



Uterine Fibroids

*A report on the condition and
its impact on women in the U.S.*

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INTRODUCTION

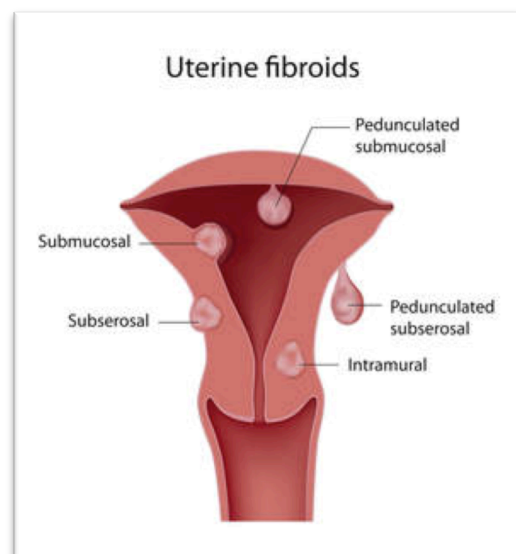
Uterine fibroids are the most common gynecological condition among women, with lifetime prevalence exceeding 80% among black women and approaching 70% among white women.¹ Uterine fibroids are usually noncancerous growths that develop within the muscle tissue of the uterus. Some fibroids never cause any symptoms or problems, and many women will never know they have this condition.² But in rare circumstances, uterine fibroids may lead to devastating personal health consequences for women and their loved ones.

Since most women *have* fibroids, the line between normal and abnormal can be blurry. For example, is having uterine fibroids actually the norm? And are fibroid symptoms therefore “normal,” or should they be cause for concern? When is it time to see a health care provider? When is treatment appropriate and what treatment best meets each woman’s needs and preferences? This understandable and common confusion unfortunately results in an underappreciation of fibroids as a clinical problem, delay in identification of symptoms and treatment, and avoidable economic and emotional costs.

WHAT ARE UTERINE FIBROIDS?

Uterine fibroids, also called leiomyomas or myomas, are common, usually noncancerous growths of the uterus. They are of varying size and are distinct from the surrounding tissue.³ Some are so small, they are undetectable to the human eye; others are large enough to reshape the uterus itself, particularly when multiple fibroids are present.

Uterine fibroids grow in various locations within the uterus.⁴ Intramural fibroids are found within the muscular uterine wall; submucosal fibroids grow into the uterine cavity; subserosal fibroids extend beyond the uterus into the pelvic cavity. Uterine fibroids also grow at different rates and in different ways: some very slowly, others very quickly. Some fibroids grow and then stop; some get smaller on their own. Fibroids tend to shrink after menopause as hormone production decreases.⁵ Exactly why or how uterine fibroids grow is unknown, but ongoing research indicates genetic changes, hormones, and other growth factors in the body seem to play a role.



While it is extremely rare, there is a very small chance (less than one in 1,000) that a woman will have a cancerous fibroid, called a leiomyosarcoma.⁶ Importantly, existing, noncancerous fibroids cannot become cancerous and there is no known association between leiomyosarcoma and other forms of cancer.

Uterine fibroids are the most common gynecological condition among women.⁷ While prevalence estimates vary, lifetime prevalence of uterine fibroids among black women exceeds 80%, and approaches 70% for white women.⁸ Prevalence estimates for other racial and ethnic groups are not available in the literature. Many of these women will have asymptomatic or undiagnosed uterine fibroids. However, one study estimates that about 25% of all white and 50% of all black women will experience symptomatic fibroids during their lifetime.⁹

RISK FACTORS

While the exact cause of uterine fibroids is unknown, the greatest risk factor is simply being a woman of reproductive age with a uterus.¹⁰ Other major risk factors include increasing age up to menopause and black race.¹¹ (This paper offers a detailed discussion of the specific impact for African American women below.) But other factors may contribute as well, including hereditary risk, specific genetic mutations, environmental factors, onset of early menstruation, oral contraceptive use before age 16, obesity, alcohol use, vitamin D deficiency, and a nutritional intake higher in red meat and lower in green vegetables, fruit, and dairy. Use of progestin-only injectable contraceptives, a diet higher in fruit, vegetables, and low-fat dairy products, and having more pregnancies that reach a viable gestational age are associated with a reduced risk of fibroids.¹²

SYMPTOMS

Common symptoms of uterine fibroids include heavy menstrual bleeding, menstrual periods lasting more than a week, pelvic or lower abdominal pain or pressure, frequent urination, difficulty emptying the bladder, constipation, pain during intercourse, and backache or leg pain.¹³ Large fibroids that lead to an enlarged uterus can also cause symptoms including bowel and bladder dysfunction and abdominal protrusion.¹⁴ Severe fibroid symptoms can be disabling, leading to anemia, urinary tract infections, and kidney damage.¹⁵

Women with uterine fibroids may also be more likely to experience difficulties during pregnancy and childbirth. Though it is uncommon, fibroids are associated with infertility.¹⁶ Most women, however, experience healthy pregnancies and births.¹⁷

DETECTION AND DIAGNOSIS

Uterine fibroids are often found during a routine pelvic exam. If uterine fibroids are suspected, a patient's health care provider may order imaging tests.¹⁸ Ultrasound, which uses sound waves to allow mapping and measurement of fibroids within the uterus, is often

the first imaging test used in fibroid diagnosis. An ultrasound may be done on the abdomen (transabdominal) or inside the vagina (transvaginal).

If additional information is needed after an ultrasound, a provider might order:

- Magnetic Resonance Imaging (MRI);
- Hysterosonography, which uses sterile saline (salt water) to distend the uterine cavity to obtain better images;
- Hysterosalpingography, which uses dye to highlight the uterine cavity and fallopian tubes on x-ray images; or
- Hysteroscopy, which uses a small endoscope and fluid to examine the walls of the uterus and openings to the fallopian tubes.¹⁹

Health care providers may also order lab tests such as a complete blood count (CBC) for patients reporting abnormal menstrual bleeding.²⁰ A CBC can determine if abnormal bleeding has led to anemia, a deficiency of red blood cells or hemoglobin in the blood.

DIAGNOSIS CHALLENGES

Sadly, even with all the diagnostic tools described above, women with symptomatic uterine fibroids wait an average of 3.6 years before seeking diagnosis or treatment, and nearly one-third wait more than five years.²¹ When women do seek care, they see two or more providers in order to obtain a proper diagnosis.

