Dr. Lisa Larkin

Leadership – Ms.Medicine (msmedicine.com)

Tanika Gray Valbrun

The White Dress Project

Dr. Sawsan (Suzie) As-Sanie

University of Michigan School of Medicine

The Strength of Primary Care Providers to Educate and Empower Women to Receive Evidence-based Care for Heavy Menstrual Bleeding (HMB) Associated with Uterine Fibroids (UF)

Program Disclosures

- This presentation is not intended for promotional purposes
- This presentation highlights the views and perspectives of the participating speakers and not necessarily the views of Pfizer, Inc or Myovant
- Myovant and Pfizer, Inc have provided funding to the speakers to support this program

Speaker Disclosures

- Dr. Lisa Larkin: Consultant for Proctor and Gamble, Solv Wellness, Astellas, Therapeutics MD, Pharmavite, Movant, Pfizer Inc; Speakers bureau for Abbvie; Non-profit board member for Healthy Women, North American Menopause Society, HERMedicine.org
- Dr. Sawsan (Suzie) As-Sanie: Consultant for Myovant, Pfizer Inc, Abbvie, Bayer, and Eximis; Author Royalties from UpToDate
- Tanika Gray Valbrun: Consultant for Myovant, Pfizer Inc.

Presentation Goal: To Create Awareness of UF and Help to Eliminate Barriers in Care and Empower Your Patients, Apply Evidence-based Care, and Help to Improve Overall Satisfaction with Healthcare Delivery

Participant Objectives

- Review the pathophysiology, diagnosis, and evidence-based treatment recommendations for HMB associated with UF
- Evaluate patient needs/gaps in care that may lead to a delay in diagnosis or treatment; and strategies to help reduce these delays
- Provide ways to promote fibroid awareness and patient advocacy and help to eliminate gaps in care

Patient Story

“For me, this is what having fibroids looks like. Not being able to get out of the shower because blood clots pour out of me continuously, blood clots the size of my fist. It looks like so much blood that I only have energy to get up to go to the bathroom.”

Women Are Not Getting the Health Care They Need or Deserve!

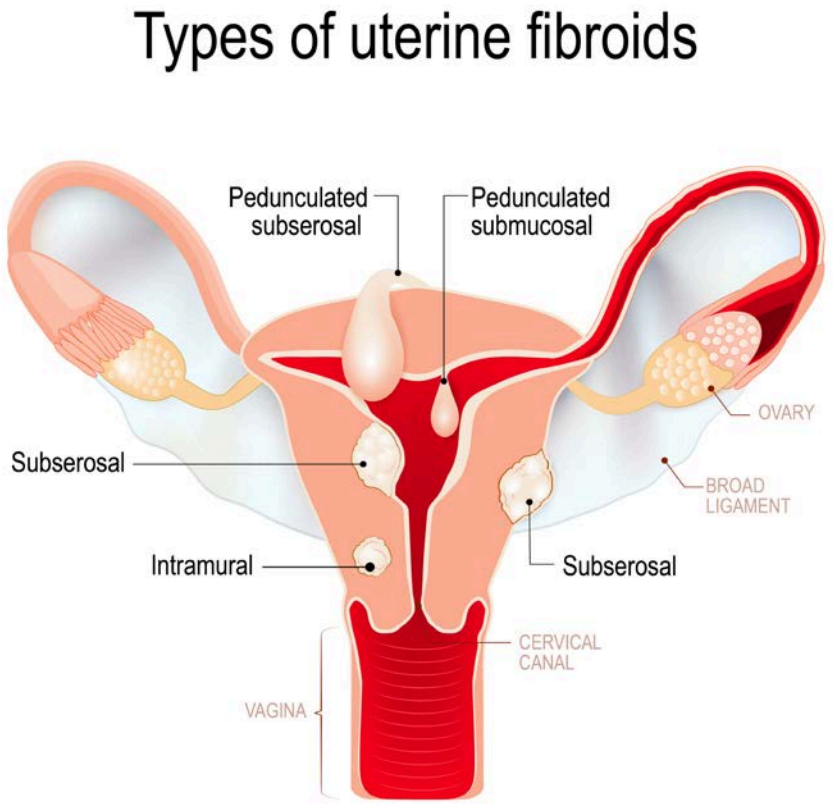
Women-only Diseases Are Studied Less, and Women Are Undertreated

- Endometriosis
- Polycystic Ovary Syndrome
- Fibroids
- Menopause
- Women's Sexual Health

DusenBery M. Doing Harm. 2019

What Are Uterine Fibroids (UF)?

Noncancerous Tumors That Grow in, On, or Around the Uterus



Uterine Fibroids (UF): Treatment Gaps & Unmet Needs

- Women's Lack of Awareness of Uterine Fibroid Disease and Normal Menstruation
- Women Seeking Medical Care Who Are Diagnosed with Symptomatic UF, Do Not Always Receive Treatment
- Limited Long-term Medical Therapy or Therapies That Provide Symptom Relief with Minimal Risk or Complications
- Preservation of Fertility

94% of Women Are Uninformed About the Health Issues That Affect Them Most

https://www.mdvip.com/patients/womens-health-center#blog. Accessed 7 December 2021

Uterine Fibroids (UF): Treatment Gaps & Unmet Needs (cont.)

Lack of Awareness of UF and Normal Menstruation

- Despite 25% to 50% of women with fibroids being symptomatic, UF is likely undiagnosed and undertreated due to lack of awareness, societal stigma around menstruation, and the uncertainty of normal bleeding[1]
- Even with UF disease having a significant psychological impact on women, few seek help from mental health professionals[2]

- An average of 3.6 years to seek treatment[3]
- 41% visited at least 2 healthcare providers before diagnosis[3]

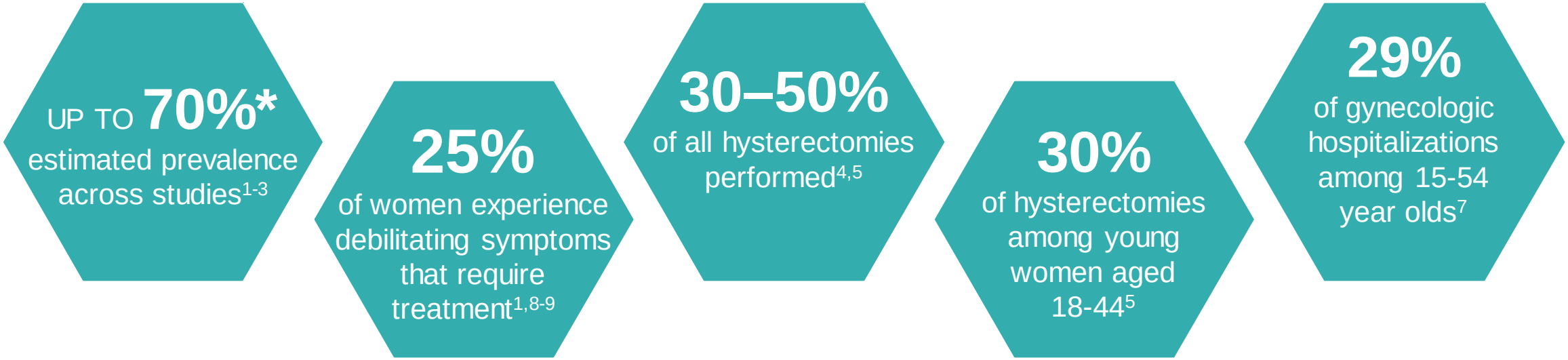
- Limited knowledge of UF and normal menstruation may lead to distorted view of what is normal and when to seek medical treatment[4]
- Women do not seek treatment due to lack of clear understanding about gynecological diseases including UF[4]
- Most common cited reason for delayed diagnosis was perception that what they were experiencing was normal[4]

