Abnormal Uterine Bleeding and Uterine Fibroids (for Ohio Only)

Policy Number: CS002OH.A
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Instructions for Use

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Related Policy

- Hysterectomy (for Ohio Only)

Application

This Medical Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

Endometrial Ablation

Endometrial ablation is proven and medically necessary for treating abnormal uterine bleeding in premenopausal individuals. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Hysteroscopy, Operative, Endometrial ablation for abnormal bleeding in premenopausal individual.

Click here to view the InterQual® criteria.

Levonorgestrel-Releasing Intrauterine Device

Levonorgestrel-releasing intrauterine devices (LNG-IUD) (e.g., Mirena®, Skyla®, Liletta® or Kyleena™) are proven and medically necessary for treating menorrhagia. Refer to the U.S. Food and Drug Administration (FDA) section for additional information.

Uterine Fibroids

Uterine artery embolization (UAE) is proven and medically necessary for treating symptomatic uterine fibroids when there is documentation of evaluation of abnormal uterine bleeding (AUB) including endometrial biopsy for individuals > 40 years of age and a pap smear screening consistent with current guidelines. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Uterine Artery Embolization (UAE).

Click here to view the InterQual® criteria.

Laparoscopic ultrasound guided radiofrequency ablation (Acessa) or transcervical ultrasound guided radiofrequency ablation (Sonata) is medically necessary as an alternative to myomectomy or hysterectomy for treating symptomatic uterine fibroid(s) when all the following criteria are met:

- Uterine preservation is desired, and
- Fibroid(s) < 10 cm (in any diameter), and
- Uterine size < 16 gestational weeks, and
- No history of gynecologic malignancy or pre-malignancy within the past 5 years, and
- No history of cervical dysplasia, and
- Member has received counseling regarding the lack of data for individuals that want to become pregnant

Magnetic resonance-guided focused ultrasound ablation (MRgFUS) is considered unproven and not medically necessary for treating uterine fibroids due to insufficient evidence of efficacy.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
Uterine Fibroids	
0071T	Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume less than 200 cc of tissue
0072T	Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume greater or equal to 200 cc of tissue
0404T	Transcervical uterine fibroid(s) ablation with ultrasound guidance, radiofrequency
37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction
58563	Hysteroscopy, surgical; with endometrial ablation (e.g., endometrial resection, electrosurgical ablation, thermoablation)
58674	Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency

HCPCS Code	Description
Levonorgestrel-Releasing Intrauterine Device	
J7296	Levonorgestrel-releasing intrauterine contraceptive system, (Kyleena), 19.5 mg
J7297	Levonorgestrel-releasing intrauterine contraceptive system (Liletta), 52 mg
J7298	Levonorgestrel-releasing intrauterine contraceptive system (Mirena), 52 mg
J7301	Levonorgestrel-releasing intrauterine contraceptive system (Skyla), 13.5 mg
J7306	Levonorgestrel (contraceptive) implant system, including implants and supplies
S4981	Insertion of levonorgestrel-releasing intrauterine system

Description of Services

Abnormal uterine bleeding (AUB) in women of childbearing age is defined as any change in menstrual period frequency or duration, a change in amount of flow, or any bleeding between cycles. In postmenopausal women, AUB includes vaginal

bleeding 12 months or more after the cessation of menstruation, or unpredictable bleeding in patients who have been receiving hormone therapy for 12 months or more. AUB terms include oligomenorrhea (bleeding occurs at intervals of more than 35 days), polymenorrhea (bleeding occurs at intervals of less than 21 days), menorrhagia (bleeding occurs at normal intervals but with heavy flow or duration of more than 7 days), menometrorrhagia (bleeding occurs at irregular, noncyclic intervals and with heavy flow or duration more than 7 days), and metrorrhagia (irregular bleeding occurs between ovulatory cycles). Menorrhagia can be idiopathic or can be associated with underlying uterine lesions such as fibroids or polyps, pelvic pathology, anatomical abnormalities, systemic illness, hormonal imbalance or certain medications. Idiopathic menorrhagia that is not related to a specific underlying condition is called AUB. All these conditions associated with menorrhagia can be referred to as AUB, although it is also possible to have some conditions such as fibroids or an anatomical abnormality with normal menses. The focus in this policy is on treatment options when the bleeding pattern is abnormal.

Conservative management of AUB includes watchful waiting and pharmacological therapy. Hormone therapy may cause the fibroids to shrink; however, they will quickly return to their original mass once therapy has been discontinued. Another treatment option is dilation and curettage. Hysterectomy is available when symptoms cannot be controlled by conservative treatment.

According to ACOG, fibroids, are most commonly found in women aged 30-40 years, but can occur at any age. Uterine fibroids (also known as leiomyomata) are benign tumors of the uterus. They have a rich blood supply and may cause excessive uterine bleeding, uterine enlargement and mass or bulk related symptoms such as pelvic pain and pressure, urinary frequency and abdominal distension. Uterine fibroid embolization (UFE) is indicated for individuals with clinically documented fibroids and fibroid-related symptoms and a viable alternative to hysterectomy surgery. Recommendations prior to UFE treatment include an endometrial biopsy to rule out malignancy or hyperplasia (Bradley 2018). Alternate minimally invasive procedures such as UFE are performed in an outpatient setting resulting in shorter recovery times, less complications and elimination of overnight hospital stays.

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)

The local administration of the progestin levonorgestrel is delivered via an intrauterine device (IUD). The local delivery of this hormone causes the endometrium to become insensitive to ovarian estradiol leading to atrophy of the endometrial glands, inactivation of the endometrial epithelium and suppression of endometrial growth and activity.

Uterine Artery Embolization (UAE)

This procedure injects particles via the uterine arteries to block blood supply to uterine fibroids, causing them to shrink.

Magnetic Resonance Guided Focused Ultrasound (MRgFUS)

This procedure combines real-time MR-guidance with high-intensity focused ultrasound for the noninvasive thermal ablation of uterine fibroids. Tumor ablation is performed by focusing a collection of ultrasonic beams to increase sonic beam intensity at a point deep within the tissue to cause thermal coagulation while sparing normal tissues.

Ultrasound-Guided Radiofrequency Ablation

- Laparoscopic Ultrasound-Guided Radiofrequency Ablation: This minimally invasive procedure uses a laparoscopic ultrasound probe to determine the location and size of fibroids. Then a small electrode array delivers radiofrequency energy to destroy the fibroids.
- Transcervical Ultrasound-Guided Radiofrequency Ablation: This minimally invasive procedure destroys fibroids using a transcervical radiofrequency ablation device under integrated, real-time, intrauterine ultrasound imaging guidance.

Clinical Evidence

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD)

A 2020 Cochrane Systematic Database Review by Bofill Rodriguez, Lethaby and Jordan found that the levonorgestrel-releasing intrauterine system (LNG-IUS) had a greater reduction in menstrual blood loss for women with HMB when compared to other medical treatments or placebos; the authors' conclusion was LNG-IUS appears to be more effective than oral medical therapies and results in better (QOL) and higher satisfaction. The analysis included 25 RCTs which included a total of 2511 women; most

studies did not provide long-term data beyond 2 years. Limitations included the small number of participants in the differing trials and a high risk of bias for blinding.

Cim et al. (2018) reported two-year follow-up data of patients with AUB after insertion of the LNG-IUS. One hundred and six parous women aged 33-48 years with recurrent HMB participated in this study, and were followed for 1, 3, 6, 12, 18, and 24 months following the insertion. The authors reported that the LNG-IUS was well tolerated by all women. Pre-treatment of the use of the LNG-IUS, endometrial biopsy patterns for irregular proliferative endometrium and for atypical simple hyperplasia were 34/106 (32.08%) and 61/106 (57.55%) respectively and after treatment no abnormal pathologic findings were determined ($p < 0.001$).

Louie et al. (2017) evaluated comparative clinical outcomes after placement of LNG-IUS, ablation, or hysterectomy for AUB. A decision tree was generated to compare clinical outcomes in a hypothetical cohort of 100, 000 premenopausal women with nonmalignant AUB. Complications, mortality, and treatment outcomes were evaluated over a 5-year period, with calculated cumulative quality-adjusted life years (QALYs), and probabilistic sensitivity analysis. The LNG-IUS had the highest number of QALYs (406, 920), followed by hysterectomy (403, 466), non-resectoscopic ablation (399, 244), and resectoscopic ablation (395, 827). Ablation had more treatment failures and complications than LNG-IUS and hysterectomy. According to the authors, findings were robust in sensitivity analysis.

A Cochrane review (Marjoribanks et al., 2016) compared the effectiveness, safety and acceptability of surgery versus medical therapy for heavy menstrual bleeding. Fifteen randomized controlled trials (RCTs) (n = 1289) comparing surgery versus oral medication or LNG-IUD for treating HMB were included. The authors concluded that hysterectomy, endometrial surgery and the LNG-IUD were all effective in reducing heavy menstrual bleeding, though surgery was most effective, at least over the short term. These treatments suited most women better than oral medication. Although hysterectomy will stop heavy menstrual bleeding, it is associated with serious complications. Both conservative surgery and LNG-IUD appear to be safe, acceptable and effective.

An updated Cochrane systematic review by Lethaby et al. (2015) evaluated the safety and efficacy of the LNG-IUD for HMB. Twenty-one RCTs in women of reproductive age treated with progesterone or progestogen-releasing intrauterine devices versus no treatment, placebo or other medical or surgical therapy for HMB were included. The authors concluded that the LNG-IUD is more effective than oral medication as a treatment for HMB. The device is associated with a greater reduction in HMB, improved QOL and appears to be more acceptable long term but is associated with more minor adverse effects than oral therapy. When compared to endometrial ablation, it is not clear whether the LNG-IUD offers any benefits with regard to reduced HMB, and satisfaction rates and QOL measures were similar. Limitations included inconsistency and inadequate reporting of study methods.

