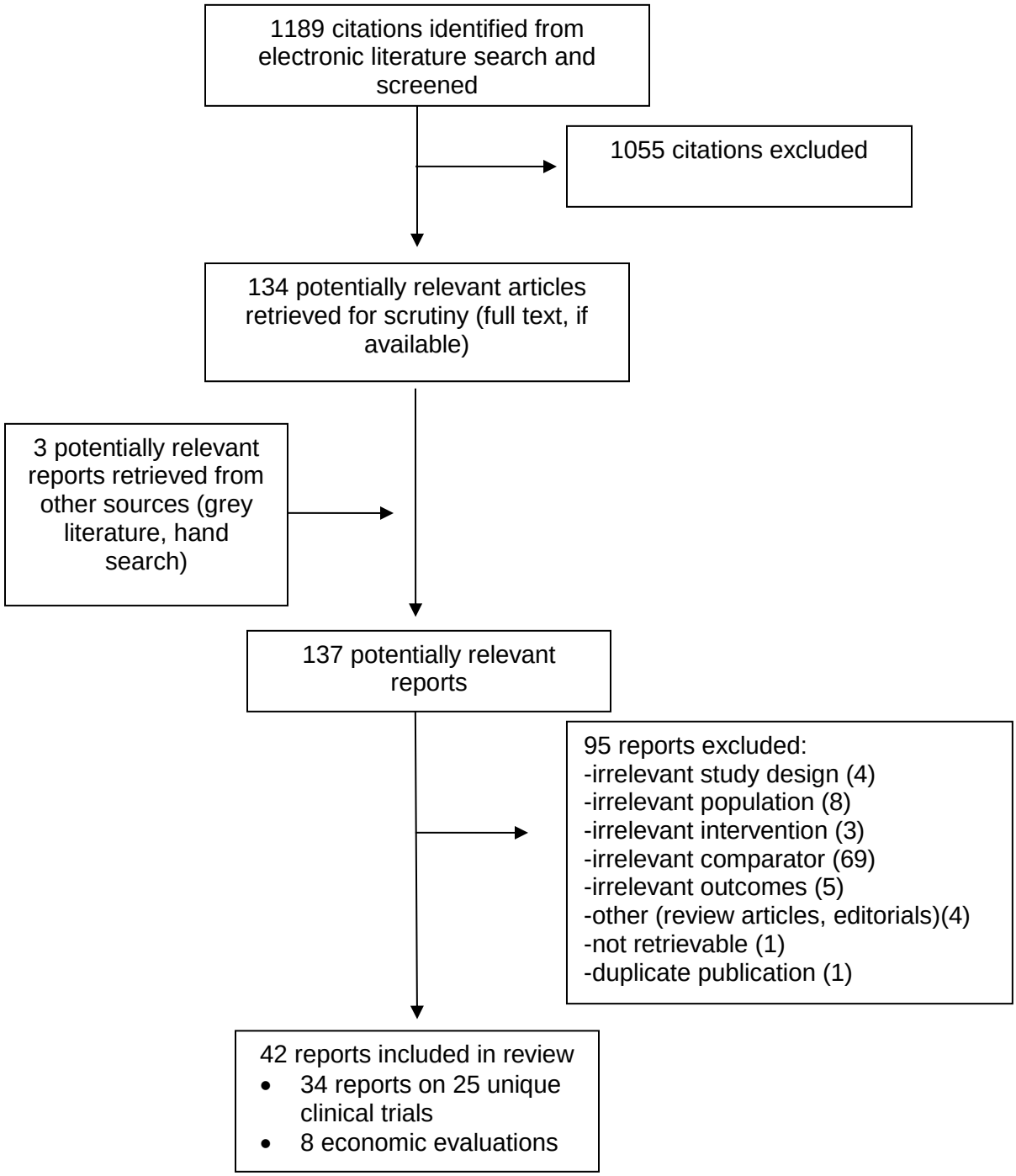
GREY LITERATURE

Dates for Search:	May 2015
Keywords:	Uterine fibroids, fibroids, leiomyoma
Limits:	No publication date limit; English or French language only

Relevant websites from the following sections of the CADTH grey literature checklist, “Grey matters: a practical tool for evidence-based searching” (https://www.cadth.ca/resources/finding-evidence/grey-matters-practical-search-tool-evidence-based-medicine) were searched:

- Health Technology Assessment Agencies
- Drug & Device Regulatory Approvals
- Advisories & Warnings
- Clinical Practice Guidelines
- Health Economics
- Databases (free)
- Statistics/Prevalences
- Internet Search
- Open Access Journals

APPENDIX 2: SELECTION OF INCLUDED STUDIES



APPENDIX 3: INCLUDED STUDIES FOR CLINICAL EVIDENCE

Ambat S, Mittal S, Srivastava DN, Misra R, Dadhwal V, Ghosh B. Uterine artery embolization versus laparoscopic occlusion of uterine vessels for management of symptomatic uterine fibroids. Int J Gynaecol Obstet. 2009 May;105(2):162-5.

Brochner AC, Mygil B, Elle B, Toft P. Inflammatory response in patients undergoing uterine artery embolization as compared to patients undergoing conventional hysterectomy. Acta Radiol. 2009 Dec;50(10):1193-7.

Broder MS, Goodwin S, Chen G, Tang LJ, Costantino MM, Nguyen MH, et al. Comparison of long-term outcomes of myomectomy and uterine artery embolization. Obstet Gynecol. 2002 Nov;100(5 Pt 1):864-8.

Cunningham E, Barreda L, Ngo M, Terasaki K, Munro MG. Uterine artery embolization versus occlusion for uterine leiomyomas: a pilot randomized clinical trial. J Minim Invasive Gynecol. 2008 May;15(3):301-7.

The EMMY study:

Hehenkamp WJ, Volkers NA, Birnie E, Reekers JA, Ankum WM. Symptomatic uterine fibroids: treatment with uterine artery embolization or hysterectomy--results from the randomized clinical Embolisation versus Hysterectomy (EMMY) Trial. Radiology [Internet]. 2008 Mar [cited 2015 May 28];246(3):823-32. Available from: http://pubs.rsna.org/doi/pdf/10.1148/radiol.2463070260

Hehenkamp WJ, Volkers NA, Donderwinkel PF, de Blok S, Birnie E, Ankum WM, et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): peri- and postprocedural results from a randomized controlled trial. Am J Obstet Gynecol. 2005 Nov;193(5):1618-29.

Volkers NA, Hehenkamp WJ, Birnie E, Ankum WM, Reekers JA. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2 years' outcome from the randomized EMMY trial. Am J Obstet Gynecol. 2007 Jun;196(6):519-21.

Hehenkamp WJ, Volkers NA, Birnie E, Reekers JA, Ankum WM. Pain and return to daily activities after uterine artery embolization and hysterectomy in the treatment of symptomatic uterine fibroids: results from the randomized EMMY trial. Cardiovasc Intervent Radiol. 2006 Mar;29(2):179-87.

Hehenkamp WJ, Volkers NA, Bartholomeus W, de Blok S, Birnie E, Reekers JA, et al. Sexuality and body image after uterine artery embolization and hysterectomy in the treatment of uterine fibroids: a randomized comparison. Cardiovasc Intervent Radiol [Internet]. 2007 Sep [cited 2015 May 28];30(5):866-75. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2039794

van der Kooij SM, Hehenkamp WJ, Volkers NA, Birnie E, Ankum WM, Reekers JA. Uterine artery embolization vs hysterectomy in the treatment of symptomatic uterine fibroids: 5-year outcome from the randomized EMMY trial. Am J Obstet Gynecol. 2010 Aug;203(2):105-13.

Goodwin SC, Bradley LD, Lipman JC, Stewart EA, Nosher JL, Sterling KM, et al. Uterine artery embolization versus myomectomy: a multicenter comparative study. Fertil Steril. 2006 Jan;85(1):14-21.

Hahn et al.

Hahn M, Brucker S, Kraemer D, Wallwiener M, Taran FA, Wallwiener CW, et al. Radiofrequency volumetric thermal ablation of fibroids and laparoscopic myomectomy: long-term follow-up from a randomized trial. Geburtshilfe Frauenheilkd [Internet]. 2015 May [cited 2015 Jul 2];75(5):442-9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4461677

Brucker SY, Hahn M, Kraemer D, Taran FA, Isaacson KB, Kramer B. Laparoscopic radiofrequency volumetric thermal ablation of fibroids versus laparoscopic myomectomy. Int J Gynaecol Obstet [Internet]. 2014 Jun [cited 2015 May 28];125(3):261-5. Available from: http://www.sciencedirect.com/science/article/pii/S0020729214001040

Hald et al.

Hald K, Noreng HJ, Istre O, Klow NE. Uterine artery embolization versus laparoscopic occlusion of uterine arteries for leiomyomas: long-term results of a randomized comparative trial. J Vasc Interv Radiol. 2009 Oct;20(10):1303-10.

Hald K, Kløw NE, Qvigstad E, Istre O. Laparoscopic occlusion compared with embolization of uterine vessels: a randomized controlled trial. Obstet Gynecol. 2007 Jan;109(1):20-7.

Helal A, Mashaly A, Amer T. Uterine artery occlusion for treatment of symptomatic uterine myomas. J Soc Laparoendosc Surg [Internet]. 2010 Jul [cited 2015 May 28];14(3):386-90. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3041036

Holub Z, Mara M, Eim J. Laparoscopic uterine artery occlusion versus uterine fibroid embolization. Int J Gynaecol Obstet. 2007;96(1):44-5.

HOPEFUL

Hirst A, Dutton S, Wu O, Briggs A, Edwards C, Waldenmaier L, et al. A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study. Health Technol Assess [Internet]. 2008 Mar;12(5):1-248. Available from: http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0006/64671/FullReport-hta12050.pdf

Dutton S, Hirst A, McPherson K, Nicholson T, Maresh M. A UK multicentre retrospective cohort study comparing hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids (HOPEFUL study): main results on medium-term safety and efficacy. BJOG. 2007 Nov;114(11):1340-51.

Ikink ME, Nijenhuis RJ, Verkooijen HM, Voogt MJ, Reuwer PJ, Smeets AJ, et al. Volumetric MR-guided high-intensity focused ultrasound versus uterine artery embolisation for treatment of

symptomatic uterine fibroids: comparison of symptom improvement and reintervention rates. Eur Radiol. 2014 Oct;24(10):2649-57.

Iverson RE Jr, Chelmow D, Strohbehn K, Waldman L, Evantash EG. Relative morbidity of abdominal hysterectomy and myomectomy for management of uterine leiomyomas. Obstet Gynecol. 1996 Sep;88(3):415-9.

Manyonda IT, Bratby M, Horst JS, Banu N, Gorti M, Belli AM. Uterine artery embolization versus myomectomy: impact on quality of life--results of the FUME (Fibroids of the Uterus: Myomectomy versus Embolization) Trial. Cardiovasc Intervent Radiol. 2012 Jun;35(3):530-6.

Mara M, Kubinova K, Maskova J, Horak P, Belsan T, Kuzel D. Uterine artery embolization versus laparoscopic uterine artery occlusion: the outcomes of a prospective, nonrandomized clinical trial. Cardiovasc Intervent Radiol. 2012 Oct;35(5):1041-52.

Mara et al.

> Mara M, Maskova J, Fucikova Z, Kuzel D, Belsan T, Sosna O. Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. Cardiovasc Intervent Radiol [Internet]. 2008 Jan [cited 2015 May 28];31(1):73-85. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2700241
>
> Mara M, Fucikova Z, Maskova J, Kuzel D, Haakova L. Uterine fibroid embolization versus myomectomy in women wishing to preserve fertility: preliminary results of a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2006 Jun 1;126(2):226-33.

Narayan A, Lee AS, Kuo GP, Powe N, Kim HS. Uterine artery embolization versus abdominal myomectomy: a long-term clinical outcome comparison. J Vasc Interv Radiol [Internet]. 2010 Jul [cited 2015 May 28];21(7):1011-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2900435

Odejinmi F, Maclaran K, Agarwal N. Laparoscopic treatment of uterine fibroids: a comparison of peri-operative outcomes in laparoscopic hysterectomy and myomectomy. Arch Gynecol Obstet. 2015 Mar;291(3):579-84.

Pinto I, Chimeno P, Romo A, Paul L, Haya J, de la Cal MA, et al. Uterine fibroids: uterine artery embolization versus abdominal hysterectomy for treatment--a prospective, randomized, and controlled clinical trial. Radiology [Internet]. 2003 Feb [cited 2015 May 28];226(2):425-31. Available from: http://pubs.rsna.org/doi/pdf/10.1148/radiol.2262011716

Razavi MK, Hwang G, Jahed A, Modanlou S, Chen B. Abdominal myomectomy versus uterine fibroid embolization in the treatment of symptomatic uterine leiomyomas. AJR Am J Roentgenol [Internet]. 2003 Jun [cited 2015 May 28];180(6):1571-5. Available from: http://www.ajronline.org/doi/pdf/10.2214/ajr.180.6.1801571

Ruuskanen A, Hippelainen M, Sipola P, Manninen H. Uterine artery embolisation versus hysterectomy for leiomyomas: primary and 2-year follow-up results of a randomised prospective clinical trial. Eur Radiol. 2010 Oct;20(10):2524-32.

Sawin SW, Pilevsky ND, Berlin JA, Barnhart KT. Comparability of perioperative morbidity between abdominal myomectomy and hysterectomy for women with uterine leiomyomas. Am J Obstet Gynecol. 2000 Dec;183(6):1448-55.

Siskin GP, Shlansky-Goldberg RD, Goodwin SC, Sterling K, Lipman JC, Nosher JL, et al. A prospective multicenter comparative study between myomectomy and uterine artery embolization with polyvinyl alcohol microspheres: long-term clinical outcomes in patients with symptomatic uterine fibroids. J Vasc Interv Radiol. 2006 Aug;17(8):1287-95.

Spies JB, Bradley LD, Guido R, Maxwell GL, Levine BA, Coyne K. Outcomes from leiomyoma therapies: comparison with normal controls. Obstet Gynecol. 2010 Sep;116(3):641-52.

Spies JB, Cooper JM, Worthington-Kirsch R, Lipman JC, Mills BB, Benenati JF. Outcome of uterine embolization and hysterectomy for leiomyomas: results of a multicenter study. Am J Obstet Gynecol. 2004;191(1):22-31.

APPENDIX 4: EXCLUDED STUDIES FOR CLINICAL REVIEW

Irrelevant Study Design

Mettler L, Schollmeyer T, Lehmann-Willenbrock E, Dowaji J, Zavala A. Treatment of myomas by laparoscopic and laparotomic myomectomy and laparoscopic hysterectomy. Minim Invasive Ther Allied Technol. 2004 Feb;13(1):58-64.

Rabinovici J, David M, Fukunishi H, Morita Y, Gostout BS, Stewart EA, et al. Pregnancy outcome after magnetic resonance-guided focused ultrasound surgery (MRgFU) for conservative treatment of uterine fibroids. Fertil Steril. 2010 Jan;93(1):199-209.

Radosa MP, Owsianowski Z, Mothes A, Weisheit A, Vorwergk J, Asskaryar FA, et al. Long-term risk of fibroid recurrence after laparoscopic myomectomy. Eur J Obstet Gynecol Reprod Biol. 2014 Sep;180:35-9.

Volkers NA, Hehenkamp WJ, Birnie E, de Vries C, Holt C, Ankum WM, et al. Uterine artery embolization in the treatment of symptomatic uterine fibroid tumors (EMMY trial): periprocedural results and complications. J Vasc Interv Radiol. 2006 Mar;17(3):471-80.

Irrelevant Population

Aboulghar MM, Al-Inany HG, Aboulghar MA, Serour GI, Mansour RT. The effect of intramural fibroids on the outcome of IVF. Middle East Fertility Society Journal [Internet]. 2004 [cited 2015 Jun 2];9(3):263-7. Available from: http://www.bioline.org.br/pdf?mf04048

Calin D, Haradja H, Pacu I, Bratila E, Gheorghiu D, Rahimian H, et al. Laparoscopic myomectomy in infertility treatment. ARS Medica Tomitana. 2015;20(3):139-43.

Chong GO, Lee YH, Hong DG, Cho YL, Lee YS. Robotic hysterectomy or myomectomy without power morcellation: a single-port assisted three-incision technique with manual morcellation. Int J Med Robot. 2015 Jun 8. Epub ahead of print.

Iverson RE Jr, Chelmow D, Strohbehn K, Waldman L, Evantash EG, Aronson MP. Myomectomy fever: testing the dogma. Fertil Steril. 1999 Jul;72(1):104-8.

Lin JY, Lee WL, Wang PH, Lai MJ, Chang WH, Liu WM. Uterine artery occlusion and myomectomy for treatment of pregnant women with uterine leiomyomas who are undergoing cesarean section. J Obstet Gynaecol Res. 2010 Apr;36(2):284-90.

Mastrominas M, Pistofidis GA, Dimitropoulos K. Fertility outcome after outpatient hysteroscopic removal of endometrial polyps and submucous fibroids. J Am Assoc Gynecol Laparosc. 1996 Aug;3(4, Supplement):S29.

Shokeir T, El-Shafei M, Yousef H, Allam AF, Sadek E. RETRACTED: Submucous myomas and their implications in the pregnancy rates of patients with otherwise unexplained primary infertility undergoing hysteroscopic myomectomy: a randomized matched control study. Fertil Steril. 2010 Jul;94(2):724-9.

You JH, Sahota DS, Yuen PM. Uterine artery embolization, hysterectomy, or myomectomy for symptomatic uterine fibroids: a cost-utility analysis. Fertil Steril. 2009 Feb;91(2):580-8.

Irrelevant Intervention

Aleyasin A, Hayatshahi A, Saffarieh E, Torkamandi H, Aghahosseini M, Hanafi S, et al. No superiority of granisetron over metoclopramide in prevention of post-operative nausea and vomiting: a randomized clinical trial. J Obstet Gynaecol India [Internet]. 2014 Feb [cited 2015 May 28];64(1):59-62. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3931901

Jacoby VL, Jacoby A, Learman LA, Schembri M, Gregorich SE, Jackson R, et al. Use of medical, surgical and complementary treatments among women with fibroids. Eur J Obstet Gynecol Reprod Biol. 2014 Nov;182:220-5.

Liu M, Cheng Z, Zhu Y, Dai H, Hu L, Xu L. Prospective comparison of laparoscopic uterine artery occlusion plus myomectomy with classic intrafascial supracervical hysterectomy for symptomatic fibroid treatment: differences in post-operative quality-of-life measures. Eur J Obstet Gynecol Reprod Biol. 2011 Mar;155(1):79-84.

Irrelevant Comparator

Alborzi S, Ghannadan E, Alborzi S, Alborzi M. A comparison of combined laparoscopic uterine artery ligation and myomectomy versus laparoscopic myomectomy in treatment of symptomatic myoma. Fertil Steril. 2009 Aug;92(2):742-7.

Alessandri F, Lijoi D, Mistrangelo E, Ferrero S, Ragni N. Randomized study of laparoscopic versus minilaparotomic myomectomy for uterine myomas. J Minim Invasive Gynecol. 2006 Mar;13(2):92-7.

Ananthakrishnan G, Murray L, Ritchie M, Murray G, Bryden F, Lassman S, et al. Randomized comparison of uterine artery embolization (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): subanalysis of 5-year MRI findings. Cardiovasc Intervent Radiol. 2013 Jun;36(3):676-81.