Surveys of women with symptomatic or recently-treated uterine fibroids reveal some reasons for this behavior. First, women report limited knowledge of fibroids: 48 percent of women with fibroids indicated no knowledge of the condition before diagnosis.²² Second, about two-thirds of women did not believe they were at risk for developing fibroids. Third, women try to ignore the issue altogether, using “avoidance-based coping strategies” and dissociating, or distancing themselves, from their fibroid symptoms.

A final, key reason cited for delayed diagnosis is the perception that the symptoms - heavy menstrual bleeding, lengthy menstrual periods, or pain during intercourse - are “normal” and therefore not deserving of personal or medical attention.²³

WHAT IS NORMAL?

So what is normal? The average length of a menstrual cycle, measured from the first day of one period to the first day of the next period, is 28 days long.²⁴ However, cycles ranging from 21 to 35 days are considered normal. Menstrual cycles tend to become shorter and more consistent as women age, but may become less consistent as menopause approaches. The length of a period can also vary by month and among different women, but is typically three to five days.²⁵ A period lasting two to seven days is considered normal.

On average, a woman loses approximately two to three tablespoons of blood during her period.²⁶ (Menstrual blood comprises approximately 30-50% of menstrual flow, which also includes endometrial lining, cervical mucus, and other components.²⁷) However, measuring blood loss can be challenging for a woman in the absence of clinical tools to measure hemoglobin contained in used menstrual sanitary supplies.²⁸

Given these challenges in measuring blood loss, the following guidelines have been developed to help identify heavy menstrual bleeding. A call to a health care provider may be warranted if the following heavy menstrual bleeding symptoms are present:

- A period that lasts longer than 8 days;
- Using (bleeding through) one or more pads or tampons every two to three hours;
- Passing menstrual clots larger than the size of a quarter;
- Feeling lightheaded, weak, dizzy, out of breath, or tired, which may be symptoms of anemia, a condition that occurs due to a lack of iron that impedes the ability of blood cells to carry oxygen around the body.²⁹

Menstrual pain and cramping are also hard to measure. Menstrual pain, or dysmenorrhea, is the most common problem women have with periods, affecting more than half of women.³⁰ Some pain, called primary dysmenorrhea, is common and is caused by the uterus contracting to shed the endometrial lining. This type of menstrual pain typically lessens as women age. However, secondary dysmenorrhea may indicate another health problem. This type of pain worsens as a woman ages and also lasts longer than typically period cramps. Menstrual pain that cannot be managed with over-the-counter pain medication or that interferes with work or school is reason to speak with a health care provider.³¹

MENTAL HEALTH CHALLENGES

Once diagnosed, some women and their families suffer major emotional health consequences. In a 2015 study of patients with symptomatic, diagnosed uterine fibroids, most women reported fear, anxiety, anger, and/or depression.³² Half of the women reported feeling helpless and without control over their fibroids. Many of these women worried that their fibroids would grow, that they would have additional health complications, that they would need a hysterectomy, or that their fibroids could become cancerous (though, as described above, noncancerous fibroids do not become cancerous).³³

Many women with symptomatic, diagnosed uterine fibroids also report a negative self-image, including feeling less attractive, which can lead to intimacy challenges with their partners.³⁴ In fact, loss of sexual intimacy is among the greatest fears for women with symptomatic uterine fibroids, with 52% of women concerned about their sexual function.³⁵ A diagnosis of uterine fibroids may also negatively influence women's non-sexual relationships, with more than one in five women with

symptomatic fibroids reporting that fibroids impede their ability to care for their home and children and interfere with relationships with family and friends.³⁶

ECONOMIC COSTS

In addition to the emotional and mental health costs of uterine fibroids, fibroids are also financially costly both for patients and the health care system. Direct annual health care system costs attributable to uterine fibroids exceed \$9.4 billion.³⁷ Patients themselves also bear costs associated with lost wages, lost productivity, and short-term disability. In fact, nearly one-third of women with symptomatic uterine fibroids report missing work due to their condition, and 24% believe their symptoms prevented them from reaching their career potential.³⁸ Altogether, these costs to patients amount to roughly \$4,624 per woman in the first year of diagnosis, and between \$5 billion and \$17 billion for all women.³⁹

UTERINE FIBROIDS AND AFRICAN AMERICAN WOMEN

African American women are more likely to have fibroids than women of other racial groups – a threefold greater incidence and relative risk of fibroids – and they are more likely to have fibroids at younger ages, to have bigger fibroids, and to have multiple fibroids.⁴⁰ Sadly, with such high incidence, uterine fibroid symptoms might seem even more “normal” in this cohort.

African American women are also 2.4 times more likely to undergo a hysterectomy to treat fibroids and 6.8 times more likely to undergo myomectomy (which removes the fibroids but leaves the uterus intact).⁴¹ (See below for more information on these and other treatment options.) African American women with fibroids are also more likely to have preoperative anemia and severe pelvic pain.⁴²

A 2012 survey of women with symptomatic uterine fibroids also revealed that African American women were significantly more likely to have severe or very severe symptoms including⁴³:

- Heavy or prolonged menses;
- Menstrual cramps;
- Passage of clots during their period;
- Interference with physical activities;
- Interference with relationships; and
- Missed days of work.

In fact, this same survey revealed that African American women with fibroids report abdominal bloating, pressure, and protrusion at two times the rate of Caucasian women. They report anemia at three times the rate of Caucasian women.

African American women also report greater disruption to everyday life. Twenty-two percent report that fibroids affected their relationship with a significant other and 14% report that fibroids

affected their ability to care for their home or children. Fibroids also cause a disproportionate economic impact on African American women, as they are 77% more likely to miss work due to fibroids than Caucasian women.

A diagnosis of uterine fibroids also seems to cause greater emotional distress and anxiety for African American women than for Caucasian women.⁴⁴ While black and white women report equal levels of concern about needing a future hysterectomy or that fibroids might cause cancer, black women report certain anxieties with much greater frequency, including that:

- Fibroids will affect my sex life;
- Fibroids will affect my relationship with my significant other;
- Fibroids will affect my ability to have a successful and healthy pregnancy; and
- Fibroids will make me depressed.