In a systematic review of twenty-six studies, Matteson et al. (2013) compared the effectiveness of nonsurgical AUB treatments for bleeding control, QOL, pain, sexual health, patient satisfaction, additional treatments needed and adverse events. Interventions included the levonorgestrel intrauterine system, combined oral contraceptive pills (OCPs), progestins, nonsteroidal anti-inflammatory drugs (NSAIDs) and antifibrinolytics. For reduction of menstrual bleeding in women with AUB presumed secondary to endometrial dysfunction, the levonorgestrel intrauterine system (71-95% reduction), combined OCPs (35-69% reduction), extended cycle oral progestins (87% reduction), tranexamic acid (26-54% reduction) and NSAIDs (10-52% reduction) were all effective treatments. The levonorgestrel intrauterine system, combined OCPs and antifibrinolytics were all superior to luteal phase progestins (20% increase in bleeding to 67% reduction). The levonorgestrel intrauterine system was superior to combined OCPs and NSAIDs. Antifibrinolytics were superior to NSAIDs for menstrual bleeding reduction. Data were limited on other important outcomes such as QOL for women with AUB presumed secondary to endometrial dysfunction and for all outcomes for women with AUB presumed secondary to ovulatory dysfunction.

In another systematic review, Matteson et al. (2012) compared hysterectomy with less-invasive alternatives for AUB. Nine RCTs comparing bleeding, QOL, pain, sexual health, satisfaction, need for subsequent surgery and adverse events were included. Endometrial ablation, levonorgestrel intrauterine system and medications were associated with lower risk of adverse events but higher risk of additional treatments than hysterectomy. Compared to ablation, hysterectomy had superior long-term pain and bleeding control. Compared with the levonorgestrel intrauterine system, hysterectomy had superior control of bleeding. No other differences between treatments were found. The review group concluded that less-invasive treatment options for AUB result in improvement in QOL but carry significant risk of retreatment caused by unsatisfactory results. Although hysterectomy is the most effective treatment for AUB, it carries the highest risk for adverse events.

Kaunitz et al. (2010) compared the efficacy and safety of the LNG-IUS and oral medroxyprogesterone acetate in the treatment of idiopathic heavy menstrual bleeding. In this multicenter, randomized, controlled study, women aged 18 years or older with HMB (menstrual blood loss 80 mL or more per cycle) were randomly assigned to six cycles of treatment with either LNG-IUS or oral medroxyprogesterone acetate. Of 807 women screened, 165 were randomly assigned to treatment (LNG-IUS n = 82, oral medroxyprogesterone acetate n = 83). At the end of the study, the absolute reduction in median menstrual blood loss was significantly greater in the LNG-IUS group than in the medroxyprogesterone acetate arm, and the proportion of women with successful treatment was significantly higher for the LNG-IUS (84.8%) than for medroxyprogesterone acetate (22.2%).

Kaunitz et al. (2009) compared the effects of the levonorgestrel intrauterine system and endometrial ablation in reducing heavy menstrual bleeding. The systematic review and meta-analysis were restricted to RCTs in which menstrual blood loss was reported using pictorial blood loss assessment chart scores. Six RCTs that included 390 women (levonorgestrel intrauterine system, n = 196; endometrial ablation, n = 194) were reviewed. Three studies pertained to first-generation endometrial ablation (manual hysteroscopy) and three to second-generation endometrial ablation (thermal balloon). Both treatment modalities were associated with similar reductions in menstrual blood loss after 6 months, 12 months and 24 months. In addition, both treatments were generally associated with similar improvements in QOL in five studies that reported this as an outcome. No major complications occurred with either treatment modality in these small trials. The authors concluded that the efficacy of the levonorgestrel intrauterine system in the management of HMB appears to have similar therapeutic effects to that of endometrial ablation up to 2 years after treatment.

Uterine Artery Embolization (UAE)

A systematic review by Liu, Wang and Lei (2021) compared UAE against high-intensity focused ultrasound (HIFU) ablation for the treatment of symptomatic uterine fibroids. A total of 7 articles were found which included one RCT. 4,592 women met the inclusion criteria; 4,365 of them underwent UAE and 227 underwent HIFU. Primary outcome measurements included UFS-QoL scores, reintervention rate, pregnancy rate, and adverse events. For the group of women who had UAE, the authors found the QoL scores were higher at follow-up, the reintervention rate, adverse outcomes and pregnancy rates were all lower. The authors' concluded while both procedures appear to be promising, UAE seems to have significant improvement of symptoms over HIFU. Limitations included small sample size of articles, lack of comparison with regards to recovery time, postop complications and cost and lack of consistency in follow-up times amongst the studies. The authors indicate there is still a lack of good quality comparative data and further RCTs are needed.

Xu et al. (2021) conducted a meta-analysis of 31 studies (6 RCTs and 25 cohort studies) with a total of 42,103 individuals that was designed to compare re-intervention rates of myomectomy, MRgFUS, and UAE, for uterine fibroids. Twelve- month re-intervention rates of myomectomy, UAE, and MRgFUS for uterine fibroids were 0.06, 0.07, and 0.12 respectively. The 24-month re-intervention rates were 0.10, 0.08, and 0.14 respectively. The 36-month re-intervention rates were 0.09, 0.14, and 0.22 respectively. Additionally, the 60-month re-intervention rates were 0.19, 0.21 and 0.49 respectively. The authors concluded MRgFUS has the highest re-intervention rate and increases rapidly in the 60th month after treatment. Myomectomy was found to have the lowest re-intervention rate of the three regimens; UAE re-intervention rate was higher than myomectomy but lower than MRgFUS. Furthermore, the authors note that UAE is less invasive, and associated with a shorter hospital stay and a quicker recovery regimen. Limitations include insufficient number of available RCTs may lead to selection bias, observed substantial heterogeneity, and patients treated by ultrasound image-guided focused ultrasound surgery were not included due to lack of data. (Froeling 2013, Goodwin 2008, Moss 2011, and van der Kooij 2010 which were previously cited in this policy, are included in this meta-analysis).

Manyonda et al. (2020) conducted a multicenter, randomized, open-label trial which compared myomectomy and UAE in women with symptomatic uterine fibroids. 254 women were recruited out of a potential 650 and randomly assigned in a 1:1 ratio to undergo a myomectomy or uterine artery embolization. Myomectomy was performed by the route preferred by the operating gynecologist (e.g., open abdominal, hysteroscopic, laparoscopic, or a combination of these). Embolization of the uterine arteries was performed under fluoroscopic guidance and the specific embolic agent used was at the discretion of the interventional radiologist. The tool used for primary outcome was the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire; scores ranged from 0 to 100 with higher scores indicating a better QOL. Primary and secondary outcome data was collected from each participant at 6 months, 1 year, and 2 years after randomization. The authors found the mean scores on UFS-QOL at two years were substantially higher in both groups, but the magnitude of improvement was greater in the myomectomy group. At 2 years, 93% of the women in the myomectomy group would recommend the procedure to a friend versus only 84% in the embolization group would make their procedure recommendation. Complications associated with both procedures were low. Limitations included loss to follow-up, lack of blinding, a substantial amount of missing data on the FSH

and luteinizing hormone levels due to lack of collection of blood samples, a number of participants did not receive the intervention to which they had been assigned despite randomization and many women declined to participate in the trail due to wanting a specific treatment option. The authors concluded this multicenter trial showed the superiority of myomectomy over UAE with respect to health-related QOL.

Karlsen et al. (2018) conducted a systematic review of the reported rates of pregnancy and miscarriage after treatment of uterine fibroids with UAE. Randomized controlled trials, controlled clinical trials, comparative before-after trials, cohort studies, case-control studies and case series where UAE treatment of premenopausal women was performed for uterine fibroids with and where a control intervention was included. The PRISMA guideline was used to do a systematic review using the main outcomes pregnancy rate and miscarriage rate. Risk of bias was assessed by the Cochrane risk of bias tool or by ROBINS-I. The quality of evidence was assessed by the GRADE approach. 17 studies comprising 989 patients were selected and included 1 RCT, 2 cohort studies, and 14 case series. The results showed pregnancy rates after UAE were 50% in the RCT and 51 and 69% in the cohort studies. Among the case series median pregnancy rate was 29%. Miscarriage rates were 64% in the RCT. Miscarriage rates at 56 and 34% were found in the cohort studies after UAE. The median miscarriage rate was 25% in the case series. The authors concluded that pregnancy rate was found to be lower and miscarriage rate higher after UAE than after myomectomy. However, they found very low quality of evidence regarding the assessed outcomes and the reported proportions are uncertain. There is a need for improved prospective randomized studies to improve the evidence base.

Fonseca et al. (2017) conducted a meta-analysis and indirect treatment comparison to examine the comparative efficacy and safety of surgical procedures to treat symptomatic uterine leiomyomas compared with UAE. Data from 986 patients submitted to UAE (n = 527) or surgery (n = 459) were analyzed. UAE had a lower risk of major complications and a higher risk of minor complications; UAE had a higher risk of re-intervention up to 2 years and up to 5 years; UAE had a similar risk of follicle-stimulating hormone levels > 40 IU/L after 6 months and of recommending the procedure to another patient up to 5 years after treatment. Compared with surgery, UAE had lower rates of major complications with an increased risk of re-intervention up to 2 and 5 years after the first procedure. Surgery had a similar risk of ovarian failure and similar recommendation of the procedure to another patient. However, the number of trials was limited, and there was a high risk of bias in at least 2 domains, and non-blinding of study participants and staff occurred.

The Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review on management of uterine fibroids that was designed to review the treatment effectiveness and the risk of leiomyosarcoma in women with fibroids. The review found high strength evidence that UAE is effective for reducing the size of fibroids and total fibroid volume. Improvements in bleeding and QOL had a moderate strength of supporting evidence. Over half of the women who received UAE did not require a subsequent intervention after a 5 year follow-up period. Additionally, insufficient evidence was found to determine safety of the UAE on reproductive outcomes (Hartmann et al., 2017).

Havryliuk et al. (2017) conducted a systematic review and meta-analysis from clinical studies that described populations of pre-menopausal women seeking surgical management (both uterine-sparing and hysterectomy) for their symptomatic fibroids. Procedures included in the analysis were myomectomy, UAE, Lap-RFA, MRgFUS, and hysterectomy. For UAE (n = 1154), the mean follow-up period was 13.5 months, overall complication rate 16.8% (2.7% major, 14.0% minor), and reintervention rate 14.8%. Patients reported, however, greater improvement of their fibroid symptoms as reflected by post-treatment high HRQL and EQ-5D scores and low symptom severity scores. Patients who underwent UAE had the largest fibroid diameters compared to all other treatment groups and the largest proportion of intramural myomas; these factors may have contributed to the observed outcomes. The chance of developing premature ovarian failure was very low in patients who were younger than 40 years of age; however, this risk increased in women older than 45 years. The authors state that limitations of this review include the inherent heterogeneity among studies; only a portion of the included studies were RCTs, most were not and were assigned an ACOG quality score of B; and lack of uniformity in reporting conventions. Further comprehensive prospective research, ideally in the form of well-powered RCTs, is needed to validate the specific treatment modality preferred for specific anatomical variances of fibroids.