Ardovino M, Ardovino I, Castaldi MA, Trabucco E, Colacurci N, Cobellis L. Minilaparoscopic myomectomy: a mini-invasive technical variant. J Laparoendosc Adv Surg Tech A. 2013 Oct;23(10):871-5.

Asgari Z, Hafizi L, Hosseini R, Javaheri A, Rastad H. Intrauterine synechiae after myomectomy; laparotomy versus laparoscopy: non-randomized interventional trial. Iran J Reprod Med. 2015;13(3):161-8.

Bae JH, Chong GO, Seong WJ, Hong DG, Lee YS. Benefit of uterine artery ligation in laparoscopic myomectomy. Fertil Steril. 2011 Feb;95(2):775-8.

Behera MA, Likes CE III, Judd JP, Barnett JC, Havrilesky LJ, Wu JM. Cost analysis of abdominal, laparoscopic, and robotic-assisted myomectomies. J Minim Invasive Gynecol. 2012 Jan;19(1):52-7.

Benassi L, Marconi L, Benassi G, Accorsi F, Angeloni M, Besagni F. Minilaparotomy vs laparotomy for uterine myomectomies: a randomized controlled trial. Minerva Ginecol. 2005 Apr;57(2):159-63.

Birsan A, Deval B, Detchev R, Poncelet C, Darai E. Vaginal and laparoscopic myomectomy for large posterior myomas: results of a pilot study. Eur J Obstet Gynecol Reprod Biol. 2003 Sep 10;110(1):89-93.

Cagnacci A, Pirillo D, Malmusi S, Arangino S, Alessandrini C, Volpe A. Early outcome of myomectomy by laparotomy, minilaparotomy and laparoscopically assisted minilaparotomy. A randomized prospective study. Hum Reprod [Internet]. 2003 Dec [cited 2015 Jun 8];18(12):2590-4. Available from: http://humrep.oxfordjournals.org/content/18/12/2590.full.pdf+html

Chang WC, Huang PS, Wang PH, Chang DY, Huang SC, Chen SY, et al. Comparison of laparoscopic myomectomy using in situ morcellation with and without uterine artery ligation for treatment of symptomatic myomas. J Minim Invasive Gynecol. 2012 Nov;19(6):715-21.

Chen I, Lisonkova S, Joseph KS, Williams C, Yong P, Allaire C. Laparoscopic versus abdominal myomectomy: practice patterns and health care use in British Columbia. J Obstet Gynaecol Can. 2014 Sep;36(9):817-21.

Ciavattini A, Tsiroglou D, Tranquilli AL, Litta P. Laparoscopic versus ultraminilaparotomic myomectomy for the treatment of large uterine myomas. Acta Obstet Gynecol Scand. 2010;89(1):151-5.

Cicinelli E, Tinelli R, Colafiglio G, Saliani N. Laparoscopy vs minilaparotomy in women with symptomatic uterine myomas: a prospective randomized study. J Minim Invasive Gynecol. 2009 Jul;16(4):422-6.

Cooper JM, Anderson TL, Fortin CA, Jack SA, Plentl MB. Microwave endometrial ablation vs. rollerball electroablation for menorrhagia: a multicenter randomized trial. J Am Assoc Gynecol Laparosc. 2004 Aug;11(3):394-403.

Dubuisson JB, Malartic C, Jacob S, Chapron C, Rambaud D. Preventive uterine artery occlusion combined with laparoscopic myomectomy: a valid procedure to prevent bleeding. J Gynecol Surg. 2004;20(4):105-12.

Edwards RD, Moss JG, Lumsden MA, Wu O, Murray LS, Twaddle S, et al. Uterine-artery embolization versus surgery for symptomatic uterine fibroids. N Engl J Med. 2007 Jan 25;356(4):360-70.

Gargiulo AR, Srouji SS, Missmer SA, Correia KF, Vellinga TT, Einarsson JI. Robot-assisted laparoscopic myomectomy compared with standard laparoscopic myomectomy. Obstet Gynecol. 2012 Aug;120(2 Pt 1):284-91.

Gocmen A, Sanlikan F, Ucar MG. Comparison of robotic-assisted laparoscopic myomectomy outcomes with laparoscopic myomectomy. Arch Gynecol Obstet. 2013 Jan;287(1):91-6.

Goldman KN, Hirshfeld-Cytron JE, Pavone ME, Thomas AP, Vogelzang RL, Milad MP. Uterine artery embolization immediately preceding laparoscopic myomectomy. Int J Gynaecol Obstet [Internet]. 2012 Feb [cited 2015 Jun 1];116(2):105-8. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4034570/pdf/nihms580802.pdf

Holub Z. Surgical results of myomectomy using laparoscopic and minilaparotomic access. Womens Health (Lond Engl). 2007 Sep;3(5):537-9.

Holzer A, Jirecek ST, Illievich UM, Huber J, Wenzl RJ. Laparoscopic versus open myomectomy: a double-blind study to evaluate postoperative pain. Anesth Analg. 2006 May;102(5):1480-4.

Hsiao SM, Lin HH, Peng FS, Jen PJ, Hsiao CF, Tu FC. Comparison of robot-assisted laparoscopic myomectomy and traditional laparoscopic myomectomy. J Obstet Gynaecol Res. 2013 May;39(5):1024-9.

Jun F, Yamin L, Xinli X, Zhe L, Min Z, Bo Z, et al. Uterine artery embolization versus surgery for symptomatic uterine fibroids: a randomized controlled trial and a meta-analysis of the literature. Arch Gynecol Obstet. 2012 May;285(5):1407-13.

Kim JY, Kim KH, Choi JS, Lee JH. A prospective matched case-control study of laparoendoscopic single-site vs conventional laparoscopic myomectomy. J Minim Invasive Gynecol. 2014 Nov;21(6):1036-40.

Kim SK, Lee JH, Lee JR, Suh CS, Kim SH. Laparoendoscopic single-site myomectomy versus conventional laparoscopic myomectomy: a comparison of surgical outcomes. J Minim Invasive Gynecol. 2014 Sep;21(5):775-81.

Likes C, Behera M, Judd J, Barnett JC, Havrilesky L, Wu J. Cost minimization analysis of abdominal, laparoscopic, and robotic-assisted myomectomies [abstract]. J Pelvic Med Surg. 2010;16(2):S11.

Litta P, Fantinato S, Calonaci F, Cosmi E, Filippeschi M, Zerbetto I, et al. A randomized controlled study comparing harmonic versus electrosurgery in laparoscopic myomectomy. Fertil Steril. 2010 Oct;94(5):1882-6.

Liu WM, Wang PH, Chou CS, Tang WL, Wang IT, Tzeng CR. Efficacy of combined laparoscopic uterine artery occlusion and myomectomy via minilaparotomy in the treatment of recurrent uterine myomas. Fertil Steril. 2007 Feb;87(2):356-61.

Liu WM, Tzeng CR, Yi-Jen C, Wang PH. Combining the uterine depletion procedure and myomectomy may be useful for treating symptomatic fibroids. Fertil Steril. 2004 Jul;82(1):205-10.

Loffer FD. Improving results of hysteroscopic submucosal myomectomy for menorrhagia by concomitant endometrial ablation. J Minim Invasive Gynecol. 2005 May;12(3):254-60.

Loffer FD, Grainger D. Five-year follow-up of patients participating in a randomized trial of uterine balloon therapy versus rollerball ablation for treatment of menorrhagia. J Am Assoc Gynecol Laparosc. 2002 Nov;9(4):429-35.

Ludwin A, Ludwin I, Pitynski K, Basta P, Basta A, Banas T, et al. Transrectal ultrasound-guided hysteroscopic myomectomy of submucosal myomas with a varying degree of myometrial penetration. J Minim Invasive Gynecol. 2013 Sep;20(5):672-85.

Mais V, Ajossa S, Guerriero S, Mascia M, Solla E, Melis GB. Laparoscopic versus abdominal myomectomy: a prospective, randomized trial to evaluate benefits in early outcome. Am J Obstet Gynecol. 1996 Feb;174(2):654-8.

Malzoni M, Tinelli R, Cosentino F, Iuzzolino D, Surico D, Reich H. Laparoscopy versus minilaparotomy in women with symptomatic uterine myomas: short-term and fertility results. Fertil Steril. 2010 May 1;93(7):2368-73.

McLucas B, Chespak L, Kaminsky D. Myoma necrosis following Gelfoam embolization of uterine myomata. Minim Invasive Ther Allied Technol. 2008;17(3):200-4.

Meng X, He G, Zhang J, Han Z, Yu M, Zhang M, et al. A comparative study of fibroid ablation rates using radio frequency or high-intensity focused ultrasound. Cardiovasc Intervent Radiol. 2010 Aug;33(4):794-9.

Moss JG, Cooper KG, Khaund A, Murray LS, Murray GD, Wu O, et al. Randomised comparison of uterine artery embolisation (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. BJOG. 2011 Jul;118(8):936-44.

Nezhat C, Lavie O, Hsu S, Watson J, Barnett O, Lemyre M. Robotic-assisted laparoscopic myomectomy compared with standard laparoscopic myomectomy--a retrospective matched control study. Fertil Steril. 2009 Feb;91(2):556-9.

Palomba S, Zupi E, Falbo A, Russo T, Marconi D, Zullo F. New tool (Laparotenser) for gasless laparoscopic myomectomy: a multicenter-controlled study. Fertil Steril. 2010 Aug;94(3):1090-6.

Palomba S, Zupi E, Falbo A, Russo T, Marconi D, Tolino A, et al. A multicenter randomized, controlled study comparing laparoscopic versus minilaparotomic myomectomy: reproductive outcomes. Fertil Steril. 2007 Oct;88(4):933-41.

Palomba S, Zupi E, Russo T, Falbo A, Marconi D, Tolino A, et al. A multicenter randomized, controlled study comparing laparoscopic versus minilaparotomic myomectomy: short-term outcomes. Fertil Steril. 2007 Oct;88(4):942-51.

Phillips DR, Milim SJ, Nathanson HG, Haselkorn JS. Experience with laparoscopic leiomyoma coagulation and concomitant operative hysteroscopy. J Am Assoc Gynecol Laparosc. 1997;4(4):425-33.

Phillips DR. A comparison of endometrial ablation using the Nd:YAG laser or electrosurgical techniques. J Am Assoc Gynecol Laparosc. 1994 May;1(3):235-9.

Pisco JM, Bilhim T, Duarte M, Ferreira A, Santos D, Pires FM, et al. Pelvic pain after uterine artery embolization: a prospective randomized study of polyvinyl alcohol particles mixed with ketoprofen versus bland polyvinyl alcohol particles. J Vasc Interv Radiol. 2008 Nov;19(11):1537-42.

Pynna K, Vuorela P, Lodenius L, Paavonen J, Roine RP, Rasanen P. Cost-effectiveness of hysterectomy for benign gynecological conditions: a systematic review. Acta Obstet Gynecol Scand. 2014;93(3):225-32.

Quinn SD, Vedelago J, Regan L, Gedroyc WM. Safety and treatment volumes achieved following new developments of the magnetic resonance-guided focused ultrasound system in the treatment of uterine fibroids: a cohort study. J Ther Ultrasound [Internet]. 2013 [cited 2015 Jun 8];1:20. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4265952/pdf/2050-5736-1-20.pdf

Rossetti A, Sizzi O, Soranna L, Cucinelli F, Mancuso S, Lanzone A. Long-term results of laparoscopic myomectomy: recurrence rate in comparison with abdominal myomectomy. Hum Reprod [Internet]. 2001 Apr [cited 2015 May 28];16(4):770-4. Available from: http://humrep.oxfordjournals.org/content/16/4/770.full.pdf+html

Seracchioli R, Rossi S, Govoni F, Rossi E, Venturoli S, Bulletti C, et al. Fertility and obstetric outcome after laparoscopic myomectomy of large myomata: a randomized comparison with abdominal myomectomy. Hum Reprod [Internet]. 2000 Dec [cited 2015 Jun 8];15(12):2663-8. Available from: http://humrep.oxfordjournals.org/content/15/12/2663.full.pdf+html

Sesti F, Capobianco F, Capozzolo T, Pietropolli A, Piccione E. Isobaric gasless laparoscopy versus minilaparotomy in uterine myomectomy: a randomized trial. Surg Endosc. 2008 Apr;22(4):917-23.

Shlansky-Goldberg RD, Rosen MA, Mondschein JI, Stavropoulos SW, Trerotola SO, Diaz-Cartelle J. Comparison of polyvinyl alcohol microspheres and tris-acryl gelatin microspheres for uterine fibroid embolization: results of a single-center randomized study. J Vasc Interv Radiol. 2014 Jun;25(6):823-32.

Silva BA, Falcone T, Bradley L, Goldberg JM, Mascha E, Lindsey R, et al. Case-control study of laparoscopic versus abdominal myomectomy. J Laparoendosc Adv Surg Tech A. 2000 Aug;10(4):191-7.

Song YG, Jang H, Park KD, Kim MD, Kim CW. Non spherical polyvinyl alcohol versus gelatin sponge particles for uterine artery embolization for symptomatic fibroids. Minim Invasive Ther Allied Technol. 2013 Dec;22(6):364-71.

Soysal ME, Soysal SK, Vicdan K. Thermal balloon ablation in myoma-induced menorrhagia under local anesthesia. Gynecol Obstet Invest. 2001;51(2):128-33.

Spies JB, Allison S, Flick P, Cramp M, Bruno J, Jha RC, et al. Spherical polyvinyl alcohol versus tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: results of a limited randomized comparative study. J Vasc Interv Radiol. 2005 Nov;16(11):1431-7.

Spies JB, Allison S, Flick P, McCullough M, Sterbis K, Cramp M, et al. Polyvinyl alcohol particles and tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: results of a randomized comparative study. J Vasc Interv Radiol. 2004 Aug;15(8):793-800.

Su H, Han CM, Wang CJ, Lee CL, Soong YK. Comparison of the efficacy of the pulsed bipolar system and conventional electrosurgery in laparoscopic myomectomy - a retrospective matched control study. Taiwan J Obstet Gynecol. 2011 Mar;50(1):25-8.

Tan J, Sun Y, Zhong B, Dai H, Wang D. A randomized, controlled study comparing minilaparotomy versus isobaric gasless laparoscopic assisted minilaparotomy myomectomy for removal of large uterine myomas: short-term outcomes. Eur J Obstet Gynecol Reprod Biol. 2009 Jul;145(1):104-8.

Tan J, Sun Y, Dai H, Zhong B, Wang D. A randomized trial of laparoscopic versus laparoscopic-assisted minilaparotomy myomectomy for removal of large uterine myoma: short-term outcomes. J Minim Invasive Gynecol. 2008 Jul;15(4):402-9.

Vercellino G, Erdemoglu E, Joe A, Hopfenmueller W, Holthaus B, Kohler C, et al. Laparoscopic temporary clipping of uterine artery during laparoscopic myomectomy. Arch Gynecol Obstet. 2012 Nov;286(5):1181-6.

Wang F, Tang L, Wang L, Wang X, Chen J, Liu X, et al. Ultrasound-guided high-intensity focused ultrasound vs laparoscopic myomectomy for symptomatic uterine myomas. J Minim Invasive Gynecol. 2014 Mar;21(2):279-84.

Wang JJ, Yang F, Gao T, Li L, Xia H, Li HF. Gasless laparoscopy versus conventional laparoscopy in uterine myomectomy: a single-centre randomized trial. J Int Med Res. 2011;39(1):172-8.

Wang PH, Liu WM, Fuh JL, Chao HT, Yuan CC, Chao KC. Symptomatic myoma treated with laparoscopic uterine vessel occlusion and subsequent immediate myomectomy: which is the optimal surgical approach? Fertil Steril. 2009 Aug;92(2):762-9.

Wang X, Qin J, Wang L, Chen J, Chen W, Tang L. Effect of high-intensity focused ultrasound on sexual function in the treatment of uterine fibroids: comparison to conventional myomectomy. Arch Gynecol Obstet. 2013 Oct;288(4):851-8.

Wen KC, Chen YJ, Sung PL, Wang PH. Comparing uterine fibroids treated by myomectomy through traditional laparotomy and 2 modified approaches: ultraminilaparotomy and laparoscopically assisted ultraminilaparotomy. Am J Obstet Gynecol. 2010 Feb;202(2):144-8.

Wen KC, Sung PL, Chao KC, Lee WL, Liu WM, Wang PH. A prospective short-term evaluation of uterine leiomyomas treated by myomectomy through conventional laparotomy or ultraminilaparotomy. Fertil Steril. 2008 Dec;90(6):2361-6.

Worthington-Kirsch RL, Siskin GP, Hegener P, Chesnick R. Comparison of the efficacy of the embolic agents acrylamido polyvinyl alcohol microspheres and tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: a prospective randomized controlled trial. Cardiovasc Intervent Radiol. 2011 Jun;34(3):493-501.

Yu SC, Lok I, Ho SS, Tong MM, Hui JW. Comparison of clinical outcomes of tris-acryl microspheres versus polyvinyl alcohol microspheres for uterine artery embolization for leiomyomas: results of a randomized trial. J Vasc Interv Radiol. 2011 Sep;22(9):1229-35.

Yuk JS, Ji HY, Kim KH, Lee JH. Single-port laparoscopically assisted-transumbilical ultraminilaparotomic myomectomy (SPLA-TUM) versus single port laparoscopic myomectomy: a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2015 May;188:83-7.

Irrelevant Outcomes

Healey S, Buzaglo K, Seti L, Valenti D, Tulandi T. Ovarian function after uterine artery embolization and hysterectomy. J Am Assoc Gynecol Laparosc. 2004 Aug;11(3):348-52.

Pourrat XJ, Fourquet F, Guerif F, Viratelle N, Herbreteau D, Marret H. Medico-economic approach to the management of uterine myomas: a 6-month cost-effectiveness study of pelvic embolization versus vaginal hysterectomy. Eur J Obstet Gynecol Reprod Biol. 2003 Nov 10;111(1):59-64.

Qu X, Cheng Z, Yang W, Xu L, Dai H, Hu L. Controlled clinical trial assessing the effect of laparoscopic uterine arterial occlusion on ovarian reserve. J Minim Invasive Gynecol. 2010 Jan;17(1):47-52.

Rashid S, Khaund A, Murray LS, Moss JG, Cooper K, Lyons D, et al. The effects of uterine artery embolisation and surgical treatment on ovarian function in women with uterine fibroids. BJOG. 2010 Jul;117(8):985-9.

Volkers NA, Hehenkamp WJ, Smit P, Ankum WM, Reekers JA, Birnie E. Economic evaluation of uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: results from the randomized EMMY trial. J Vasc Interv Radiol. 2008 Jul;19(7):1007-16.

Duplicate Publication

Brochner AC, Mygil B, Elle B, Toft P. Inflammatory response in patients undergoing uterine artery embolization as compared to patients undergoing conventional hysterectomy. Acta Radiol. 2009 Dec;50(10):1193-7.

Publication Not Retrievable

El Gantri R, Aya L, Gawass M. Morbidity of abdominal myomectomy when compared with abdominal hysterectomy in the management of uterine fibroids. Jamahiriya Medical Journal. 2010;10(2):123-9.