1. Marsh EE et al. *J Womens Health (Larchmt)*. 2018;27:1359-1367; 2. Ghant MS et al. *J Psychosom Res*. 2015;78:499-503;
3. Borah BJ et al. *Am J Obstet Gynecol*. 2013;209:319.e1-319.e20; 4. Ghant MS et al. *J Womens Health (Larchmt)*. 2016;25:846-852.

Barriers to Care and Speaking Up

- Fear
- Mistrust of the medical establishment
- Racism & discrimination in healthcare
- Lack of information & misinformation about condition
- Gaslighting makes you question your sanity – or if your symptoms are real

Uterine Fibroids (UF): Disease Burden



The annual direct costs for uterine fibroids in the U.S. alone (including surgery, hospital admissions, outpatient visits, and medications) are estimated at:

$4.1–$9.4
BILLION dollars[10]

*The prevalence of uterine fibroids varied widely across studies, from 4.5% to 68.6%.

1. Stewart EA et al. *BJOG*. 2017;124:1501-1512; 2. Zimmermann A et al. *BMC Womens Health*. 2012;12:6; 3. Baird DD et al. *Am J Obstet Gynecol*. 2003;188:100-107.
4. Wright JD et al. *Obstet Gynecol*. 2013;122:233-241; 5. Merrill RM. *Med Sci Monit*. 2008;14:CR24-31; 6. Johns Hopkins Medicine. Available at: https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/hysterectomy 7. Whiteman MK et al. *Am J Obstet Gynecol*. 2010;202:541e1-e6; 8. Stewart EA. *Lancet*. 2001;357:293-298; 9. Islam MS et al. *Fertil Steril*. 2013;100:178-193; 10. Taylor DK et al. *F1000 Res*. 2015;4:183; 10. Cardozo ER et al. *Am J Obstet Gynecol*. 2012;206:211.e1-e9.

Risk Factors for Uterine Fibroids (UF)

Increased Age[1]	Genetics and Family History[1]	Race/ Ethnicity[1]	Reproductive Status[1]	Obesity[2,3]
▪ UF risk tends to increase with age through the reproductive years and declines in the postmenopausal years	▪ A positive history of UF carries a threefold greater risk of developing UFs versus women without	▪ Black women have two- to threefold greater risk of UFs than Caucasian women	▪ Nulliparous women are at an increased risk of UF development	▪ Obesity may increase the risk and prevalence of UFs

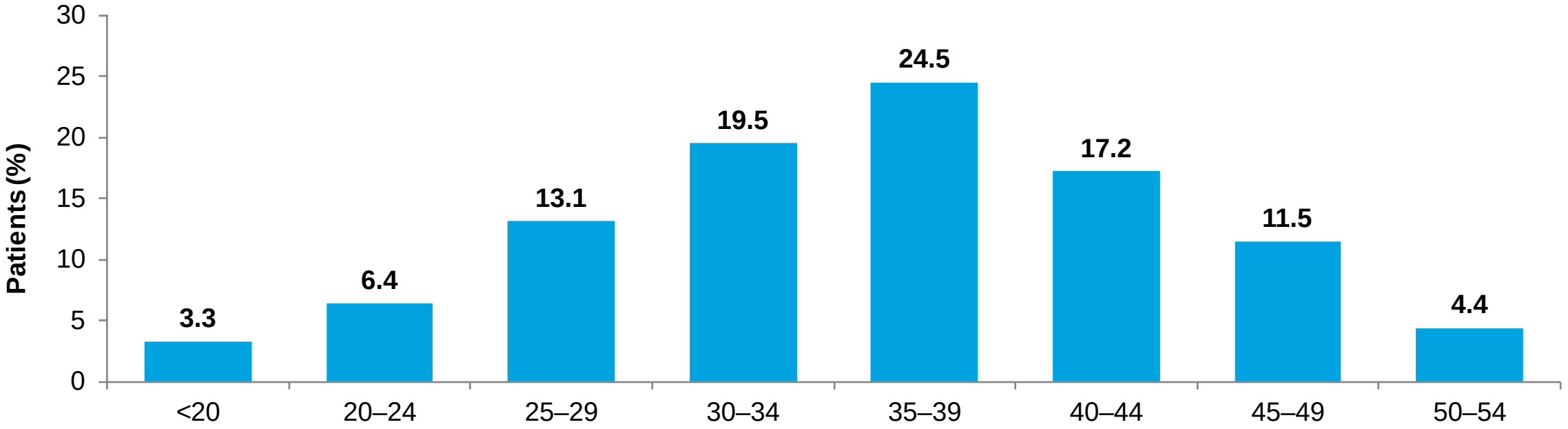
There Are Identified Risk Factors for UFs: Age, Genetics, Race, Reproductive Status and Potentially Obesity

UF=Uterine fibroids

1. Stewart EA et al. *BJOG*. 2017;124:1501-1512; 2. Pandey S, Bhattacharya D. *Women's Health*, 2010; 6; 107-17. 3. Qin H, et al. *J of Epidemiol Community Health*, 2021; 75; 197-204.