Pisco et al. (2017) conducted a retrospective analysis of prospectively collected data of 359 women with uterine fibroids and/or adenomyosis who were unable to conceive. The purpose of the study was to determine pregnancy rates after conventional and partial UFE. The mean follow-up period was 69 months. During follow-up, 149 women became pregnant, 131 women had live births, and 16 women had several pregnancies, resulting in a total of 150 live newborns. It was the first pregnancy for 85.5% (112 of 131) of women. Spontaneous pregnancy rates at 1 year and 2 years after UFE were 29.5% and 40.1%. A dominant submucosal fibroid and ischemia greater than or equal to 90% had greater likelihood of spontaneous pregnancy. Complication

rates in patients treated with partial UFE (14.6%) were not greater than rates in patients treated with conventional UFE (23.1%, p = .04). The authors concluded that partial UFE may be safe and effective outpatient procedures for women with uterine fibroids who want to conceive. Limitations included the study was performed at a single center along with a non-standardized technique utilized by the radiologists; additional RCTs comparing UFE to myomectomy are needed.

Szkodziak et al. (2017) evaluated minimally invasive procedures in the management of uterine fibroids through a systematic review. They reported that the clinical efficacy index for UAE in the treatment of excessive menstrual bleeding, pelvic pain and pressure symptoms associated with tumor mass are located in the following ranges: 81-96%, 70-100% and 46-100%. A 25-60% reduction in uterine volume has been observed within 3 to 6 months after the procedure. In a long-term (up to 5 years) follow-up after UAE, in over 70% of patients there was a significant improvement in the QOL, while 16-23% of the patients required another intervention. Potential complications include infection, expulsion of demarcated, necrotic pieces of fibroids through the cervical canal, and nontarget embolization of other pelvic organs. After UAE, a significant shortening and decrease of the amount of menstrual bleeding can be observed, which is considered by the authors to be a beneficial effect of this procedure. However, the total lack of menstruation in many studies is given as the effect of post-embolization ovarian failure.

Torre et al. (2017) conducted a non-comparative open-label trial, on 15 women ≤ 40 years, presenting with multiple symptomatic fibroids (at least 3, ≥ 3 cm), immediate pregnancy wish, and no associated infertility factor. Patients were eligible for surgical multiple myomectomy, but carefully elected UAE. During the year following UAE, 9 patients actively wishing to conceive delivered 5 live births. Women were followed for 43.1 months (95%CI 32.4-53.9); 10 live births occurred in 8 patients, and 5 patients required secondary surgeries for fibroids. Although in this study women without associated infertility factors demonstrated an encouraging capacity to deliver after UAE, RCTs comparing UAE and myomectomy are warranted.

In an updated Cochrane systematic review, Gupta et al. (2014) assessed the benefits and risks of UAE versus other medical or surgical interventions for symptomatic uterine fibroids. The primary outcomes of the review were patient satisfaction and live birth rate (among women seeking live birth). Seven RCTs (n = 793) were included in this review. Three trials compared UAE with abdominal hysterectomy, two trials compared UAE with myomectomy and two trials compared UAE with either type of surgery (53 hysterectomies and 62 myomectomies). The authors reported no evidence of a difference in patient satisfaction rates at up to two years following UAE versus surgery (myomectomy or hysterectomy). Findings at five-year follow-up were similarly inconclusive. There was very low-quality evidence to suggest that myomectomy may be associated with better fertility outcomes than UAE, but this information was only available from a selected subgroup in one small trial. The authors found no clear evidence of a difference between UAE and surgery in the risk of major complications, but UAE was associated with a higher rate of minor complications and an increased likelihood of requiring surgical intervention within two to five years of the initial procedure. Limitations included wide range in the quality of evidence, failure to clearly report methods and lack of blinding for subjective outcomes.

Panagiotopoulou et al. (2014) evaluated the effectiveness of uterine-sparing interventions for women with symptomatic uterine fibroids who wish to preserve their uterus. Five trials, involving 436 women were included. Two compared UAE with myomectomy and three compared UAE with laparoscopic uterine artery occlusion. Indirect treatment comparison showed that myomectomy and UAE resulted in higher rates of patient satisfaction and lower rates of clinical failure than laparoscopic uterine artery occlusion. Myomectomy resulted in a lower reintervention rate than UAE and laparoscopic uterine artery occlusion even though the latter techniques had an advantage over myomectomy because of shorter hospitalization and quicker recovery. There was no evidence of difference between the three techniques in ovarian failure and complications rates. The evidence for reproductive outcomes is poor. The authors concluded that these results suggest that laparoscopic uterine artery occlusion is less effective than UAE and myomectomy in treatment of symptomatic fibroids. The choice between UAE and myomectomy should be based on individuals' expectations and fully informed discussion. Limitations of the study included the relatively low number of included studies and low number of participants; further RCTs providing longer follow up and assessing the safety and efficacy of the interventions are warranted.

Torre et al. (2014) conducted a prospective cohort study of 66 consecutive patients with extensive symptomatic fibroids who desired a future pregnancy and were treated with UAE. Patients were not eligible for abdominal myomectomy because of fibroid recurrence despite previous surgery, because of current risks of surgery, or because of patient refusal. Ovarian reserve demonstrated no change after embolization. Women were followed for 33.4 ±14.5 months; only one in 31 women who were actively attempting to conceive became pregnant which ended in miscarriage. The authors concluded that the low reproductive outcomes reported in the study suggest that UAE should not be performed routinely in young women of childbearing age with extensive fibroids. Although this finding was established in a population for whom abdominal myomectomy was declined, a

possible adverse effect of UAE on fertility potential should be considered for woman of childbearing age scheduled for embolization. Limitations included lack of control group and smaller sample size.

Martin et al. (2013) performed a systematic review of complications and reinterventions in UAE for symptomatic uterine fibroids. In RCTs, common complications were discharge and fever (4%), bilateral UAE failure (4%) and postembolization syndrome (2.86%). Two trials showed a significantly decreased risk in major complications with UAE. None of the trials showed a significant difference in minor complications of UAE. None of the trials showed a significant difference in risk for overall complications of UAE. Three trials showed a significantly increased risk for reintervention with UAE. In 76 nonrandomized studies, common complications were amenorrhea (4.26%), pain (3.59%) and discharge and fever (3.37%). In 41 case studies, common complications were discharge and fever (n = 22 cases), repeat UAE (n = 6 cases) and fibroid expulsion (n = 5 cases). The authors concluded that, overall, UAE has a significantly lower rate of major complications relative to surgery, but it comes at the cost of increased risk of reintervention.

Jun et al. (2012) compared the efficacy and safety of UAE for symptomatic uterine fibroids with surgery. Patients were randomly assigned to undergo either UAE (n = 63) or surgery (n = 64). A meta-analysis of existing studies was also performed. There were significant improvements in UAE groups in most components of quality-of-life assessment at six months. The UAE group had a shorter hospital stay and a shorter recovery time compared with the surgical group. During the follow-up, there were no differences in complications incidence, but the UAE group had fewer major complications. A meta-analysis of this and existing studies further suggested that the UAE group had a shorter hospital stay, a shorter recovery time and less major complications than the surgical group. The authors concluded that more studies are needed to evaluate the long-term effects and impact of UAE on fertility.

Toor et al. (2012) performed a systematic review and meta-analysis to determine complication rates and effectiveness of UAE) in the treatment of symptomatic uterine fibroids. Fifty-four studies met the inclusion criteria (n = 8159). There were no reported deaths. Major complications occurred at a rate of 2.9%. The rate of hysterectomy for resolution of a complication from UAE was 0.7% (0.5-0.9%) and the rate of readmission was 2.7% (1.9-3.7%). Other complications recorded were leiomyoma tissue passage (4.7% [3.9-5.7%]), deep venous thrombosis or pulmonary embolism (0.2% [0.2-0.4%]) and permanent amenorrhea (3.9% [2.7-5.3%]). Reintervention rates including repeat UAE, myomectomy, or hysterectomy calculated per patient-year occurred at 5.3% (4.2-6.4%) with follow-up ranging from 0.25 to 5 years. Clinical symptomatic improvement ranged from 78% to 90%, with follow-up ranging from 0.25 to 2 years. The authors concluded that symptomatic uterine leiomyoma treatment by UAE is an effective procedure with a low rate of major complications supporting its use as an alternative to hysterectomy. Limitations include only using English language articles which may have missed other valid studies and underestimation of complications due to variable follow up durations between studies.

In a retrospective analysis, Pisco et al. (2011) evaluated the outcome of pregnancy after UFE in 74 patients who wanted to conceive. The length of the follow-up period was 4.5 years; however, all the pregnancies occurred between 4 and 22 months after UFE. Of the study participants, 44 became pregnant (59.5%). There are five (11.3%) ongoing pregnancies and 39 (88.7%) finished pregnancies, with 33 successful live births (84.6%), four spontaneous abortions (10.3%), one induced abortion, and one stillbirth. There were 22 cesarean deliveries (66.6%), two preterm deliveries at 36 weeks (6.1%), and five low birth weights. Although the authors concluded that UFE appears to be safe, study limitations include non-randomization in comparison with myomectomy, and small patient population.

In a systematic review and meta-analysis, van der Kooij et al. (2011) analyzed the evidence on short-, mid- and long-term results of UAE compared to surgery (hysterectomy/myomectomy) in premenopausal women with HMB caused by symptomatic uterine fibroids. Four RCTs with a total of 515 patients were included. Short-term advantages of UAE over surgery included less blood loss, shorter hospital stays and quicker return to usual activities. Mid- and long-term results showed comparable health-related QOL results and a higher reintervention rate in the UAE group.

