

# **National Urogynecology Research Agenda 2023**

***A Path Forward for Advancing the  
Treatment and Management of  
Pelvic Floor Disorders***

Developed by the AUGS Scientific Committee

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It should be noted, the use of gender terminology fluctuates throughout the report based upon how the referenced studies refer to the patient population. The term “women” has been used to describe adult females aged 18 and older.

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## Introduction

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### Background

Pelvic floor disorders (PFDs) are common conditions that can significantly affect a woman's quality of life and include pelvic organ prolapse (POP), urinary incontinence (UI), and fecal incontinence (FI). Approximately 25% of women experience at least one PFD and this percentage is likely higher in those who are older than 65 years, as it is well established that all PFDs increase after menopause.<sup>1,2</sup>

Women's health research is woefully underfunded. A 2021 study found that in disease states that unequally affect one gender, a disproportionate amount of funding from the National Institute of Health (NIH) went to male-dominated diseases. The authors found that in approximately 75% of cases the funding was provided to male dominated diseases.<sup>3</sup> In addition to the disproportionately smaller amount of NIH research funding that is allocated to women's health, the majority goes to research involving reproductive-aged women and is often allocated specifically to pregnancy and maternity issues

([https://orwh.od.nih.gov/sites/orwh/files/docs/ORWH\\_BiennialReport2019\\_20\\_508.pdf](https://orwh.od.nih.gov/sites/orwh/files/docs/ORWH_BiennialReport2019_20_508.pdf)).<sup>4</sup> The Office of Research of Women's Health (ORWH) noted that of the proportion of the overall NIH research spending by disease, condition, and special initiative from FY 2017 to FY 2019, only 10% was allocated to women's health research; however, in that same year the proportion of that money spent on contraception and pregnancy was 78.6% of the total, despite the fact that women spend the minority of their lives bearing children

([https://orwh.od.nih.gov/sites/orwh/files/docs/ORWH\\_BiennialReport2019\\_20\\_508.pdf](https://orwh.od.nih.gov/sites/orwh/files/docs/ORWH_BiennialReport2019_20_508.pdf)).<sup>4</sup>

The American Urogynecologic Society (AUGS) recognizes the importance of evaluating the conditions women face throughout their lives, including conditions that become more prevalent in the post-reproductive years. There is an urgent need to increase the amount of research funding directed towards women's health beyond maternity and reproductive care.

Women's health care should encompass the full life span of women, including conditions affecting post-reproductive and geriatric women, the fastest growing segment of the U.S. population. As a result, AUGS undertook an advocacy campaign, with national funding institutions, to help promote funding to women's health,

which is fundamentally necessary for improvement in women's health care. In addition, AUGS serves as a champion for increased national support for the training and career development of clinician scientists to promote continued research in women's health across the age spectrum.

A result of this advocacy was that the FY 2021 House report 116-450 adopted the below language:

#### **Office of the NIH Director**

*Pelvic Floor Disorders—The committee recognizes that pelvic floor disorders, including such conditions as urinary incontinence, accidental bowel leakage, and pelvic organ prolapse, have a large financial impact on individuals and society, and significant negative quality of life impact for more than 25 million women annually, in the U.S. alone. The Committee urges NICHD, NIDDK, and NIA to collaborate, on the development of universally accepted disorder specific data sets for the purpose of research studies on patient outcomes of current and future therapies used to treat pelvic floor disorders and the pathogenesis of these conditions. The Committee requests that NICHD, NIDDK and NIA provide a report on current research and future initiatives to address pelvic floor disorders in the fiscal year 2022 Congressional Justification and provide timely updates to the Committee on advances being made with respect to prevention, treatment and understanding the mechanisms of these conditions.*

AUGS' advocacy continued with Congress in 2022 with a result of the FY 2023 House 117-403 and the Senate Explanatory Statement FY 2023 Labor-HHS Bill adopting the following language:

#### **Office of the NIH Director**

*Overactive Bladder Treatment—The Committee remains concerned about the safety of medications used to treat overactive bladder, which may be increasing risk of Alzheimer disease and related dementias (ADRD). Overactive bladder affects 38 million Americans, and one in three older adults in this country. Overactive bladder has a significant impact on quality of life and the healthcare system. The anticholinergic medications typically used first-line to treat overactive bladder have been shown to increase the risk of developing dementia. Dementia continues to grow as a prevalent and serious public health issue. The Committee urges NIA to study anticholinergic medications and alternative treatments to determine the safety and effectiveness of medications for*

*overactive bladder, and their potential risks related to ADRD. The Committee requests an update on the status of research activities focused on this issue in the fiscal year 2024 CJ.*

**National Institute of Child Health and Human Development (NICHD)**

**Pelvic Floor Disorders** - Pelvic floor disorders, including urinary incontinence, accidental bowel leakage, and pelvic organ prolapse, negatively impact the quality of life of more than 25 million U.S. women each year. There are socioeconomic disparities amongst women suffering from pelvic floor disorders, with differences in symptoms, knowledge, access to care, availability of treatments and treatment outcomes noted in patients from different backgrounds. The Committee urges NICHD to prioritize research activities into underrepresented patient populations and pelvic floor disorders. Such activities may include the development of educational programs for general practitioners, the evaluation of effectiveness of screening protocols for pelvic floor disorders in the primary care setting, investigating medical literacy amongst minority women as it pertains to pelvic floor disorders, as well as assessing socioeconomic and socio-cultural disease perspectives by designing qualitative studies using focus groups of women with varying socio-economic, cultural, and ethnic backgrounds, evaluating current educational resources, determining gaps in patient knowledge, and designing culture-specific educational materials and resources. The Committee requests an update on this research in the fiscal year 2024 Congressional Justification.

**Purpose**

At the direction of the AUGS Board of Directors, the AUGS Scientific Committee was charged with the task of creating a Research Agenda. The overarching goal of this document was to synthesize research priorities in the field of urogynecology, provide summaries of each condition, introduce current key gaps/priorities, and provide recommendations based on these gaps. Given their importance, the specific topics and opportunities to address health care disparities, multidisciplinary research, and training of future scientists are each highlighted in their own unique section.

**Methods**

The AUGS Scientific Committee first met virtually, and reviewed research guidance documents published by other societies (American Society of Hematology Agenda for Hematology Research, American Urological Association National Urology Research Agenda, Federation of American Societies for Experimental Biology Recommendations for the Biden Administration, Society of Gynecologic Oncology Pathways to Progress in Women’s Cancer, and American Society of Clinical

Oncology Research Priorities), as well as the previous AUGS Research Recommendation statement that was published in 2011.<sup>5</sup> This review allowed the committee to become familiar with the process required to create such a document and helped generate a template that the committee felt was appropriate for the intended agenda.

The Scientific Committee met and worked on generating topics felt to be of utmost importance to research in urogynecology. The contributors acknowledge that many of the research topics are complex and may require a multidisciplinary approach or have an etiology outside the purview of Urogynecology. However, all the topics identified were felt to be essential research areas related to pelvic floor disorders. Six topics were decided upon (Table 1) along with three overarching themes (Table 2).

Table 1: Identified Research Topics for Urogynecology
<ul style="list-style-type: none"> <li>• Lower Urinary Tract Symptoms/Urinary Incontinence</li> <li>• Pelvic Organ Prolapse</li> <li>• Fecal Incontinence</li> <li>• Recurrent Urinary Tract Infections</li> <li>• Sexual Health in Women with Pelvic Floor Disorders</li> <li>• Bladder Pain Syndrome/Interstitial Cystitis and Myofascial Pelvic Pain</li> </ul>

A call was then sent out to the membership of AUGS looking for clinicians and researchers that would be interested in volunteering to work on the Research Agenda within one of these six topics. In choosing those who would be a part of these working groups, the Scientific Committee was looking for representation from across the United States and Canada, sought to have at least one basic science researcher in each group, and directly contacted certain researchers that were known to have expertise in particular areas of interest for each of the working groups. After the selection process was complete, each group had 7–10 volunteers. One member from the Scientific Committee then volunteered to be the lead for each of the groups. In addition, groups were provided with administrative support from AUGS. Each working group functioned independently and, therefore, individual sections will have unique differences in language and format.