Uterine Fibroids (UF): Epidemiology

Prevalence by Age at Time of Diagnosis

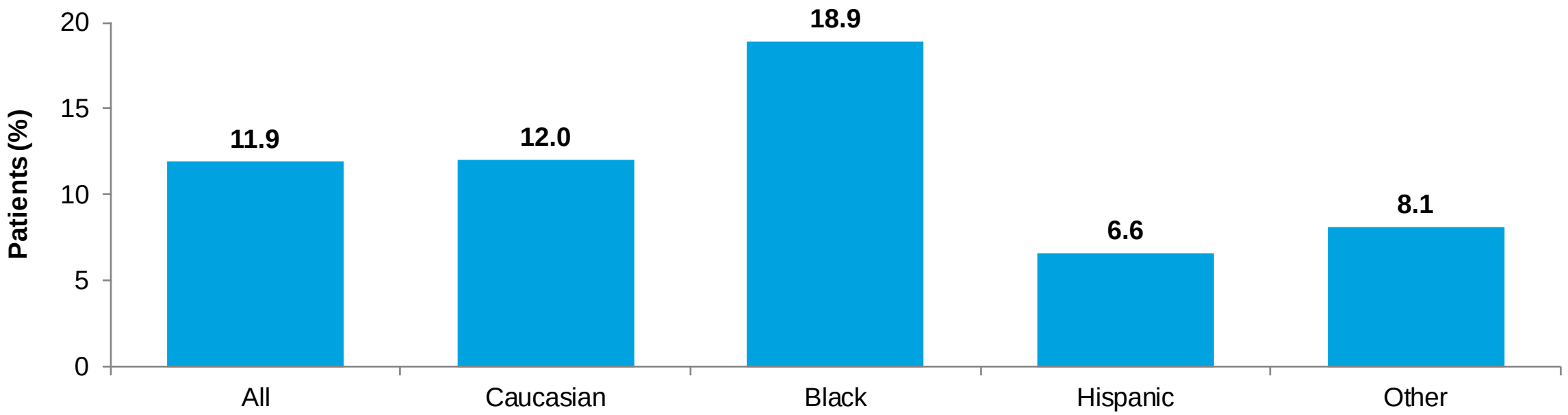


Over 60% of Women Were Between the Ages of 30–44 When Diagnosed with Uterine Fibroids

The dataset used in the analysis covered 41,474 women in the U.S. who participated in one of the eight NHANES Reproductive Health surveys conducted from 1999 to 2006.
NHANES=National Health and Nutrition Examination Survey.
Cacheris WP and Hunsche EGI. Poster PIH15 presented at ISPOR Europe 2018, Barcelona, Spain.

Uterine Fibroids (UF): Epidemiology

Prevalence Rates by Race/Ethnicity



Uterine Fibroids Are Most Prevalent in Black Women

The dataset used in the analysis covered 41,474 women in the U.S. who participated in one of the eight NHANES Reproductive Health surveys conducted from 1999 to 2006.
NHANES=National Health and Nutrition Examination Survey.
Cacheris WP and Hunsche EGI. Poster PIH15 presented at ISPOR Europe 2018, Barcelona, Spain.

Huge Disparities Exist in the Frequency and Severity of Uterine Fibroids with Black Women

Symptoms of Uterine Fibroids (UF): Heavy Menstrual Bleeding (HMB)

HMB is Defined as Excessive Menstrual Blood Loss (MBL) That Interferes with a Woman's Emotional, Physical, and Social Quality of Life (QoL)[1,2]

Characteristics of HMB:

- Manifest by flooding (defined as a change of pad or tampon more frequently than hourly) and/or prolonged menses[3]
- Quantitatively defined as MBL >80 mL per cycle in both research and clinical settings[4,5]

Approximately **1/3** of women with UF will **suffer from heavy menstrual bleeding**[6]

HMB is the Most Common and Burdensome Symptom of UF

HMB=heavy menstrual bleeding; MBL=menstrual blood loss; QoL=quality of life; UF=uterine fibroids.

1. Marsh EE et al. *J Womens Health (Larchmt)*. 2018;27:1359-1367; 2. Hapangama DK et al. *Womens Health (Lond)*. 2016;12:3-13;
3. James AH. *Hematology Am Soc Hematol Educ Program*. 2016;2016:236–242; 4. Quinn SD et al. *Womens Health (Lond)*. 2016;12:21-26;
5. Sriprasert I et al. *Contracept Reprod Med*. 2017;2:20; 6. Al-Hendy A et al. *Semin Reprod Med*. 2017;35:473-480.

Symptoms of Uterine Fibroids (UF): Anemia

Anemia Can Result as a Consequence of Excessive Blood Loss from Heavy Menstrual Bleeding[1] and is Defined by the Degree of Severity

Hemoglobin Levels to Diagnose Anemia*[2]

Normal (g/dL)	Mild (g/dL)	Moderate (g/dL)	Severe (g/dL)
≥ 12.0	11.0–11.9	8.0–10.9	< 8.0

- Anemia may cause fatigue, weakness, pallor, and dizziness[3]
- Severe anemia can be life-threatening because of the chronic, excessive menstrual blood loss[4]

Severe Anemia Resulting from Heavy Menstrual Bleeding Can Be Potentially Life-threatening, Leading to Hospitalization and Blood Transfusions

*For non-pregnant women (15 years of age and above).

1. Al-Hendy A et al. *Semin Reprod Med*. 2017;35:473-480; 2. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. 2011;
3. Sriprasert I et al. *Contracept Reprod Med.* 2017;2:20; 4. Nelson A et al. *Am J Obstet Gynecol*. 2015;213(1):97.e1-97.e6.

Symptoms of Uterine Fibroids (UF): Associated Pain

- Pain is the **second most burdensome symptom for women** with UF[1]
- Pain experience in women with UF is individual and spans a range of pain symptoms, with **dysmenorrhea and pelvic pain frequently encountered**[2]
- Pain **significantly impacts a woman's QoL** and impairs daily activities[2]

UF-associated Pain is Common and Frequently Experienced, But Remains Poorly Studied

QOL=Quality of Life.

1. Zimmermann A et al. *BMC Womens Health*. 2012;12:6; 2. Donnez J et al. *Hum Reprod Update*. 2016;22:665-686.

Uterine Fibroids (UF): Impact of Symptoms on Emotional & Psychological Well-being

- **The chronicity of UF symptoms can have a significant negative impact on overall QoL**
- UF makes it challenging to maintain emotional and psychological well-being, causing significant mental distress and an overall reduction in QoL[1-3]
- UF symptoms reportedly affects sexual life[1-3] and relationships with family and friends[1-4]
- Reported emotional responses included sadness,[1,2] depression,[1] discouragement,[2] hopelessness,[1,2] tired or worn out (little or some of the time)[2]
- Fatigue,[2-4] decreased work productivity,[2,3,5] including missing work,[2,3,5] and work performance,[2,3,5] played a substantial role in women's perceptions of their health-related QoL[1-3,5]
- Women expressed worry about disease progression,[4] side effects of treatment,[4] and loss of the uterus[1-5]