Ultrasound-Guided Radiofrequency Ablation Procedures (Laparoscopic and Transcervical)

Yu et al. (2022) conducted a secondary analysis of the TRUST (Treatment Results of Uterine Sparing Technologies) RCT to determine the efficacy, safety, and healthcare resource use of laparoscopic RFA compared with myomectomy in patients with symptomatic uterine leiomyomas. A total of 57 individuals were randomized to either laparoscopic RFA (n = 30) or myomectomy (n = 27), and followed over a 12-month period after the procedure. This analysis reports secondary outcomes of the original TRUST study. Reduction of symptoms and the improvement in patient-reported outcomes scores were the primary focus of this study. Post procedure hospitalization, length of stay, complications, reinterventions, and recovery time were

secondary outcomes. There was an improvement in symptoms up to12-months in both groups, with better results for myomectomy compared to laparoscopic RFA. At three and 12 months after the procedure, the percentages of patients who were hospitalized in the laparoscopic RFA group were 74% and 49% lower than those in the laparoscopic myomectomy group, respectively. The length of hospital stay was significantly shorter in the laparoscopic RFA group. The total number of days until back to normal activity was significantly lower in the laparoscopic RFA group compared with the myomectomy. The authors concluded laparoscopic RFA has a lower post procedure hospitalization rate and shorter length of stay and is a safe, effective, uterine-sparing alternative to laparoscopic myomectomy. Limitations include the original TRUST study was not designed to test the findings reported in this study, lack of masking, more than 25 percent of the randomized participants were excluded after randomization and data are not provided on these participants, and the two groups differed significantly at baseline.

Arnreiter and Oppelt (2021, included in ECRI report below), evaluated the success of treatment, possible side effects and safety for the Sonata® system. The systematic review included ten studies, and none were RCTs. The authors found the safety and efficacy of the Sonata® system for women that desired future childbearing could not be established. While myomectomy is the gold standard for infertility patients with myomas, there is a growing body of literature identifying positive pregnancies when treated with RFA, however limitations of this study showed lack of randomization for the participants and lack of long-term results.

The Sonata® Transcervical Ablation System is a minimally invasive procedure intended to reduce uterine fibroid symptoms by using RFA to ablate fibroids. An evidence assessment by ECRI identifies this technology as inconclusive due to the lack of evidence available. While the available evidence suggests transcervical fibroid ablation with Sonata® appears to be safe, additional studies are needed that compares Sonata® with other uterine-sparing treatments. In addition, further studies including multi-center trials with larger sample sizes, randomization, and long-term outcomes are necessary (ECRI June 2020; updated August 2021).

Based on evidence from a systematic review, three RCTs and two case series, an ECRI report (updated 2022) demonstrates Acessa to be safe and at least as effective as other minimally invasive ablation surgeries such as myomectomy for symptoms relief of uterine fibroids. Additional RCTs comparing Acessa with other treatment modalities are needed to clarify further benefits and help identify the gaps in long-term outcomes.

A Hayes report cites a very low-quality body of evidence which is insufficient to draw conclusions regarding the safety and efficacy of the Sonata® system. While the Sonata® procedure has been associated with significant improvement in patients' symptoms, fibroid volume and QOL, consistency of the results cannot be determined. Additional studies comparing the Sonata® procedure with established treatments for uterine fibroids are needed (Hayes 2020; updated November 2022).

A Hayes report evaluated the safety and efficacy of the Acessa System for treating uterine fibroids. Overall, a low-quality, limited body of evidence suggests that radiofrequency volumetric thermal ablation (RFVTA) consistently reduces the symptoms of uterine fibroids and improves health-related QOL; however, substantial uncertainty exists regarding the comparative effectiveness and continued durability of this treatment. Limitations of the studies include small sample size, lack of a control group, and limited follow-up and substantial attrition (Hayes 2019; updated February 2023).

The Uterine Leiomyoma Treatment with Radiofrequency Ablation (ULTRA) trial was an investigator-initiated single-arm clinical trial conducted by Jacoby et al. (2020). Twenty-six women were recruited from 2013 through 2015 from five academic institutions across California. The women received laparoscopic RFA treatment with the Acessa device for their uterine leiomyomas. Seven surgeons obtained a one-day training on how to use the device. All women received counseling about the risks and benefits of the surgical procedure and its lack of FDA approval. No intraoperative complications or serious adverse events were discovered. However, the sample size is too small to adequately assess surgical complications. The authors concluded that the laparoscopic RFA surgical procedure may be quickly adopted for patients with symptomatic leiomyomas. Limitations of this study included a very small sample size and lack of randomization; future studies should focus on comparative analysis with other available surgeries. Clinicaltrials.gov number NCT02100904.

In 2020, Lukes and Green (2020, included in ECRI report above) reported 3-year results from the Sonata pivotal trial which included a 147 participants. Clinical outcome assessments included symptom severity score (SSS) and health-related quality of life (HRQoL) subscales of the Uterine Fibroid Symptom and Quality-of-Life (UFS-QoL) Questionnaire. Following the procedure, the participants returned for follow up at 10 days, 30 days, 3 months, 6 months, and annually thereafter through the final visit at 3 years. The authors concluded the Sonata system appeared to be safe with a low rate of adverse events; women treated with

Sonata for symptomatic uterine fibroids experienced a significant reduction in fibroid related symptoms with a low surgical reintervention rate over 3 years.

Bradley et al. (2019) performed a systematic review and meta-analysis for treatment of fibroids with radiofrequency ablation (RFA). The authors identified 32 articles which included 1283 patients that were treated with either laparoscopic, transvaginal or transcervical RFA. It was hypothesized that RFA would significantly reduce fibroid volume and improve the patient's QOL. The authors found that transcervical and transvaginal ablation were associated with a shorter length of stay on average and transcervical RFA had a faster return to normal activities when compared to laparoscopic RFA. Main strengths of the review included adherence to PRISMA guidelines, inclusion of almost 1300 patients and excellent generalization of results. The authors concluded that RFA was effective for symptomatic uterine fibroids and improved the QOL for patients. Limitations included lack of long-term data after 12 months, insufficient number of studies to perform statistical comparison among RFA delivery approaches and inability to determine if RFA efficacy was influenced by fibroid type or volume.

Chudnoff et al. (2019, included in Bradley 2019 systematic review) conducted a prospective, multicenter, single-arm interventional trial of patients treated in the United States and Mexico, to evaluate the 12-month safety and effectiveness of transcervical ablation for the treatment of symptomatic uterine leiomyomas. Transcervical ablation using the Sonata System was performed on 1-10 leiomyomas in 147 patients with leiomyoma diameters ranging from 1 to 5 cm. Treated leiomyomas included all nonpedunculated types. Primary endpoints assessed at 12 months were reduction in menstrual blood loss and absence of surgical reintervention. Additional assessments included symptom severity, QOL, patient satisfaction, reductions in uterine and leiomyoma volumes, and safety. The study met its primary endpoints at 12 months, because 64.8% of patients experienced 50% or greater reduction in menstrual bleeding and 99.3% of patients were free from surgical reintervention. The mean pictorial blood loss assessment chart score decreased by 38.9%, 48.4%, and 51.1% at 3, 6, and 12 months, respectively, and 95.1% of patients experienced a reduction in menstrual bleeding at 12 months. There were significant mean improvements in symptom severity and health-related QOL of 32.1 points and 43.7 points, respectively, at 12 months. Mean maximal leiomyoma volume reduction per patient was 62.4%. More than half of patients returned to normal activity within 1 day, 96.3% of patients reported symptom improvement at 12 months, and 97% expressed satisfaction with the treatment at 12 months. There were no device-related adverse events. The authors concluded that transcervical ablation was associated with a significant reduction in leiomyoma symptoms with no device-related adverse events and a low surgical reintervention rate through 12 months, demonstrating its potential to treat safely and effectively all nonpedunculated leiomyoma types through a uterus-conserving, incisionless approach.

In February 2019, Garza-Leal (included in Bradley 2019 systematic analysis) reported on the long-term (> 5 years) clinical outcomes of transcervical RFA of uterine fibroids. For this retrospective, single-arm, long-term data-collection study, 23 women with HMB secondary to fibroids were treated with transcervical RFA guided by integrated intrauterine sonography (using the Sonata® System, Gynesonics, Redwood City, CA). This study was within the 12-month Fibroid Ablation Study-EU clinical trial in Mexico. Symptoms were assessed using the Uterine Fibroid Symptom and Quality-of-Life's Symptom Severity Score (SSS) and Health-Related Quality of Life (HRQoL) subscales. Patients were queried regarding pregnancy and surgical reinterventions. The results showed seventeen women (73.9%) provided long-term follow-up information, with a mean of 64.4 months ±4.5 months. From baseline, mean SSS decreased significantly from 64.9 ± 6.9 to 27.6 ±36.1, and mean HRQoL improved significantly from 27.2 ±22.4 to 76.0 ±32.6 respectively. There were no surgical reinterventions through the first 3.5 years post-treatment. There was an 11.8% incidence of surgical reinterventions over 5.4 years of average follow-up, with 2 hysterectomies occurring after 3.5 and 4 years post ablation, respectively (event rate: 2.2% per year; 95% confidence interval; 0.3%, 7.9%). Freedom from surgical reintervention at 1, 2, and 3 years was 100%, and, at 4 and 5 years, was 88.2% ±7.8%. There was a single pregnancy occurring within the first year of treatment leading to a normal-term delivery by elective repeat cesarean section. The authors concluded that transcervical RFA with the Sonata System produced substantial durable clinical benefits beyond 5 years with a low reintervention rate. This study is limited by a lack of randomization and small number of participants and the results should be validated in larger patient populations.

Lin et al. (2019) conducted a meta-analysis assessing the short-term (3 and 6 months) and long-term (12, 24, and 36 months) symptom relief and QOL improvement, procedure-related adverse event rate, reintervention rate, and days missed from work after laparoscopic radiofrequency ablation. Eight studies with a total of 581 patients were included in this review. Based on validated questionnaires, QOL improved significantly until 36 months after laparoscopic RFA therapy, with a maximum improvement (Health-Related Quality of Life [HRQL] questionnaire score of +41.64 [95% confidence interval (CI), 38.94-44.34] and a transformed Symptom Severity Score [tSSS] of -39.37 [95% CI, 34.70-44.04]) at 12 months after laparoscopic radiofrequency ablation. All subscales of QOL improved significantly, and most of the changes remained stable in long-term

follow-up. The overall reintervention rate was 4.39% (95% CI, 1.60%-8.45%), and the median uterine volume reduction was 69.17 cm^3 (95% CI, 35.87-102.46 cm^3). The overall procedure-related adverse events rate was 1.78% (95% CI, 0.62%-3.53%), and patients missed an average of 4.35 days (95% CI, 2.55-6.15 days) of work. In conclusion, laparoscopic RFA therapy is an efficacious way to treat small-sized and nonpedunculated symptomatic uterine fibroids, providing stable long-term symptom relief and QOL improvement with a low risk of adverse events and reintervention and just a few days of missed work. The authors identified several limitations. First, because most of the studies were non-comparative, differences in study types, inclusion and exclusion criteria, and study methodology were inevitable. Second, symptoms might be related to fibroid locations; however, not all studies classified patients by FIGO type, and so we could not analyze fibroids at different positions separately. In addition, the definition of procedure-related adverse events varied between studies, resulting in related data being based partially on the subjective judgment of the authors, not on objective definitions. Owing to the high loss to follow-up, the longest follow- up among the studies was 36 months. Therefore, long term follow-up data are still urgently needed.