Other (protocols, conference abstracts, editorials)

Kim HS, Kim JW, Kim MK, Chung HH, Lee TS, Jeon YT, et al. A randomized prospective trial of the postoperative quality of life between laparoscopic uterine artery ligation and laparoscopy-assisted vaginal hysterectomy for the treatment of symptomatic uterine fibroids: clinical trial design. Trials [Internet]. 2009 [cited 2015 Jun 1];10(8). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2645389/pdf/1745-6215-10-8.pdf

Magos A, Al-Shabibi N. Prospective randomised trial comparing gonadotrophin-releasing hormone analogues with triple tourniquets at open myomectomy: authors' reply. BJOG. 2009;116(11):1532.

McPherson K, Manyonda I, Lumsden MA, Belli AM, Moss J, Wu O, et al. A randomised trial of treating fibroids with either embolisation or myomectomy to measure the effect on quality of life among women wishing to avoid hysterectomy (the FEMME study): study protocol for a randomised controlled trial. Trials [Internet]. 2014 [cited 2015 May 28];15:468. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4258053

Talbird SE, Bell KF, Graham JB, Deal LS, Mauskopf J. Cost-effectiveness analysis for treatment of symptomatic uterine fibroids among premenopausal women seeking to retain uterus [abstract]. Value Health. 2010;13(3):A183.

APPENDIX 5: CLINICAL EVIDENCE – CRITICAL APPRAISAL OF STUDIES

First author, publication year, country	Strengths	Limitations
Randomized controlled trials		
Brucker 2014, Germany[41]	• Patients were blinded • Interventions and outcomes were described • Loss to follow up was reported • Power calculation was conducted • COI was reported	• Unclear if the participants were representative of the entire population • Analysis was based on the patients who received allocated intervention
Manyonda 2012, United Kingdom[27]	• Interventions and outcomes were described • Loss to follow up was reported • ITT analysis was performed • Power calculation was conducted • COI was reported	• Unclear if the participants were representative of the entire population
Helal 2010, Egypt[34]	• Interventions and outcomes were described • Power calculation was performed • All patients completed the study, no lost to follow up	• Unclear if the randomization was conducted appropriately • Unclear if the participants were representative of the entire population • Unclear if ITT analysis was performed • Results were insufficiently reported, i.e. complications • COI was not reported
Ruuskanen 2010, Finland[21]	• Interventions and outcomes were described • Loss to follow up was reported • ITT analysis was performed • Funding source was reported	• Unclear if the randomization was conducted appropriately • Power calculation was not conducted • Unclear if the participants were representative of the entire population
Ambat 2009, India[35]	• Computer-generated random number • Interventions and outcomes were described	• No power calculation; 20 patients were enrolled in this study • Unclear if the participants were representative of the entire population

First author, publication year, country	Strengths	Limitations
		• Unclear if ITT analysis was performed • Loss to follow up was not reported • COI was not reported
Cunningham 2008, United States[36]	• Interventions and outcomes were described • Loss to follow up was reported • COI was reported	• Unclear if the randomization was conducted appropriately • Power calculation was not conducted • Unclear if ITT analysis was performed • Only preliminary results were available
Mara 2008, Czech Republic[28]	• Interventions and outcomes were described • Loss to follow up was reported • ITT analysis was performed • Funding source was reported	• Power calculation was not conducted • Unclear if the participants were representative of the entire population
Hald 2007, Norway[37]	• Interventions and outcomes were described • Loss to follow up was reported • Both ITT and per-protocol analysis were performed • Power calculation was conducted	• Unclear if the participants were representative of the entire population • The study had no sufficient power to detect between-group differences • Funding source was not reported
Hehenkamp 2005, Netherlands[22]	• Interventions and outcomes were described • Loss to follow up was reported • Power calculation was conducted • ITT analysis was performed • Funding source was reported	• Unclear if the participants were representative of the entire population
Pinto 2002, Spain[23]	• Interventions and outcomes were described • Power calculation was performed • ITT analysis was performed	• Data on most of the outcomes were analyzed based on the treatment that patient actually received • COI was not reported

First author, publication year, country	Strengths	Limitations
Non-randomized controlled trials		
Odejinmi 2015, United States[18]	• Interventions and outcomes were described • COI was reported	• Retrospective study • Unclear if patients in different intervention groups were recruited over the same period of time • Treatment was self-selected by the patient and physician • Baseline patient characteristics differed between groups • Sample size determination was reported • Unclear if the participants were representative of the entire population
Ikink 2014, Netherlands[40]	• Interventions and outcomes were described • Potential confounders were identified a priori • Loss to follow up was reported • COI was reported	• Patients in different intervention groups were recruited from different sites; unclear if patients were recruited over the same period of time • Sample size determination was not described • Imbalanced baseline patient characteristics between groups • Unclear if the participants were representative of the entire population
Mara 2012, Czech Republic[38]	• Prospective study • Patients were enrolled over same period of time • Interventions and outcomes were described • COI was reported	• Treatment was chosen based on patient's preferences • Sample size determination was not reported • Imbalanced baseline patient characteristics between groups • Unclear if the participants were representative of the entire population
Narayan 2010,	• Interventions and outcomes were	• Unclear if patients in different

First author, publication year, country	Strengths	Limitations
United States[29]	described • Potential confounders were identified a priori • Missing data imputation was performed • Long term data (≥ 5 years) were available	intervention groups were recruited over the same period of time • Treatment was self-selected by the patients • Some baseline patient characteristics were not comparable between groups • Per-protocol analysis was performed • Unclear if the participants were representative of the entire population • Funding source was not reported
Spies 2010, United States[17]	• Prospective study • Interventions and outcomes were described • Loss to follow up was reported • Sample size determination was reported • Funding source was reported	• Unclear if patients in different intervention groups were recruited over the same period of time • Treatment was self-selected by the patients • Some baseline patient characteristics were not comparable between groups • Per-protocol analysis was performed • Unclear if the participants were representative of the entire population
Brochner 2009, Denmark[24]	• Prospective study • Patients were enrolled over same period of time • Interventions and outcomes were described • COI was reported	• Treatment selection was made by the patients • Sample size determination was not reported • Baseline patient characteristics was not reported in details • Results were reported graphically, or briefly described without providing p values • Unclear if the participants were

First author, publication year, country	Strengths	Limitations
		representative of the entire population
Dutton 2007, United Kingdom[25]	• Large clinical study with long term effectiveness and safety data • Interventions and outcomes were described • Potential confounders were identified a priori • Missing data were estimated using various methods • Sample size determination was described • Funding source was reported	• Retrospective study • Patients in different intervention groups were recruited over the different period of time • Some baseline patient characteristics were not comparable between groups
Goodwin 2006, United States[30]	• Prospective study • Patients were enrolled over same period of time • Interventions and outcomes were described • Independent committee assisted in results interpretation • ITT analysis was performed • Funding source was reported	• Treatment was selected by patients and physicians according to the standard of care at respective site • Sample size determination was not reported • imbalanced baseline patient characteristics between groups • Unclear if the participants were representative of the entire population
Siskin 2006, United States[31]	• Prospective study • Patients were enrolled over same period of time • Interventions and outcomes were described • Independent committee was responsible for adverse events review • All images were evaluated by a central core laboratory • ITT analysis was performed • Funding source was reported	• Sample size determination was not reported • imbalanced baseline patient characteristics between groups • Unclear if the participants were representative of the entire population
Holub 2006, Czech	• Prospective study	• Data on 34 patients were presented

First author, publication year, country	Strengths	Limitations
Republic[39]		• Patient characteristics were not reported in details • No sufficient details of data analysis
Spies 2004, United States[26]	• Prospective study • Interventions and outcomes were described • Funding source was reported	• Sample size determination was not reported in details; no power calculation • Unclear if patients in the two treatment groups were enrolled over same period of time • imbalanced baseline patient characteristics between groups • no information of loss to follow up • Unclear if the participants were representative of the entire population
Razavi 2003, United States[32]	• Interventions and outcomes were described • Patients in the two treatment groups were enrolled over the same period of time • Sample size determination was reported • ITT analysis was performed	• Retrospective study • Some baseline patient characteristics were not comparable between groups • No information on loss to follow up • Unclear if the participants were representative of the entire population • Funding source was not reported
Broder 2002, United States[33]	• Interventions and outcomes were described • Patients in the two treatment groups were enrolled over the same period of time • COI was reported	• Retrospective study • Insufficient power to detect significant difference in the primary outcome • imbalanced baseline patient characteristics between groups • Unclear if the participants were representative of the entire population
Sawin 2000,	• Interventions and outcomes were described	• Retrospective study • Unclear if patients in the two

First author, publication year, country	Strengths	Limitations
United States[19]	• Sample size calculation was described	treatment groups were enrolled over the same period of time • imbalanced baseline patient characteristics between groups • Unclear if the participants were representative of the entire population • COI was not reported
Iverson 1996, United States[20]	• Interventions and outcomes were described • ITT analysis was performed	• Retrospective study • Patients in the two treatment groups were enrolled over a wide range period of time • imbalanced baseline patient characteristics between groups • Unclear if the participants were representative of the entire population • COI was not reported

COI=conflict of interest; ITT=intention-to-treat

APPENDIX 6: CLINICAL EVIDENCE – STUDY CHARACTERISTICS

Studies (first author, year, country)	Study design (RCT/non-RCT, follow-up period)	Population (# in each arm and total)	Intervention and comparators	Key outcomes
Myomectomy versus Hysterectomy				
RCTs (no studies)				
Non-RCTs				
Odejinmi 2015, United Kingdom[18]	Retrospective cohort study. Choice of treatment was decided by the patient and surgeon.	Women undergoing laparoscopic MYO or HYS for UF. Exclusion: uterine size > 28 weeks or presence of > 10 fibroids in the MYO group. N=400 - MYO 216 - HYS 184	- laparoscopic MYO - laparoscopic HYS	Peri-operative morbidity
Sawin 2000, United States[19]	Single-center retrospective cohort study	All women who underwent abdominal MYO and an equal number of women who underwent abdominal HYS. The procedure was the primary procedure and not incidental to a more involved operation. Exclusion: if the surgery involved a malignancy, pregnancy, gynecologic infection or performed on an emergency basis. N=394 - MYO 197 - HYS 197	- abdominal MYO - abdominal HYS	Perioperative morbidity (febrile morbidity, hemorrhage, unintended major surgical procedures, life-threatening events and rehospitalisation).
Iverson 1996, United States[20]	Single-center retrospective cohort study.	All women with hospital procedure codes for total abdominal HYS and MYO, from May 1988 through May 1993 were identified and included. Excluded: age > 45 years, surgery for conditions other than UF and intended vaginal HYS. N=177	- abdominal MYO (vasopressin injection was used in 95% of MYO) - total abdominal HYS	Peri-procedural complications: blood loss, febrile morbidity, organ injuries.

		- MYO 103 - HYS 89		
Uterine Artery Embolization versus Hysterectomy				
RCTs				
Ruuskanen 2010, Finland[21]	Single-center RCT, 2-year follow up.	Symptomatic UF, severe enough to consider HYS. Exclusion: fertility preservation, myoma suitable for hysteroscopic MYO. N=57 - MYO 27 (93% technical success) - HYS 30 (81% technical success)	- UAE - HYS (type and route of access were not standardized)	Symptom improvement, complications, re-interventions and satisfaction.
Hehenkamp 2005 (EMMY), the Netherlands[22,42-44,59,60]	Multicenter RCT, up to 5 years follow-up data after the primary intervention were presented.	Premenopausal women with symptomatic ultrasound-confirmed UF that were eligible for HYS Excluded: submucosal fibroids with 50% of diameter within the uterine cavity or dominant pedunculated serosal fibroids were present. N=177 - UAE 88 (88.9% technical success) - HYS 89 (100% technical success)	- UAE - HYS via different routes (84% abdominal)	Menorrhagia after 2 years, complications, HRQOL (measured by SF-36, EuroQol 5D, HUI-3, UDI, IIQ, DDI and SAQ), duration of hospital stay, re-intervention, patient satisfaction.
Pinto 2002, Spain[23]	Single-center RCT, patients were followed up to 2 years.	Women with bleeding UF who were candidates for HYS. Excluded: who wished to maintain fertility, UF > 10 cm in diameter. N=57 - UAE 38 (1 crossovered to HYS) - HYS 19 (3 crossovered to UAE)	- UAE - abdominal HYS	Length of hospital stay, change in bleeding, change in dominant UF volume, complications, patient satisfaction.
Non-RCTs				
Brochner 2009, Denmark[24]	Single-center prospective study.	Women scheduled for HYS or UAE. The treatment was decided by the patient prior to inclusion in the study.	- UAE - abdominal HYS	Inflammatory markers, patient satisfaction, hospital stay,

		Excluded: patients treated with steroids, with rheumatologic disease/diabetes/ongoing malignant disease. N=40 - UAE 20 - HYS 20		
Dutton 2007 (HOPEFUL), United Kingdom[25,48]	Multi-center retrospective cohort study. The mean follow up in the UAE groups was 4.6 years, and 8.6 years in the HYS group.	Women with symptomatic UFs and received UAE from 1996 to 2002 or HYS from 1994 to 1995 in 18 UK NHS hospital trusts. No exclusions by age, other medical conditions or any other variables. N=1108 - UAE 649 - HYS 459	- UAE - HYS (total abdominal 86.7%)	Safety (severe/ major/ minor complications), treatment effect (resolution of fibroid symptoms, patient satisfaction, further treatments for continuing or recurrent symptoms, pregnancy outcomes after UAE).
Spies 2004, United States[26]	Multi-center prospective study, patients were followed up to 1 year.	Women aged ≥ 30 years and ≤ 50 years with symptomatic UF. Women in the UAE group would be excluded if had submucosal UF with > 50% of their diameter within the uterine cavity or dominant pedunculated serosal UF. N=152 - UAE 102 - HYS 50	- UAE - HYS via various routes	Change in bleeding (measured with a menorrhagia questionnaire, UAE arm only), change in other symptoms, general HRQOL (measured with SF-12), length of hospital stay, AEs, patient satisfaction.
Uterine Artery Embolization versus Myomectomy				
RCTs				
Manyonda 2012 (FUME), United Kingdom[27]	Single-center RCT. Patients were followed for at least 1 year.	Premenopausal women with symptomatic UF, desired uterine preserving treatment, fibroid ≥ 4 cm in diameter. Exclusion: pedunculated fibroid, the fibroid mass extended beyond the level of umbilicus, were pregnant or actively planning or trying to conceive.	- UAE - open abdominal MYO	HRQOL (measured by UFS-QOL), hospital stay, complications and re-intervention.

		N=163 - UAE 82 (97% technical success), 8 withdrawals - MYO 81, 8 withdrawals		
Mara 2008, Czech Republic[28,61]	Single-center RCT. Mean follow-up in the study was 24.9 months.	Age < 40 years, planned pregnancy, ultrasound-verified intramural UF of ≥ 4 cm. Exclusion: nonintramural localization of the main UF, UF of ≥ 12 cm by ultrasound or uterus greater than the 4th month of pregnancy by palpation, or with previous UF treatment (MYO, UAE or hormonal therapy). N=121 - UAE 58 (89.7% technical success) - MYO 63 (92.1% technical success)	- UAE - abdominal MYO, open or laparoscopy	Peri-procedural complications, early post-procedural (first 30 days after procedure) complications and late post-procedural (> 30 days after procedure); reproductive outcomes, re-intervention, symptom relief and length of hospital stay. The preliminary results from 63 patients in this study are not presented in this report.
Non-RCTs				
Narayan 2010, United States[29]	Single-center prospective cohort study. Patients were followed for at least 5 years	Women with symptomatic UF and received UAE or abdominal MYO. Patients were included if the procedure was performed 5 years prior to the study. N=185 - UAE 87 - MYO 98	- UAE - open abdominal MYO	Symptom evaluations (measured by SSS) and patient satisfaction.
Goodwin 2006, United States[30]	Multi-center prospective cohort study. Treatment was assigned based on a best treatment decision made by the patient and physician as per the standard of care at each site. 6-month follow-up for both groups, and 1-year follow-up in UAE group	Age ≥ 30 years, Ultrasound or MRI-confirmed symptomatic UF (severe enough to warrant therapy). Patients with a UFQoL score ≥ 90 at baseline was excluded unless she planned to undergo MYO for infertility. Patients with hysteroscopically resectable UFs were excluded. Patients in the UAE group would be excluded if they wished to become pregnant in the future. N=209	- UAE - Abdominal MYO	Improvement in the UFQoL score from baseline to 6 months postoperatively, adverse events, overall HRQOL (instrument not specified), change in size of the dominant UF, uterine volume change, menstrual bleeding changes (with Ruta scale) and hospitalization days. Some outcomes (UFQoL, bleeding changes, AEs, pregnancies and

	only.	- UAE 149 (using irregularly shaped particles: "Contour PVA Emboli") - MYO 60		fibroid treatments) were followed up to 1 year for UAE patients only.
Siskin 2006, United States[31]	Multi-center prospective cohort study. Treatment was assigned on the basis of treatment decisions made by the patients and physician according to the standard of care at each site. 6-month follow-up for MYO; 2-year follow-up for UAE	Age ≥ 30 years, MRI-confirmed symptomatic UF, regular menstrual cycles, have not had any drug treatments for UF within 3 months of the procedure. Patients with a UFQoL score ≥ 90 at baseline was excluded unless she planned to undergo MYO for infertility. Patients in the UAE group would be excluded if they wished to become pregnant in the future, severe contrast agent allergy or pedunculated subserosal UF. N=146 - UAE 77 (using spherical embolic agent: "Contour SE Microspheres") - MYO 69 This study was overlapped with the Goodwin 2006 study.[30] Most of the patients in the MYO group in Siskin 2006 study[31] has been described in the Goodwin study. Patients in the UAE group were using a different embolic agent for embolization. The Siskin study had longer follow-up period.	- UAE - abdominal MYO	Improvement in the UFQoL score from baseline to 6 months postoperatively, AE, changes in tumor symptom scores, menorrhagia bleeding scores, change in uterine volume and UF size, additional treatment and pregnancy. Some outcomes were measured at months 12 and 24.
Razavi 2003, United States[32]	Single-center retrospective study Mean follow-up time: UAE 14.3 months; MYO 14.6 months	Women with symptomatic UF and had strong desire to avoid HYS. N=111 - UAE 67 - MYO 44	- UAE - Abdominal MYO	Successful symptom control (reporting category 5 or 6 in a scale), major AEs (leading to death, additional procedures, prolongation of hospital stay, any procedure-related undesirable outcome requiring treatment or clinic visits ≤ 30 days of the index procedure), and bleeding complications requiring nonautologous blood transfusion. Secondary

				outcomes: hospital stay and secondary interventions.
Broder 2002, United States[33]	Single-center retrospective study Patients were surveyed 37-59 months after the primary procedure.	Women with symptomatic UF in one institution, and underwent UAE or MYO. N=81 - UAE 51 - MYO 30	- UAE - Abdominal MYO	Success/failure (required additional invasive treatment, no improvement or worsening of the overall symptoms score, or patient dissatisfaction) of the procedure at the time of survey, symptom improvement (using an investigator-developed scale), patient satisfaction and re-intervention.
Uterine Artery Embolization versus Uterine Artery Occlusion				
RCTs				
Helal 2010, Egypt[34]	Single-center RCT. Patients were followed for 1 year.	Premenopausal women with symptomatic UF and did not desire further pregnancy. Excluded: subserous UF that could be easily removed by laparoscopic surgery, known adenomyosis, uterus size exceeded the umbilical level, submucous UF with a diameter of < 3.5 cm situated completely intracavitarily or with an intramural extension of > 50% N=96 (90 received treatment) - UAE 45 - UAO 45	- UAE - UAO via laparoscopy	Menstrual blood loss, postoperative complications, and re-interventions.
Ambat 2009, India[35]	Single-center RCT Patients were followed for 6 months.	Women with symptomatic UF, uteri size corresponded to 12-20 weeks of pregnancy. Excluded: had taken hormones during the last 3 months, and women had suspected submucosal UFs based on ultrasound scan. N=20 - UAE 10	- UAE - UAO via laparoscopy	Menstrual blood loss (measured by PBAC score), reduction in uterine and UF volumes, AEs and complications (pain, measured by a visual analog scale) following procedures.