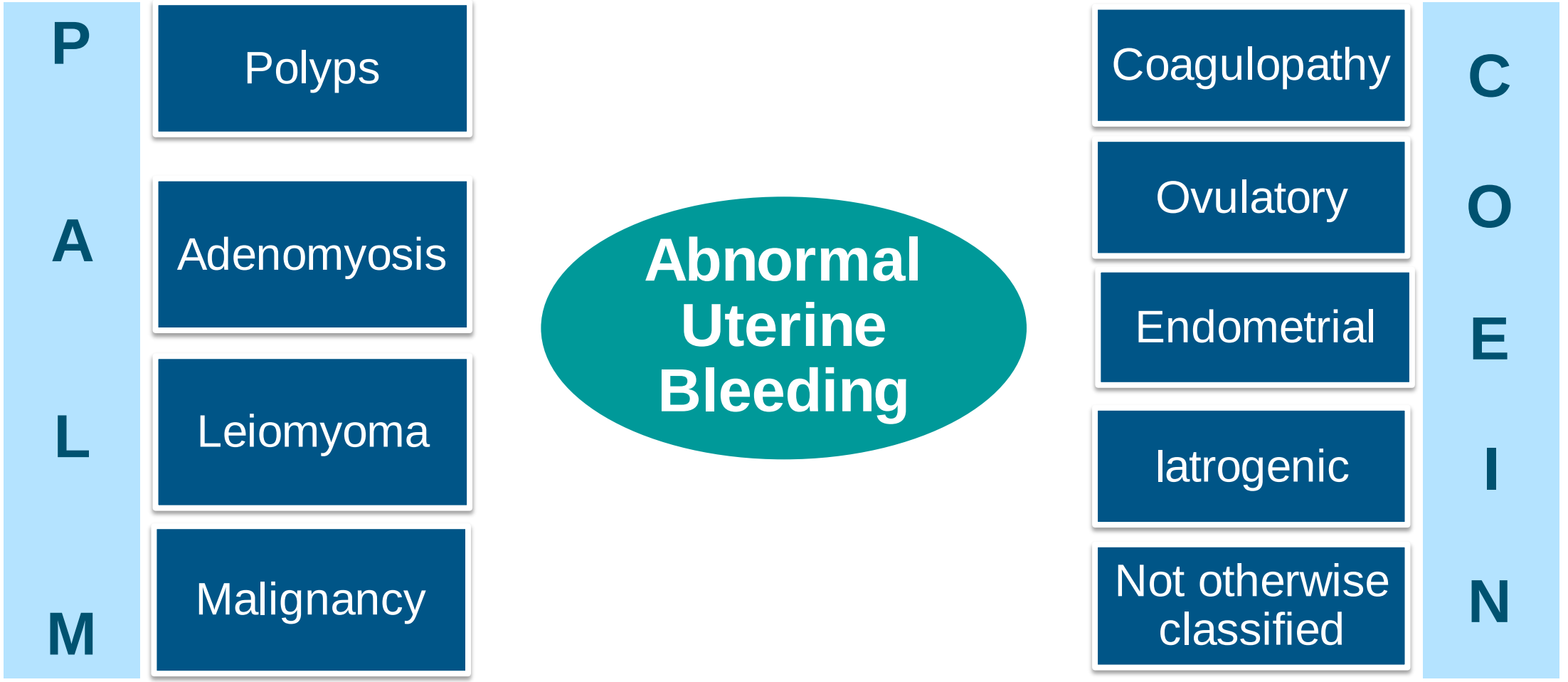
QOL=Quality of Life.

1. Ghant MS et al. *J Psychosom Res*. 2015;78:499-503; 2. Borah BJ et al. *Am J Obstet Gynecol*. 2013;209:319.e1–319.e20;
3. Al-Hendy A et al. *Semin Reprod Med*. 2017;35:473-480; 4. Knudsen NI et al. *Geburtshilfe Frauenheilkd*. 2017;77:976-983; 5. Hasselrot K et al. *PLoS One*. 2018;13:e0197958.

Our Pain is Invisible, But We Are Not!

“NO, I’M NOT PREGNANT. I’ve repeated this statement for 1½ years. I have fibroids. The reality is my condition is not uncommon… Like many women, I was told to just ‘wait and watch’ and when they grew I was uninsured and they went untreated.”

FIGO Abnormal Uterine Bleeding Differential Diagnosis



Whitaker L, Critchley HOD, Abnormal uterine bleeding, *Best Practice & Research Clinical Obstetrics and Gynaecology* (2015), http://dx.doi.org/10.1016/j.bpobgyn.2015.11.012

Diagnosis of Uterine Fibroids (UF)

Step 1: Ask

Symptom Screening

- Abnormal uterine bleeding (heavy, irregular)
- Bulk symptoms (pelvic pressure, urinary frequency)
- Pelvic pain, dysmenorrhea, dyspareunia
- Iron-deficiency anemia in menstruating persons

CBC=Complete Blood Count
TSH=Thyroid Stimulating Hormone

Donnez J, Dolmans MM. *Hum Reprod Update*. 2016;22:665-686; Stoehr A et al. *Arch Gynecol Obstet*. 2019;300:1029-1043.

Diagnosis of Uterine Fibroids (UF)

Step 2: Examine

Pelvic Examination

- Bimanual evaluation for pelvic mass, uterine enlargement
- OR consider referral to Ob/GYN

CBC=Complete Blood Count
TSH=Thyroid Stimulating Hormone

Donnez J, Dolmans MM. *Hum Reprod Update*. 2016;22:665-686; Stoehr A et al. *Arch Gynecol Obstet*. 2019;300:1029-1043.

Diagnosis of Uterine Fibroids (UF)

Step 3: Evaluate

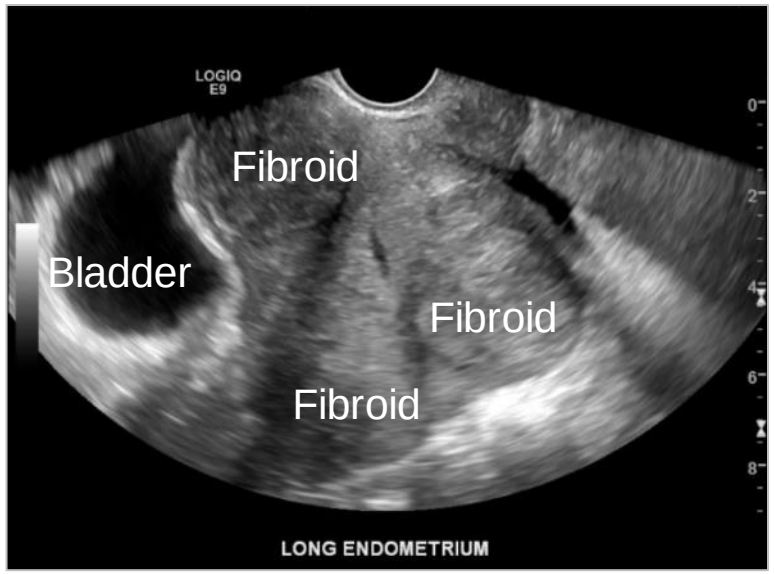
Labs

- Pregnancy test
- CBC
- TSH
- Pap smear
- Endometrial biopsy (all women >45 yo with abnormal bleeding & in women <45 yo with unopposed estrogen exposure or failed medical treatment)
- Pelvic ultrasound