Miller and Osman (2019) reported results from a 2-year study of sonography-guided transcervical fibroid ablation (TFA) using the Sonata® device. 147 premenopausal women with a mean age of 43 years were enrolled at 22 different sites. Inclusion criteria consisted of up to 10 uterine fibroids ranging in size from 1 to 5 cm in diameter. The mean value on the symptom severity score (SSS) decreased from 55-19 to 24-18 ($p < 0.001$), health-related quality of life (HRQL) scores increased from 40-21 to 83-19 ($p < 0.001$), and EuroQol 5-Dimension (EQ-5D) scores increased from 0.72-0.21 to 0.89-0.14 ($p < 0.001$). The results for the 125 participants that made it through to the 2-year follow up demonstrated the use of the Sonata® device was a safe and effective outpatient procedure which provided significant symptom relief and improved the quality of life for the patient. Patient satisfaction was 94%.

Huirne and Brooks (2018) conducted a prospective, single-arm European trial in which 49 women with fibroids were treated with transcervical, intrauterine ultrasound- guided RFA with the Sonata System. The EQ-5D-3L system was utilized to collect patient health status at baseline, 3, 6, and, 12 months post-procedure. Patient-reported health states at each time point were converted into a health utility value using time-trade off methodology. Patient health utility increased from a mean of 0.745 at baseline, to means of 0.838, 0.852, and 0.914 at 3 months, 6 months, and 12 months, respectively. The change from baseline at 12 months was significant. Randomized controlled trials with larger patient populations and longer follow-up periods are needed to further evaluate the Sonata system.

Rattray et al. (2018) conducted a RCT to compare laparoscopic ultrasound-guided RFA of fibroids and laparoscopic myomectomy in terms of health care utilization and serious complication rates in 45 women with symptomatic uterine fibroids who desired uterine conservation. The secondary objectives were comparison of subject responses to validated symptom and QOL questionnaires. Inclusion criteria for the participants were females > 18 years of age with symptomatic uterine fibroids ≥ 10 cm and a uterine size of ≤16 gestational weeks and a desire for uterine preservation. Hospitalization time was 6.7±3.0 hours for the laparoscopic RFA group and 9.9 ±10.7 hours for the myomectomy group. Intraoperative blood loss was less for laparoscopic RFA subjects: 25.2 ±21.6 versus 82.4 ±62.5 mL. Laparoscopic RFA procedures took less time than myomectomy procedures: 70.0 versus 86.5 minutes. At three months, both cohorts reported the same significant symptom severity reduction. Laparoscopic RFA subjects also took less time from work: 11.1 ±7.6 versus 18.5 ±10.6 days. The authors concluded that laparoscopic RFA has less intraoperative blood loss, shorter hospitalization and procedure times and faster return to work. Limitations include recall bias, lack of long-term data, and small sample size.

In a systematic review prepared for AHRQ, the strength of evidence for RFA in the management of uterine fibroids is noted as insufficient to inform care (Hartmann et al., 2017).

In a systematic review and meta-analysis, Havryliuk et al. (2017) evaluated data from clinical studies that described populations of pre-menopausal women seeking surgical management (both uterine-sparing and hysterectomy) of their symptomatic fibroids. Procedures included in the analysis were myomectomy, UAE, Lap-RFA, MRgFUS, and hysterectomy. Based on 209 patients (4 cohorts), the complication rate for Lap-RFA was overall 6.9% (1.7 major, 4.4% minor) with the reintervention rate 5.2%. Long-term follow-up averaged 27 months. The authors concluded that based on their analysis, Lap-RFA is associated with low complication rates, minimal EBL, and low reintervention rates. In addition, patients reported major improvement in their HRQL, and symptom severity scores compared to reports of more traditional interventions, such as hysterectomy, myomectomy, and UAE. Because of the precise placement of RF probe into a targeted myoma, which is confirmed by laparoscopic ultrasound before ablation, there is minimal disruption of normal myometrium and ovarian function. This is advantageous for patients who may desire future pregnancy. Pregnancy data are limited; however, normal full-term pregnancies resulting in vaginal deliveries have been reported after Lap-RFA. The authors state that limitations of this study include the

inherent heterogeneity among studies; only a portion of the included studies were RCTs, most were not and were assigned an ACOG quality score of B; and lack of uniformity in reporting conventions. Further comprehensive prospective research, ideally in the form of well-powered RCTs, is needed to validate the specific treatment modality preferred for specific anatomical variances of fibroids.

Iversen and Dueholm (2017) conducted a retrospective, multicenter, case series to access the long-term efficacy and rate of intervention for uterine myomas of 66 women who underwent abdominal or vaginal ultrasound-guided RFA. The patients were contacted for long-term follow up to complete the Uterine Fibroid Symptom and Quality of Life Score (UFS-QOL) questionnaire and optional ultrasound and examination. Forty of 62 patients underwent no/minor hysteroscopic reinterventions; 35 patients from this group completed the UFS-QOL questionnaire and showed sustained and improved symptom severity scores from baseline to long-term follow-up. Twenty-two patients had major reinterventions (15 hysterectomies and myomectomies). Six of the 22 patients underwent major reinterventions for reasons other than myoma-related complaints. The estimated major reintervention rate because of myoma-related symptoms was 13.5% after two years and 29.1% after five years. Women ≥ 45 years of age had a major reintervention rate of 12% after two years and 19% after five years, and women < 45 years had a major reintervention rate of 35.0% and 73.8% after two and five years, respectively. Fewer major reinterventions occurred in women with only one RFA-treated myoma than women with more than one RFA-treated myoma. The authors concluded that especially for women ≥ 45 years of age with only one myoma, ultrasound-guided RFA is an alternative treatment option that merits further evaluation with larger studies. Limitations include the retrospective nature of the study, small study size, and broad inclusion criteria.

Toub (2017) evaluated the clinical evidence for the Sonata System, the results of which showed significant median reductions in total (73.3%) and perfused (73.3%) uterine fibroid volume, menstrual bleeding (72.3%), symptom severity (62.5%), and improvements in health-related QOL (127%) at 12 months post-ablation. In the author's opinion, the Sonata System is a promising treatment modality for uterine fibroids that does not require general anesthesia or hospitalization, and has the potential for redefining the current paradigm for management of symptomatic fibroids. Randomized controlled trials with longer follow-up periods are needed to evaluate the safety and reliability of this procedure.

Krämer et al. (2016, included in Hayes report and Bradley 2019 systematic review) analyzed 51 patients that were randomized to either undergo RFVTA treatment (n = 26) or a laparoscopic myomectomy (LM) (n = 25). Inclusion criteria included premenopausal women of at least 18 years of age, experiencing symptomatic fibroids and desired uterine preservation; in addition, the participants had a uterine size < 16 gestational weeks, fibroid diameter < 10 cm (diagnosed by transvaginal ultrasound) and a normal PAP test. At 24 months, the authors found no significant differences observed between the treatment groups; however a significant improvement in health-related QOL was observed in the LM group. A trocar-site hematoma occurred in one patient in the LM group. Further surgical interventions were recorded in three patients in the RFVTA group, but these were unrelated to fibroid symptoms. The data suggested RFVTA and LM were equal when it came to safety, symptom reduction, and improvements in quality of life. Limitations included small sample size and a racially homogenous group.

Hahn et al. (2015, included in Hayes report and Bradley 2019 systematic review) conducted a 1:1 parallel, randomized, prospective, single-center, comparative analysis of RFVTA to LM for fibroid treatment in women ≥ 18 years of age who desired uterine preservation and had symptomatic fibroids (less than 10 cm) detected by transvaginal ultrasound. Fifty women were equally randomized to either RFVTA or LM. At 12 months, the authors reported similar clinical benefits in both groups. Mean symptom severity scores decreased (improved) by -7.8 for the ablation subjects and by -17.9 for the myomectomy subjects. Health-related QOL improved (increased) by 7.5 and 13.1, respectively, for the two groups. Two myomectomy subjects had pregnancies that ended in a Cesarean delivery and a vaginal delivery of healthy infants. Two pregnancies in the RFVTA group ended in full-term vaginal deliveries of healthy infants. Limitations included age discrepancy between the groups (RFVTA had older participants) along with small sample size. In addition, despite randomization of the trial, the participants were told postoperatively their assigned surgical treatment thus this may have impacted their post-surgical questionnaire responses.

Bongers et al. (2015, included in Bradley 2019 systematic review) conducted a prospective, longitudinal, multicenter, single-arm controlled trial to establish the effectiveness and confirm the safety of transcervical, intrauterine, ultrasound-guided RFA in the treatment of uterine fibroids. Fifty consecutive women with symptomatic uterine fibroids (n = 92 fibroids) received treatment with the VizAblate System. The primary study endpoint was the percentage change in perfused fibroid volume at 3 months. Secondary endpoints, reached at 6 months, included safety, symptom reduction, rate of surgical reintervention and number of days to return to normal activity. Perfused fibroid volumes were reduced at 3 months by an average of 68.8 ±27.8%. Six-month

results suggest that the VizAblate System is safe and effective in providing relief of AUB associated with fibroids, with appropriate safety and a low reintervention rate. Similar results were reported at 12 months (Brölmann et al., 2016).

Berman et al. (2014, included in Bradley 2019 systematic review) reported 3-year outcomes of 104 patients from the Halt trial conducted by Chudnoff (2013). Questionnaire responses indicated sustained relief from symptoms and continued improvement in health-related QOL through 36 months after ablation. The cumulative repeat intervention rate was 11% (14 of 135 participants) at 36 months. This study is supported by the study sponsor Halt Medical Inc., and limitations include lack of randomization and control.