		- UAO 10		
Cunningham 2008, United States[36]	Single-center double-blind RCT (patient, the study gynecologist and the team performing the follow-up interviews were blinded),	Premenopausal women with ultrasound-confirmed UF and associated heavy uterine bleeding, and seeking UAE for the treatment; eligible participants should have no desire for fertility for ≥ the next 3 years; AMSS score ≥ 22; at least 1 UF, which was submucosal and > 3 cm in diameter, or more than 3 in number. Excluded: use of GnRH in the last 3 months N=14 - UAE 8 - UAO 6	- UAE - UAO	Post-procedural pain, length of post-procedural institutional stay, bleeding symptoms (measured by AMSS)
Hald 2007, Norway[37,62]	Single-center RCT 6 months and 48 months follow up	Premenopausal women with symptomatic UF, and did not want to have HYS. Excluded: uterus size exceeded the umbilical level, submucous myoma < 3.5 cm and was completely intracavitarily or with an intramural extension of > 50%, and those wished to have children. N=58 - UAE 29 - UAO 29	- UAE - UAO via laparoscopy	Reduction of blood loss from pre-treatment to 6 months postoperatively (using the PBAC), symptom reduction, postoperative pain, complications, secondary interventions, and clinical failure (defined as persisting symptoms requiring secondary treatment or no improvement at month 6).
Non-RCTs				
Mara 2012, Czech Republic[38]	Single-center prospective study. Treatment was chose based on the patient's preferences. Mean length of follow-up was 45.5 months for the UAE group and 40.4 months for the UAO	Premenopausal women with symptomatic UF. UF ≥ 3cm in diameter. Excluded: > 40 years, submucous myomas largely prominent into cavity, largely subserous or pedunculated myoma, predominantly cervical myoma, myoma with no perfusion or atypical pelvic tumor or of suspicious appearance. Preference for MYO or HYS, or myoma suited for	- UAE - UAO via laparoscopy	Early post-procedural (first 30 days after procedure) complications including fever, infection, need for blood transfusion; late post-procedural (> 30 days after procedure) including uterine infection, requiring hormone replacement therapy, sudden severe uterine bleeding,

	group.	laparoscopic MYO. N=200 - UAE 100 (95% technical success) - UAO 100 (96% technical success)		emergent MYO or HYS, trans-cervical expulsion of myoma and uterine rupture; re-intervention; reproductive outcomes.
Holub 2006, Czech Republic[39]	Multi-center prospective study. Follow-up period was unclear.	Inclusion/ exclusion criteria NR. N=295 - UAE 102 (14 patients conceived) - UAO 195 (20 patients conceived)	- UAE - UAO	Pregnancy outcomes
Myomectomy versus Radiofrequency Thermal Ablation				
RCTs				
Brucker 2014,[41] **Hahn 2015,**[16] **Germany**	Single-center RCT with non-inferiority design, margin 16.5 hours. Patients were blinded to the treatment assignment. Patients were followed for 1 year. 5 years follow-up was planned.	Age ≥ 18 years, symptomatic UFs, uterine size ≤ 16 gestational weeks, UF < 10 cm in any diameter, desire uterine conservation. Excluded: high risk for or were known to have significant intra-abdominal adhesions, had taken any depot GnRH agonist ≤ 3 months prior to the screening, had pelvic radiation, cervical myoma; had UFs that were better treated via hysteroscopic methods. MYO was not performed on intramural myomas that were 1.0-1.5 cm in diameter, although this was not an exclusion criterion. N=51 - MYO 25 - RFVTA 26 (1 patient did not receive allocated treatment and was excluded from analysis)	- Laparoscopic MYO - Laparoscopic RFVTA	Length of hospital stay, procedure-related complications, symptom improvement (measured by OTE and MIQ), HRQOL (measured by UFS-QOL, EQ-5D), re-intervention for UF, and pregnancy outcomes.
Non-RCTs (no studies)				
Uterine Artery Embolization versus Hysterectomy versus Myomectomy				
RCTs (no studies)				
Non-RCTs				
Spies 2010, United States[17]	Multi-center prospective study, patients were	Premenopausal women aged ≥ 30 years and ≤ 50 years. Women in the UF treatment	- UAE	HRQOL measured by UFS-QOL and SF-36, length of

	followed up to 1 year.	groups had to be scheduled to undergo HYS, MYO or UAE. Women in the normal control group had no history of UF, had normal gynecologic examination with regular menstrual cycle at enrollment. N=375 - UAE 107 - HYS 106 - MYO 61 - normal control 101	- HYS, various types - MYO, various types - Normal control	hospital stay, AEs
Uterine Artery Embolization versus Magnetic Resonance-guided Focused Ultrasound Ablation				
RCTs (no studies)				
Non-RCTs				
Ikink 2014, Netherlands[40]	Single-center prospective study.	Premenopausal women treated with MRgFU or UAE. UF size ≤ 12 cm and number ≤ 5. N=119 -UAE 68 -MRgFU 51	-UAE -MRgFU	Symptom relief (measured by UFS-QOL), re-intervention.

AE=adverse event; AMSS=Aberdeen Menorrhagia Severity Scale (also known as Ruta Score); DDI=defecation distress inventory; GnRH=gonadotropin-releasing hormone; HRQOL=health-related quality of life; HYS=hysterectomy; IIQ=incontinence impact questionnaire; MIQ=Menstrual impact questionnaires; MRgFU=Magnetic resonance-guided focused ultrasound; MYO=myomectomy; N=number of patients; OL=open-label; OTE=Overall Treatment Effect Survey; PBAC=Pictorial Blood Loss Assessment Chart; RCT=randomized controlled trial; RFVTA=radiofrequency volumetric thermal ablation; SAQ=the Sexual Activity Questionnaire; SF-36=Medical Outcome Study Short Form 36; SSS=Symptom Severity Scale (of UFS-QOL, higher scores indicate more severe symptoms); UAE=uterine artery embolization; UAO=uterine artery occlusion; UDI=urogenital distress inventory; UF=uterine fibroid; UFQoL=the Uterine Fibroid Quality of Life Questionnaire (a scale of 0-100; 100 indicates the best outcome while 0 indicates the worst outcome); UFS-QOL=the Uterine Fibroid Symptom and Quality of Life questionnaire (consists of Symptom Severity scale and health-related quality of life questions. Higher scores in the former indicate greater symptom severity, while higher scores in the latter indicate better quality of life);

APPENDIX 7: CLINICAL EVIDENCE – STUDY RESULTS

Table 7-1. Patient Baseline Characteristics (Myomectomy *versus* Hysterectomy)

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment, n (%)
RCTs (no studies)						
Non-RCTs						
Odejinmi 2015[18]						
MYO (n=216)	38.0±5.4	26.7±5.0	0.54±0.97	Uterine size (weeks): 14.1±4.1	Menorrhagia: 43.0% Pain: 22.7% Pressure: 5.1% Infertility: 29.2%	C-section, MYO or laparotomy: 13.9%
HYS (n=184)	46.5±4.5	30.5±6.3	1.93±1.37	Uterine size (weeks): 17.1±5.9	Menorrhagia: 92.9% Pain: 3.8% Pressure: 3.3% Infertility: 0	C-section, MYO or laparotomy: 13.0%
Spies 2010[17]						
MYO (n=61)	40.6±5.6	27.2±6.7	Previous pregnancy: 36 patients (59.0%)	Uterus volume (ml): 430.86± SD371.62 Number of UF: ≤ 5: 43 patients (70.5%) > 5: 18 patients (29.5%) Size of dominant UF (cm): 5.9± SD3.3	NR	NR
HYS (n=106)	44.5±3.9	28.5±7.4	Previous pregnancy: 92 patients (87.6%)	Uterus volume (ml): 549.44± SD419.54 Number of UF: ≤ 5: 74 patients (69.8%) > 5: 25 patients (23.6%) Size of dominant UF (cm): 5.9± SD3.1	NR	NR
Sawin 2000[19]						
MYO (n=197)	36.1±5.5	NR	0.5± SD0.9	Uterine size: 14.4± SD5.0 weeks	Bleeding: 35.6% Pain: 38.7%	GnRH agonists: 9.1% Previous MYO: 7.1%

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment, n (%)
HYS (n=197)	43.9±5.9	NR	1.6± SD1.3	Uterine size: 15.6± SD4.9 weeks	Bleeding: 61.9% Pain: 30.8%	GnRH agonists: 10.2% Previous MYO: 11.7%
Iverson 1996[20]						
MYO (n=103)	34.4	NR	Gravidity: 0.9 Parity: 0.2	Uterine size: 11.5 weeks Volume of dominant UF (ml): 193.2	Bleeding: 18 patients (17.5%) Pain/dysmenorrhea: 6 patients (5.8%)	GnRH agonist: 57 patients (55.3%)
HYS (n=89)	39.2	NR	Gravidity: 1.8 Parity: 1.3	Uterine size: 15.2 weeks Volume of dominant UF (ml): 247.7	Bleeding: 44 patients (49.4%) Pain/dysmenorrhea: 10 patients (11.2%)	GnRH agonist: 21 patients (23.6%)

HYS=hysterectomy; MYO=myomectomy; NR=not reported; SD=standard deviation; UF=uterine fibroid;

Table 7-2. Results (Myomectomy *versus* Hysterectomy)

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
RCTs (no studies)										
Non-RCTs										
Odejinmi 2015[18]										
MYO (n=216)	NR	NR	NR	NR	NR	-Blood loss (ml): 316.2± SD232.9 -Transfusion: 5 (2.3%)	NR	NR	NR	2.12± SD0.98
HYS (n=184)	n/a	NR	n/a	NR	NR	-Blood loss (ml): 215.1± SD136.2 -Transfusion: 1 (0.5)	NR	NR	NR	1.81± SD0.64
P for between-group comparisons	n/a	NR	n/a	NR	NR	-Blood loss: < 0.0001 -Transfusion: NR	NR	NR	NR	=0.0003
Spies 2010[17]										
MYO (n=60)	NR	NR	NR	Month 12: SSS in UFS-QOL: 23.4± SD18.9;	Month 12: 23.4± SD18.9; HRQL total in UFS-QOL: 81.1± SD23.2 Month 12: SF-36 PCS: 52.2± SD8.2 SF-36 MCS: 46.9± SD11.9	AEs: 8 patients (13.3%)	NR	3 patients (5%)	NR	2.1±1.0
HYS (n=105)	n/a	NR	n/a	Month 12: SSS in UFS-QOL: 7.6± SD8.4	Month 12: HRQL total in UFS-QOL: 92.3± SD11.0 Month 12: SF-36 PCS: 52.3± SD8.7 SF-36 MCS:	AEs: 14 patients (13.3%)	n/a	4 patients (3.8%)	NR	1.9±1.3

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
					50.0± SD10.2					
P for between-group comparisons	n/a	NR	n/a	NR	HRQL total: < 0.01 SF-36 PCS and MCS: NR	> 0.05	n/a	NR	NR	NR
Sawin 2000[19]										
MYO (n=197)	NR	NR	NR	NR	NR	- Overall morbidity: 38.6%; - Febrile: 33.0% - Hemorrhage: 9.6% - Blood loss: 226.7± SD190.5 - Patient transfused: 18 (9.1%)	NR	NR	NR	3.96± SD2.1
HYS (n=197)	n/a	NR	n/a	NR	NR	- Overall morbidity: 40.1%; - Febrile: 25.9% - Hemorrhage: 14.2%; - Blood loss: 483.6± SD375.8 - Patient transfused: 25 (12.8%)	NR	NR	NR	4.42± SD 2.4
P for between-group comparisons	n/a	NR	n/a	NR	NR	- Overall morbidity: =0.75 - Febrile: =0.12 - Hemorrhage: =0.009 - Blood loss: =0.00001 - Patient	NR	NR	NR	=0.048

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
						transfused: =0.25				
Iverson 1996[20]										
MYO (n=103)	NR	NR	NR	NR	NR	- Blood loss (ml): 796 - Transfusion: 29 (28.2%) - Temperature ≥ 38C after 48 hr: 31 (32%)	NR	NR	NR	NR
HYS (n=89)	n/a	NR	n/a	NR	NR	- Blood loss (ml): 464 - Transfusion: 29 (32.6%) - Temperature ≥ 38C after 48 hr: 44 (49.4%)				
P for between-group comparisons	n/a	NR	n/a	NR	NR	95% CIs: - Blood loss: 121-545 - Transfusion: 0.8-1.8 - Temperature ≥ 38C (relative risk): 1.1-2.2				

AE=adverse event; CI=confidence interval; HRQOL=health-related quality of life; HYS=hysterectomy; MYO=myomectomy; n/a=not applicable; NR=not reported; SD=standard deviation; SSS=Symptom severity scale

Table 7-3. Patient Baseline Characteristics (Uterine artery embolization *versus* Hysterectomy)

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment (medical/surgical)
RCTs						
Ruuskanen 2010[21]						
UAE (n=27)	48.5±3.6	26.3±6.0	1.9±0.9	Number of UF: 1: 2 patients (8%) 2-4: 12 patients (44%) ≥ 5: 13 patients (48%) Uterus volume (ml): 422± SD242 Dominant UF volume (ml): 131±149 Location of UF: - intramural: 23 patients (85%) - submucosal: 1 patients (4%) - subserosal: 3 patients (11%)	-Menorrhagia: 18 (67%) -Pain: 7 (26%) -Urinary symptoms: 20 (74%) -Anemia: 10 (37%) -Pressure symptoms: 20 (74%)	Hormonal treatment: 13 (48.1%) MYO: 2 (10%)
HYS (n=30)	48.3±3.9	26.5±4.3	1.7±1.0	Number of UF: 1: 4 patients (13%) 2-4: 12 patients (40%) ≥ 5: 14 patients (47%) Uterus volume (ml): 438± SD308 Dominant UF volume (ml): 138±161 Location of UF: - intramural: 19 patients (63%) - submucosal: 5 patients (17%) - subserosal: 6 patients (20%)	-Menorrhagia: 25 (83%) -Pain: 16 (53%) -Urinary symptoms: 26 (87%) -Anemia: 13 (43%) -Pressure symptoms: 26 (87%)	Hormonal treatment: 18 (60%) MYO: 3 (7%)
Hehenkamp 2005 (EMMY)[42]						
UAE (n=88)	44.6±4.8	26.7±5.6	0: 30 (34.1%) ≥1: 58 (65.9%)	Uterine volume (cm^3, median [range]): 321 (31-3005) Number of UF (median [range]):	-Menorrhagia: 88 (100%) -Pain: 15 (17.0%)	-No treatment: 11 (12.5%) -Hormonal: 59 (67.0%)

				2 (1-20) UF volume (cm^3, median [range]): 59 (1-673)	-Urinary symptoms: 13 (14.8%) -Anemia: 43 (48.9%) -Pressure symptoms: 23 (26.1%)	-NSAIDs/ tranexaminacid: 45 (51.1%) -Iron-supplement/ blood transfusion: 50 (56.8%) -Surgical procedures: 17 (19.3%)
HYS (n=89)	45.4±4.2	25.4±4.0	0: 20 (22.5%) ≥1: 69 (77.5%)	Uterine volume (cm^3, median [range]): 313 (58-3617) Number of UF (median [range]): 2 (1-9) UF volume (cm^3, median [range]): 87 (4-1641)	-Menorrhagia: 89 (100%) -Pain: 14 (15.7%) -Urinary symptoms: 20 (22.5%) -Anemia: 42 (47.2%) -Pressure symptoms: 25 (28.1%)	-No treatment: 15 (16.9%) -Hormonal: 59 (66.3%) -NSAIDs/ tranexaminacid: 45 (51.1%) -Iron-supplement/ blood transfusion: 50 (56.8%) -Surgical procedures: 17 (19.3%)
Pinto 2002[23]						
UAE (n=38)	46.4±4.4	NR	Previous pregnancy: 2.6± SD1.2	Number of UF: 1.6± SD0.5 Location of UF: - intramural: 16 patients (42%) - submucosal: 15 patients (40%) - subserous: 7 patients (18%) UF volume (cm^3): 72.0± SD86	Menorrhagia: 37 patients (97%) Metrorrhagia: 19 patients (50%)	None: 23 (61%) Hormonal: 14 (37%) MYO: 1 (3%)
HYS (n=19)	44.6±5.0	NR	Previous pregnancy: 3.2± SD1.8	Number of UF: 1.6± SD0.5 Location of UF: - intramural: 13 patients (68%) - submucosal: 2 patients (11%) - subserous: 4 patients (21%) UF volume (cm^3): 113± SD138	Menorrhagia: 17 patients (90%) Metrorrhagia: 9 patients (47%)	None: 9 (47%) Hormonal: 10 (53%) MYO: 0
Non-RCTs						
Spies 2010[17]						

UAE (n=107)	43.2±3.7	28.4±6.5	Previous pregnancy: 77 (73.3%)	Uterus volume (ml): 579.54± SD339.85 Number of UF: ≤ 5: 63 patients (58.9%) > 5: 42 patients (39.3%) Size of dominant UF (cm): 6.0± SD2.3	NR	NR
HYS (n=106)	44.5±3.9	28.5±7.4	Previous pregnancy: 92 (87.6%)	Uterus volume (ml): 549.44± SD419.54 Number of UF: ≤ 5: 74 patients (69.8%) > 5: 25 patients (23.6%) Size of dominant UF (cm): 5.9± SD3.1	NR	NR
Brochner 2009[24]						
UAE (n=20)	The 2 groups were comparable in age, BMI and comorbidity. Data were not provided		NR	Average number of UF: 1.8 Average diameter of UF: 6.8 cm	NR	NR
HYS (n=20)			NR	Average number of UF: 1.6 Average diameter of UF: 7.5 cm		
Dutton 2007 (HOPEFUL)[25,48]						
UAE (n=649)	43.8±6.5	26.5±5.5	Nulliparous: 296 (45.6%) Multiparous: 328 (50.5%) Missing: 25 (3.9%)	Number of UF: 1-3: 155 patients (23.9%) > 3: 97 patients (14.9%) Volume of dominant UF (cm^3): 330.1± SD379.2 Maximum diameter of dominant UF (cm): 8.5±3.5 Location of UF: - submucosal: 44 patients (6.8%) - intramural: 130 (20.0%) - subserosal: 26 patients (4.0%)	Menstrual only: 133 patients (20.5%) Bulk only: 72 patients (11.1%) Both: 384 patients (59.2%)	Pelvic surgery: 169 patients (26.0%)