CBC=Complete Blood Count
TSH=Thyroid Stimulating Hormone

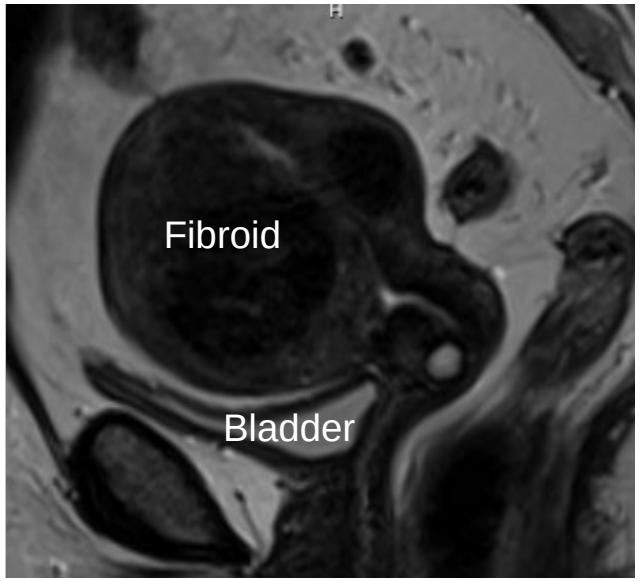
Donnez J, Dolmans MM. *Hum Reprod Update*. 2016;22:665-686; Stoehr A et al. *Arch Gynecol Obstet*. 2019;300:1029-1043.

Diagnosis of Uterine Fibroids (UF): Imaging



Transvaginal Pelvic Ultrasound

- Preferred initial imaging
- Evaluates fibroid size and location
- 90%–99% sensitive for detecting fibroids
- Sonohysterography and 3D ultrasound improves detection of submucosal fibroids



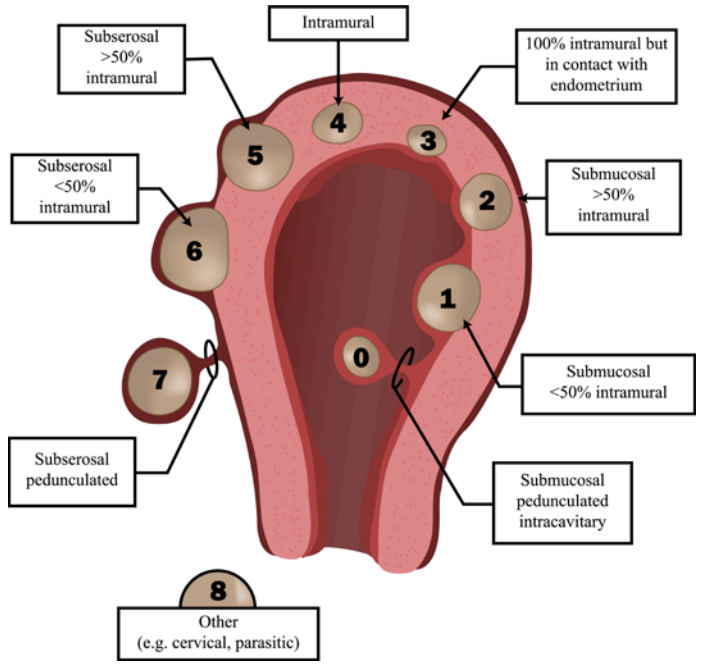
Magnetic Resonance Imaging (MRI)

- Provides information on location, size, and distance from the endometrium, as well as vascularization
- Indicated in women who are considering myomectomy, uterine artery embolization, or at increased risk of sarcoma

Donnez J, Dolmans MM. *Hum Reprod Update*. 2016;22:665-686, De La Cruz MSD, Buchanan EM. *Am Fam Physician*. 2017;95:100-107.

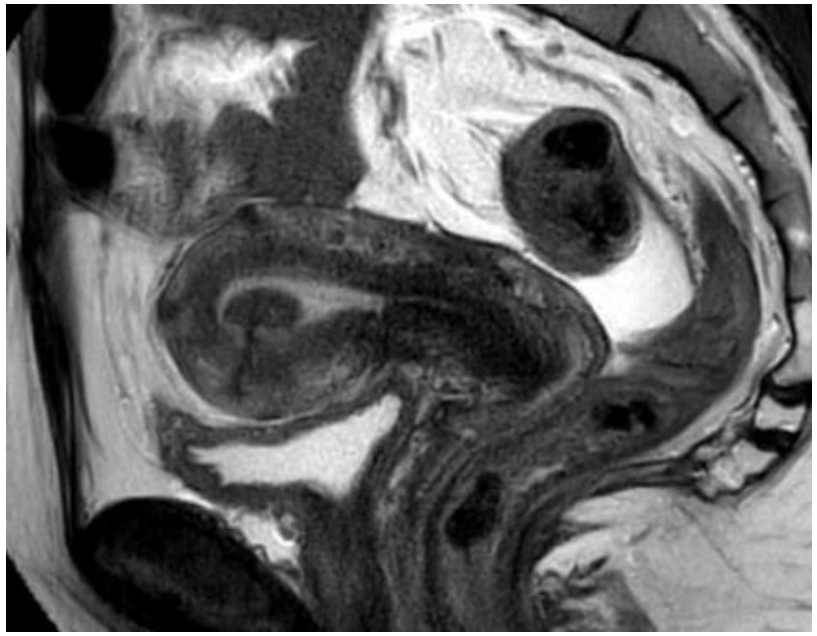
Figo Classification of Fibroids

Submucosal	**0**	Pedunculated Intracavity
	1	<50% Intramural
	2	≥50% Intramural
Intramural	**3**	Contacts endometrium; 100% Intramural
	4	Intramural
Subserosal	**5**	Subserosal, ≥50% Intramural
	6	Subserosal, <50% Intramural
	7	Subserosal Pedunculated

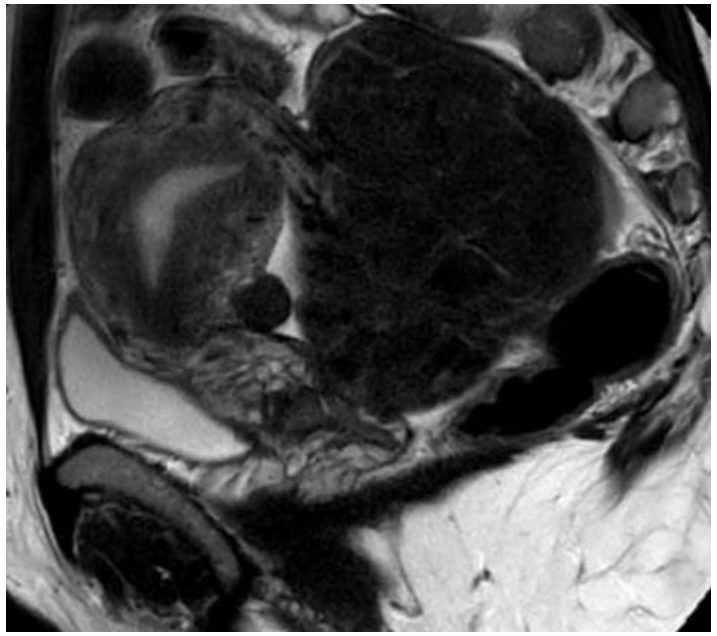


Transmural	Two numbers are listed separated by a dash. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below.	
	2–5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities respectively