Table 2: Overarching Themes / Additional Topics
<ul style="list-style-type: none"> <li>• Health Disparities</li> <li>• Moving Beyond Multidisciplinary Research</li> <li>• Training Future Scientists</li> </ul>

Each group first created a Background section for their topic. This section was focused on reviewing the literature and then describing the etiology and pathophysiology of the condition, the rationale and importance of studying the condition, as well as the societal and economic burden of each condition. The final Background document was generated and edited by each group after two to three meetings, followed by a final edit by a separate member of the Scientific Committee.

For the next section, each group member developed three to five Knowledge Gaps and/or Research Priorities within their topics. For those that were generated, the group members were also asked to develop Recommendations in response to the Knowledge Gaps and/or Research Priorities they had identified. Once a list of Knowledge Gaps and/or Research Priorities with corresponding Recommendations was generated based on the input of individual group members, each group independently met and discussed what broad themes had been recognized for each topic. Based on these themes, the list of Gaps/Priorities and Recommendations were categorized, and the group members worked together to decide which items should be included in or excluded from the document. Upon finalization of the list items, group members were each asked to edit a category to ensure accurate content and references. These were then sent back to the group lead who collated and refined the document. We acknowledge that there are a multitude of research gaps in each of these topics. However, through the process described above, the working groups identified and concluded upon these highlighted areas as the focus of this document. The revised product was sent back to the Scientific Committee where it underwent a final review by a separate committee member.

Once internal revisions were complete, the Research Agenda was reviewed and edited by nine external reviewers, and then subsequently by the AUGS Publications Committee and the AUGS Board of Directors. Edits were considered and revisions made accordingly to create this final document.

## Results

The following is a summary of the six topics of interest identified for this Research Agenda.

### **Lower Urinary Tract Symptoms/Urinary Incontinence**

Overactive bladder (OAB) in women has been estimated to affect millions with its greatest prevalence (over 50%) in adults  $\geq 60$  years old.<sup>12</sup> Stress urinary incontinence (SUI) affects 14-41% of biologic females between the ages of 30 years and 60 years.<sup>6, 7</sup> Numerous studies have demonstrated the negative impact of OAB and SUI on independence, self-esteem, mental health conditions, and interpersonal relationships.<sup>8-11</sup> Voiding dysfunction is

described using a variety of symptoms that depart from normal voiding sensation and function.<sup>12</sup> A large international survey study of a cohort of women older than 40 years reported 5.2% experienced voiding symptoms and 14.9% experienced coexisting voiding and storage symptoms.<sup>13, 14</sup> The etiologies of voiding dysfunction in women are not well understood. Further, the understanding of the impact of voiding dysfunction on quality of life is limited in part due to the historic lack of validated questionnaires for female voiding dysfunction.

The following categories were identified as outstanding knowledge gaps for conditions of lower urinary tract symptoms:

- Clinical phenotyping
- Combined therapies
- Voiding dysfunction
- Health disparities
- CNS control mechanisms, neuromodulation and electrostimulation outcomes
- Biomaterials for stress urinary incontinence treatment
- Impact of pregnancy/childbirth on LUTS management
- Impact of anticholinergic medications on cognition

### **Pelvic Organ Prolapse**

Pelvic organ prolapse (POP) is the descent of one or more of the anterior, posterior, or apical pelvic floor compartments that affects up to 50% of all women.<sup>15</sup> This condition can severely impact quality of life, prompting 1 in 7 women in the United States to undergo surgical correction of POP.<sup>16, 17</sup> Worsening POP has also been associated with deteriorating physical function, anxiety, depression, fatigue, sleep disturbance, and lower satisfaction with participation in social roles.<sup>18</sup> Overall, the pathophysiologic mechanisms underlying the development, progression, and severity of POP are inadequately understood. No effective preventative strategies exist against POP and current treatment modalities are delayed and compensatory.