				- pedunculated: 6 (0.9%) - missing: 443 (68.3%)		
HYS (n=459)	46.5±6.8	26.7±4.9	Nulliparous: 65 (14.2%) Multiparous: 391 (85.2%) Missing: 3 (0.6%)	Number of UF: 1-3: 94 patients (20.5%) > 3: 50 patients (10.9%) Volume of dominant UF (cm^3): 289.0± SD400.6 Maximum diameter of dominant UF (cm): 6.5±3.9 Location of UF: - submucosal: 10 patients (2.2%) - intramural: 44 (9.6%) - subserosal: 12 patients (2.6%) - pedunculated: 12 (2.6%) - missing: 381 (83.0%)	Menstrual only: 173 patients (37.7%) Bulk only: 59 patients (12.9%) Both: 165 patients (35.9%)	Pelvic surgery: 65 patients (14.2%)
Spies 2004[26]						
UAE (n=102)	42.6± 4.0	NR	Previous pregnancy: 0: 19 (19%) ≥ 1: 83 (81%)	Uterus volume (ml): 689.4± SD466.1 Number of UF: 1: 27 patients (26%) > 1: 75 patients (73%) Size of dominant UF (ml): 146.8± SD158.5 Location of UF: - intramural: 61 patients (60%) - subserosal: 19 (19%) - submucosal: 17 patients (17%) - transmural: 11 patients (11%) - pedunculated: 2 (2%)	Self-assessment of menstrual flow: Extremely/ moderately heavy: 98 patients (96%) UF-related pain: 94 patients (93%) UF-related discomfort: 98 patients (97%) Urinary dysfunction: 93 patients (92%)	None: 53 (52%) Hormonal: 39 (39%) Invasive: 53 (53%)
HYS (n=50)	41.6±5.3	NR	Previous pregnancy: 0: 8 (16%)	Uterus volume (ml): 389.2± SD521.2	Self-assessment of menstrual flow: Extremely/	None: 35 (70%) Hormonal: 12 (24%) Invasive: 10 (20%)

			≥ 1: 42 (84%)	Number of UF: 1: 20 patients (40%) > 1: 29 patients (58%) Size of dominant UF (ml): 90.6± SD354.8 Location of UF: - intramural: 32 patients (64%) - subserosal: 8 (16%) - submucosal: 13 patients (26%) - transmural: 1 patient (2%) - pedunculated: 4 (8%)	moderately heavy: 42 patients (84%) UF-related pain: 47 patients (96%) UF-related discomfort: 44 patients (90%) Urinary dysfunction: 41 patients (84%)	

HYS=hysterectomy; MYO=myomectomy; NR=not reported; NSAID=nonsteroidal anti-inflammatory drug; SD=standard deviation; UAE=uterine artery embolization; UF=uterine fibroid;

Table 7-4. Results (Uterine artery embolization *versus* Hysterectomy)

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
RCTs										
Ruuskanen 2010[21]										
UAE (n=27)	Year-2: Substantial improvement in menorrhagia: 12/18 patients (67%)	Year-2: Substantial improvement in pressure symptoms: 19/20 patients (95%)	NR	Year-2: 22 patients (82%) reported substantial symptom relief	NR	Major complication: 0 Minor complication: 1 patient	NR	5 patients	24 patients (89%) would have chosen their performed treatment again.	NR
HYS (n=30)	Year-2: Substantial improvement in menorrhagia: 25/25 patients (100%)	Year-2: Substantial improvement in pressure symptoms: 18/26 patients (69%)	n/a	Year-2: 28 patients (93%) reported substantial symptom relief	NR	Major complication: 2 patients Minor complication: NR	NR	3 patients	29 patients (97%) would have chosen their performed treatment again.	NR
P for between-group comparisons	=0.002	=0.029	n/a	=0.173	NR	Major: =0.492	NR	NR	=0.336	NR
Hehenkamp 2005 (EMMY)[22,42-44,59,60,63]										
UAE (n=88)	2-year: 50/81 showed improvement or free of menorrhagia; 3 had no change in menorrhagia. 5-year: Of the 58 patients who still had uterus, 44 (75.9%) were free of menorrhagia	2-year: Bulk-related complaints eased in 66.2%; Moderate to greater improvement in pain: 84.9%	2-year: Uterine volume: ↓48.2% Fibroid size: ↓60.5%	NR	2-year change from baseline: *SF-36 MCS*: 5.80; *SF-36 PCS*: 9.42; *HUI-3*: 0.068; *EuroQol-5D*: 0.086; *UDI*: -17.03; *IIQ*: -7.14; *DDI*: -14.42; *SAQ* [c] (dimensions of pleasure/	Blood loss: 30.9 ml Pain (24 hr post intervention): Data were presented graphically Minor [a] complication (from procedure until 6-week visit): 64.2%	NR	2-year: 20/81 patients (24.7%) required re-interventions, including 19 secondary HYS, due to bilateral UAE failure or clinical failure during 2-year follow up	2-year: 74/81 (92%) patients were at least moderately satisfied. 5-year: 68/81 (84.0%) patients were at least moderately satisfied.	2.0± SD2.1

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
	or reported great or moderate improvement; 8 (13.8%) reported unchanged menstrual bleeding compared with baseline; 10 patients were menopause.				discomfort/ habit): 0.89/ -0.43/ 0.28. 5-year change from baseline: *SF-36 MCS*: 6.31; *SF-36 PCS*: 8.47; *UDI*: -10.70; *DDI*: -12.72.	Major [b] complication (from procedure until 6-week visit: 4.9%		2-5 year: 8 patients needed re-interventions, including 4 new secondary HYS In total, 28/81 (34.6%) patients required re-interventions after the primary intervention.		
HYS (n=89)	n/a	2-year: Bulk-related complaints eased in 69.2%; Moderate to greater improvement in pain: 78.0%	n/a	NR	2-year change from baseline: *SF-36 MCS*: 7.26; *SF-36 PCS*: 9.32; *HUI-3*: 0.094; *EuroQol-5D*: 0.102; *UDI*: -14.66; *IIQ*: 1.59; *DDI*: -5.39; *SAQ* (dimensions of pleasure/ discomfort/ habit): 1.18/ -0.49/ 0.22. 5-year change from	Blood loss: 436.1 ml Pain (24 hr post intervention): Higher pain scores, data were presented graphically Minor complication: 56.0% Major complication: 2.7%	n/a	2-year: 5/75 patients (6.7%) required re-interventions 2-5 year: 3 patients needed re-interventions In total, 8/75 (10.7%) patients required re-interventions after the primary intervention.	2-year: 66/75 (88%) patients were at least moderately satisfied. 5-year: 66/75 (88%) patients were at least moderately satisfied.	5.1± SD1.3

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
					baseline: *SF-36 MCS*: 6.87; *SF-36 PCS*: 7.20; *UDI*: -8.41; *DDI*: 0.01.					
P for between-group comparisons	n/a	2-year: Bulk-related symptoms change: =0.71; Moderate to greater improvement in pain: =0.30	n/a	NR	2-year: *SF-36 MCS*: =0.496; *SF-36 PCS*: =0.948; *HUI-3*: =0.462; *EuroQol-5D*: =0.620; *UDI*: =0.656; *IIQ*: =0.226; *DDI*: =0.072; *SAQ* (dimensions of pleasure/ discomfort/ habit): =0.74/ 0.88/ 0.74 5-year: *SF-36 MCS*: =0.806; *SF-36 PCS*: =0.468; *UDI*: =0.686; *DDI*: =0.010.	Blood loss: < 0.001 Pain (24 hr post intervention): =0.012 Minor complication: 0.38 Major complication: 0.68	n/a	NR	2-year: =0.02 5-year: =0.13	NR
Pinto 2002[23] e										
UAE (n=38)	Month 6: Cessation of bleeding: 31/36 patients (86%)	NR	Month 6: mean dominant UF volume ↓ 46%,	NR	NR	Intra-procedural complication: 10/40 patients (25%) ≤ 30 days post-	NR	2/37 patients (5.4%) received HYS due to UAE failure	28/36 patients (78%) indicated they would undergo the	1.71± SD1.59

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
			from 84.42 cm^3 at baseline to 45.46 cm^3			procedure complication: 29/40 patients (72%)			same treatment again; 5 (14%), no; 3 (8%), maybe.	
HYS (n=19)	n/a	NR	n/a	NR	NR	Intra-procedural complication: 4/20 patients (20%) ≤ 30 days post-procedure complication: 9/20 patients (45%)	NR	NR	15/17 patients (88%) indicated they would undergo the same treatment again; 2 (12%), no.	5.85± SD2.52
P for between-group comparisons	n/a	NR	n/a	NR	NR	Intra-procedural complication:=0.8 ≤ 30 days post-procedure complication: =0.05	NR	n/a	NR	< 0.001
Non-RCTs										
Spies 2010[17]										
UAE (n=105)	NR	NR	NR	Month- 12: SSS in UFS-QOL: 24.9± SD18.6	Month-12: HRQL total in UFS-QOL: 82.9± SD20.0 Month 12: SF-36 PCS: 51.6± SD6.7 SF-36 MCS: 50.8± SD8.9	AEs [d]: 7 patients (6.7%)	NR	0	NR	1.0± SD0.0
HYS (n=105)	n/a	NR	n/a	Month- 12: SSS in UFS-QOL:	Month-12: HRQL total in UFS-	AEs: 14 patients (13.3%)	n/a	4 patients (3.8%)	NR	1.9± SD1.3

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
				7.6± SD8.4	QOL: 92.3± SD11.0 Month 12: SF-36 PCS: 52.3± SD8.7 SF-36 MCS: 50.0± SD10.2					
P for between-group comparisons	n/a	NR	n/a	NR	HRQL total: < 0.01 SF-36 PCS and MCS: NR	> 0.05	n/a	NR	NR	NR
Brochner 2009[24]										
UAE (n=20)	NR	NR	NR	NR	NR	NR	NR	3 patients (15%)	17 patients (85%)	< 24 hours
HYS (n=20)	n/a	NR	n/a	NR	NR	NR	n/a	NR	NR	Median 4 days (range 3-5)
P for between-group comparisons	n/a	NR	n/a	NR	NR	NR	n/a	NR	NR	NR
Dutton 2007 (HOPEFUL)[25,48]										
UAE (n=649)	NR	NR	NR	Symptom relieved: 472 patients (85.2%)	NR	Total complications 114 patients (17.6%) Severe complications 1 patient (0.2%) Major complications 24 patients (3.7%) Minor	In 303 women who indicated that they wished or were uncertain of their wish for children, 27 women (8.5%) had 37 pregnancies: 19 live births (79% C-section), 15	119 patients (18.3%) needed further treatments for UF.	Recommend to friend: 510 patients (91.4%) Expectation fulfilled: 417 patients (73.5%)	NR

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
						complications 89 patients (13.7%) No complication: 535 (82.4%)	miscarriages, 2 ectopic pregnancies, and 1 termination.			
HYS (n=459)	n/a	NR	n/a	Symptom relieved: 352 patients (99.2%)	NR	Total complications 120 patients (26.1%) Severe complications 3 patients (0.7%) Major complications 49 patients (10.7%) Minor complications 68 patients (14.8%) No complication: 339 patients (73.9%)	n/a	n/a	Recommend to friend: 278 patients (85.5%) Expectation fulfilled: 343 patients (93.5%)	NR
P for between-group comparisons	n/a	NR	n/a	< 0.0001	NR	Total complications: = 0.001 Severe/ major complications: < 0.0001	n/a	n/a	Recommend to friend: =0.007 Expectation fulfilled: < 0.0001	NR
Spies 2004[26]										
UAE	*Self-assessed*	Month 6:	Month-3:	NR	*SF-12*	% of patients	NR	NR	% of	0.83

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
(n=102)	*blood loss score*: Month 3:↓55.6% (435.6± SD286.5 at baseline to 161.1± SD133.3); Month 6:↓58.1% (to 140.6± SD110.1) *Menorrhagia questionnaire*: Month 3: ↓46.8% (47.2± SD13.8 at baseline to 23.3± SD11.2); Month 6: ↓56.6% (to 19.2± SD8.3); Year-1: ↓61.3% (to 17.3± SD10.2).	% of patients with improved pelvic pain: 83%; % of patients with improved pelvic discomfort: 80%; improved urinary dysfunction: 75%. Year-1: % of patients with improved pelvic pain: 84%; % of patients with improved pelvic discomfort: 83%; improved urinary dysfunction: 80%.	↓45.8% Month-6: ↓54.0%		*Physical summary*: Month 3: ↑19.5% (45.1± SD8.2 at baseline to 52.3± SD6.0); Month 6: ↑22.3% (to 53.4± SD5.0); Year-1: ↑22.6% (to 53.6± SD6.1). *SF-12 Mental summary*: Month 3: ↑21.4% (45.4± SD11.5 at baseline to 52.0± SD7.5); Month 6: ↑24.5% (to 53.1± SD7.6); Year-1: ↑23.4% (to 52.6± SD7.9). Overall health status at Month 3: from 71.1 at	with ≥ 1 AE: 28 (27.5%) Complications ≤ 30 days of procedure: 17.6% Complications > 30 days of procedure: 12.7% Minor [f] complications: 29 patients (28.4%) Major [g] complications: 4 patients (3.9%)			moderately/very satisfied at Month-3: 89%; Month-6: 88%; Year-1: 90%.	

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
					baseline ↑to 83.6.					
HYS (n=50)	n/a	Month 6: % of patients with improved pelvic pain: 88%; % of patients with improved pelvic discomfort: 80%; improved urinary dysfunction: 73%. Year-1: % of patients with improved pelvic pain: 98%; % of patients with improved pelvic discomfort: 95%; improved urinary dysfunction: 79%.	n/a		*SF-12 Physical summary*: Month 3: ↑22.3% (43.0± SD9.9 at baseline to 50.7± SD6.6); Month 6: ↑26.0% (to 51.6± SD7.5); Year-1: ↑25.4% (to 51.4± SD6.9). *SF-12 Mental summary*: Month 3: ↑38.4% (40.6± SD11.1 at baseline to 51.7± SD10.5); Month 6: ↑32.3% (to 49.7± SD11.8); Year-1: ↑39.1% (to 51.1± SD11.2). Overall	% of patients with ≥ 1 AE: 25 (50%) Complications ≤ 30 days of procedure: 28% Complications > 30 days of procedure: 32% Minor complications: 26 patients (52%) Major complications: 6 patients (12%)	n/a	NR	% of moderately/very satisfied at Month-3: 94%; Month-6: 94%; Year-1: 97%.	2.3

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
					health status at Month 3: from 67.5 at baseline ↑to 86.1.					
P for between-group comparisons	n/a	Month 6: pelvic pain: =0.478; Pelvic discomfort: =1.0; urinary dysfunction: =0.841. Year-1: pelvic pain: =0.021; Pelvic discomfort: =0.055; urinary dysfunction: =0.819.	n/a		Overall health status at Month 3: =0.26	% of patients with ≥ 1 AE: =0.01 Early complications: =0.15 Late complications: =0.01 Major complications: =0.08	n/a	NR	All > 0.05	< 0.001

DDI=defecation distress inventory (higher score indicates worse outcome); HRQOL=health-related quality of life; HUI-3=the Health Utilities Index Mark 3 (higher score indicates favorable outcome); HYS=hysterectomy; IIQ= incontinence impact questionnaire (higher score indicates worse outcome); MCS=mental component summary (higher score indicates more favorable outcome); n/a=not applicable; NR=not reported; PCS=physical component summary (higher score indicates more favorable outcome); SAQ=the Sexual Activity Questionnaire (for dimensions of pleasure and habit, higher scores indicate more favorable outcome, while for dimension of discomfort, higher score indicates worse outcome); SD=standard deviation; SF-36: Short Form 36; SSS=Symptom severity scale (of UFS-); UAE=uterine artery embolization; UDI=urogenital distress inventory (higher score indicates worse outcome); UFS-QOL=the Uterine Fibroid Symptom and Quality of Life questionnaire (higher scores in Symptom Severity subscale indicate greater symptom severity; higher quality of life scores indicate better quality of life);

a "Minor complication" was listed for all non-major complications.

b "Major complication" was defined when the events were potentially life-threatening, could lead to permanent sequelae, or required surgical intervention.

c SAQ was only filled out by patients who were sexually active during the month before receiving the questionnaire. At 24-month, 52% of patients in UAE and 31% of patients in HYS groups were sexually active (p=0.118).

d "Adverse event" was not defined in the Spies study. This outcome included: required unanticipated medical therapy, delayed normal hospital discharge by > 24 h, need for emergency department evaluation or care, readmission to hospital, need for increased level of care (intensive care unit), additional surgery or invasive procedures, permanent injury or death.

e all outcomes were measured in per-treatment population, except for "length of hospital stay" where an intention-to-treat analysis was performed.

f "minor complication" was defined as no therapy, no consequences, requiring nominal therapy, observation but no consequences.

g "major complication" was defined as requiring therapy, minor hospitalization (< 48 hours), major therapy, unplanned increase level of care, prolonged hospitalization (≥ 48 hours), permanent adverse sequelae, or death.