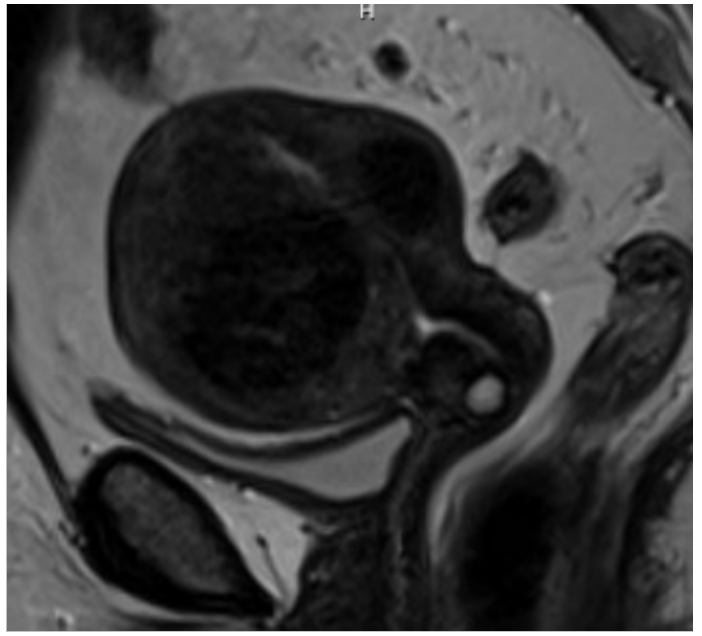
Munro M, et al. Int Gynaecol Obstet. 2011. April;113(1):3-13.



2cm, type 0 submucosal-heavy menstrual bleeding

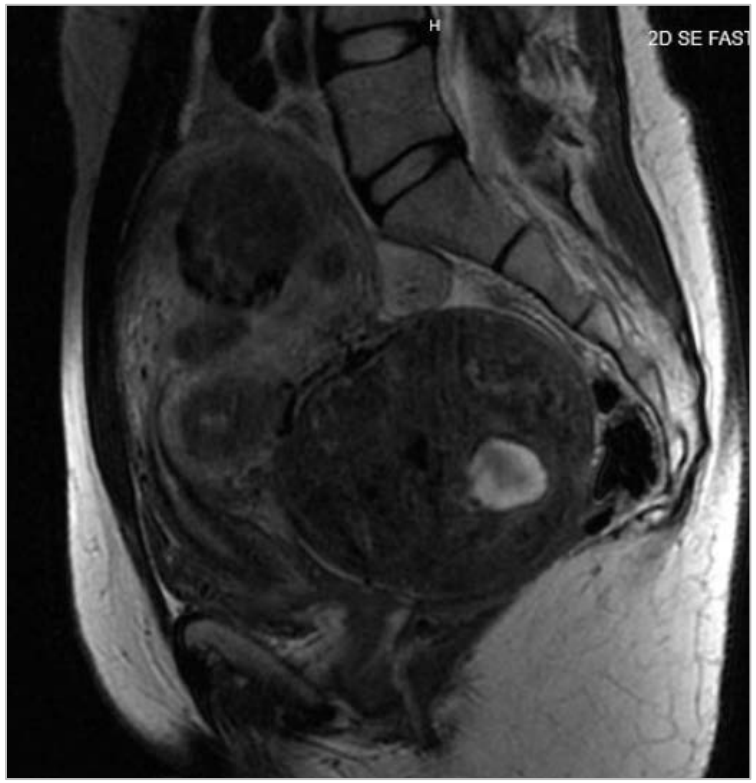


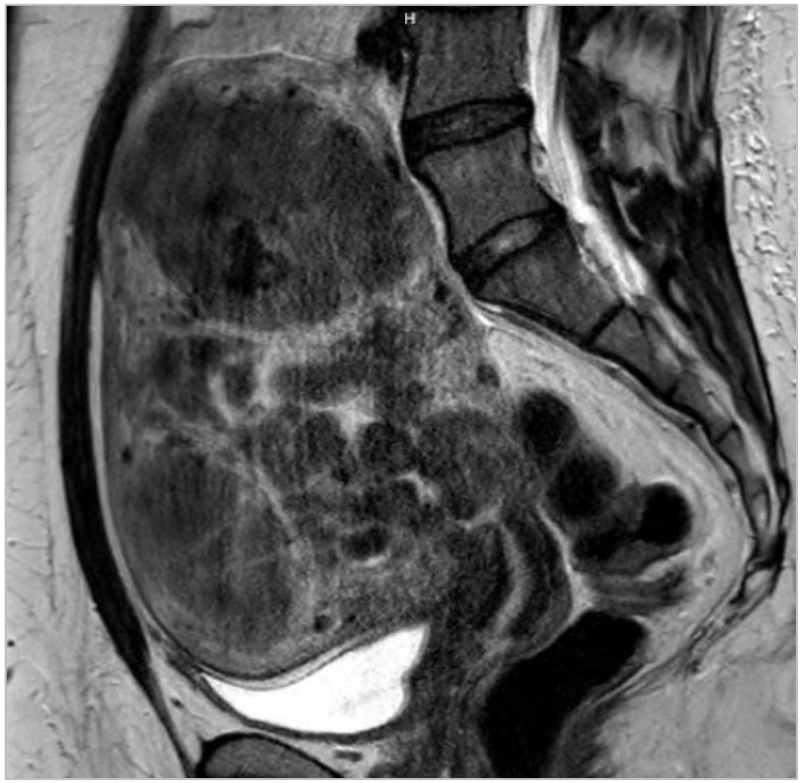
10cm, type 7 pedunculated subserosal – bulk symptoms only



5cm, type 2–5 intramural heavy menstrual bleeding

- Symptoms vary based on number, size, and location of uterine fibroids
- Classified on degree of extension into the myometrium and/or the uterine cavity





Numerous Intramural, Subserosal and Submucosal Fibroids-heavy Menstrual Bleeding + Bulk Symptoms

- Symptoms vary based on number, size, and location of uterine fibroids
- Classified on degree of extension into the myometrium and/or the uterine cavity

Selection of Therapy Depends on Severity of Symptoms and:

Patient Age (Pre- or Peri-menopausal)

Desire to Preserve Uterus and/or Fertility

Fibroid Location and Size

Mas A et. al. *Int J Womens Health*. 2017;9:607-617.