This working group elucidated Knowledge Gaps and Research Recommendations within each of the 6 areas noted below. With such research, knowledge around the pathophysiology of POP and the relative risk of whom it afflicts would be vastly increased. This would in turn improve our ability to predict or influence POP and, thereby, greatly impact the counseling and care of these patients. The 6 identified themes within POP that require further exploration in well-designed studies are the following:

- Normal and abnormal functional anatomy and biomechanics
- Molecular, cellular, genetic and biomechanical factors

- Therapies for prevention
- Treatment, treatment failure and recurrence
- Health disparities
- Societal impact and financial burden of treatment modalities

### **Fecal Incontinence**

Fecal incontinence (FI), or accidental bowel leakage, defined as unintentional leakage of mucous, liquid, or solid stool is a prevalent condition, affecting up to 24% of women.<sup>19</sup> FI has a profound negative impact on women's quality of life, as well as a substantial economic burden both at the individual and health care system levels. As a result of the associated stigma, women with FI often suffer in silence. As the prevalence increases with age, paralleling the rapidly growing aging population, the impact of FI on society will continue to expand.

Two broad themes to reduce the burden of FI were recognized:

- To optimize the effectiveness of existing treatments and to develop more effective treatments through various research initiatives (basic science, translational, and clinical research)
- To better understand the psychosocial consequences and provide support to alleviate the burden of living with FI

Research gaps were identified, and recommendations were provided for the following categories:

- Pathogenesis
- Classifications of FI Types
- Treatments and Prevention
- Reporting/Validated Measures
- Psychosocial Consequences and Providing Support
- Research Inclusion/Diversity

### **Recurrent Urinary Tract Infections**

Urinary tract infections (UTIs) are some of the most common bacterial and fungal infections, and they disproportionately affect women. More than one half of women have one UTI in their lifetime, and approximately one third develop recurrent UTI (rUTI). Women suffering from rUTIs experience burdens related to symptoms and treatment, including side-effects from antibiotics and risks posed by multi-drug and azole resistant bacteria. Despite the substantial impact of rUTI, there is a paucity of evidence upon which to base accurate diagnosis, treatment, and prevention.

The rUTI working group identified the following research categories:

- Characterization of host-microbial interaction in the female bladder and with neighboring microbial niches
- Biomarker rapid detection

- Patient centered outcomes and care equity
- Recommendations around these categories generally focused on large, multi-center, socioeconomically diverse studies that explore patient-centered outcomes and the impact of rUTI in diverse communities.

### **Sexual Health in Women with Pelvic Floor Disorders**

Patients with pelvic floor disorders (PFD) have a high prevalence of sexual dysfunction and lack of improvement in sexual function after pelvic reconstructive surgery is viewed by patients as a serious complication. Patients may be embarrassed by urine loss during sexual activity, how their genitalia look, and/or express concerns that their prolapse may prohibit sexual activity.<sup>20, 21</sup> The societal and economic burden of sexual dysfunction in women with PFDs is high. A more thorough understanding of the prevalence of sexual dysfunction among each of the individual pelvic floor disorders is essential. There is an urgent need to raise awareness and the importance of sexual function in women with PFDs and to investigate treatments and solutions rather than simply defining the conditions.<sup>22, 23</sup>

Knowledge gaps included the need to:

- Improve Overall Understanding of Basic Anatomy and Physiology and How They Relate to Sexual Function
- Standardization in Terminology, Screening and Reporting
- Patient Centered Counseling and Changes with PFDs Surgery on Sexual Function
- Explore Sexual Health and Dysfunction in Understudied Populations with PFDs