Notably, anxiety about treatment for fibroids revealed an even greater racial gap.⁴⁵ African American women reported much higher rates of concern that fibroid treatments would compromise their fertility, their ability to have a healthy pregnancy, their own sense of femininity, and the potential for scarring.

TREATMENT OPTIONS

Following diagnosis, uterine fibroid treatment and care options depend upon the severity of a woman's symptoms, the location of the fibroids, the type of fibroids, and personal preferences, particularly with regard to pregnancy. In surveys, women, especially African American women, express clear preferences for treatment options that avoid invasive surgery, preserve the uterus, and preserve fertility for those of childbearing age.⁴⁶

For women with asymptomatic fibroids, treatment is generally unnecessary and is not supported by evidence.⁴⁷ For these women, as well as for those who report mild symptoms that are not measurably affecting their lives, "watchful waiting" is often the chosen treatment course. "Watchful waiting" involves monitoring the fibroid(s) for growth and monitoring symptom presentation or progression. This approach is often selected by women with mild symptoms who are approaching menopause, when fibroids typically shrink and symptoms decrease.

For symptomatic uterine fibroids, patients and their health care providers have a variety of options including medication, noninvasive procedures, minimally invasive procedures, and traditional surgical procedures. Ongoing research seeks to compare all of the treatment options outlined below, and to better understand the risks and benefits of each, with the goal of helping women and their loved ones make informed treatment decisions.⁴⁸ The treatment options presented here may not be appropriate for all women and should be considered only when under the care of a trained health care provider.

MEDICATION

Medication may be used to treat fibroid symptoms, including cramping, heavy bleeding, and painful periods, or to temporarily shrink fibroids, sometimes in preparation for surgical treatment options.⁴⁹

Medications approved to treat symptoms associated with uterine fibroids (but that do not treat the fibroids directly):

- **Over-the-counter pain medications**, including acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen or naproxen, can help relieve pain, cramping, and decrease menstrual bleeding, but do not treat the fibroids themselves.
- **Iron supplementation** may help treat symptoms of anemia, which may be caused by heavy menstrual periods.⁵⁰
- **Hormonal birth control**, including oral contraceptives, combined hormonal vaginal rings, and levonorgestrel-releasing intrauterine devices (IUDs) and other long-acting reversible contraceptive (LARC) methods, can help treat heavy and prolonged menstrual bleeding that often accompanies uterine fibroids, though they are not approved by the U.S. Food and Drug Administration (FDA) for this purpose. The Mirena (L-IUD) is FDA approved for the treatment of heavy menstrual bleeding.
- **Tranexamic acid**, an oral antifibrinolytic agent approved for the treatment of heavy menstrual bleeding, is taken only during heavy menstrual bleeding and can help decrease bleeding, usually with minimal side effects.⁵¹

Medications to temporarily shrink fibroids (upon cessation of medication, fibroids return in size):

- **Gonadotropin-releasing Hormone (GnRH) agonists and antagonists** may shrink fibroids, but only during treatment.⁵² These medications temporarily place a woman's body into menopause and are primarily indicated for short-term use, such as to reduce fibroid size in preparation for a less invasive surgical procedure or when a woman is approaching menopause.⁵³ One GnRH agonist, leuprolide, is approved for short-term use in a specific population of women with symptomatic uterine fibroids while another, elagolix, is approved to manage moderate to severe pain associated with endometriosis.⁵⁴
- **Progesterone receptor modulators**, such as mifepristone and ulipristal acetate, use a different mechanism to shrink fibroids, also helping to decrease symptoms. Although both are approved by the FDA for other purposes, they are not FDA approved to treat uterine fibroids or symptoms.⁵⁵ At the time of publication, the FDA has not yet approved ulipristal acetate for the treatment of abnormal uterine bleeding in women with fibroids.
- **Aromatase inhibitors and androgenic steroids** have shown some promising results in treating fibroids but they are not FDA approved for this use and more evidence is required to support their use.

NONINVASIVE PROCEDURES

Focused ultrasound surgery, guided by magnetic resonance imaging (MRI), is a noninvasive surgical procedure that uses sound waves to heat and destroy fibroid tissue.⁵⁶ Side effects for this procedure are rare and there is some evidence for high rates of successful pregnancy following the procedure, but more research is necessary.⁵⁷

MINIMALLY INVASIVE PROCEDURES

Various minimally invasive procedures, which minimize surgical incisions and are often performed using thin needles and/or small scopes, are available for the treatment of uterine fibroids:

- **Myomectomy**, which may be performed using minimally invasive or traditional surgical techniques, is an option for women with symptomatic uterine fibroids. In this procedure, fibroids are removed but the uterus is left intact.⁵⁸ Depending on the type, size, and location of fibroids, a physician may perform a hysteroscopic myomectomy, in which instruments are inserted through the vagina, or a laparoscopic or robotic myomectomy, using small incisions made in the abdomen.⁵⁹ Myomectomy is the first-line therapy for most women in whom submucosal fibroids are the cause of bleeding, and results in rapid recovery and a beneficial effect on future pregnancy.⁶⁰
- **Radiofrequency ablation**, which gained FDA approval in 2012, directs radiofrequency energy directly into each uterine fibroid, causing cell death.⁶¹ Known as the Acessa procedure, this treatment innovation can target almost all fibroid sizes and locations and, because it requires just two, one-centimeter abdominal incisions, recovery is measured in days, rather than weeks.⁶² Due to its more recent approval, limited data on side effects and the impact on subsequent pregnancy are available.⁶³ A similar device, the Sonata system, gained FDA approval in August 2018.⁶⁴ Like the Acessa system, the Sonata system provides radiofrequency ablation of uterine fibroids, but uses a transcervical approach that does not require incisions.⁶⁵
- **Uterine artery embolization**, which eliminates the flow of blood to the fibroids, can shrink fibroids and relieve symptoms.⁶⁶ In this minimally invasive procedure, an interventional radiologist uses either the femoral or radial artery to gain access to the vessels that supply blood to the uterus. The impact of embolization on future pregnancies requires future study. While successful deliveries have been reported, a randomized trial found a higher rate of delivery and lower rate of miscarriage following myomectomy compared to embolization.⁶⁷
- **Endometrial ablation** is another minimally invasive procedure that uses various agents, such as heat, electric current, or microwave energy, to destroy the endometrium.⁶⁸ This option either eliminates menstruation or significantly reduces menstrual bleeding. Because it increases the risk of pregnancy complications, pregnancy is not recommended after this procedure.