Table 7-5. Patient Baseline Characteristics (Uterine Artery Embolization *versus* Myomectomy)

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment
RCTs						
Manyonda 2012[27]						
UAE (n=74)	44±5.7	NR	NR	Size of dominant fibroid (cm): 7.7± SD3.8 Uterine volume (ml): 973± SD946.8	UFS-QOL: -Symptom severity score: 59.8± SD22.1 -total HRQL: 40.2± SD23.1	NR
MYO (n=73)	43.2±5.3	NR	NR	Size of dominant fibroid (cm): 6.5± SD2.8 Uterine volume (ml): 707.1± SD511.8	UFS-QOL: -Symptom severity score: 55.9± SD21.2 -total HRQL: 46.4± SD22.5	NR
Mara 2008[28]						
UAE (n=58)	32.4	NR	Sterile: 11 patients (19.0%)	Size of dominant fibroid (mm): 62.3± SD19.1 Number of UF: 1: 39 (67.2%) ≥ 2: 19 (32.8%)	110 (90.9%) were symptomatic. No details were provided.	Previous UF treatment not allowed
MYO (n=63)	32.0	NR	Sterile: 24 patients (38.1%)	Size of dominant fibroid (mm): 59.8± SD16.5 Number of UF: 1: 40 (63.5%) ≥ 2: 23 (36.5%)		Previous UF treatment not allowed
Non-RCTs						
Spies 2010[17]						
UAE (n=107)	43.2±3.7	28.4±6.5	Previous pregnancy: 77 (73.3%)	Uterus volume (ml): 579.54± SD339.85 Number of UF: ≤ 5: 63 patients (58.9%) > 5: 42 patients (39.3%)	NR	NR

				Size of dominant UF (cm): 6.0± SD2.3		
MYO (n=61)	40.6±5.6	27.2±6.7	Previous pregnancy: 36 (59.0%)	Uterus volume (ml): 430.86± SD371.62 Number of UF: ≤ 5: 43 patients (70.5%) > 5: 18 patients (29.5%) Size of dominant UF (cm): 5.9± SD3.3	NR	NR
Narayan 2010[29]						
UAE (n=87)	42.9±7.8	NR	0.8±0.9	NR	SSS score: 53.6 (95%CI 44.9-62.4)	History of medication use: 29.2%
MYO (n=98)	37.7±5.8	NR	0.4±0.6	NR	SSS score: 48.6 (95%CI 40.7-56.4)	History of medication use: 63.4%
Goodwin 2006[30]						
UAE (n=149)	43.9, SD NR	NR	Previous pregnancy: 75.2%	Uterine volume (cm^3): 658.4 Number of UF: ≤ 5: 47 (31.5%) > 5: 102 (68.5%) Size of dominant fibroid (cm^3, mean±SD): 182.1±209.0 Location: Intramural: 88 (59.1%) Submucosal and submucosal pedunculated: 18 (12.1%) Subserosal and subserosal pedunculated: 39 (26.2%)	Abnormal bleeding: 77 (51.7%) Bulk/pressure: 38 (25.5%) Pelvic pain: 29 (19.5%)	NR
MYO (n=60)	38.2, SD NR	NR	Previous pregnancy: 48.3%	Uterine volume (cm^3): 590.6 Number of UF: ≤ 5: 27 (45.0%) > 5: 27 (45.0%)	Abnormal bleeding: 20 (33.3%) Bulk/pressure: 16 (26.7%)	NR

				Missing: 6 (10.0%) Size of dominant fibroid (cm^3, mean±SD): 226.9±196.4 Location: Intramural: 26 (43.3%) Submucosal and submucosal pedunculated: 5 (8.3%) Subserosal and subserosal pedunculated: 21 (35.0%)	Pelvic pain: 18 (30%)	
Siskin 2006[31]						
UAE (n=77)	43.9, SD NR	NR	Previous pregnancy: 80.5%	Uterine volume (cm^3): 706.4 (range 134-3101) Number of UF: ≤ 5: 19 patients (24.7%) > 5: 54 patients (70.2%) Missing: 4 patients (5.2%) Size of dominant fibroid (cm^3): 134.84± SD159.91 Location: Intramural: 45 (58.4%) Submucosal and submucosal pedunculated: 12 (15.6%) Subserosal and subserosal pedunculated: 15 (19.5%)	Abnormal bleeding: 53 patients (68.8%) Bulk/pressure: 11 patients (13.4%) Pelvic pain: 12 patients (15.6%)	NR
MYO (n=69)	37.8, SD NR	NR	Previous pregnancy: 50.7%	Uterine volume (cm^3): 618.0 (range 99.9-2131) Number of UF: ≤ 5: 32 patients (46.2%) > 5: 31 patients (44.9%) Missing: 6 patients (8.7%) Size of dominant fibroid (cm^3): 230.30± SD192.62	Abnormal bleeding: 21 patients (30.4%) Bulk/pressure: 20 patients (29.0%) Pelvic pain: 21 patients (30.4%)	NR

				Location: Intramural: 32 (46.4%) Submucosal and submucosal pedunculated: 5 (7.2%) Subserosal and subserosal pedunculated: 24 (34.8%)		
Razavi 2003[32]						
UAE (n=67)	44.2 (range 31-56)	NR	NR	NR	Bleeding: 52/62 patients (84%) Pelvic pain: 34/62 patients (55%) Mass effect: 37/62 patients (60%)	NR
MYO (n=44)	37.7 (range 28-28)	NR	NR	NR	Menorrhagia: 22/40 patients (55%) Pelvic pain: 26/40 patients (65%) Mass effect: 23/40 patients (58%)	NR
Broder 2002[33]						
UAE (n=51)	43.5 (range 27-66)	NR	NR	NR	Menorrhagia: 40 patients (78%) Abdominal/pelvic pain: 20 patients (39%) Overall symptom score: 13 (range 6-28)	Hormonal: 13 patients (25%) All had prior surgery. Prior MYO: 40 patients (78%)
MYO (n=30)	37.6 (range 28-45)	NR	NR	NR	Menorrhagia: 25 (83%) Abdominal/pelvic pain: 19 (63%) Overall symptom score: 15 (range 9-29)	Hormonal: 9 (30%) MYO: 1 (3%)

MYO=myomectomy; NR=not reported; SD=standard deviation; SSS=Symptom Severity Scale (of UFS-QOL); UAE=uterine artery embolization; UF=uterine fibroid;

Table 7-6. Results (Uterine Artery Embolization *versus* Myomectomy)

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
RCTs										
Manyonda 2012[27]										
UAE (n=74)	NR	NR	NR	Year-1: SSS: ↓ 30.4± SD25.3 from baseline	Year-1: Total HRQL: ↑ 32.3± SD28.8 from baseline	Minor: 9 patients (13.2%) Major: 2 patients (2.9%)	NR	9 patients (14.8%)	NR	2.0
MYO (n=73)	NR	NR	NR	Year-1: SSS: ↓ 37.6± SD27.2 from baseline	Year-1: Total HRQL: ↑ 39.9± SD27.3 from baseline	Minor: 8 patients (10.9%) Major: 6 patients (8%)	NR	3 patients (4%)	NR	6.0
P for between-group comparisons	NR	NR	NR	=0.13	=0.14	Minor: =0.4 Major: =0.28	NR	=0.067	NR	< 0.0001
Mara 2008[28]										
UAE (n=58)	NR	NR	Mean ↓ of diameter of dominant UF by ultra-sound: 31.7%	Symptom relief at month 6: 46/52 (88.5%)	NR	Peri-procedural complications: 4 patients (6.9%) Early post-procedural complications: 12 patients (20.7%) Late post-procedural complications: 8 patients (13.8%) Transfusion: 0	26 patients tried to conceive: 13 (50%) became pregnant, 5 (19.2%) had delivered. 5 deliveries: 0 preterm delivery, 3 C-sections, 1 postpartum hemorrhage, 0 fetal intrauterine growth restriction.	19 patients (32.8%), mean interval from initial UAE to re-intervention was 12.4 months.	NR	60.2± SD32.3 hours

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
MYO (n=63)	NR	NR	n/a	Symptom relief at month 6: 51/58 (87.9%)	NR	Peri-procedural complications: 5 patients (7.9%) Early post-procedural complications: 10 patients (15.9%) Late post-procedural complications: 8 patients (13.8%) Transfusion: 2 (3.2%)	40 patients tried to conceive: 31 (77.5%) became pregnant, 19 (47.5%) had delivered. 19 deliveries: 5 preterm delivery, 13 C-sections, 0 postpartum hemorrhage, 2 fetal intrauterine growth restriction.	2 patients (3.2%), 15- and 30-month after initial MYO, respectively.	NR	86.1± SD40.4
P for between-group comparisons	NR	NR	n/a	Symptom relief at month 6: > 0.05	NR	> 0.05 for peri/ early post-/late post-procedural complications and transfusion.	Became pregnant: > 0.05 Delivery: < 0.05 > 0.05 for all perinatal outcomes.	< 0.0001	NR	< 0.0001
Non-RCTs										
Spies 2010[17]										
UAE (n=105)	NR	NR	NR	NR	Month 12: - SSS in UFS-QOL: 24.9± SD18.6; - HRQL total in UFS-QOL: 82.9± SD20.0	AEs: 7 patients (6.7%)	NR	0	NR	1.0±0.0

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
					Month 12: - SF-36 PCS: 51.6± SD6.7 - SF-36 MCS: 50.8± SD8.9					
MYO (n=60)	NR	NR	NR	NR	Month 12: - SSS in UFS-QOL: 23.4± SD18.9; - HRQL total in UFS-QOL: 81.1± SD23.2 Month 12: - SF-36 PCS: 52.2± SD8.2 - SF-36 MCS: 46.9± SD11.9	AEs: 8 patients (13.3%)	NR	3 patients (5%)	NR	2.1±1.0
P for between-group comparisons	NR	NR	NR	NR	> 0.05 for all comparisons	> 0.05	NR	NR	NR	NR
Narayan 2010[29]										
UAE (n=87)	NR	NR	NR	SSS: ↓ from 53.6 pre-procedure to 15.0 post-procedure	NR	Transfusion: adjusted OR, UAE vs. MYO: 0.049 (95% CI: 0.006, 0.42)	NR	Adjusted OR, UAE vs. MYO: 0.97 (95% CI: 0.27, 3.52)	Adjusted OR, UAE vs. MYO: 1.36 (95% CI: 0.47, 3.96)	Adjusted OR, UAE vs. MYO: 0.0036 (95% CI: 0.0003, 0.0377)
MYO (n=98)	NR	NR	NR	SSS: ↓ from 48.6 pre-procedure to 22.6 post-procedure	NR		NR			
P for between-group	NR	NR	NR	NR	NR	Transfusion: =0.006	NR	NR	=0.57	=0.000

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
comparisons										
Goodwin 2006[30]										
UAE (n=149)	Change in mean menstrual bleeding scores from baseline: Month 3: -24.5 (-49.2%) Month 6: -26.6 (-55.2%) Year-1: -28.6 (-61.1%)	NR	Change from baseline: Month 3: -37.7% Month 6: -53.9%	NR	Month-6: 141 patients (94.6%) achieved a ≥ 5-point increase in UFQoL score Overall HRQOL: Significantly improved at month 6 from baseline in all domains.	% of patients with AEs: 33 (22.1%) Number of AEs: 53 in total, 24 (45.3%) were procedure-related. Major events [a]: 6, 3 were procedure-related.	Year-1: no pregnancy was reported.	3 (2.0%) Year-1: 2/120 required additional pharmaceutical therapy.	NR	23.8 hours, SD NR
MYO (n=60)	Change in mean menstrual bleeding scores from baseline: Month 3: -22.8 (-43.0%). Month 6: -24.1 (-46.1%).	NR	n/a	NR	Month-6: 55 patients (91.7%) achieved a ≥ 5-point increase in UFQoL score. Overall HRQOL: Significantly improved at month 6 from baseline in all domains.	% of patients with AEs: 24 (40%) Number of AEs: 43 in total, 22 (51.2%) were procedure-related. Major events: 1, procedure-related.	NR	1 (1.7%) converted to HYS at time of MYO	NR	61.6 hours, SD NR
P for between-group comparisons	> 0.05 for both month 3 and month 6	NR	n/a	NR	Overall HRQOL: > 0.05 for all comparison at month 6.	% of patients with AEs: =0.01 Major events: > 0.05	NR	NR	NR	< 0.0001
Siskin 2006[31]										
UAE (n=77)	Change in mean	NR	Change from	NR	*UFQoL*: - Month-6:	% of patients with AEs:	Year-1: No	Year-1: 3/71 patients	NR	22.0 hours

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
	menorrhagia bleeding scores from baseline: Month 3: `1-46.0% Month 6: -52.1% Year-1: -58.2% Year-2: 61.0%		baseline: Month 3: -38.5% Month 6: -43.7%		68 patients (88.3%) achieved a ≥ 5-point increase in UFQoL score - Year-1 and Year-2: Significant change from baseline scores in all measures, except for hot flashes. *Overall HRQOL*: Significantly improved from baseline in all domains.	20 patients (26.0%) Number of AEs: 26 in total, 12 (46.2%) were procedure-related – all minor [b].	pregnancy. Year-2: 2 unplanned pregnancy (1 spontaneous abortion, 1 elective termination)	required additional treatment (1 drug therapy, 2 HYS)		(range 2-47)
MYO (n=69)	Change in mean menorrhagia bleeding scores from baseline: Month 3: -40.0% Month 6: -43.7%	NR	n/a	NR	*UFQoL*: Month-6: 52 (75.4%) achieved a ≥ 5-point increase in UFQoL score. *Overall HRQOL*: Significantly improved from baseline in all domains.	% of patients with AEs: 29 patients (42.0%) Number of AEs: 53 in total, 30 (56.6%) were procedure-related – 28 were minor, 2 were major [a].	NR	1 (1.4%) patients converted to HYS during the baseline MYO	NR	60.2 hours (range 7-196)
P for between-group comparisons	NR				≥ 5-point increase in UFQoL: =0.041 No significant differences	% of patients with AEs: =0.041				NR

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
					found in the overall HRQOL measures between groups. P value NR.					
Razavi 2003[32]										
UAE (n=67)	Completely resolved or significantly improved: 48/52 patients (92%)	Completely resolved or significantly improved: 28/37 patients (76%)	NR	NR	NR	AEs: 7 patients (11%)	NR	5/62 patients (8%)	NR	0
MYO (n=44)	Completely resolved or significantly improved: 14/22 patients (64%)	Completely resolved or significantly improved: 21/23 patients (91%)	n/a	NR	NR	AEs: 10 patients (25%)	NR	4/40 patients (10%)	NR	2.9 (range 2-7)
P for between-group comparisons	< 0.05	< 0.05	n/a	NR	NR	< 0.05	NR	> 0.05	NR	< 0.05
Broder 2002[33]										
UAE (n=51)	NR	NR	NR	Median score improved: 6 points (range -3 to 15)	NR	NR	NR	15 (29%)	34/36 (94%) at least somewhat satisfied	NR
MYO (n=30)	NR	NR	NR	Median score improved: 5 points (range -1 to 23)	NR	NR	NR	1 (3%)	23/29 (79%) somewhat/very dissatisfied	NR

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
P for between-group comparisons	NR	NR	NR	=0.44	NR	NR	NR	=0.004	=0.06	NR

AE=adverse event; CI=confidence interval; HRQOL=health-related quality of life; HYS=hysterectomy; MYO=myomectomy; n/a=not applicable; NR=not reported; OR=odds ratio; SD=standard deviation; SSS=Symptom Severity Scale (of UFS-QOL); UAE=uterine artery embolization; UFS-QOL=the Uterine Fibroid Symptom and Quality of Life questionnaire (consists of Symptom Severity scale and health-related quality of life questions. Higher scores in the former indicate greater symptom severity, while higher scores in the latter indicate better quality of life);
a “Major event” was defined as requiring major therapy or increase in care beyond 48 hours, permanent adverse sequelae, or death.
b “minor event” was defined as not requiring therapy or result in any consequences, requiring nominal therapy including observational overnight admission, or requiring treatment and/or hospitalization for ≤ 48 hours without sequelae.

Table 7-7. Patient Baseline Characteristics (Uterine Artery Embolization *versus* Uterine Artery Occlusion)

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2 (median, range)	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment, n (%)
RCTs						
Helal 2010, Egypt[34]						
UAE (n=45)	The study indicated that the 2 groups were similar with respect to age, BMI and parity and baseline symptom. Data were not reported.			NR	The study indicated that the 2 groups were similar in baseline symptom. Data were not reported.	NR
UAO (n=45)				NR		NR
Ambat 2009[35]						
UAE (n=10)	40.8	NR	2.4± SD1.4	Dominant UF was intramural in all. Multiple UF: 9 patients (90%) UF volume (ml): 58.0 Uterine volume (ml): 222.7	-Menorrhagia: 10 (100%) -Dysmenorrhea: 2 (20%) -Bulk-related symptoms: 1 (10%) -PBAC score: 267.3	NR
UAO (n=10)	40.5	NR	2.9± SD1.0	Dominant UF was intramural in all. Multiple UF: 7 patients (70%) UF volume (ml): 38.4 Uterine volume (ml): 224.7	-Menorrhagia: 10 (100%) -Dysmenorrhea: 7 (70%) -Bulk-related symptoms: 1 (10%) -PBAC score: 444.9	NR
Cunningham 2008[36]						
UAE (n=8)	46.5 (range35-53)	NR	NR	Uterine volume (cm^3): 557.3 (range 225-1133)	AMSS score: 53 (range 51.1-76.7)	NR
UAO (n=6)	47.5 (range37-53)	NR	NR	Uterine volume (cm^3): 612.4 (range 225-1133)	AMSS score: 54 (range 51.1-69.8)	NR
Hald 2007[37]						
UAE (n=29)	42.5±4.3	23.0 (19.3-37.3)	nullipara: 11 (37.9%)	-Uterine volume (ml): 598 (171-1276) -Size of dominant UF (ml): 257 (35-530) -Submucous/ subserous/ transmural UF: 6/ 3/ 20	-Menorrhagia: 29 (100%) PBAC score: 358 (63-1257) -Bulk symptoms: 24 (82.8%)	NR

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2 (median, range)	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment, n (%)
				patients	-Hemoglobin (g/100 ml): 11.6±1.5	
UAO (n=29)	43.3±5.2	23.5 (20.2-39.2)	nullipara: 11 (37.9%)	-Uterine volume (ml): 557 (128-1921) -Size of dominant UF (ml): 137 (6-847) -Submucous/ subserous/ transmural UF: 6/ 6/ 17 patients	-Menorrhagia: 28 (96.6%) -PBAC score: 317 (108-1200) -Bulk symptoms: 20 (69.0%) -Hemoglobin (g/100 ml): 11.7±1.6	NR
Non-RCTs						
Mara 2012, Czech Republic[38]						
UAE (n=100)	33.1±3.7	25.2±5.0	NR	Number of UF: 2.4±2.4 Size of dominant UF (mm): 68.2± SD18.2 Volume of dominant UF: 188.7± SD39.6	NR	NR
UAO (n=100)	34.9±4.0	23.4±3.5	NR	Number of UF: 2.3±1.4 Size of dominant UF (mm): 48.3± SD11.1 Volume of dominant UF: 59.9± SD41.2	NR	NR
Holub 2006, Czech Republic[39]						
UAE (n=14 conceived)	NR					
UAO (n=20 conceived)						

AMSS=Aberdeen Menorrhagia Severity Scale; HYS=hysterectomy; MYO=myomectomy; NR=not reported; PBAC=Pictorial Bleeding Assessment Chart; SD=standard deviation; UAE=uterine artery embolization; UAO=uterine artery occlusion; UF=uterine fibroid

Table 7-8. Results (Uterine Artery Embolization *versus* Uterine Artery Occlusion)

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
RCTs										
Helal 2010[34]										
UAE (n=45)	Year-1: bleeding reduction in 40 patients (88.9%) Year-1 mean reduction in bleeding: 91.9%.	Year-1: pressure reduction in 36 patients (80%)	NR	NR	NR	NR	NR	NR	NR	NR
UAO (n=45)	Year-1: bleeding reduction in 39 patients (86.7%) Year-1 mean reduction in bleeding: 93.3%.	Year-1: pressure reduction in 35 patients (80%)	NR	NR	NR	NR	NR	NR	NR	NR
P for between-group comparisons	Number of patients reporting bleeding reduction: =0.69	=0.88	NR	NR	NR	NR	NR	NR	NR	NR
Ambat 2009[35]										
UAE (n=10)	NR	NR	Month-3:	Month-3:	NR	Post-operative	NR	NR	NR	3.5

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
			UF volume ↓15.8% Month 6: UF volume ↓43%	Mean PBAC score ↓47.3% Month 6: Mean PBAC score ↓59.6%		pain score: 2.75				(range 2-7)
UAO (n=10)	NR	NR	Month-3: UF volume ↓34.3% Month 6: UF volume ↓33.6%	Month-3: Mean PBAC score ↓69.2% Month 6: Mean PBAC score ↓41%	NR	Post-operative pain score: 6.5	NR	NR	NR	3.5 (range 2-10)
P for between-group comparisons	NR	NR	Month-3: =0.075 Month-6: =1.0	Month-3: =0.165 Month-6: =0.436	NR	=0.0002	NR	NR	NR	=1.0
Cunningham 2008[36]										
UAE (n=8)	NR	NR	NR	Month 3: Mean AMSS score ↓58%	NR	Post-procedural pain score: 5± SD3.2	NR	NR	NR	6± SD0.7
UAO (n=6)	NR	NR	NR	Month 3: Mean AMSS score ↓63%	NR	Post-procedural pain score: 1± SD1.5	NR	NR	NR	1± SD0.4