### **Bladder Pain Syndrome/Interstitial Cystitis and Myofascial Pelvic Pain**

Bladder pain syndrome/interstitial cystitis (BPS/IC) and myofascial pelvic pain (MFPP) are two chronic pain conditions that are commonly assessed and treated by urogynecologists. BPS/IC is characterized by bladder pain with associated urinary urgency, frequency, and nocturia lasting greater than 6 weeks in the absence of other identifiable causes.<sup>24</sup> BPS/IC symptoms are common, yet the condition is often underdiagnosed with a lack of understanding the disease pathogenesis. The etiology of BPS/IC is multifactorial with interactions between autoimmune, neuroendocrine, allergic, and infectious pathways.<sup>25, 26</sup> MFPP can be acute; however the chronic syndrome is characterized by pain originating from the pelvic floor muscles.<sup>27</sup> MFPP is persistent or episodic and occurs in the absence of a local pathological condition with symptoms suggestive of lower urinary tract, sexual, bowel or gynecological dysfunction.<sup>28-32</sup> The etiology of MFPP is also not well understood and is likely



multifactorial. Several theories have been suggested including metabolic imbalance at the motor end plate in peripheral tissue, central sensitization of pain, and neuromuscular microtrauma.<sup>33-36</sup>

Both pain conditions warrant significant research attention as they are underrecognized and/or disregarded but are notable sources of pelvic pain and other pelvic symptoms. For BPS/IC, four categories were identified:

- Diagnosis
- Disease Phenotypes
- Current Treatments
- Treatments on the Horizon

For MFPP, the following categories were included:

- Prevalence
- Etiology
- Diagnosis
- Treatment

For each of these categories, Knowledge Gaps/Research Priorities were elaborated on with Recommendations given for each.

## Conclusion

There are extensive areas to be explored in women's health research. The main goal of this Research Agenda was to synthesize and present key gaps and research priorities for a variety of PFDs. There is a clear need to increase funding to investigate these crucial topics. The intention is that this agenda will serve as a living document to be updated as knowledge advances and research priorities evolve. This document will also help to guide researchers when putting forth funding applications and should be used by PFD advocates when championing for research dollars that can be directed toward women's health care beyond reproduction.

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## Research Priorities

### Section 1: Lower Urinary Tract Symptoms/Urinary Incontinence

#### Background

“Lower urinary tract symptoms (LUTS)” is an umbrella descriptor for symptoms related to the storage and voiding of urine. Conditions associated with lower urinary tract symptoms include overactive bladder (OAB), stress urinary incontinence (SUI), as well as neurogenic and non-neurogenic voiding dysfunction.

#### Overactive Bladder

OAB is a sudden urge to urinate that may be associated with one or all of the following symptoms: frequency (voiding 8 or more times per day), nocturia, and urgency urinary incontinence (UUI).<sup>1</sup> OAB may be due to an overt pathologic process such as an underlying neurologic disease, cardiovascular condition, side-effect of medication, or prior bladder surgery. However, the majority of OAB is classified as idiopathic.<sup>2-7</sup> The inability to differentiate forms of OAB is reflected in the current treatment algorithms, which are based on the invasiveness and risk of each modality and often recommended globally regardless of the etiology of a particular patient’s symptoms.<sup>8,9</sup> This approach results in relatively high-treatment failure rates and often with only moderate resolution of symptoms.<sup>10</sup>

OAB is estimated to affect millions of women globally, particularly those older than 60 years (as more than 50% in this group reported OAB symptoms).<sup>11</sup> OAB has a significant impact on quality of life, with almost 40% reporting interference with activities of daily living, including the inability to leave the house.<sup>12-14</sup> Studies have also found that OAB negatively impacts mental health conditions, self-esteem, sexual function, and interpersonal relationships.<sup>15,16</sup> Estimates of OAB in the long-stay nursing facilities is limited. However, an analysis of Medicare beneficiaries demonstrated that 36% of residents had OAB, and that UUI is one of the most important predictors of future institutionalization in older adults.<sup>17,18</sup> In addition, there are significant medical consequences associated with this condition. An epidemiological study of patients with OAB demonstrated that these patients had an increased risk of falls and fractures by 28% and 32%, respectively.<sup>19</sup>