TRADITIONAL SURGICAL PROCEDURES

Hysterectomy, which is complete removal of the uterus, is a common option for women who have completed childbearing, accounting for nearly three quarters of all fibroid surgical procedures.⁶⁹ It also provides the most effective treatment for fibroids since it eliminates the risk of new fibroid formation.⁷⁰ It is, however, a major surgery and comes with a higher risk of complications and longer recovery time than other nonsurgical or minimally invasive treatment options.⁷¹

Laparoscopic hysterectomy is an alternative to traditional hysterectomy and does not require a large incision. Until 2014, when the FDA began issuing safety warnings about its use, some laparoscopic hysterectomies were accompanied by power morcellation. Power morcellation divides the uterus so it can be removed through small incisions. However, it may also introduce a risk that undiagnosed uterine cancer may be spread throughout the abdomen and pelvis, and the FDA now discourages the use of power morcellation during hysterectomy or myomectomy for uterine fibroids.⁷² The use of power morcellation dropped significantly following the FDA's safety communications.⁷³

HEALTH SYSTEM CHALLENGES

The U.S. health care system presents several challenges to detecting, diagnosing, and treating uterine fibroids and furthering understanding and awareness of the condition among patients and health care providers.

First, insurance coverage may be a barrier to accessing care. While most insurance plans are now required to provide coverage of an annual well women visit without cost-sharing, any non-routine screening or testing, such as that conducted to diagnose fibroids, or fibroid treatment is generally subject to the health plan's typical cost-sharing requirements.

Second, the health system is also challenged by the insufficiency of research on uterine fibroids and significant gaps in the existing research. In 2011, the U.S. Agency for Healthcare Research and Quality (AHRQ) offered an assessment of current evidence on fibroids. They concluded that current literature is limited by significant gaps.⁷⁴ Some of these relate to key components of study design, including validity, study population size, use of validated measures, and the direct comparison of treatment options. AHRQ also called for the development of "patient centered outcome measures for fibroid care."

AHRQ also noted lack of content in certain key areas, such as disease burden, predictors of symptom development and resolution, variation in care-seeking, health and quality of life outcomes, risks to fertility and future pregnancy complications, and specific disparities between white and black women, among other areas.⁷⁵ While research indicates that uterine fibroids are most common among black women and least common among Asian women, data regarding other racial differences are more limited, though one study of women in the first trimester of pregnancy did find differences in incidence for black, Hispanic, and Caucasian women.⁷⁶

The reasons for these differences are largely unknown, though researchers have explored potential explanations, including racial differences in the biosynthesis and metabolism of the hormone estrogen, differences in how the body receives and expresses steroid hormones, and differences in RNA.⁷⁷ Other studies have analyzed genetic, lifestyle, dietary, and stress factors in these racial differences, but these factors do not completely explain observed incidence.⁷⁸

PATIENT AND FAMILY AWARENESS

Women must be advocates for their own health, and for the health of their loved ones to support them in seeking care when any symptoms of uterine fibroids are present. Health care providers also must understand what is considered a “normal” menstrual cycle and ask patients about these and other uterine fibroid symptoms.

CARE About Fibroids developed the Fibroid MAP to help women and their health care providers detect symptomatic uterine fibroids. Using the MAP acronym can help women and their providers flag any **M**enstrual changes, **A**bdominal, urinary, or bowel problems, or **P**ain, pressure, and reproductive problems for discussion and follow up.

Following the **Fibroid MAP** can help detect symptomatic uterine fibroids.

- M**enstrual Changes
 - Longer, more frequent or heavier periods
 - Menstrual cramps
 - Vaginal bleeding at times other than during period
 - Heavy vaginal bleeding may cause anemia
- A**bdominal, Urinary and Bowel Problems
 - Abdominal cramps
 - Pain in the abdomen and lower back
 - Difficulty urinating or frequent urination
 - Constipation, rectal pain
- P**ain, Pressure and Reproductive Problems
 - Enlargement, bloating of the lower abdomen
 - Pain during sex
 - Complications during pregnancy and labor
 - Infertility (a rare problem)

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In addition, the American College of Obstetricians and Gynecologists has developed a list of signs and symptoms that may signal the need for fibroid treatment, including:

- Heavy or painful menstrual periods that cause anemia or that disrupt a woman's normal activities
- Bleeding between periods
- Uncertainty whether the growth is a fibroid or another type of tumor, such as an ovarian tumor
- Rapid increase in growth of the fibroid
- Infertility
- Pelvic pain."⁷⁹

LOOKING AHEAD

Improved awareness and understanding of the signs and symptoms of uterine fibroids is imperative. Patients, their loved ones, and their health care providers must work towards earlier diagnosis and access to appropriate care. In addition, more research is needed to shed greater light on differences in uterine fibroid incidence among many different racial and ethnic groups, as well as to better understand causes for and potential mitigation of the disproportionate impact of uterine fibroids on black women. When treatment is indicated, insurance coverage policies must ensure that women can access that treatment with reasonable cost-sharing requirements. All of these things must be supported by thoughtful public policy that places focus on women and their loved ones who are navigating a complicated health care system, often with little knowledge of their condition, or even awareness that their symptoms are not "normal."

In spite of these challenges, there is reason for hope. Women and their families today have a number of effective diagnosis and treatment options for uterine fibroids and symptoms, including medication as well as noninvasive, minimally invasive, and traditional surgical procedural options. In addition, research continues on innovative new diagnosis and treatment options that preserve women's fertility, as well as on comparative effectiveness research to help women, their loved ones, and their health care providers make informed treatment decisions.⁸⁰ For example, research is underway on screening methods to determine if a uterine tumor or fibroid is cancerous prior to treatment.⁸¹ With a reliable method to determine that tumors are not cancerous, power morcellation, which helps to reduce complications in laparoscopic uterine fibroid procedures, may become more prevalent, helping women avoid a more invasive, traditional hysterectomy.