Uterine Fibroids (UF): Current Treatment Landscape

Treatment Goals[1]

- Relieve signs and symptoms, such as abnormal uterine bleeding, pelvic pressure, bowel dysfunction, etc.
- Sustain reduction of the size of fibroids
- Maintain fertility (if desired)
- Avoid harm

Asymptomatic UFs[4]

- Watchful waiting and clinical surveillance are recommended

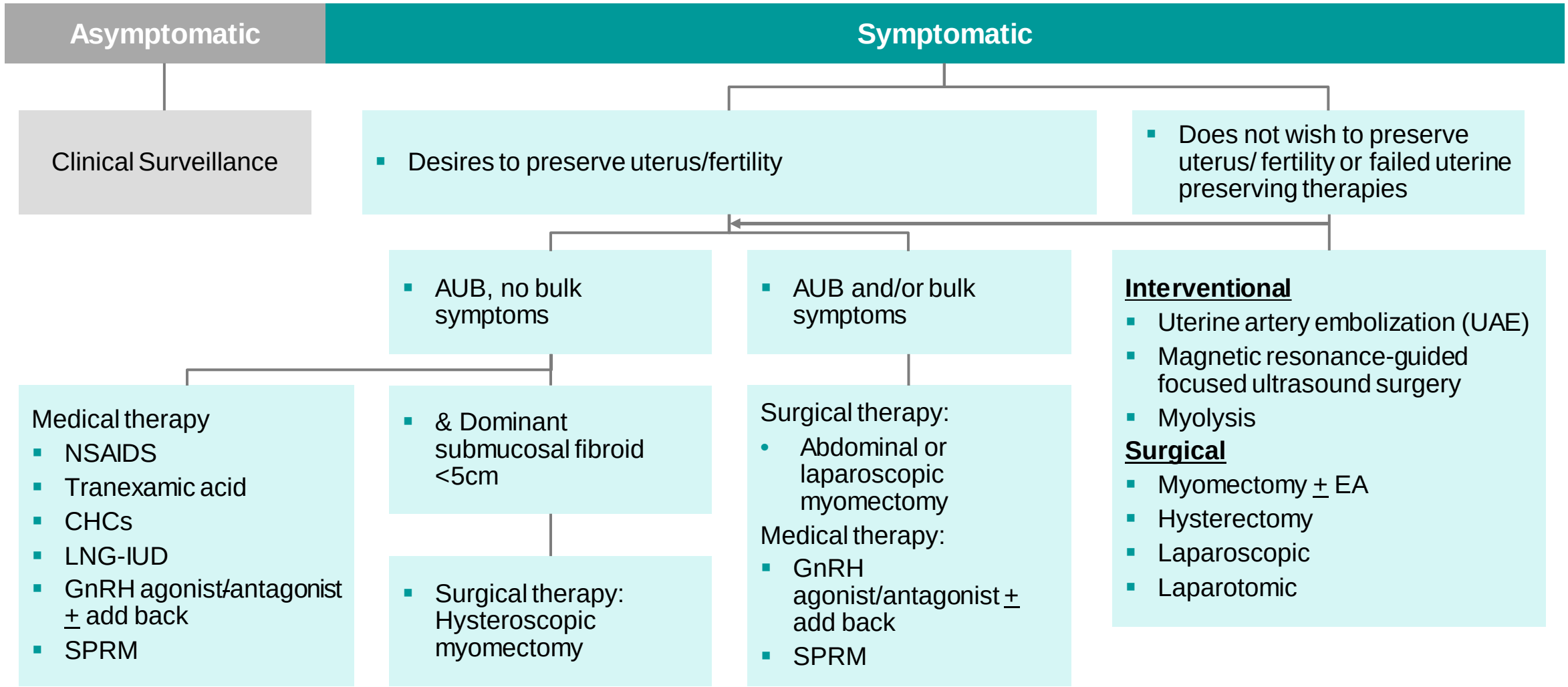
Treatment Options[1-4]

Medical	Procedural Interventions	Surgical
• Combined oral contraceptives* • GnRH agonists† • GnRH antagonist combination therapy‡ • NSAIDs* • Progestins: oral, intrauterine system* • Selective progesterone receptor modulators (SPRMs)* • Tranexamic acid*	• Endometrial ablation§ • Fibroid radio-frequency ablation (RFA)§ • Focused ultrasound (MRgFUS)§ • Uterine artery embolization§	• Hysterectomy (laparoscopic, vaginal or abdominal)§ • Myomectomy (laparoscopic, hysteroscopic or abdominal)

*Not FDA approved for UFs or UF-related symptoms
†FDA approved for improving hematologic parameters prior to surgery for UFs
‡FDA approved for heavy menstrual bleeding associated with UFs
§ Not fertility-sparing
GnRH=gonadotropin-releasing hormone; MRgFUS=magnetic resonance-guided focused ultrasound; RF=radiofrequency.

1. De La Cruz MS et al. *Am Fam Physician*. 2017;95:100-107; 2. Mas A et al. *Int J Womens Health*. 2017;9:607-617; 3. Schlaff WD et al. *N Engl J Med*. 2020;382:328-340. 4. ACOG Practice Bulletin No. 228. *Obstet Gynecol.* 2021; 137:e100-e109.