A 2009 analysis found that annual spending in the United States on OAB was over \$65 billion, with an estimate to be between \$76 and \$83 billion.<sup>20,21</sup> Further, it has been reported that OAB patients spent a median of 2.5 times

more on care than similar patients without OAB.<sup>20,21</sup> A similar study in the United Kingdom found expenditures exceeding 7 billion euros annually for OAB patients.<sup>22</sup> The overall global burden of OAB is not well described, but it is believed to occur with similar frequency in most localities. It is estimated that the total number of patients with OAB will increase to over 400 million by 2030 in the 8 major markets of China, United States, United Kingdom, Germany, Japan, Spain, Italy, and France (GlobalData website).<sup>23</sup> The true global incidence of OAB, as well as the economic and social burden, is unknown and likely much greater.

#### Stress Urinary Incontinence

SUI is the leakage of urine associated with increased intra-abdominal pressure, such as with coughing, sneezing, physical exertion. Leakage occurs when pressure on the bladder contents overcomes the outlet resistance provided by the anatomical continence mechanism. It occurs in approximately 14-41% of women between the ages of 30 and 60 years, peaking in the fifth decade of life.<sup>24,25</sup> The major risk factors for SUI in women are pregnancy, vaginal delivery, increasing parity, obesity, increasing age, and postmenopausal status.<sup>26,27</sup>

Studies have reported that many women with SUI suffer from depression, introverted behavior, and dysfunctional interpersonal relationships attributable to SUI symptoms.<sup>27,28</sup> Additionally, studies have reported women with SUI often withdraw from regular physical activities, which can lead to impairments in overall health.<sup>27</sup> Among women who are moderately to extremely bothered by SUI symptoms, only 46.6% reported having ever talked with a physician about incontinence.<sup>29</sup>

In the United States, SUI is an enormous financial burden with over \$12 billion spent annually on the condition, and patients paying 70% out-of-pocket for routine care costs including expenditures for pads, diapers, laundry, and dry cleaning.<sup>30</sup> A large study recently found that women spent nearly \$750 per year for incontinence management and that women were willing to pay nearly \$1,400 per year for a cure.<sup>31</sup>

## Voiding Dysfunction

Voiding symptoms are a departure from normal sensation or function during or following the act of micturition.<sup>11</sup> Voiding symptoms may be described as a delay (hesitancy) in initiating micturition, a need to strain to void, a sensation of incomplete bladder emptying, and a need to void again soon after passing urine. The relationship of postvoid residual volumes with voiding symptoms is unclear in the existing literature; in part due to lack of diagnostic criteria for chronic urinary retention.<sup>32</sup> A 2017 consensus report from the American Urological Association defined non-neurogenic chronic urinary retention as an elevated postvoid residual of > 300 mL that has persisted for at least 6 months on two or more separate occasions.<sup>33</sup> The etiology of voiding symptoms is generally not well understood. In an international survey of women who were older than 40 years, 5.2% had isolated voiding symptoms while 14.9% had coexisting voiding and storage symptoms.<sup>32, 34</sup> Neurogenic voiding dysfunction is characterized by the presence of relevant neurological pathology in the setting of voiding symptoms as described above.<sup>35</sup> For this research agenda, the writing group decided to focus on non-neurogenic voiding dysfunction.

Non-neurogenic voiding dysfunction, a diagnosis by symptoms and urodynamic investigations, is defined as abnormally slow and/or incomplete micturition.<sup>11</sup> Pressure-flow studies estimate etiologies such as detrusor underactivity or bladder outflow obstruction; however, there is no consensus in female bladder outlet obstruction and detrusor underactivity diagnostic criteria.<sup>11</sup> Management of voiding dysfunction depends on etiologies, which may be functional, anatomic (prolapse, urethral stricture), or iatrogenic.