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
P for between-group comparisons	NR	NR	NR	NR	NR	=0.03	NR	NR	NR	=0.09
Hald 2007[37]										
UAE (n=29)	Month 6: Bleeding reduction in 26 patients (89.7%)	Month-6: Reduction in 20 patients (69.0%)	Month-6: % reduction in dominant UF volume: 62.8± SD27.0 (based on 26 patients)	Symptom-free at month-6: 20 (69.0%) Month-3: Mean PBAC score ↓45% Month 6: Mean PBAC score ↓52%	NR	Pain after UAE measured by VAS: 2.41±SEM0.27 cm AEs during hospitalization: 4 patients (13.8%) AEs from discharge to month 6: 15 patients (51.7%)	NR	7 patients (24.1%)	Partly or totally satisfied: 27 (93.1%)	Average 57 hours (range 24-108)
UAO (n=29)	Month-6: Bleeding reduction in 25 patients (86.2%)	Month-6: Reduction in 17 patients (58.6%)	Month-6: % reduction in dominant UF volume: 55± SD22.1 (based on 22 patients)	Symptom-free at month-6: 15 (51.7%) Month-3: Mean PBAC score ↓47% Month-6: Mean PBAC score ↓53%	NR	Pain after UAE measured by VAS: 1.00±SEM0.27 cm AEs during hospitalization: 3 patients (10.3%) AEs from discharge to month 6: 9 patients (31.0%)	NR	6 patients (20.7%)	Partly or totally satisfied: 24 (93.1%)	Average 46 hours (range 24-72)

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
P for between-group comparisons	=0.69	=0.88	=0.083	Symptom-free: =0.18	NR	Pain: =0.026	NR	NR	=0.23	=0.001
Non-RCTs										
Mara 2012, Czech Republic[38]										
UAE (n=100)	NR	NR	Based on 90 patients, month 6: ↓ in diameter of dominant UF: 28.5% ↓ in volume of dominant UF: 53.0%	Patients with persistent symptoms at month 6: 7 (7%) Patients with symptom recurrence after month 6: 3 (3%)	NR	Overall complications: 28 events Peri-procedural complications: 1 event Early post-procedural complications: 19 events Late post-procedural complications: 8 events	Number of pregnant women: 29/42 (69.0%) Number of deliveries: 23/42 (54.8%) Number of post-procedural sterility: 13/42 (31.0%) Mean gestation week in women who delivered: 38.1± SD1.6 Preterm delivery: 1/23 (4.3%) C-section rate: 78.3%	39 patients (39%) Re-intervention due to failure, recurrence or complication: 12 patients (12%)	NR	2.4± SD1.1
UAO (n=100)	NR	NR	Based on 92 patients,	Patients with persistent	NR	Overall complications: 11 events	Number of pregnant women: 32/48	15 patients (15%)	NR	2.3±0.8

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
			month 6: ↓ in diameter of dominant UF: 22.3% ↓ in volume of dominant UF: 39.0%	symptoms at month 6: 8 (8%) Patients with symptom recurrence after month 6: 3 (3%)		Peri-procedural complications: 1 event Early post-procedural complications: 8 events Late post-procedural complications: 2 events	(66.7%) Number of deliveries: 22/48 (45.8%) Number of post-procedural sterility: 16/48 (33.3%) Mean gestation week in women who delivered: 38.0± SD3.5 Preterm delivery: 2/22 (9.1%) C-section rate: 78.3%	Re-intervention due to failure, recurrence or complication: 10 patients (10%)		
P for between-group comparisons	NR	NR	↓ in diameter and volume of UF: > 0.05	> 0.05	NR	Overall: =0.002 Peri-procedural: > 0.05 Early: =0.023 Late: =0.048	All > 0.05	Number of patients required re-intervention: =0.001	NR	> 0.05
Holub 2006[39]										
UAE (n=14 conceived)	NR	NR	NR	NR	NR	NR	-Number of pregnancy: 17 -Abortion: 7/16 (43.7%) -Preterm delivery: 1	NR	NR	NR

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
							(12.5%) -C-section: 6 (75%) -mean gestational age: 38.3 weeks			
UAO (n=20 conceived)	NR	NR	NR	NR	NR	NR	-Number of pregnancy: 22 -Abortion: 3/20 (15%) -Preterm delivery: 2 (14.2%) -C-section: 8 (57.2%) -mean gestational age: 38.8 weeks	NR	NR	NR
P for between-group comparisons	NR	NR	NR	NR	NR	NR	Abortion: < 0.05. All others: > 0.05	NR	NR	NR

AMSS=Aberdeen Menorrhagia Severity Scale; HRQOL=health-related quality of life; n/a=not applicable; NR=not reported; PBAC=Pictorial Bleeding Assessment Chart; SD=standard deviation; SEM=standard error of the mean; UAE=uterine artery embolization; UAO=uterine artery occlusion; VAS=visual analog scale

Table 7-9. Patient Baseline Characteristics (Uterine Artery Embolization *versus* Magnetic Resonance-guided Focused Ultrasound)

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment
RCTs (no studies)						
Non-RCTs						
Ikink 2014[40]						
UAE (n=68)	43 (IQR 41-46)	NR	NR	Number of UF: 1: 23 patients (34%) > 1: 45 patients (66%) Dominant UF volume (cm^3): 166 (IQR 65-236) Maximum diameter of dominant UF (cm): 7.2 (IQR 5.5-8.4) Uterus volume (cm^3): 486 (IQR 347-689) Location of UF: - intramural: 38 patients (56%) - subserosal: 8 (12%) - submucosal: 22 patients (32%)	Menorrhagia: 63 patients (93%) Bulky symptoms: 50 patients (74%) Pain: 31 patients (46%) UFS-QOL: - tSSS: 65.3 (IQR 56.3-74.2) - total HRQOL: 48.5 (IQR 33.8-65.1)	NR
MRgFU (n=51)	46 (IQR 43-49)	NR	NR	Number of UF: 1: 12 patients (24%) > 1: 39 patients (76%) Dominant UF volume (cm^3): 273 (IQR 142-478) Maximum diameter of dominant UF (cm): 8.5 (IQR 6.5-10.7) Uterus volume (cm^3): 792 (IQR 454-1104) Location of UF:	Menorrhagia: 37 patients (73%) Bulky symptoms: 47 patients (92%) Pain: 36 patients (71%) UFS-QOL: - tSSS: 53.1 (IQR 40.6-68.8) - total HRQOL: 60.3 (IQR 40.4-81.0)	NR

				- intramural: 30 patients (59%) - subserosal: 13 (25%) - submucosal: 8 patients (16%)		

IQR=interquartile range; MRgFU=Magnetic resonance-guided focused ultrasound; NR=not reported; SD=standard deviation; tSSS=transformed Symptom Severity Score (higher scores indicate more severe symptoms); UAE=uterine artery embolization; UF=uterine fibroid;

Table 7-10. Results (Uterine Artery Embolization *versus* Magnetic Resonance-guided Focused Ultrasound)

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL (mean±SD)	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day (mean±SD)
RCTs										
Ikink 2014[40]										
UAE (n=68)	NR	NR	Month-3: ↓ in UF volume: 43.3% (IQR 29.9-65.0)	Month-3: tSSS ↓ from 65.3 at baseline to 21.9 (IQR 9.4-34.4)	Month-3: Total HRQOL score in UFS-QOL: ↑from 48.5 at baseline to 85.4 (IQR 75.2-94.6)	13 events.	NR	Year-1: 3 patients (4.5%) Median follow-up of 24 months: 5 patients (7%)	NR	NR
MRgFU (n=51)	NR	NR	Month-3: ↓ in UF volume: 17.2% (IQR 3.2-34.5)	Month-3: tSSS ↓ from 53.1 at baseline to 34.4 (IQR 21.9-46.9)	Month-3: Total HRQOL score in UFS-QOL: ↑from 60.3 at baseline to 81.5 (IQR 57.6-90.3)	No complications or AEs reported.	NR	Year-1: 18 patients (35%) Median follow-up of 15 months: 24 patients (47%)	NR	NR
P for between-group comparisons	NR	NR	< 0.001	< 0.001	< 0.001	NR	NR	Year-1: =0.002	NR	NR
Non-RCTs (no studies)										

AE=adverse event; HRQOL=health-related quality of life; IQR=interquartile range; MRgFU=Magnetic resonance-guided focused ultrasound; n/a=not applicable; NR=not reported; SD=standard deviation; UAE=uterine artery embolization; UFS-QOL=the Uterine Fibroid Symptom and health-related Quality of Life;

Table 7-11. Patient Baseline Characteristics (Myomectomy *versus* Radiofrequency Volumetric Thermal Ablation)

Studies (first author, year)	Demographic characteristics			Disease characteristics		
	Age, year (mean±SD)	BMI, kg/m^2	Parity	Diagnosis (UF location/size/number)	Symptoms	Previous treatment
RCTs						
Brucker 2014,[41] Hahn 2015[16]						
MYO (n=25)	34.4±6.1	24.0	NR	Number of UF: 2.4± SD1.6 Diameter of dominant UF (cm): 9.2 Location of UF: - submucosal: 2 patients (3.3%) - transmural: 3 patients (4.9%) - intramural: 26 patients (42.6%) - intramural UF abutting the endometrium: 0 - subserosal: 34 (55.7%) - pedunculated subserosal: 2 (3.3%)	Heavy menstrual bleeding: 18 patients (72%) Pelvic discomfort/pain: 6 patients (24%) UFS-QOL -Symptom severity subscale score: 41.8 -Quality of life subscale score: 70.2	NR
RFVTA (n=25)	40.0±7.8	22.6	NR	Number of UF: 2.9± SD2.6 Diameter of dominant UF (cm): 8.7 Location of UF: - submucosal: 0 - transmural: 0 - intramural: 33 patients (45.8%) - intramural UF abutting the endometrium: 2 (2.8%) - subserosal: 37 (51.4%) - pedunculated subserosal: 0	Heavy menstrual bleeding: 21 patients (84%) Pelvic discomfort/pain: 3 patients (12%) UFS-QOL -Symptom severity subscale score: 39.9 -Quality of life subscale score: 77.2	NR
Non-RCTs (no studies)						

MYO=myomectomy; NR=not reported; RFVTA=radiofrequency volumetric thermal ablation; SD=standard deviation; UF=uterine fibroid; UFS-QOL=the Uterine Fibroid Symptom and Quality of Life questionnaire (consists of Symptom Severity scale and health-related quality of life questions. Higher scores in the former indicate greater symptom severity, while higher scores in the latter indicate better quality of life);

Table 7-12. Results (Myomectomy *versus* Radiofrequency Volumetric Thermal Ablation)

Studies	Change in abnormal uterine bleeding	Change in pelvic pressure	Change in fibroid size	Symptom scores	HRQOL	Complications (operational, pregnancy)	Pregnancy outcomes (infertility, miscarriage, bleeding during pregnancy, full-term delivery)	Relapse/ re-intervention	Patient satisfaction, n (%)	Length of hospital stay, day
RCTs										
Brucker 2014,[41] Hahn 2015[16]										
MYO (n=25)	Year-1 heavy uterine bleeding: 2/22 patients (9.1%) MIQ at Year-1: 84.3% reported "better" or "about the same" for the perception of blood loss from the previous period.	Year-1 pelvic discomfort: 2/22 patients (9.1%)	Number of treated UFs: 2.0± SD1.4	Year-1 SSS score in UFS-QOL: ↓ 17.9 to 23.4	Year-1 EQ-5D: ↑8.9 from 72.3 at baseline. HRQOL total score in UFS-QOL ↑ 13.1 to 83.2.	Blood loss (ml): 51± SD57 1 suprapubic port site hematoma, no other complications.	3 pregnancies, 2 full-term deliveries.	No re-intervention.	Year-1: 86.5% reported "very satisfied"; 13.6% reported "moderately satisfied"	29.9± SD14.2 hours
RFVTA (n=25)	Year-1 heavy uterine bleeding: 7/21 patients (33.3%) MIQ at Year-1: 94.4% reported "better" or "about the same" for the perception of blood loss from the previous period.	Year-1 pelvic discomfort: 1/21 patients (4.8%)	Number of treated UFs: 2.8± SD2.6	Year-1 SSS score in UFS-QOL: ↓ 7.8 to 26.2	Year-1 EQ-5D: ↑2.0 from 81.7 at baseline. HRQOL total score in UFS-QOL: ↑ 7.5 to 86.4.	Blood loss (ml): 16± SD9 1 unplanned hospitalization due to vertigo, no other complications.	2 pregnancies, 2 full-term deliveries.	3 re-interventions.	Year-1: 42.9% reported "very satisfied"; 42.9% reported "moderately satisfied"	10.0± SD5.5 hours
P for between-group comparisons	Heavy uterine bleeding: =0.088 MIQ: =0.12	=1.00	=0.30	=0.16	EQ-5D: =0.24 HRQL total score: =0.46	Blood loss: < 0.001	NR	NR	=0.004	< 0.001
Non-RCTs (no studies)										

HRQOL=health-related quality of life; MIQ=Menstrual Impact Questionnaire; MYO=myomectomy; n/a=not applicable; NR=not reported; RFVTA=radiofrequency volumetric thermal ablation; SD=standard deviation; SSS=Symptom Severity Scale (of UFS-QOL); UFS-QOL=the Uterine Fibroid Symptom and Quality of Life questionnaire (consists of Symptom Severity scale and health-related quality of life questions. Higher scores in the former indicate greater symptom severity, while higher scores in the latter indicate better quality of life);

Appendix 8: Economic Evidence – Study Characteristics

Table 8-1: Characteristics of Included Economic Evaluations

First author, Publication Year, Country	Type of Analysis, Perspective	Intervention and Comparator(s)	Study Population	Time Horizon	Main Assumptions
Babashov 2015, Canada[45]	Cost-utility analysis Ontario public payer perspective	MRgFU, UAE, myomectomy, hysterectomy	Premenopausal women with symptomatic uterine fibroids, for whom pharmacotherapy had been ineffective	11 years (ages 40 to 51)	• Women reach menopause at age 51 • All patients eligible for hysterectomy and myomectomy, 90% eligible for UAE • 35% (base case) or 100% (alternative scenario) of patients eligible for MRgFU • Patients with symptom recurrence would be re-treated with the same intervention (maximum three rounds of treatment) • Patients with first-line treatment failure would receive second-line treatment with the next least invasive procedure (maximum three rounds of treatment) • Third-line treatment was always hysterectomy • 5% discount rate
Cain-Nielsen 2014, United States[46]	Cost-utility analysis Societal perspective	MRgFU, UAE, myomectomy	Premenopausal women with symptomatic uterine fibroids who wish to retain their uteri	5 years	• 35% of patients eligible for MRgFU, 90% eligible for UAE, 100% eligible for myomectomy • Patients would undergo myomectomy if they failed either MRgFU or UAE or had fibroid recurrence • Costs of major complications were assumed to be captured by the top 25% of costliest patients • QoL scores for UAE were used to approximate those of

Table 8-1: Characteristics of Included Economic Evaluations

First author, Publication Year, Country	Type of Analysis, Perspective	Intervention and Comparator(s)	Study Population	Time Horizon	Main Assumptions
					myomectomy • Patients who experienced a major complication would have a 20% reduction in QoL at time of treatment • Sensitivity analysis: 75% 5 year recurrence rate • 3% discount rate
Kong 2014, United States[47]	Cost-utility analysis Societal perspective	MRgFU, UAE, hysterectomy	Premenopausal women with symptomatic uterine fibroids	11 years (ages 40 to 51)	• Women reach menopause at age 51 • 35% of patients eligible for MRgFU, 90% eligible for UAE, 100% eligible for hysterectomy • Patients with no symptom relief would be re-treated with the next least invasive strategy • Patients with symptom recurrence would be re-treated with the same first-line intervention • Patients are treated either until their symptoms resolve or until menopause at age ≥ 51 • Fibroids are assumed to resolve after age 51 • No major or minor complications for MRgFU • Lost productivity costs for hysterectomy complications included within the lost-productivity costs of the procedure • 3% discount rate
O'Sullivan 2009, United States[2]	Cost-utility analysis	MRgFU, UAE, myomectomy, hysterectomy,	Premenopausal women with symptomatic	Lifetime horizon (patients enter the model at age 40)	• All women are eligible for treatment with hysterectomy, myomectomy, or

Table 8-1: Characteristics of Included Economic Evaluations

First author, Publication Year, Country	Type of Analysis, Perspective	Intervention and Comparator(s)	Study Population	Time Horizon	Main Assumptions
	Societal perspective	pain management with pharmacotherapy	uterine fibroids		pharmacotherapy, 90% eligible for UAE, 35% eligible for MRgFU • Patients ineligible for MRgFU or UAE assumed to prefer least invasive of remaining treatment options (except pharmacotherapy) • Patients are treated until symptoms have resolved; constant risk of symptom recurrence until menopause • Patients with symptom recurrence would be re-treated with the same intervention • Patients with first-line treatment failure receive second-line treatment with an alternative, more invasive procedure • Third-line treatment is always hysterectomy • Reference case analysis: productivity costs assumed to be reflected in the utility estimates (omitted from cost estimates) • Major complication rates equal for myomectomy and hysterectomy • No further treatment modeled for pharmacotherapy • 3% discount rate
Hirst 2008 (HOPEFUL), United Kingdom[48]	Cost-utility analysis United Kingdom public payer perspective	UAE, hysterectomy	Premenopausal women with symptomatic uterine fibroids	11 years (ages 44 to 55)	• Women undergo menopause at age 55 • Patients with UAE failure would have additional procedures (UAE, myomectomy, or hysterectomy) • Complete symptom resolution

Table 8-1: Characteristics of Included Economic Evaluations

First author, Publication Year, Country	Type of Analysis, Perspective	Intervention and Comparator(s)	Study Population	Time Horizon	Main Assumptions
					assumed following a hysterectomy • Myomectomy assumed to have the same cost and utilities as hysterectomy • Utility decrements applied for complications • 3.5% discount rate
Zowall 2008, United Kingdom[49]	Cost-utility analysis United Kingdom public payer perspective	MRgFU, UAE, myomectomy, hysterectomy	Women for whom surgical treatment for symptomatic uterine fibroids is being considered	17 years (39 to 56)	• Base case assumed that patients are distributed across the three treatments: 25% to UAE, 25% to myomectomy and 50% to hysterectomy • Initial in-hospital cost of UAE, hysterectomy and myomectomy assumed to be the same • No clinical or cost differences for treatments after menopause • Patients with first-line treatment failure receive second-line treatment with an alternative, more invasive procedure • QoL assumed to be the same for all successful treatments and assumed not to change beyond 6 months post-treatment • 3.5% discount rate
Wu 2007 (HOPEFUL), United Kingdom[50]	Cost-utility analysis United Kingdom public payer perspective	UAE, hysterectomy	Premenopausal women with symptomatic uterine fibroids	11 years (ages 44 to 55)	• Women undergo menopause at age 55 • Patients with UAE failure would have additional procedures (UAE, myomectomy, or hysterectomy) • Complete symptom resolution assumed following a hysterectomy