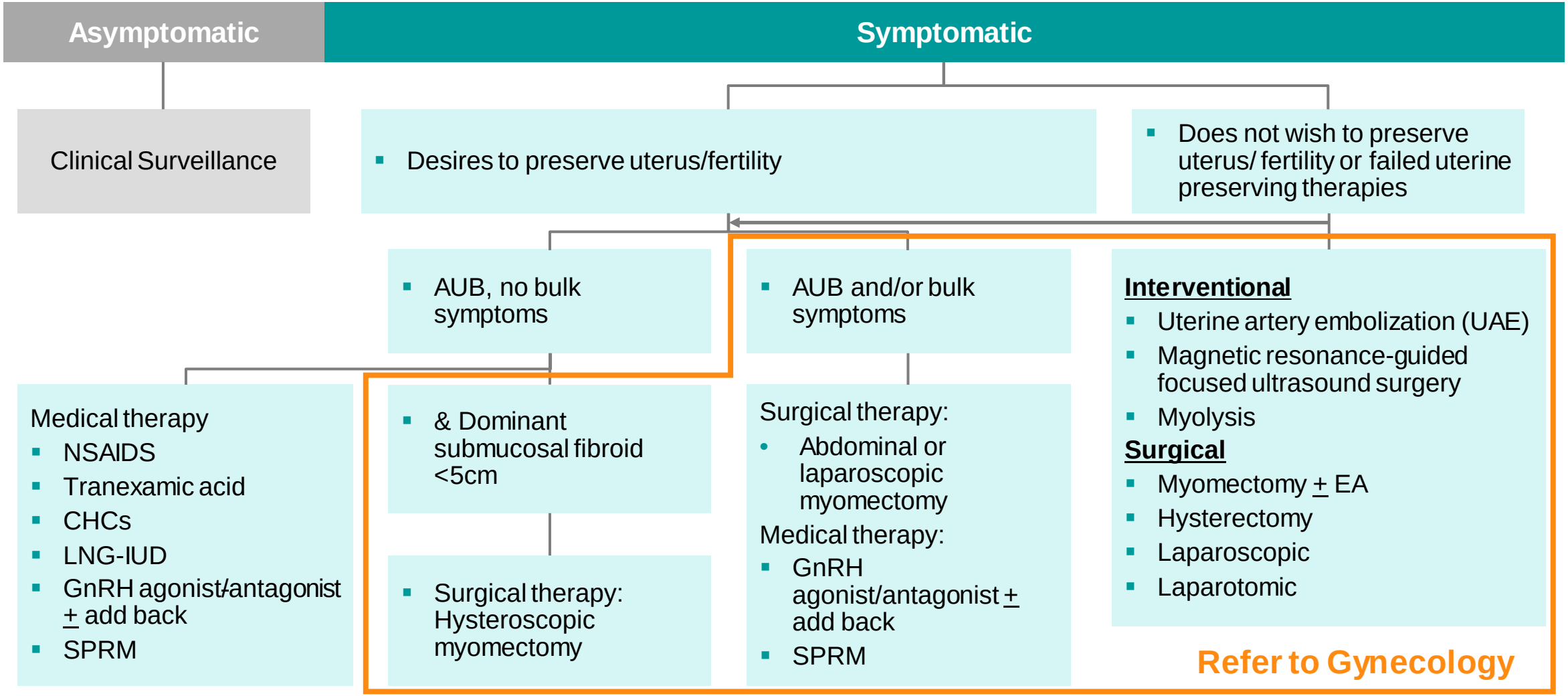
Example Treatment Selection Algorithm



Adapted from: De La Cruz MSD, Buchanan EM. *Am Fam Physician*. 2017;95:100-107 and Vilos GA et al. J Obstet Bynaecol Can 2015;37(2):157-78

CHCs=Combination Hormonal Contraceptives; LNG-IUD= Levonorgesterol releasing IUD; GnRH=Gonadotropin-Releasing Hormone; SPRM=selective progesterone receptor modulators; AUB=Abnormal Uterine Bleeding; EA=Endometrial Ablation

Example Treatment Selection Algorithm



Adapted from: De La Cruz MSD, Buchanan EM. *Am Fam Physician*. 2017;95:100-107 and Vilos GA et al. J Obstet Bynaecol Can 2015;37(2):157-78

CHCs=Combination Hormonal Contraceptives; LNG-IUD= Levonorgesterol releasing IUD; GnRH=Gonadotropin-Releasing Hormone; SPRM=selective progesterone receptor modulators; AUB=Abnormal Uterine Bleeding; EA=Endometrial Ablation

American College of Obstetricians and Gynecologists (ACOG) 2021 Practice Bulletin Management of Symptomatic Uterine Leiomyomas

Key to Treatment Selection

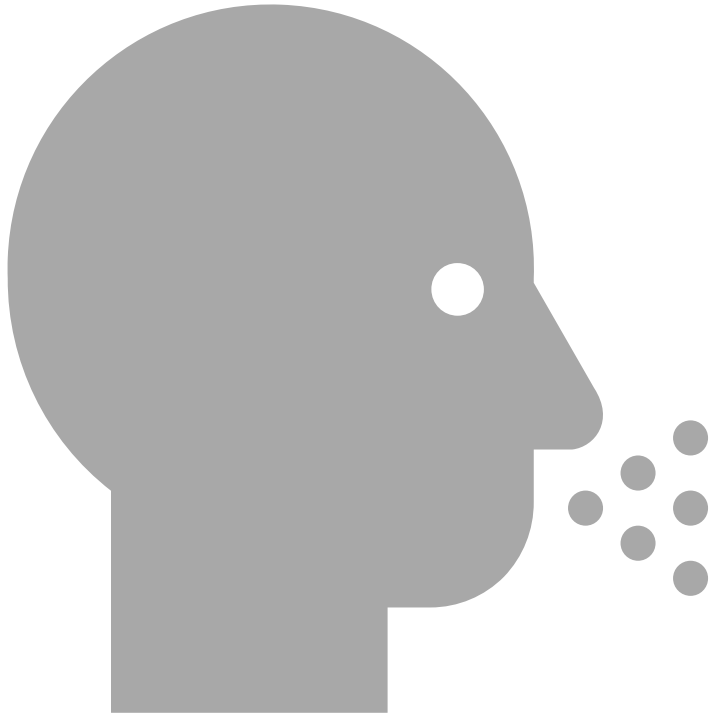
- Provide evidence-based recommendations for the management of symptomatic leiomyomas

CLINICAL SURVEILLANCE | MEDICAL MANAGEMENT | PROCEDURAL INTERVENTIONS | SURGICAL MANAGEMENT

- Acknowledge that comparative evidence is lacking for leiomyoma management options
- Emphasize counseling and a patient-centered shared decision-making approach
- Acknowledge and focus on racial disparities in disease presentation, severity, treatment, outcomes, and quality of life for Black women compared with White women with UF

ACOG Practice Bulletin Summary, Number 228. *Obstet Gynecol*. Jun 1 2021;137(6):1131-1133.

Communication Considerations: The Patient's Perspective



Key Takeaways

Participant Takeaways

- Create awareness of Uterine Fibroids
- Help to eliminate barriers in care
- Empower your patients
- Apply evidence-based care
- Improve overall satisfaction with healthcare deliver

Dr. Lisa Larkin

Leadership – Ms.Medicine (msmedicine.com)

Tanika Gray Valbrun

The White Dress Project

Dr. Sawsan (Suzie) As-Sanie

University of Michigan School of Medicine

The Strength of Primary Care Providers to Educate and Empower Women to Receive Evidence-based Care for Heavy Menstrual Bleeding (HMB) Associated with Uterine Fibroids (UF)

Patient Case: Kathryn

- New patient presenting to primary care clinic for annual wellness exam
- 47 years old
- G2P2 sp tubal

Patient Case: Kathryn

Ask

- Discuss patient's menstrual cycle (including probing if heavy bleeding)

Examine

- Bimanual evaluation for pelvic mass, uterine enlargement
- OR consider referral to OB/GYN

Evaluate

- Assess necessary laboratory values

Patient Case: Kathryn

- 47 years old
- G2P2 sp tubal
- Over the last 2–3 years her periods have become irregular and much heavier. She needs to change tampons every hour, and soaks through them at night.
- PE: 16-week uterus (confirmed on US)
- Hct 29 MCV 79
- She would like to discuss options. She does not want surgery.

Patient Case: Kathryn

- Shared decision-making is key to address patient-specific needs
- Things to consider
  - Fibroids with:
    - HMB with anemia
    - Large uterus
    - Does not desire fertility
    - Failed OCP's
    - Close to menopause

Patient Age (Pre- or Peri-menopausal)

Desire to Preserve Uterus and/or Fertility

Fibroid Location and Size

Dr. Lisa Larkin

Leadership – Ms.Medicine (msmedicine.com)

Tanika Gray Valbrun

The White Dress Project

Dr. Sawsan (Suzie) As-Sanie

University of Michigan School of Medicine

The Strength of Primary Care Providers to Educate and Empower Women to Receive Evidence-based Care for Heavy Menstrual Bleeding (HMB) Associated with Uterine Fibroids (UF)