In addition, as briefly mentioned above, as of this writing, the FDA has not yet approved the pharmaceutical ulipristal acetate for treatment of uterine fibroids. Ulipristal acetate is approved in the U.S. for another indication, as emergency contraception, and approved in Europe and Canada for pre-surgical treatment of fibroids.⁸² Studies have found the drug can induce cell death in the fibroids, decrease proliferation of fibroids, and reduce fibroid size. In addition, ulipristal acetate shows great promise in fertility preservation, with one study finding 71% of women treated with

ulipristal acetate for uterine fibroids achieved pregnancy following conclusion of ulipristal, and 66% of these pregnancies resulted in live births.⁸³

More pharmaceutical treatment options may soon be available, with clinical trials of three drugs to treat heavy menstrual bleeding due to uterine fibroids currently underway. One trial is evaluating elagolix, a gonadotropin-releasing hormone agonist, alone and in combination with estradiol/norethindrone acetate, an estrogen progestin combination therapy.⁸⁴ This Phase 3 trial is estimated to be completed by December 21, 2018. Phase 3 trials are underway for a gonadotropin-releasing hormone receptor antagonist, relugolix, which also treats heavy menstrual bleeding due to uterine fibroids.⁸⁵ Two different trials of relugolix are anticipated to be completed in June 2019 and January 2020. Finally, a Phase 3 trial investigating the safety and efficacy of vilaprisan, a selective progesterone receptor modulator, to treat heavy menstrual bleeding in women with uterine fibroids is anticipated to be complete in May 2020.⁸⁶ Experts note that vilaprisan works very quickly, in just three days, to control fibroid-related heavy menstrual bleeding.⁸⁷

With regard to procedural treatment options, in August 2018, the FDA approved the Sonata system, mentioned above. By offering radiofrequency ablation of uterine fibroids using a transcervical approach, a woman can preserve her uterus while avoiding all incisions, speeding her return to daily activities. The makers of the Sonata system continue to follow patients who volunteer via a registry that collects questionnaire data on a number of treatment recovery, patient satisfaction, pregnancy, and other issues.⁸⁸

Research also continues on procedural treatment options for uterine fibroids. For example, the makers of the Acessa procedure, described above, continue to evaluate the efficacy of their product, which uses radiofrequency to destroy fibroid tissues in a minimally invasive procedure. One current study is evaluating fibroid-related symptoms at various points up to 36 months after the Acessa procedure. It is also assessing operative outcomes, such as time to return to activities, post-operative pain, blood loss, complications, and more.⁸⁹

Many academic medical centers are also involved in uterine fibroid research. For example, experts at Johns Hopkins Medicine have spent more than a decade studying the cellular structure of uterine fibroids, seeking to understand why fibroids form.⁹⁰ Using this knowledge, researchers led by Dr. James Segars aim to develop an enzyme that could be injected into uterine fibroids and cause them to shrink or disappear completely. Meanwhile, researchers at Mount Sinai Hospital in Canada are comparing patient satisfaction and quality outcomes among women who undergo uterine artery embolization using either femoral artery access (in the groin) or radial artery access (in the wrist).⁹¹ Observational studies comparing the two access methods for heart procedures have generally confirmed reduced risk of complications and improved patient outcomes, including faster recovery, with transradial access.⁹²

CONCLUSION

Uterine fibroids are the most common gynecological condition among women, yet many women suffer devastating and debilitating symptoms and complications of uterine fibroids for years before seeking care.⁹³ This is due in part to the belief that fibroid symptoms are normal. By increasing awareness of uterine fibroids and their symptoms among women, loved ones, and health care providers, women may achieve earlier diagnosis and access an appropriate treatment that meets their needs and preferences. Once patients have been properly diagnosed, their health care providers must present the range of treatment options so women and their families can determine the best course for them. In addition, it is essential that they have adequate coverage to ensure that they can access the right care. Earlier diagnosis, treatment, and adequate coverage can help mitigate the physical, emotional, and economic toll the uterine fibroids take on women, their families, and our health care system.

ENDNOTES

- 1 Stewart EA. Uterine Fibroids. *New England Journal of Medicine*. April 23, 2015. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 2 Stewart EA. Uterine Fibroids. *Lancet*. 2001 Jan;257(9252):293-298
- 3 Mayo Clinic. Uterine Fibroids: Symptoms & Causes. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/symptoms-causes/syc-20354288>
- 4 Mayo Clinic. Uterine Fibroids: Symptoms & Causes. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/symptoms-causes/syc-20354288>
- 5 Mayo Clinic. Uterine Fibroids: Symptoms & Causes. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/symptoms-causes/syc-20354288>
- 6 CARE About Fibroids. Fibroids: The 411. 2018. Accessed July 25, 2018. Available at: <http://www.careaboutfibroids.org/411.html>
- 7 Stewart EA. Uterine Fibroids. *Lancet*. 2001 Jan;257(9252):293-298
- 8 Stewart EA. Uterine Fibroids. *New England Journal of Medicine*. April 23, 2015. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 9 Mutch DG et al. Uterine Fibroids. *Merck Manual*. November 2017. Accessed July 25, 2018. Available at: <https://www.merckmanuals.com/professional/gynecology-and-obstetrics/uterine-fibroids/uterine-fibroids>. See also Fuldeore MJ and Soliman AM. Patient-reported prevalence and symptomatic burden of uterine fibroids among women in the United States: findings from a cross-sectional survey analysis. *International Journal of Women's Health*. June 7, 2017. Accessed July 25, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5476627/>
- 10 Mayo Clinic. Uterine Fibroids: Symptoms & Causes. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/symptoms-causes/syc-20354288>
- 11 Stewart EA. Uterine Fibroids. *New England Journal of Medicine*. April 23, 2015. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 12 Stewart EA. Uterine Fibroids. *New England Journal of Medicine*. April 23, 2015. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 13 Mayo Clinic. Uterine Fibroids: Symptoms & Causes. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/symptoms-causes/syc-20354288>. See also National Women's Health Network. Fibroids Overview. February 2018. Accessed July 25, 2018. Available at: <https://nwhn.org/fibroids/>. See also <https://www.acog.org/~media/For%20Patients/faq074.pdf?dmc=1&ts=20131008T1955356950>
- 14 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 15 CARE About Fibroids. Fibroids: The 411. 2018. Accessed July 25, 2018. Available at: <http://www.careaboutfibroids.org/411.html>
- 16 National Women's Health Network. Fibroids Overview. February 2018. Accessed July 25, 2018. Available at: <https://nwhn.org/fibroids/>
- 17 National Women's Health Network. Fibroids Overview. February 2018. Accessed July 25, 2018. Available at: <https://nwhn.org/fibroids/>
- 18 Mayo Clinic. Uterine Fibroids: Diagnosis & Treatment. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/diagnosis-treatment/drc-20354294>
- 19 Mayo Clinic. Uterine Fibroids: Diagnosis & Treatment. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/diagnosis-treatment/drc-20354294>
- 20 Mayo Clinic. Uterine Fibroids: Diagnosis & Treatment. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/diagnosis-treatment/drc-20354294>
- 21 Borah BJ, Nicholson WK, Bradley L, and Stewart EA. The Impact of Uterine Leiomyomas: A National Survey of Affected Women. October 2013. *American Journal of Obstetrics & Gynecology*. Accessed July 26, 2018. Available at: [https://www.ajog.org/article/S0002-9378\(13\)00749-7/abstract](https://www.ajog.org/article/S0002-9378(13)00749-7/abstract)
- 22 Ghant MS et al. An Altered Perception of Normal: Understanding Causes for Treatment Delay in Women with Symptomatic Uterine Fibroids. August 1, 2016. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4982946/>
- 23 Ghant MS et al. An Altered Perception of Normal: Understanding Causes for Treatment Delay in Women with Symptomatic Uterine Fibroids. August 1, 2016. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4982946/>
- 24 Cleveland Clinic. Abnormal Menstruation (Periods). January 16, 2015. Accessed July 26, 2018. Available at: <https://my.clevelandclinic.org/health/diseases/14633-abnormal-menstruation-periods> See also WebMD. What is a Normal Period? January 11, 2018. Accessed July 26, 2018. Available at: <https://www.webmd.com/women/normal-period>
- 25 WebMD. What is a Normal Period? January 11, 2018. Accessed July 26, 2018. Available at: <https://www.webmd.com/women/normal-period>