The impact of voiding symptoms, with or without urinary retention, on quality of life is poorly understood in part due to a historic lack of validated questionnaires for female voiding dysfunction. Previous estimates of prevalence used questionnaire tools designed for males with prostate pathology.<sup>32</sup> The single validated tool to assess storage and voiding symptoms in women, the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN) Symptom Index-10 (SI-10), is fairly new and has not yet been extensively integrated into clinical research.<sup>36</sup> Health sequelae and associated societal, economic, and personal burdens specific to non-neurogenic female voiding dysfunction are unknown. Cost analyses of such burdens require data regarding the condition-specific impact on quality of life and reported clinical outcome measures with therapy.

## Research Priorities and Opportunities

### Clinical Phenotyping

*Research Gap:* Overactive bladder syndrome is loosely defined in order to encompass a range of varying phenotypes, including nocturia and urinary urgency incontinence (UUI). However, treatment efficacy varies widely and necessitates increased attention to how particular patient characteristics and symptoms may be used to guide treatment.<sup>10, 37</sup> The Symptoms of Lower Urinary Tract Dysfunction Research Network has focused on the specification of clinical phenotypes of OAB, but an absence of knowledge remains. There are not established clinical and patient genotypes and phenotypes within OAB, UUI, urinary urgency/frequency and nocturia.

#### *Recommendations:*

- ✓ Characterize LUTS clusters and investigate their association to treatment responsiveness.
- ✓ Identify biomarkers (including brain imaging findings, serum/plasma/urine markers), functional assessment measures (including frailty evaluations and cognitive assessments), and physiologic assessment measures (including neurologic testing, POP-Q measurements, urodynamic measures) specific to individual phenotype profiles to objectively correlate symptoms and treatment outcomes.
- ✓ Examine improved diagnostic testing (including home testing, enhanced urethral testing) that may contribute to clinical phenotype profiles.

### Combined Therapies

*Research Gap:* There is a need to understand the potential benefit from combined therapies (pharmacologic and nonpharmacologic) to treat urinary incontinence (UI) in meeting patients' treatment goals compared to the use of monotherapy. Typically, UI is treated with one modality that then follows a progressive linear pathway. In this siloed approach, if one treatment modality fails, that treatment is discontinued and the next treatment in the pathway is initiated without consideration of alternate combination modalities utilizing an additive model that would combine therapies. Few studies have evaluated the effectiveness of combined therapies and have had mixed results.<sup>38, 39</sup>

#### *Recommendations:*

- ✓ Evaluate the potential synergistic benefit of combined therapies in subjective and objective patient outcomes.
- ✓ Examine predictors of patient-defined treatment success with combined therapies (which can include symptom responsiveness, satisfaction, preference, etc.) for LUTS conditions.

## Voiding Dysfunction

*Research Gap:* There is a significant knowledge gap in the understanding of the approach to better streamline patients in getting timely diagnosis, and effective treatment for voiding dysfunction. Initial treatments for voiding dysfunction include timed voiding, clean intermittent catheterization, pelvic floor muscle (PFM) relaxation training with biofeedback, and alpha-blocker pharmacotherapy. However, there remains a paucity of rigorous research examining treatment outcomes for adult women with voiding dysfunction, as the majority of nomograms of voiding parameters were collected from men.

### *Recommendations:*

- ✓ Increase the understanding of prevalence and magnitude of voiding dysfunction in women through the development of tools to assess symptoms and the establishment of standardized nomenclature and approaches to the diagnoses that connect signs/symptoms with objective findings.
- ✓ Conduct research using robust research design methodology in adult women with underactive bladder and voiding dysfunction that compares PFM relaxation and biofeedback alone to standard behavioral modifications (including hydration, scheduled voiding, toilet training, and diet) combined with PFM relaxation and biofeedback.
- ✓ Evaluate the impact of preemptive biofeedback, behavioral modifications, and pelvic floor physical therapy on treatment outcomes of subsequent sacral neuromodulation therapy.

