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

What Are Uterine Fibroids (UF)?
<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Women’s Lack of Awareness of Uterine Fibroid Disease and Normal Menstruation</td>
<td>Women seeking medical care who are diagnosed with symptomatic UF do not always receive treatment</td>
</tr>
<tr>
<td>Women Seeking Medical Care Who Are Diagnosed with Symptomatic UF, Do Not Always Receive Treatment</td>
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<tr>
<td>Limited Long-term Medical Therapy or Therapies That Provide Symptom Relief with Minimal Risk or Complications</td>
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<tr>
<td>Preservation of Fertility</td>
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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
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\(^4\)

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

- **UP TO 70%** estimated prevalence across studies\(^1-3\)
- **25%** of women experience debilitating symptoms that require treatment\(^1,8-9\)
- **30–50%** of all hysterectomies performed\(^4,5\)
- **30%** of hysterectomies among young women aged 18-44\(^5\)
- **29%** of gynecologic hospitalizations among 15-54 year olds\(^7\)

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%.*

## Risk Factors for Uterine Fibroids (UF)

<table>
<thead>
<tr>
<th>Increased Age(^1)</th>
<th>Genetics and Family History(^1)</th>
<th>Race/Ethnicity(^1)</th>
<th>Reproductive Status(^1)</th>
<th>Obesity(^2,3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UF risk tends to increase with age through the reproductive years and declines in the postmenopausal years</td>
<td>A positive history of UF carries a threefold greater risk of developing UF(s) versus women without</td>
<td>Black women have two- to threefold greater risk of UF(s) than Caucasian women</td>
<td>Nulliparous women are at an increased risk of UF development</td>
<td>Obesity may increase the risk and prevalence of UF(s)</td>
</tr>
</tbody>
</table>

### There Are Identified Risk Factors for UF\(s\): Age, Genetics, Race, Reproductive Status and Potentially Obesity

UF=Uterine fibroids
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.
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Cacheris WP and Hunsche EG. 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 \(\frac{1}{3}\) 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.

**Symptoms of Uterine Fibroids (UF): Anemia**

Anemia can result as a consequence of excessive blood loss from heavy menstrual bleeding and is defined by the degree of severity.

### Hemoglobin Levels to Diagnose Anemia*2

<table>
<thead>
<tr>
<th>Normal (g/dL)</th>
<th>Mild (g/dL)</th>
<th>Moderate (g/dL)</th>
<th>Severe (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 12.0</td>
<td>11.0–11.9</td>
<td>8.0–10.9</td>
<td>&lt; 8.0</td>
</tr>
</tbody>
</table>

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

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

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\(^2\)

QOL=Quality of Life.
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.

UF symptoms reportedly affects sexual life and relationships with family and friends.

Reported emotional responses included sadness, depression, discouragement, hopelessness, tired or worn out (little or some of the time).

Fatigue decreased work productivity including missing work and work performance played a substantial role in women’s perceptions of their health-related QoL.

Women expressed worry about disease progression, side effects of treatment, and loss of the uterus.

QOL=Quality of Life.

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)

Symptom Screening

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

Step 1: Ask

CBC=Complete Blood Count
TSH=Thyroid Stimulating Hormone
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

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

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

# Figo Classification of Fibroids

<table>
<thead>
<tr>
<th>Submucosal</th>
<th>0</th>
<th>Pedunculated Intracavity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>&lt;50% Intramural</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>≥50% Intramural</td>
</tr>
<tr>
<td>Intramural</td>
<td>3</td>
<td>Contacts endometrium; 100% Intramural</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Intramural</td>
</tr>
<tr>
<td>Subserosal</td>
<td>5</td>
<td>Subserosal, ≥50% Intramural</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Subserosal, &lt;50% Intramural</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>Subserosal Pedunculated</td>
</tr>
</tbody>
</table>

**Transmural**

|          | 2–5 | Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities respectively |

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.

Symptoms vary based on number, size, and location of uterine fibroids

- Classified on degree of extension into the myometrium and/or the uterine cavity
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
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
# Uterine Fibroids (UF): Current Treatment Landscape

## Treatment Goals

- 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

## Treatment Options

<table>
<thead>
<tr>
<th>Medical</th>
<th>Procedural Interventions</th>
<th>Surgical</th>
</tr>
</thead>
</table>
| • 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.


## Asymptomatic UFs

- Watchful waiting and clinical surveillance are recommended

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†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.

Clinical Surveillance

Asymptomatic

- Desires to preserve uterus/fertility

Symptomatic

- Does not wish to preserve uterus/fertility or failed uterine preserving therapies

Medical therapy:
- NSAIDS
- Tranexamic acid
- CHCs
- LNG-IUD
- GnRH agonist/antagonist + add back
- SPRM

- AUB, no bulk symptoms
  - & Dominant submucosal fibroid <5cm
  - Surgical therapy: Hysteroscopic myomectomy

Interventional

- Uterine artery embolization (UAE)
- Magnetic resonance-guided focused ultrasound surgery
- Myolysis

Surgical

- Myomectomy + EA
- Hysterectomy
- Laparoscopic
- Laparotomic

Surgical therapy:
- Abdominal or laparoscopic myomectomy

Medical therapy:
- GnRH agonist/antagonist + add back
- SPRM


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

**Asymptomatic**
- Clinical Surveillance
  - Desires to preserve uterus/fertility
- Medical therapy
  - NSAIDS
  - Tranexamic acid
  - CHCs
  - LNG-IUD
  - GnRH agonist/antagonist + add back
  - SPRM
- Surgical therapy
  - Hysteroscopic myomectomy

**Symptomatic**
- AUB, no bulk symptoms
- AUB and/or bulk symptoms
- Interventional
  - Uterine artery embolization (UAE)
  - Magnetic resonance-guided focused ultrasound surgery
  - Myolysis
- Surgical
  - Myomectomy + EA
  - Hysterectomy
  - Laparoscopic
  - Laparotomic

**Medical therapy**
- NSAIDs
- Tranexamic acid
- CHCs
- LNG-IUD
- GnRH agonist/antagonist + add back
- SPRM

**Surgical therapy**
- Abdominal or laparoscopic myomectomy
- GnRH agonist/antagonist + add back
- SPRM


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

Refer to Gynecology
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

- 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

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
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
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