-
- ²⁶ U.S. Department of Health & Human Services. Office on Women's Health. Your Menstrual Cycle. March 16, 2018. Accessed July 26, 2018. Available at: <https://www.womenshealth.gov/menstrual-cycle/your-menstrual-cycle>
- ²⁷ Fraser IS, Critchley HO, Broder M, Munro MG. The FIGO Recommendations on Terminologies and Definitions for Normal and Abnormal Uterine Bleeding. 2011. *Seminars in Reproductive Medicine*. Accessed July 26, 2018. Available at: <http://www.pharllc.com/wp-content/uploads/2014/03/Fraser-Semin-Reprod-Med-2011.pdf>
- ²⁸ Fraser IS, Critchley HO, Broder M, Munro MG. The FIGO Recommendations on Terminologies and Definitions for Normal and Abnormal Uterine Bleeding. 2011. *Seminars in Reproductive Medicine*. Accessed July 26, 2018. Available at: <http://www.pharllc.com/wp-content/uploads/2014/03/Fraser-Semin-Reprod-Med-2011.pdf>
- ²⁹ U.S. Department of Health & Human Services. Office on Women's Health. Period Problems. March 16, 2018. Accessed July 26, 2018. Available at: <https://www.womenshealth.gov/menstrual-cycle/period-problems>
- ³⁰ U.S. Department of Health & Human Services. Office on Women's Health. Period Problems. March 16, 2018. Accessed July 26, 2018. Available at: <https://www.womenshealth.gov/menstrual-cycle/period-problems#2>
- ³¹ U.S. Department of Health & Human Services. Office on Women's Health. Period Problems. March 16, 2018. Accessed July 26, 2018. Available at: <https://www.womenshealth.gov/menstrual-cycle/period-problems#2>
- ³² Ghant MS, et al. Beyond the Physical: A Qualitative Assessment of the Burden of Symptomatic Uterine Fibroids on Women's Emotional and Psychosocial Health. February 2, 2015. *Journal of Psychosomatic Research*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25725565>
- ³³ Borah BJ, Nicholson WK, Bradley L, and Stewart EA. The Impact of Uterine Leiomyomas: A National Survey of Affected Women. October 2013. *American Journal of Obstetrics & Gynecology*. Accessed July 26, 2018. Available at: [https://www.ajog.org/article/S0002-9378\(13\)00749-7/abstract](https://www.ajog.org/article/S0002-9378(13)00749-7/abstract)
- ³⁴ Ghant MS, et al. Beyond the Physical: A Qualitative Assessment of the Burden of Symptomatic Uterine Fibroids on Women's Emotional and Psychosocial Health. February 2, 2015. *Journal of Psychosomatic Research*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25725565>
- ³⁵ Borah BJ, Nicholson WK, Bradley L, and Stewart EA. The Impact of Uterine Leiomyomas: A National Survey of Affected Women. October 2013. *American Journal of Obstetrics & Gynecology*. Accessed July 26, 2018. Available at: [https://www.ajog.org/article/S0002-9378\(13\)00749-7/abstract](https://www.ajog.org/article/S0002-9378(13)00749-7/abstract)
- ³⁶ Borah BJ, Nicholson WK, Bradley L, and Stewart EA. The Impact of Uterine Leiomyomas: A National Survey of Affected Women. October 2013. *American Journal of Obstetrics & Gynecology*. Accessed July 26, 2018. Available at: [https://www.ajog.org/article/S0002-9378\(13\)00749-7/abstract](https://www.ajog.org/article/S0002-9378(13)00749-7/abstract)
- ³⁷ U.S. Department of Health & Human Services. Agency for Healthcare Research and Quality. Effective Health Care Program. Comparative Effectiveness Review. Management of Uterine Fibroids. December 2017. Accessed July 26, 2018. Available at: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-195-uterine-fibroids-final_0.pdf
- ³⁸ Borah BJ, Nicholson WK, Bradley L, and Stewart EA. The Impact of Uterine Leiomyomas: A National Survey of Affected Women. October 2013. November 2012. *American Journal of Obstetrics & Gynecology*. Accessed July 26, 2018. Available at: [https://www.ajog.org/article/S0002-9378\(13\)00749-7/abstract](https://www.ajog.org/article/S0002-9378(13)00749-7/abstract)
- ³⁹ U.S. Department of Health & Human Services. Agency for Healthcare Research and Quality. Effective Health Care Program. Comparative Effectiveness Review. Management of Uterine Fibroids. December 2017. Accessed July 26, 2018. Available at: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-195-uterine-fibroids-final_0.pdf
- ⁴⁰ Mayo Clinic. Uterine Fibroids: Symptoms & Causes. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/symptoms-causes/syc-20354288>
- ⁴¹ Stewart EA, Nicholson WK, Bradley L, Borah BJ. The Burden of Uterine Fibroids for African-American Women: Results of a National Survey. October 2013. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3787340/>
- ⁴² Stewart EA, Nicholson WK, Bradley L, Borah BJ. The Burden of Uterine Fibroids for African-American Women: Results of a National Survey. October 2013. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3787340/>
- ⁴³ Stewart EA, Nicholson WK, Bradley L, Borah BJ. The Burden of Uterine Fibroids for African-American Women: Results of a National Survey. October 2013. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3787340/>
- ⁴⁴ Stewart EA, Nicholson WK, Bradley L, Borah BJ. The Burden of Uterine Fibroids for African-American Women: Results of a National Survey. October 2013. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3787340/>
- ⁴⁵ Stewart EA, Nicholson WK, Bradley L, Borah BJ. The Burden of Uterine Fibroids for African-American Women: Results of a National Survey. October 2013. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3787340/>
- ⁴⁶ Borah BJ, Nicholson WK, Bradley L, and Stewart EA. The Impact of Uterine Leiomyomas: A National Survey of Affected Women. October 2013. *American Journal of Obstetrics & Gynecology*. Accessed July 26, 2018. Available at: [https://www.ajog.org/article/S0002-9378\(13\)00749-7/abstract](https://www.ajog.org/article/S0002-9378(13)00749-7/abstract) See also Stewart EA, Nicholson WK, Bradley L, Borah BJ. The Burden of Uterine Fibroids for African-American Women: Results of a National Survey. October 2013. *Journal of Women's Health*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3787340/>