Brucker et al. (2014 included in Hayes report and Bradley 2019 systematic review) conducted a randomized, single-center study comparing the perioperative outcomes of radiofrequency volumetric thermal ablation (RFVTA) and laparoscopic myomectomy (LM) in women who desired uterine conservation. Of 110 patients assessed for eligibility, 51 were randomized to the two interventions. The final analysis included 25 patients in the RFVTA group and 25 patients in the LM group. RFVTA resulted in the treatment of more fibroids, a significantly shorter hospital stay and less intraoperative blood loss than laparoscopic myomectomy. This study was sponsored by Halt Medical and is limited by small sample size and short-term follow-up.

Galen et al. (2014, included in Bradley 2019 systematic review) performed a retrospective, multicenter clinical analysis of 206 consecutive cases of ultrasound guided laparoscopic RFVTA of symptomatic uterine fibroids conducted under two phase II studies at 2 sites (n = 69) and one phase III study at 11 sites (n = 137). From baseline to 12 months in the phase II study, the mean transformed symptom severity scores improved from 53.9 to 8.8 (n = 57), HRQOL scores improved from 48.5 to 92.0 (n = 57) and mean uterine volume decreased from 204.4 cm^3 to 151.4 cm^3 (n = 58). Patients missed a median of 4 days of work. The rate of possible device-related adverse events was 1.4%. In the phase III study, approximately 98% of patients were assessed at 12 months, and their transformed symptom severity scores, HRQOL scores, mean decrease in uterine volume and mean menstrual bleeding reduction were also significant. Patients in phase III missed a median of 5 days of work. The rate of periprocedural device-related adverse events was 3.5%. This study is limited by retrospective design, lack of randomization and control and short-term follow-up.

Chudnoff et al. (2013, included in Hayes report and Bradley 2019 systematic review) reported preliminary results of a prospective clinical trial designed to evaluate laparoscopic ultrasound-guided radiofrequency volumetric thermal ablation for treating symptomatic uterine fibroids. The study clinically supported by Halt Medical, Inc. included a cohort of 135 premenopausal symptomatic women with uterine fibroids not exceeding 7 cm in any diameter, objectively confirmed heavy menstrual bleeding, uterine size of ≤ 14 weeks upon pelvic examination and desire for uterine preservation. Primary outcome measures were menstrual bleeding at 12 months compared to baseline (pre-procedure), adverse events and surgical reintervention rates. At 3-, 6- and 12-month follow-ups, menstrual blood loss decreased from baseline levels by 31.8%, 40.7% and 38.3%, respectively. Symptom severity decreased from baseline and health-related QOL improved. The authors reported one serious adverse event requiring readmission 5 weeks post procedure and one surgical reintervention for persistent bleeding. Ninety-four percent of the women reported satisfaction with the treatment. This study is limited by lack of randomization and control and short-term follow-up.

Garza-Leal et al. (2011) conducted a single center cohort study to evaluate the safety of the VizAblate transcervical device for the treatment of uterine fibroids. Nineteen women with uterine fibroids received treatment with the VizAblate System in a closed abdomen setting prior to hysterectomy. Twelve women underwent an immediate abdominal hysterectomy after RFA (acute group), while the remaining seven underwent hysterectomy on post-ablation days 16 and 17 (subacute group). Uteri were analyzed to quantify fibroid ablation dimensions and assess the serosa for thermal injury. Subjects in the subacute group were treated under conscious sedation and indicated overall procedural satisfaction. There were no complications or thermal serosal injury. For women in the subacute group receiving one ablation, the mean total procedure time was 25.8 ±6.0 minutes (range 18-32 minutes). All subjects in the subacute group were discharged within 2 hours of the procedure. For fibroids ≤ 5 cm, 67.2% ±27.0% of the fibroid volume was ablated (range 15-100%; median 75%). The authors concluded that transcervical RFA of fibroids under intrauterine sonographic guidance with the VizAblate system can be accomplished with a high degree of reliability and without adverse events.

Magnetic Resonance-Guided Focused Ultrasound Ablation (MRgFUS)

There is insufficient evidence to conclude MRgFUS is effective for the treatment of fibroids. The quality of evidence is low and additional research involving larger, robust RCTs is needed to establish its safety, efficacy and long-term outcomes.

Yu et al. (2021) conducted a comparative meta-analysis on the efficacy and safety of magnetic resonance-guided high intensity focused ultrasound (MR-HIFU) and ultrasound-guided HIFU. Forty-eight studies were included for review; twenty-eight addressed the MR-HIFU and 20 focused on US-HIFU. Uterine fibroids with of a volume of < 300 cm^3 were part of the inclusion criteria. Non-perfused volume rate (NPVR) is considered a significant parameter that is positively connected with clinical success rate. A NPVR for the MR-HIFU was 58.92% which was lower than that of the US-HIFU group which was 81.07%. A NPVR of greater than 80% is considered successful. The average treatment time for MR-HIFU was almost double that of US-HIFU which had a mean of 96.9 minutes. For treatment of symptomatic uterine fibroids, the author conclusions revealed the US procedure had greater safety and efficacy than the MR procedure. Limitations included a loss of follow-up in the majority of the studies, poor documentation for number and location of fibroids, and lack of long-term outcomes.

A Hayes report concluded that, although evidence suggests that magnetic resonance-guided focused ultrasound (MRgFUS) reduces fibroid volume in women with symptomatic fibroids, the overall quality of the evidence is low due to the lack of well-designed controlled studies. Substantial uncertainty remains regarding the effect of magnetic resonance–guided focused ultrasound ablation of uterine fibroids on symptoms and the comparative effectiveness with other treatment alternatives. (Hayes, 2019; updated 2021)

In a 2019 systematic review (included in Hayes report), Taheri et al. examined the change in uterine and fibroid volumes associated with UAE, focused ultrasound (FUS), and radiofrequency ablation (RFA). Eighty-one relevant papers were identified: 52 related to UAE, 11 to RFA, 17 to FUS, 1 compared UAE and FUS. Uterine volume and fibroid volume changes seen in these studies were at 1 to 36 months. The pooled fibroid volume reductions at six months seen with RFA were 70%, UAE 54% and FUS 32%. All three types of non-respective treatment result in fibroid volume reduction. However, fibroid volume reduction is most marked with RFA, with UAE resulting in the next most volume reduction. Additional larger cohort studies, including those that are randomized and/or comparative, would enable definitive conclusions.

Verpalen et al. (2019, included in ECRI report) reassessed the effectiveness of Magnetic Resonance-High Intensity Focused Ultrasound (MRHIFU) on reducing fibroid related symptoms. Patients with fibroids containing a high T2 signal intensity or Funaki type 3 were excluded. Eighteen articles were included for review; sixteen of them were clinical trials and all were case series. The quality of evidence ranged from 9 to 16 using the 18-point criteria tool. The level of evidence for all included studies was IV according to Oxford Centre for Evidence-based Medicine (OCEBM) guidelines. Only 6 of the 18 studies were of acceptable quality. The author's concluded all studies displayed fibroid shrinkage and demonstrated that fibroids could continue shrink up to a years' time following the procedure. Adverse events were minimal and only two patients experience a serious adverse effect (DVT and third-degree skin burn). The studies suggested that MRHIFU may be a cost-effective strategy however the topic of cost was not analyzed. Limitations included weaknesses of a meta-analysis design, potential high-risk bias related to specific study designs, different sample sizes and loss of follow-up in some sub-studies. The authors expressed additional future studies are needed, but because randomized trials are difficult to conduct and pose methodological challenges along with difficulty recruiting patients, larger comparative controlled cohort studies with longer follow-up are warranted.

Ierardi et al. (2018) performed a systematic review for percutaneous ablation on uterine fibroids. The primary endpoint was to investigate feasibility and safety of the technique. Six articles containing 541 patients was evaluated and no major complications of the procedure was found. After reviewing the data, the authors concluded microwave ablation of uterine fibroids to be safe and effective, however larger randomized prospective trials are needed to better demonstrate the benefits. The authors found a major limitation of MRgFUS is that many women are not eligible for the procedure due to potential challenges and risks associated with visceral injury.

Barnard et al. (2017, included in ECRI and Hayes reports) conducted a RCT and comprehensive cohort analysis to compare the periprocedural outcomes of fibroid embolization and focused ultrasound. Premenopausal women with symptomatic uterine fibroids seen at 3 US academic medical centers were enrolled in the RCT (n = 57). Women meeting identical criteria who declined randomization but agreed to study participation were enrolled in a nonrandomized parallel cohort (n = 34). The 2 treatment groups were analyzed by using a comprehensive cohort design. All women undergoing focused ultrasound and UAE received the same post procedure prescriptions, instructions, and symptom diaries for comparison of recovery in the first 6 weeks. Return to work and normal activities, medication use, symptoms, and adverse events were captured with post procedure diaries. Data were analyzed using the Wilcoxon rank sum test or $\chi 2$ test. Multivariable regression was used to adjust for baseline pain levels and fibroid load when comparing opioid medication, adverse events, and recovery time between treatment groups because these factors varied at baseline between groups and could affect outcomes. Adverse events were

also collected. The results showed focused ultrasound surgery was a longer procedure than embolization, with 23 (over half) women undergoing focused ultrasound 2 treatment days. Immediate self-rated post procedure pain was higher after UAE than focused ultrasound. Compared with those having focused ultrasound (n = 39), women undergoing embolization (n = 36) were more likely to use outpatient opioid (75% vs 21%) and nonsteroidal anti-inflammatory medications (97% vs 67%) and to have a longer median recovery time (days off work, 8 vs 4; days until return to normal, 15 vs 10. There were no significant differences in the incidence or severity of adverse events between treatment arms; 86% of adverse events (42 of 49) required only observation or nominal treatment, and no events caused permanent sequelae or death. After adjustment for baseline pain and uterine fibroid load, UAE was still significantly associated with higher opioid use and longer time to return to work and normal activities. Results were similar when restricted to the RCT. The authors discussed the challenges that have inhibited mainstream adoption of MRgFUS, and they include the prolonged duration of most procedures, patient eligibility with numerous exclusion criteria and restrictive selection criteria, and concluded that more comparative trials are needed to assess MRgFUS against other more established uterine-preserving treatments.

In a clinical assessment, ECRI concluded the evidence for the ExAblate Body System was inconclusive. The evidence suggests that the ExAblate reduces symptoms and improves the QOL in women up to three years, however the studies have a high risk of bias and report on too few outcomes to be conclusive on how well it works. The evidence was limited by small sample size, retrospective design, high patient attrition, lack of control groups, randomization and blinding. (ECRI 2017; updated August 2020).