Table 8-1: Characteristics of Included Economic Evaluations

First author, Publication Year, Country	Type of Analysis, Perspective	Intervention and Comparator(s)	Study Population	Time Horizon	Main Assumptions
					• 3.5% discount rate
Beinfeld 2004, United States[51]	Cost-utility analysis Societal perspective	UAE, hysterectomy	Premenopausal women with symptomatic uterine fibroids	11 years (ages 40 to 51)	• Women reach menopause at age 51 • No clinical or cost differences for treatments after menopause • Patients with UAE failure would undergo hysterectomy within 30 days • Patients with UAE followed by symptom recurrence would undergo hysterectomy within one year • Complete symptom resolution assumed following a hysterectomy • No chance of long-term fibroid recurrence after UAE • Utilities after UAE were assumed to be the same as women in the same age group in the general population • 3% discount rate

MRgFU = magnetic resonance-guided focused ultrasound; MRI = magnetic resonance imaging; QALY = quality adjusted life year; QoL = quality of life; UAE = uterine artery embolization;

APPENDIX 9: ECONOMIC EVIDENCE – STUDY RESULTS

Table 9-1: Summary of Findings of Included Economic Evaluations

Main Study Findings	Author's Conclusions
Babashov 2015[45]	
Base case (hysterectomy reference) • UAE vs. hysterectomy, ICER = $46,480/QALY • Myomectomy strictly dominated by all other interventions (higher costs, lower QALYs) • MRgFU extendedly dominated by a combination of UAE and hysterectomy Scenario 1 (uterine-preserving treatment options only; MRgFU reference) • UAE vs. MRgFU, ICER = $46,495/QALY • Myomectomy strictly dominated by all other interventions Scenario 2 (all patients eligible for MRgFU; hysterectomy reference) • MRgFU vs. hysterectomy, ICER = $32,757/QALY • UAE vs. MRgFU, ICER = $70,239/QALY • Myomectomy strictly dominated by all other interventions Scenario 3 (all patients eligible for MRgFU and UAE is not available; hysterectomy reference) • MRgFU vs. hysterectomy, ICER = $39,254/QALY • Myomectomy strictly dominated by all other interventions One-way sensitivity analyses: • UAE was the cost-effective option for most scenarios when the WTP threshold was $50,000/QALY and $100,000/QALY	From a Canadian public payer perspective, UAE was the most cost-effective treatment option for women with symptomatic uterine fibroids, unless all patients are eligible for MRgFU. MRgFU becomes the most cost-effective treatment option when all women are eligible and UAE is not available. Myomectomy was not cost-effective in any of the tested scenarios.
Cain-Nielsen 2014[46]	
Base case (myomectomy reference, WTP threshold of $50,000/QALY; ICER above the threshold are cost-effective) • Productivity costs excluded: MRgFU vs. myomectomy, ICER = $46,250/QALY • Productivity costs included: MRgFU vs. myomectomy, ICER = $341,750/QALY • UAE dominated in both scenarios One-way sensitivity analyses • Preferred treatment strategy was sensitive to several parameters, both when productivity costs were included and excluded from the model.	From an American societal perspective, myomectomy was found to be the most cost-effective treatment option when productivity costs are not considered; MRgFU is the most cost-effective option when productivity costs are included. However, due to uncertainty in the model and depending on variations in WTP thresholds, all three strategies may be cost-effective for the treatment of symptomatic uterine fibroids.

Table 9-1: Summary of Findings of Included Economic Evaluations	
Main Study Findings	**Author's Conclusions**
• All treatment strategies preferred in certain circumstances. Probabilistic sensitivity analyses • Including direct costs only: MRgFU preferred when WTP threshold $15,000/QALY to $25,000/QALY; myomectomy preferred at all other values • Low productivity costs included: UAE preferred at WTP threshold under $30,000/QALY, MRgFU preferred at $30,000/QALY to $105,000/QALY, myomectomy preferred above $105,000/QALY	
Kong 2014[47]	
Base case • MRgFU vs. hysterectomy, ICER = $33,110/QALY • UAE vs. MRgFU, ICER = $270,057/QALY • Re-intervention rates: 93/100 for MRgFU, 71/100 for UAE • Complication rates: 37/100 for hysterectomy, 16/100 for UAE, 12/100 for MRgFU Sensitivity analysis (increasing patient age at treatment start) • ICER for MRgFU improves as age increases from 40 to 49. • UAE dominated by MRgFU at all ages above 41 • UAE preferred strategy when probability of symptom relief with MRgFU below 74% or when base cost of MRgFU was above 200% • Hysterecomy preferred strategy when probability of fibroid recurrence after UAE above 4.7% • Hysterectomy dominated MRgFU at lowest long-term utility value	From an American societal perspective, MRgFU was a cost-effective first-line treatment for symptomatic uterine fibroids, and becomes more cost-effective with increasing patient age.
O'Sullivan 2009[2]	
Base case (pharmacotherapy reference) • Hysterectomy vs. pharmacotherapy, ICER = $21,800/QALY • MRgFU vs. hysterectomy, ICER = $41,400/QALY • UAE vs. MRgFU, ICER = $54,200/QALY • Myomectomy strictly dominated One-way sensitivity analyses • MRgFU was cost-effective in most scenarios when the WTP threshold was $50,000/QALY • UAE was cost-effective in most scenarios when the WTP threshold was $100,000/QALY • ICERs and most cost-effective treatment choices at each WTP threshold were most	From an American societal perspective MRgFU is cost-effective at the generally accepted WTP threshold of $50,000/QALY.

Table 9-1: Summary of Findings of Included Economic Evaluations

Main Study Findings	Author's Conclusions
sensitive to the probability of symptom relief, probability of symptom recurrence, and procedure costs for UAE and MRgFU. • ICERs from reference case analysis (productivity costs omitted from cost estimates) and alternative analyses (less conservative estimates for complications rates and costs, recurrence rates, eligibility rate for MRgFU) provided the same or similar conclusions as the base case. • Myomectomy was always dominated by the other treatment strategies.	
Hirst 2008[48]	
Base case (age at initial treatment 44 years) • UAE had lower costs (£1769 vs. £3462) and higher QALYs (0.820 vs. 0.815) than hysterectomy within the first year of treatment. • UAE incurred additional costs (£907) while hysterectomy did not, and UAE had lower QALYs (7.384 vs. 7.426) for subsequent years after treatment. Alternate analysis (age at initial treatment 35 years) • Same results as the base case were observed for the first year following treatment. • UAE incurred greater costs (overall difference £138) and fewer QALYs (overall difference 0.081) than hysterectomy in subsequent years after treatment. One-way sensitivity analyses • UAE dominant when utility associated with retaining a uterus was applied • Reduction in procedural success rate for young women (age under 30 years with less severe symptoms) revealed that UAE is more cost-effective than no treatment (ICER = £4280/QALY) • Inclusion of lost productivity costs increased the cost difference from the base case between UAE and hysterectomy (£907 to £2805) Probabilistic sensitivity analysis • In general, UAE is associated with lower costs and similar QALYs to hysterectomy • Overall, UAE is more cost-effective than hysterectomy when WTP threshold is less than £30,000/QALY	From a UK public payer perspective, UAE has lower costs and is more effective than hysterectomy within the first year of treatment for symptomatic uterine fibroids. However, this result is not maintained in subsequent years after treatment. UAE is not preferred in younger patients who may require treatment over a longer period of time, but may be a cost-effective option for women who wish to preserve their uterus.
Zowall 2008[49]	
Base case (25% UAE, 25% myomectomy, 50% hysterectomy) • MRgFU is dominant	From a UK public payer perspective, MRgFU is a cost-effective treatment strategy for symptomatic uterine fibroids compared with UAE, myomectomy,

Table 9-1: Summary of Findings of Included Economic Evaluations

Main Study Findings	Author's Conclusions
Sensitivity analyses MRgFU remains dominant under the following scenarios with alternate assumptions: • Adjusted distribution of initial treatment between UAE, myomectomy, and hysterectomy • Alternate utility values after hysterectomy • Decreased rates of recurrence for all other procedures • Long-term complications for all other treatments are reduced to zero • MRgFU complication rate set to equal that of UAE • Death rates of all other treatments reduced to zero MRgFU not dominant under the following scenarios: • Costs of all other procedures set to lower quartile hysterectomy cost (£2054); ICER = £27,845/QALY • Increased initial hospital costs of MRgFU to £2630; ICER = £33,685/QALY • MRgFU is the dominant strategy until age 43 • MRgFU is dominant in 86% of probabilistic sensitivity analyses	and hysterectomy. This result is consistent for analyses with alternate assumptions regarding clinical practice, utilities, and clinical effectiveness. The outcomes of the model are sensitive to treatment costs and age of the patients.
Wu 2007[50]	
Base case (age at initial treatment 44 years) • UAE had lower costs (£1677 vs. £3282) and higher QALYs (0.820 vs. 0.815) than hysterectomy within the first year of treatment. • UAE incurred additional costs (£860) while hysterectomy did not, and UAE had lower QALYs (7.384 vs. 7.426) for subsequent years after treatment. Alternate analysis (age at initial treatment 35 years) • Same results as the base case were observed for the first year following treatment. • UAE incurred greater costs (overall difference £129) and fewer QALYs (overall difference 0.081) than hysterectomy in subsequent years after treatment. One-way sensitivity analyses • UAE dominant when utility associated with retaining a uterus was applied • Reduction in procedural success rate for young women (age under 30 years with less severe symptoms) revealed that UAE is more cost-effective than no treatment (ICER = £4100/QALY) • Inclusion of lost productivity costs increased the cost difference from the base case between UAE and hysterectomy (£746 to £2687)	From a UK public payer perspective, UAE has lower costs and is more effective than hysterectomy within the first year of treatment for symptomatic uterine fibroids. However, this result is not maintained in subsequent years after treatment. UAE is not preferred in younger patients who may require treatment over a longer period of time, but may be a cost-effective option for women who wish to preserve their uterus.

Table 9-1: Summary of Findings of Included Economic Evaluations	
Main Study Findings	**Author's Conclusions**
Probabilistic sensitivity analysis • In general, UAE is associated with lower costs and similar QALYs to hysterectomy	
Beinfeld 2004[51]	
Base case (no treatment as reference) • UAE vs. no treatment, ICER = $2007/QALY • UAE dominated hysterectomy Sensitivity analyses • ICERs for all scenarios of UAE vs. no treatment were under $16,000/QALY • UAE was more effective and more expensive than no treatment except when the patients were under 30 and when no QoL adjustments were made. • UAE dominated hysterectomy except when cure rate of UAE was reduced to 75%, procedural costs or recovery time were increased, or post-hysterectomy recovery time was reduced. • The model was sensitive to post-treatment utility adjustments.	From an American societal perspective, UAE is a cost-effective alternative to hysterectomy for the treatment of symptomatic uterine fibroids. The results were consistent among changes to several model parameters but were sensitive to assumptions about QoL.

ICER = incremental cost-effectiveness ratio; MRgFU = magnetic resonance-guided focused ultrasound; QALY = quality adjusted life year; QoL = quality of life; UAE = uterine artery embolization; vs. = versus; UK = United Kingdom; WTP = willingness-to-pay.

APPENDIX 10: ECONOMIC EVIDENCE – CRITICAL APPRAISAL OF STUDIES

Table 10-1: Strengths and Limitations of Economic Studies using Drummond[64]

Strengths	Limitations
Babashov 2015[45]	
• Research question is clearly stated with its economic importance given the regional context • Viewpoints of the analysis clearly defined and justified • Clearly described interventions and comparators with appropriate rationale for inclusion • Choice of economic evaluation and primary outcome measures are clear and justified • Sources of natural history model parameters (treatment eligibility, efficacy, safety) clearly referenced and described (with study design and results, or methods of synthesis, where warranted) • Methods to value benefits stated • Unit costs and quantities of resources used described clearly and separately • Currency and price data are recorded • Markov model structure and key parameters well described and appropriate • Time horizon stated • Discount rate stated and justified • Appropriate approaches to scenario and sensitivity analyses used and clearly described • Uncertainty in utilities addressed in sensitivity analysis • Results are clearly described (aggregated and disaggregated form) and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	• Utilities derived from a single study that differed from those reported in other, similar publications • Assumed that post-discharge patients would not experience complications associated with significant costs • Details of statistical tests and confidence intervals not provided for stochastic data
Cain-Nielsen 2014[46]	
• Research question and associated economic importance is given • Viewpoint of the analysis clearly defined • Clearly described interventions and comparators with appropriate rationale for inclusion • Choice of economic evaluation and primary outcome measures are clear and justified	• Details of design and results of single studies used to inform model parameter estimates not provided • Quantities of resource use not described separately from costs • Costs of complications not previously published, based on assumption that top 25% of costliest patients would include cost of major complications

Table 10-1: Strengths and Limitations of Economic Studies using Drummond[64]	
Strengths	**Limitations**
• Sources of model parameters derived from multiple studies (treatment eligibility, efficacy, safety, costs) clearly referenced and described with methods of synthesis • Methods to value benefits and sources of utilities stated • Lost productivity costs reported separately from initial base case analysis • Currency and price data are recorded • Method of price adjustment for inflation stated • Markov model structure and key parameters well described and appropriate • Time horizon stated • Discount rate stated and justified • Distribution details for model parameters provided • Appropriate approaches to scenario and sensitivity analyses used and clearly described • Uncertainty in utilities addressed in sensitivity analysis • Results are clearly described (aggregated and disaggregated form) and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	• Time horizon limited to 5 years
Kong 2014[47]	
• Research question and associated economic importance is given • Viewpoint of the analysis stated • Clearly described interventions and comparators with appropriate rationale for inclusion • Choice of economic evaluation and primary outcome measures are clear and justified • Source of effectiveness estimates stated • Methods to value benefits and estimate costs stated • Lost productivity costs reported separately • Currency conversion described, where applicable • Model structure and key parameters well described and appropriate • Time horizon and discount rate stated • Approach to sensitivity analyses described • Uncertainty in costs addressed in sensitivity analysis	• Myomectomy not included as a first-line treatment option, evaluated only as a second-line option to UAE without explanation • Methods for pooling multiple model parameter estimates not provided • Details and results of single studies supporting model parameter estimates not provided • Subjects from whom utilities were obtained not described in detail • Quantities of resource use not described separately from costs • Details of statistical tests and confidence intervals not provided for stochastic data • Sensitivity analysis not performed for effectiveness parameters if base case estimate was derived from a single study (ranges for sensitivity analyses were derived from multiple studies)

Table 10-1: Strengths and Limitations of Economic Studies using Drummond[64]	
Strengths	**Limitations**
• Results are clearly described (aggregated and disaggregated form) and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	
O'Sullivan 2009[2]	
• Research question and associated economic importance is given • Viewpoint of the analysis stated • Clearly described interventions and comparators with appropriate rationale for inclusion • Choice of economic evaluation and primary outcome measures are clear and justified • Source of effectiveness estimates stated • Methods to value benefits and estimate costs stated • Lost productivity costs reported separately and discussed • Currency and price data are recorded • Markov model structure and key parameters well described and appropriate • Time horizon and discount rate stated • Appropriate approaches to scenario and sensitivity analyses used and clearly described • Results are clearly described (aggregated and disaggregated form) and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	• Methods for synthesizing multiple model parameter estimates not provided • Details and results of single studies supporting model parameter estimates not provided • Subjects from whom utilities were obtained not described in detail • Quantities of resource use not described separately from costs • Details of statistical tests and confidence intervals not provided for stochastic data
Hirst 2008 (HOPEFUL)[48]	
• Research question and associated economic importance is given • Viewpoints of the analysis clearly defined and justified • Clearly described interventions and comparators • Choice of economic evaluation and primary outcome measures are clear and justified • Source of most model parameter estimates from a single study (HOPEFUL study) stated and associated details of study design and results provided • Sources of model parameters derived from multiple studies (e.g., technical failure) clearly referenced and methods of synthesis provided	• Myomectomy discussed as an alternative surgical option to hysterectomy but not included as comparator in economic analysis • Costs associated with productivity loss are presented but relevance of these cost changes to the study question not discussed • Quantities of resource use not described separately from costs • Several variables not assessed in sensitivity analyses (e.g., range of probabilities for treatment effectiveness, complications, utilities) • Details of statistical tests and confidence intervals not provided for stochastic data • Incremental analysis not consistently reported

Table 10-1: Strengths and Limitations of Economic Studies using Drummond[64]	
Strengths	**Limitations**
• Methods to value benefits stated • Details of subjects from whom utilities were obtained were provided • Productivity loss costs reported separately • Methods to estimate costs described • Currency and price data are recorded • Model structure and key parameters well described and appropriate • Time horizon and discount rate stated • Sensitivity analyses clearly described • Results are clearly described and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	
Zowall 2008[49]	
• Research question and associated economic importance is given • Viewpoints of the analysis clearly defined and justified • Clearly described interventions and comparators • Choice of economic evaluation and primary outcome measures are clear and justified • Methods to value benefits and estimate costs stated • Currency and price data are recorded • Markov model structure and key parameters described and appropriate • Time horizon and discount rate stated • Approach to sensitivity analysis is given and reasonable • Results are clearly described (aggregated and disaggregated form) and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	• Methods for pooling multiple model parameter estimates not provided • Details and results of single studies supporting model parameter estimates not provided • Details of subjects from whom utilities were obtained not provided • Quantities of resource use not described separately from costs • Details of statistical tests and confidence intervals not provided for stochastic data
Wu 2007[50]	
• Research question and associated economic importance is given • Viewpoints of the analysis clearly defined and justified • Clearly described interventions and comparators • Choice of economic evaluation and primary outcome measures are clear and justified	• Myomectomy presented as a treatment option after failure but not included as comparator in economic analysis • Methods of synthesis for model parameter estimates derived from multiple studies (e.g., technical failure) not provided • Costs associated with productivity loss are presented but

Table 10-1: Strengths and Limitations of Economic Studies using Drummond[64]	
Strengths	**Limitations**
• Source of most model parameter estimates from a single study (HOPEFUL study) stated and reference provided for further details • Methods to value benefits stated • Productivity loss costs reported separately • Methods to estimate costs described • Currency and price data are recorded • Model structure and key parameters well described and appropriate • Time horizon and discount rate stated • Sensitivity analyses clearly described • Results are clearly described and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	relevance of these cost changes to the study question not discussed • Quantities of resource use not described separately from costs • Several variables not assessed in sensitivity analyses (e.g., range of probabilities for treatment effectiveness, complications, utilities) • Details of statistical tests and confidence intervals not provided for stochastic data • Incremental analysis not consistently reported
Beinfeld 2004[51]	
• Research question and associated economic importance is given • Viewpoints of the analysis clearly defined and justified • Clearly described interventions and comparators • Choice of economic evaluation and primary outcome measures are clear and justified • Source of model parameter estimates (probabilities, costs, utilities) stated • Methods to estimate costs described • Currency and price data are recorded • Details for currency conversion given • Model structure and key parameters well described and appropriate • Time horizon and discount rate stated • Sensitivity analyses clearly described and appropriate • Results are clearly described (aggregated and disaggregated form) and the research question is adequately addressed • Conclusions clearly follow the reported data and include appropriate caveats	• Details and results of single studies supporting model parameter estimates not provided • Details of subjects from whom utilities were obtained not provided • Productivity changes and associated costs not reported separately • Quantities of resource use not described separately from costs • Details of statistical tests and confidence intervals not provided for stochastic data