-
- 47 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 48 Patient-Centered Outcomes Research Institute. Comparing Options for Treating Uterine Fibroids through a Patient Information Registry – The COMPARE-UF Study. May 30, 2018. Accessed July 26, 2018. Available at: <https://www.pcori.org/research-results/2014/comparing-options-treating-uterine-fibroids-through-patient-information>
- 49 Olive DL. The Medical Treatment of Uterine Fibroids. In *Radiological Interventions in Obstetrics and Gynaecology*, J. Reidy et al. (eds). July 4, 2013. Accessed July 26, 2018. Available at: https://www.springer.com/cda/content/document/cda_downloaddocument/9783642279744-c2.pdf?SGWID=0-0-45-1463910-p174286561
- 50 American Society of Hematology, Iron-Deficiency Anemia. Accessed October 18, 2018. Available at: <http://www.hematology.org/Patients/Anemia/Iron-Deficiency.aspx>.
- 51 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 52 Parlikar, Urmila. No “Best” Treatment of Common Uterine Fibroids. Harvard Health Publishing. Harvard Medical School. Blog. April 23, 2016. Accessed July 26, 2018. Available at: <https://www.health.harvard.edu/blog/no-best-treatment-for-common-uterine-fibroids-201504237918>
- 53 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 54 Ali M, Al-Hendy A. Selective Progesterone Receptor Modulators for Fertility Preservation in Women with Symptomatic Uterine Fibroids. August 28, 2017. *Biology of Reproduction*. Accessed July 26, 2018. Available at: <https://academic.oup.com/biolreprod/article/97/3/337/4096253>. See also Food and Drug Administration, Drugs@FDA: FDA Approved Drug Products, *New Drug Application 210450*. Accessed October 16, 2018. Available at: <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process>.
- 55 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029> See also <https://www.fda.gov/Drugs/DrugSafety/ucm111323.htm>
- 56 Mayo Clinic. Uterine Fibroids: Diagnosis & Treatment. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/diagnosis-treatment/drc-20354294>
- 57 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 58 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 59 Mayo Clinic. Myomectomy. January 5, 2018. Accessed July 26, 2018. Available at: <https://www.mayoclinic.org/tests-procedures/myomectomy/about/pac-20384710>
- 60 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 61 Lee BB, Yu SP. Radiofrequency Ablation of Uterine Fibroids: A Review. November 4, 2016. *Current Obstetrics and Gynecology Reports*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5114324/>
- 62 Accessa. The Accessa Procedure. Accessed October 18, 2018. Available at: <http://accessaprocedure.com/accessa-procedure-overview/>
- 63 Lee BB, Yu SP. Radiofrequency Ablation of Uterine Fibroids: A Review. November 4, 2016. *Current Obstetrics and Gynecology Reports*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5114324/>
- 64 United States Department of Health and Human Services, Food and Drug Administration, Devices@FDA, Sonata Sonography-Guided Transcervical Fibroid Ablation System. August 15, 2018. Accessed October 18, 2018. Available at: <https://www.accessdata.fda.gov/SCRIPTS/cdrh/devicesatfda/index.cfm?db=pmn&id=K173703>.
- 65 Gynesonics, The Sonata System. Accessed October 18, 2018. Available at: <https://gynesonics.com/us/sonata-system/>.
- 66 Mayo Clinic. Uterine Fibroids: Diagnosis & Treatment. March 6, 2018. Accessed July 25, 2018. Available at: <https://www.mayoclinic.org/diseases-conditions/uterine-fibroids/diagnosis-treatment/drc-20354294>
- 67 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 68 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 69 Parlikar, Urmila. No “Best” Treatment of Common Uterine Fibroids. Harvard Health Publishing. Harvard Medical School. Blog. April 23, 2016. Accessed July 26, 2018. Available at: <https://www.health.harvard.edu/blog/no-best-treatment-for-common-uterine-fibroids-201504237918> See also Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- 70 Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>