According to a systematic review prepared for the AHRQ, high intensity focused ultrasound reduced fibroid and uterine size, but strength of evidence is low because of short follow-up and poor quality of overall study design. Evidence related to patient reported outcomes is insufficient (Hartmann et al., 2017, included in Hayes report).

Havryliuk et al. (2017, included in Hayes report) conducted a systematic review and meta-analysis from clinical studies that described populations of pre-menopausal women seeking surgical management (both uterine-sparing and hysterectomy) for their symptomatic fibroids. Procedures included in the analysis were myomectomy, UAE, Lap-RFA, MRgFUS, and hysterectomy. The complication rate for MRgFUS was 6.0% (1.3% major; 5.1% minor) (n = 298), and long-term follow-up averaged 12.6 months (n = 209). The reintervention rate was highest of all the procedures at 30.5% (145 combined patients). Based on their analysis, the authors concluded that MRgFUS carries low complication rates, no blood loss, and moderate improvement in HRQL scores. However, there is also a significant concern for injury of organs that may be in the way for focused ultrasound such as bowel, bladder, and sacral nerves. The authors state that limitations of this review include the inherent heterogeneity among studies; only a portion of the included studies were RCTs, most were not and were assigned an ACOG quality score of B; and lack of uniformity in reporting conventions. Further comprehensive prospective research, ideally in the form of well-powered RCTs, is needed to validate the specific treatment modality preferred for specific anatomical variances of fibroids.

In a pilot study (PROMISe), Jacoby et al. (2016, included in Hayes report) assessed the feasibility of a full-scale, randomized, placebo-controlled trial to evaluate the safety and efficacy of MRgFUS in premenopausal women with symptomatic uterine fibroids. Twenty women (mean 44 years of age) were enrolled. Thirteen were randomly assigned to MRgFUS and 7 to sham therapy. The primary outcome was a change in fibroid symptoms from baseline to 4 and 12 weeks after treatment assessed by the Uterine Fibroid Symptom Quality of Life Questionnaire (UFS-QOL). Secondary outcome was incidence of surgery or procedures for recurrent symptoms at 12 and 24 months. Four weeks after treatment, all participants reported improvement in the UFS-QOL: a mean of 10 points in the MRgFUS group and 9 points in the placebo group. By 12 weeks, the MRgFUS group had improved more than the placebo group (mean 31 points and 13 points, respectively). The mean fibroid volume decreased 18% in the MRgFUS group with no decrease in the placebo group at 12 weeks. After unblinding at 12 weeks, 5 patients in the sham group opted for treatment by MRgFUS and were followed for an additional 12 weeks. Two years after MRgFUS, 4 of 12 women who had a follow-up evaluation (30%) had undergone another fibroid surgery or procedure. The authors noted that a placebo effect may explain some of the improvement in fibroid-related symptoms observed in the first 12 weeks after MRgFUS. This study is limited by very small sample size and substantial loss to follow-up.

In a nonrandomized clinical trial, Froeling et al. (2013, included in Hayes report) compared the long-term outcome after UAE (n = 41) versus magnetic resonance-guided high-intensity focused ultrasound (MR-g HIFU) (n = 36) in women with symptomatic uterine fibroids. Symptom severity and total health-related QOL scores were assessed by questionnaire before treatment and at long-term follow-up after UAE (median 61.9 months) and after MR-g HIFU (median: 60.7 months). Reintervention was significantly lower after UAE (12.2%) than after MR-g HIFU (66.7%) at long-term follow-up. The authors reported that

improvement of symptom severity and health-related QOL scores was significantly better after UAE resulting in a significant lower reintervention rate compared to MR-g HIFU.

In a prospective cohort study, Dobrotwir and Pun (2012) evaluated the efficacy and safety of MRgFUS in 100 patients (mean age 42 years) with symptomatic fibroids (n = 104 treatments). Mean pretreatment fibroid volume was 185 cm^3 (range 2 to 1109). The authors reported that fibroid volume significantly decreased by the 12-month follow-up, and that the symptom severity score decreased by 55%. However, 14% of these patients required reintervention for persistent or recurrent fibroid disease. This study is limited by lack of randomization and control and short-term follow-up.

A retrospective study of 130 patients with symptomatic uterine leiomyomas treated with MRgFUS reported that the cumulative incidence of subsequent treatments for leiomyomas, such as hysterectomy or myomectomy, was 7.4% at 12-months. Patients were followed through retrospective review of medical records and phone interviews. At 3-, 6- and 12-month follow-up, 86% (90 of 105), 93% (92 of 99), and 88% (78 of 89) of patients reported relief of symptoms, respectively. Treatment-related complications were observed in 17 patients (13.1%): 16 patients had minor complications and one had a major complication (deep vein thrombosis). All complications were resolved within the 12-month follow-up period. This study is limited by its retrospective design (Gorny et al., 2011).

Clinical Practice Guidelines

American Academy of Family Physicians

An endometrial biopsy is an office procedure that serves as a helpful tool in diagnosing various uterine abnormalities. Endometrial biopsy is a safe and accepted method for the evaluation of abnormal or postmenopausal bleeding. The procedure is often performed to exclude the presence of endometrial cancer or its precursors such as AUB (Zuber 2001).

American Association of Gynecologic Laparoscopists (AAGL)

In a position statement on the treatment of submucous leiomyomas, the AAGL (2012) states that with currently available evidence, embolic and ablative therapies are not appropriate for women with submucous myomas who have current infertility or who wish to conceive in the future. These techniques include UAE and occlusion, as well as leiomyoma ablation with radiofrequency electricity, cryotherapy, and MRgFUS (based primarily on consensus and expert opinion [Level C]). The AAGL recommends long-term studies on the impact of various ablation techniques on the symptom of HMB in women with submucous leiomyomas.

American College of Obstetricians and Gynecologists (ACOG)

An ACOG committee opinion on uterine morcellation for presumed leiomyomas recommends women should be evaluated to determine increased risk of malignancy of the uterine corpus before considering morcellation of the uterus. The preoperative evaluation should include risk stratification and use of imaging, cervical cancer screening, and endometrial tissue sampling to identify malignancy. Additionally, the patient should be informed of the possible risk of disseminating and occult uterine malignancy by open morcellation, as well as the risk disseminating benign uterine tissue. Shared decision making, between the obstetrician-gynecologist and patient should include informed consent, explanation of risk and benefits of each approach to surgery for presumed leiomyomas, alternatives to morcellation, and the risk and benefits of morcellation (ACOG, 2021).

An ACOG committee opinion on acute AUB concludes that surgical management should be considered for patients who are not clinically stable, are not suitable for medical management or have failed to respond appropriately to medical management. The choice of surgical management should be based on the patient's underlying medical conditions, underlying pathology and desire for future fertility. (ACOG, 2013; reaffirmed 2020).

Clinical management guidelines from ACOG (updated 2021) addressing management of symptomatic uterine leiomyomas makes the following recommendations:

- Laparoscopic RFA can be considered as a minimally invasive treatment option for the management of symptomatic leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes.
- Myomectomy is recommended as a surgical management option for symptomatic leiomyomas in patients who desire uterine preservation or future pregnancy and are counseled about the risk of recurrence.

Levonorgestrel-Releasing Intrauterine Device

In a practice bulletin on management of symptomatic uterine leiomyomas, ACOG states that the levonorgestrel-releasing intrauterine devices (LNG-IUD) may be considered for treatment of abnormal uterine bleeding, however there is insufficient evidence to support their use for the treatment of any other uterine leiomyoma symptoms other than bleeding (ACOG, June 2021).

An ACOG practice bulletin on the use of non-contraceptive uses of hormonal contraceptives states the following:

- Combined oral contraceptives (OC) have been shown to regulate and reduce menstrual bleeding, treat dysmenorrhea, reduce premenstrual dysphoric disorder symptoms and ameliorate acne. (Evidence Level A – Based on good and consistent scientific evidence.)
- Hormonal contraception should be considered for the treatment of menorrhagia in women who may desire further pregnancies (ACOG, 2010; reaffirmed 2020). (Evidence Level B – Based on limited or inconsistent scientific evidence.)

Magnetic Resonance Imaging-Guided Focused Ultrasound Ablation

In a practice bulletin on management of symptomatic uterine leiomyomas ACOG states that while limited, low quality data suggests MRgFUS is associated with a reduction in leiomyoma and uterine size, smaller randomized comparative data suggests when compared with UAE, MRgFUS is associated with less improvement in symptoms and a higher rate of reintervention (ACOG, 2008; reaffirmed 2021).

Radiofrequency Ablation

Based on limited or inconsistent scientific evidence, an ACOG practice bulletin on management of symptomatic uterine leiomyomas states laparoscopic RFA can be considered as a minimally invasive treatment option for the management of symptomatic leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes (ACOG 2021).

Uterine Artery Embolization

In a practice bulletin for AUB, ACOG states an office endometrial biopsy is the first-line procedure for tissue sampling in the evaluation of patients with AUB. Endometrial sampling should be performed on patients younger than 45 years of age for persistent AUB and failed medical management. (ACOG 2012, reaffirmed 2016).

In a practice bulletin on management of symptomatic uterine leiomyomas, ACOG states UAE is recommended as a procedure for the treatment of uterine leiomyomas in women who desire uterine preservation and that they be counseled on the limited available data for reproductive outcomes (ACOG, 2008; reaffirmed 2021).

American College of Radiology (ACR)

ACR appropriateness criteria conclude the following:

- UAE is effective in managing symptomatic uterine fibroids.
- UAE and myomectomy have similar clinical success and complication rates.
- There is little long-term information on the efficacy of MRgFUS.
- A full gynecologic workup, including a Pap smear every 3 years and/or an endometrial biopsy if a patient has menometrorrhagia before UAE is performed (ACR, 2018).

National Institute of Health and Care Excellence (NICE)

A NICE guideline on transcervical ultrasound-guided RFA for symptomatic uterine fibroids states there are no major safety concerns. However, there is limited quality evidence on efficacy and this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. NICE recommends further research, preferably RCTs that include disease-specific QOL and long-term outcomes, as well as details of patient selection (NICE, 2021).

A NICE guideline on assessment and management of HMB recommends LNG-IUS as the first treatment for women with no identified pathology, fibroids less than 3 cm in diameter, or suspected or diagnosed adenomyosis. If the treatment is unsuccessful, the patient declines pharmacological treatment, or symptoms are severe, referral to a specialist is recommended to discuss additional options. For women with fibroids greater than 3 cm in diameter, LNG-IUS is listed as a pharmacologic option. (NICE, 2018; updated 2021)

The NICE guideline on the management of HMB lists UAE as an option for women with fibroids 3 cm or more in diameter. They recommend that the woman's uterus and fibroid(s) be assessed by ultrasound prior to the procedure, and if further information about fibroid position, size, number and vascularity is needed, MRI should be considered (NICE, 2018; updated 2021).

A NICE guidance document states that current evidence on the efficacy of MRgFUS for uterine fibroids in the short term is adequate, although further treatment may be required and the effect on subsequent pregnancy is uncertain. There are well-recognized complications, but the evidence on safety is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance and audit. NICE encourages further research into the efficacy of MRgFUS for uterine fibroids. Research studies should report long-term outcomes, including the need for further treatment (NICE, 2011).

The NICE guidance document states that current evidence on UAE for fibroids shows that the procedure is efficacious for symptom relief in the short and medium term for a substantial proportion of patients. There are no major safety concerns. Therefore, this procedure may be used provided that normal arrangements are in place for clinical governance and audit (NICE, 2010).

Society of Interventional Radiology (SIR)

SIR quality improvement guidelines (Dariushnia et al., 2014) state that UAE is indicated for the treatment of uterine leiomyomata that are causing significant symptoms, occasionally a single symptom, but more commonly a combination of symptoms. The most common of these are:

- Heavy or prolonged menstrual bleeding
- Severe menstrual cramping
- Pelvic pressure, discomfort, excessive bloating or fullness, particularly perimenstrual, or bothersome abdominal wall distortion caused by the enlarged uterus
- Pelvic pain related to identified leiomyomas, including dyspareunia
- Urinary urgency, frequency, nocturia or retention related to the enlarged leiomyomatous uterus
- Hydronephrosis caused by the enlarged uterus

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Levonorgestrel-Releasing Intrauterine Device

Mirena® received FDA approval on December 8, 2000 for use as an intrauterine contraceptive. Treatment of HMB for women who choose to use intrauterine contraception as their method of contraception was approved as an additional indication on October 1, 2009. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed April 14, 2023)

Skyla® received FDA approval on January 9, 2013 for use as an intrauterine contraceptive. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed April 14, 2023)

Liletta™ received FDA approval on February 26, 2015 for use as an intrauterine contraceptive. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed April 14, 2023)

Kyleena™ received FDA approval on September 16, 2016 for use as an intrauterine contraceptive. Search the following website for more information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed April 14, 2023)

Uterine Artery Embolization

Uterine artery embolization (UAE) is a procedure and, therefore, not subject to FDA regulation. However, the embolic agents used are subject to FDA oversight. A number of agents are approved by the FDA for embolization procedures of the neurological system, but several have been specifically approved for UAE. Search the following website for additional information: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. (Accessed April 14, 2023)

Magnetic Resonance-Guided Focused Ultrasound (MRgFUS)

The ExAblate 2000/2100 System (Insightec) received premarket approval (PMA) on October 22, 2004 (P040003); approval for updated labeling was given on August 9, 2011. The device is indicated for ablation of uterine fibroid tissue in pre- or perimenopausal women with symptomatic uterine fibroids who desire a uterine sparing procedure and whose uterine size is less than 24 weeks. On August 31, 2015, the indications were modified to remove the restriction of treatment to women who had completed childbearing. Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P040003S009. (Accessed April 14, 2023)

Laparoscopic Ultrasound-Guided Radiofrequency Ablation

The Acessa System received FDA clearance for marketing on November 5, 2012 (K121858). The device is indicated for use in percutaneous, laparoscopic coagulation and ablation of soft tissue, including treatment of symptomatic uterine fibroids under laparoscopic ultrasound guidance. Refer to the following website for additional information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K132744. (Accessed April 14, 2023)

The Acessa ProVu System, the next generation of the Acessa System, received FDA clearance on September 28, 2018. It is indicated for use in percutaneous, laparoscopic coagulation and ablation of soft tissue, including treatment of symptomatic uterine fibroids under laparoscopic ultrasound guidance. Refer to the following website for additional information: https://www.accessdata.fda.gov/cdrh_docs/pdf18/K181124.pdf. (Accessed April 14, 2023)

The Sonata® Sonography-Guided Transcervical Fibroid Ablation System received FDA clearance for marketing on August 15, 2018. This device is intended for diagnostic intrauterine imaging and transcervical treatment of symptomatic uterine fibroids, including those associated with heavy menstrual bleeding. Refer to the following website for additional information: https://www.accessdata.fda.gov/cdrh_docs/pdf17/K173703.pdf . (Accessed April 14, 2023)

Laparoscopic Power Morcellation Warning

A February 25, 2020 FDA Safety Communication recommends performing laparoscopic power morcellation for myomectomy or hysterectomy only with a tissue containment system (legally marketed in the U.S.) for use during laparoscopic power morcellation and performing only in appropriately selected patients.

Refer to the following website for additional information: https://www.fda.gov/medical-devices/safety-communications/update-perform-only-contained-morcellation-when-laparoscopic-power-morcellation-appropriate-fda. (Accessed April 14, 2023)

A November 24, 2014 FDA Safety Communication recommends that manufacturers of laparoscopic power morcellators with a general indication or a specific gynecologic indication prominently include the following black box warning and contraindications in their product labeling:

Warning

Uterine tissue may contain unsuspected cancer. The use of laparoscopic power morcellators during fibroid surgery may spread cancer and decrease the long-term survival of patients. This information should be shared with patients when considering surgery with the use of these devices.

Contraindications

- Laparoscopic power morcellators are contraindicated in gynecologic surgery in which the tissue to be morcellated is known or suspected to contain malignancy.
- Laparoscopic power morcellators are contraindicated for removal of uterine tissue containing suspected fibroids in patients who are peri- or post-menopausal, or are candidates for an bloc tissue removal, for example through the vagina or via a mini-laparotomy incision.

Refer to the following website for additional information:http://wayback.archive-it.org/7993/20170722215727/https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm424443.htm. (Accessed April 14, 2023)

In December 2017, the FDA released new findings on the risks of spreading hidden uterine cancer through the use of laparoscopic power morcellators which suggests that approximately 1 in 225 to 1 in 580 women who undergo surgery (hysterectomy or myomectomy) for presumed benign uterine growths may have occult or hidden uterine cancers known as sarcomas. This is generally consistent with the 1 in 350 incidences estimated by the FDA in a 2014 review. The FDA also estimates the rate of occult leiomyosarcoma, a particularly aggressive type of sarcoma, to be approximately 1 in 495 to 1 in 1100, again in general agreement with our previous assessment of 1 in 498. Ranges in incidence represent estimates based on differing statistical analyses of available study data.

A white paper published in December 2017 provides an update on medical device reports the FDA received through April 2017 related to the use of laparoscopic power morcellators and how hysterectomy and myomectomy procedure selection has changed since the FDA's 2014 warning against the routine use of morcellators to treat suspected uterine fibroids. This data demonstrates that overall, use of laparoscopic power morcellators has decreased since the FDA warned about it in 2014.

Refer to the following website for additional information: https://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/SurgeryandLifeSupport/UCM584539.pdf. (Accessed April 14, 2023)

In December of 2020, the FDA provided final guidance for product labeling for laparoscopic power morcellators which includes recommendations on the content and format for certain labeling to better inform patients and health care providers of the risks associated with these devices. Refer to the following website for additional information: https://www.fda.gov/medical-devices/surgery-devices/laparoscopic-power-morcellators. (Accessed April 14, 2023)

Transcervical Ultrasound-Guided Radiofrequency Ablation

The Sonata® Sonography-Guided Transcervical Fibroid Ablation System received FDA 510(k) marketing clearance on August 15, 2018. It is intended for diagnostic intrauterine imaging and transcervical treatment of symptomatic uterine fibroids, including those associated with heavy menstrual bleeding. Refer to the following website for additional information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K173703. (Accessed July 5, 2022)

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Policy History/Revision Information

Date	Summary of Changes
08/01/2023	**Related Policies** • Added reference link to the Medical Policy titled *Hysterectomy (for Ohio Only)* **Application** • Added language to indicate any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using *Ohio Administrative Code 5160-1-01* **Coverage Rationale** ***Endometrial Ablation*** • Added language to indicate endometrial ablation is proven and medically necessary for treating abnormal uterine bleeding in premenopausal individuals; for medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Hysteroscopy, Operative, Endometrial ablation for abnormal bleeding in premenopausal individual ***Uterine Fibroids*** Ultrasound-Guided Radiofrequency Ablation • Changed coverage status for ultrasound-guided radiofrequency ablation from "unproven and not medically necessary" to "proven and medically necessary when [listed] criteria are met" ○ Added language to indicate laparoscopic ultrasound guided radiofrequency ablation (Acessa) or transcervical ultrasound guided radiofrequency ablation (Sonata) is medically necessary as an alternative to myomectomy or hysterectomy for treating symptomatic uterine fibroid(s) when all the following criteria are met: ▪ Uterine preservation is desired • Fibroid(s) < 10 cm (in any diameter) ▪ Uterine size < 16 gestational weeks • No history of gynecologic malignancy or pre-malignancy within the past 5 years ▪ No history of cervical dysplasia • Member has received counseling regarding the lack of data for individuals that want to become pregnant ○ Removed language indicating ultrasound-guided radiofrequency ablation (e.g., Acessa™, Sonata®) is unproven and not medically necessary for treating uterine fibroids due to insufficient evidence of efficacy

Date	Summary of Changes
	Uterine Artery Embolization (UAE) • Removed language indicating uterine artery embolization (UAE) is unproven and not medically necessary for the purpose of preserving childbearing potential for women with symptomatic uterine fibroids due to insufficient evidence of efficacy **Applicable Codes** • Added CPT code 58563 • Removed CPT codes 58578 and 58999 **Supporting Information** • Updated *Description of Services*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version CS002OH.X – P

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]) or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC) or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC) or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC) or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare uses InterQual® for the primary medical/surgical criteria, and the American Society of Addiction Medicine (ASAM) for substance use, in administering health benefits. If InterQual® does not have applicable criteria, UnitedHealthcare may also use UnitedHealthcare Medical Policies, Coverage Determination Guidelines, and/or Utilization Review Guidelines that have been approved by the Ohio Department for Medicaid Services. The UnitedHealthcare Medical Policies, Coverage Determination Guidelines, and Utilization Review Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.