-
- ⁷¹ Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>
- ⁷² Stewart EA. Uterine Fibroids. April 23, 2015. *New England Journal of Medicine*. Accessed July 25, 2018. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMcp1411029>. See also U.S. Department of Health & Human Services. U.S. Food & Drug Administration. Updated Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy: FDA Safety Communication. November 24, 2014. Accessed July 26, 2018. Available at: <https://wayback.archive-it.org/7993/20170722215727/https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm424443.htm>.
- ⁷³ Wright JD, Chen L, Burke WM, et al. Trend in Use and Outcomes of Women Undergoing Hysterectomy with Electric Power Morcellation. August 23, 2018. *Journal of the American Medical Association*. Accessed September 25, 2018. Available at: <https://jamanetwork.com/journals/jama/fullarticle/2545671>
- ⁷⁴ U.S. Department of Health & Human Services. Agency for Healthcare Research and Quality. Effective Health Care Program. Comparative Effectiveness Review. Management of Uterine Fibroids. December 2017. Accessed July 26, 2018. Available at: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-195-uterine-fibroids-final_0.pdf
- ⁷⁵ U.S. Department of Health & Human Services. Agency for Healthcare Research and Quality. Effective Health Care Program. Comparative Effectiveness Review. Management of Uterine Fibroids. December 2017. Accessed July 26, 2018. Available at: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/cer-195-uterine-fibroids-final_0.pdf
- ⁷⁶ Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of Uterine Myomas: A Review. December 23, 2015. *International Journal of Fertility & Sterility*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4793163/> See also Laughlin SK, Baird DD, Savitz DA, Herring AH, Hartmann KE. Prevalence of Uterine Leiomyomas in the First Trimester of Pregnancy: An Ultrasound Screening Study. March 2009. *Obstetrics & Gynecology*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3384531/>
- ⁷⁷ Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of Uterine Myomas: A Review. December 23, 2015. *International Journal of Fertility & Sterility*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4793163/>
- ⁷⁸ Sparic R, Mirkovic L, Malvasi A, Tinelli A. Epidemiology of Uterine Myomas: A Review. December 23, 2015. *International Journal of Fertility & Sterility*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4793163/>
- ⁷⁹ The American College of Obstetricians and Gynecologists. Frequently Asked Questions Gynecologic Problems. May 2011. Accessed July 26, 2018. Available at: <https://www.acog.org/Patients/FAQs/Uterine-Fibroids>
- ⁸⁰ U.S. Department of Health & Human Services. National Institutes of Health. Yesterday, Today & Tomorrow: NIH Research Timeline. Uterine Fibroids. October 2010. Accessed July 26, 2018. Available at: <https://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=50>
- ⁸¹ Taylor DK, Holthouser K, Segars JH, Leppert PC. Recent Scientific Advances in Leiomyoma (Uterine Fibroids) Research Facilitates Better Understanding and Management. July 6, 2015. *F1000Research*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4513689/>
- ⁸² Taylor DK, Holthouser K, Segars JH, Leppert PC. Recent Scientific Advances in Leiomyoma (Uterine Fibroids) Research Facilitates Better Understanding and Management. July 6, 2015. *F1000Research*. Accessed July 26, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4513689/>
- ⁸³ Mathieu Luyckx, et al. First series of 18 pregnancies after ulipristal acetate treatment for uterine fibroids. September 18, 2014. *Fertility and Sterility*. Accessed October 16, 2018. Available at: [https://www.fertstert.org/article/S0015-0282\(14\)02024-X/fulltext](https://www.fertstert.org/article/S0015-0282(14)02024-X/fulltext)
- ⁸⁴ National Institutes of Health, U.S. National Library of Medicine, ClinicalTrials.gov, Efficacy and Safety of Elagolix in Combination with Estradiol/Norethindrone Acetate for the Management of Heavy Menstrual Bleeding Associated with Uterine Fibroids in Premenopausal Women. January 13, 2016. Accessed October 16, 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT02654054>.
- ⁸⁵ National Institutes of Health, U.S. National Library of Medicine, ClinicalTrials.gov, LIBERTY 2: Efficacy & Safety of Relugolix in Women with Heavy Menstrual Bleeding Associated with Uterine Fibroids. April 6, 2017. Accessed October 16, 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT03103087>. See also National Institutes of Health, U.S. National Library of Medicine, ClinicalTrials.gov, LIBERTY EXTENSION: Efficacy and Safety Extension Study of Relugolix in Women with Heavy Menstrual Bleeding Associated with Uterine Fibroids. January 29, 2018. Accessed October 16, 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT03412890>.
- ⁸⁶ National Institutes of Health, U.S. National Library of Medicine, ClinicalTrials.gov, Assess Safety and Efficacy of Vilaprisan in Subjects with Uterine Fibroids (ASTEROID 3). January 17, 2018. Accessed October 16, 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT03400943>.
- ⁸⁷ Melis GB, et al. Vilaprisan for treating uterine fibroids. *Expert Opinion on Investigational Drugs*. May 7, 2018. Accessed October 16, 2018. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29718788>.
- ⁸⁸ National Institutes of Health, U.S. National Library of Medicine, ClinicalTrials.gov, Transcervical Radiofrequency Ablation of Uterine Fibroids Global Registry (SAGE). April 18, 2017. Accessed October 18, 2018. Available at: <https://clinicaltrials.gov/ct2/show/NCT03118037?recrs=abdf&cond=Uterine+Fibroids&rank=5>.

⁸⁹ National Institutes of Health, U.S. National Library of Medicine, ClinicalTrials.gov, Uterine Leiomyoma Treatment with Radiofrequency Ablation (ULTRA). April 25, 2013. Accessed October 18, 2018. Available at: <https://www.clinicaltrials.gov/ct2/show/NCT01840124?term=acessa&rank=2>.

⁹⁰ Johns Hopkins Gynecology and Obstetrics, *Finding a Way to Attack Fibroids Through Their Extracellular Matrix*, Winter 2016, December 8, 2015. Accessed October 18, 2018. Available at:

<https://www.hopkinsmedicine.org/news/articles/finding-a-way-to-attack-fibroids-through-their-extracellular-matrix>.

⁹¹ National Institutes of Health, U.S. National Library of Medicine, ClinicalTrials.gov, Satisfaction of Patients With Trans-Arterial Radial Access: Quality of Life in Uterine Fibroid Embolization Trial (SPARQLE), January 16, 2017. Accessed October 18, 2018. Available at:

<https://clinicaltrials.gov/ct2/show/NCT03021720?recrs=abdf&cond=Uterine+Fibroids&rank=2>.

⁹² Cohen MG, Magnus Ohman E. Should the Benefit of Transradial Access Still Be Questioned? *Journal of the American College of Cardiology: Cardiovascular Interventions*. May 9, 2016; Vol 9, No 9. Accessed October 18, 2018. Available at:

<http://interventions.onlinejacc.org/content/jint/9/9/908.full.pdf>.

⁹³ Stewart EA. Uterine Fibroids. *Lancet*. 2001 Jan;257(9252):293-298.