## Health Disparities

*Research Gap:* Health disparities are a major public health issue, which influence urogynecologic care and outcomes. Their impact on LUTS has not been well examined and necessitates further research. While barriers to care for specific minority populations have been identified, race/ethnic information is frequently not reported in research and often such cohorts are racially/ethnically homogenous. Current guidelines for the treatment of LUTS rely on studies with cohorts of participants that do not represent the racial and ethnic distributions in our communities.<sup>40-42</sup>

### *Recommendations:*

- ✓ Establish self-report methods that are all-inclusive when attaining race and ethnicity information from study participants.
- ✓ Examine the role of discrimination, marginalization, and systemic racism on access to care and management/treatment outcomes in racial/ethnic minority populations, particularly including studies with the framework that disparities in LUTS experience, treatment, and outcomes between racial

and ethnic groups are not issues with a biological basis.

- ✓ Improve racial/ethnic representation by championing efforts to recruit racial and ethnic minority individuals into LUTS research studies at proportions similar to national racial/ethnic distributions.

## CNS Control Mechanisms, Neuromodulation and Electrostimulation Outcomes

*Research Gap:* There is a paucity of knowledge on the impact of changing the stimulation pattern and/or location of CNS control mechanisms, neuromodulation and electrostimulation therapy performance. Neuromodulation and electrostimulation therapies for incontinence, specifically sacral nerve stimulation and tibial nerve stimulation, have been used in people for over two decades. Advances throughout the years have occurred in device design (including magnetic resonance imaging [MRI] compatibility, battery, implantable tibial stimulator) and technical advances in surgical approach (including curved stylet, importance of low thresholds). However, to date there have been no changes in CNS control mechanisms, neuromodulation or electrostimulation that improve efficacy based on changes in stimulation pattern or location.

### *Recommendations:*

- ✓ Examine changes in physiology with responders and non-responders to CNS control mechanisms, neuromodulation and electrostimulation to determine mechanisms of action.
- ✓ Compare physiological measurements before and after stimulation in both groups to gain insight into how these therapies work.
- ✓ Utilize animal models to focus on the examination of changes in physiological parameters beyond just functional (including beyond bladder capacity, voiding efficiency, intermicturition interval) in response to changing stimulation location and stimulation pattern.

## Materials for Stress Urinary Incontinence Treatment

*Research Gap:* The safety and efficacy of treatment for SUI using biomaterials is not fully understood. Current treatments include procedures using synthetic materials to address the mechanical deficiencies of the urethra and its support structures; synthetic material complications remain a concern. The complications associated with autologous fascial slings and ineffectiveness of allograft biological materials have limited their clinical use.<sup>43</sup>

### *Recommendations:*

- ✓ Examine biologic and/or synthetic materials that can provide biocompatibility without sacrificing durability.

- ✓ Evaluate regenerative therapies to restore the strength and function of the urethral sphincter and support structures.

### Impact of Pregnancy/Childbirth on LUTS Management

*Research Gap:* There is a significant depth and breadth of literature on how pregnancy impacts LUTS in later life. However, other than childbirth injury, relatively little is known about what anatomic and physiologic changes related to pregnancy and the peripartum period (including the first year after delivery) lead to the development of LUTS, what qualities are associated with spontaneous resolution of symptoms, and how quality of life is impacted in young adults compared to older adults. Even less is known about what the optimal treatment options are for people who have not yet completed childbearing.

#### *Recommendations:*

- ✓ Attain a better understanding of how pregnancy and the peripartum period lead to the development of LUTS through examination of predisposing factors (including genetics, family history, neurologic symptoms, pelvic floor muscle loading function in peripartum/intrapartum states, labor, route of delivery).
- ✓ Examine factors associated with symptom resolution versus symptom persistence in parous women which could ultimately lead to the provision of targeted treatment for those patients who may most benefit from intervention without overtreatment.
- ✓ Evaluate the impact of future childbirth among people who have not yet completed childbearing with regards to the continued efficacy of conservative treatments (pelvic floor therapy, tibial nerve stimulation, behavioral modification, intravaginal devices) as compared to mid-urethral sling placement, urethral bulking, and sacral neuromodulation.

### Impact of Anticholinergic Medications on Cognition

*Research Gap:* There is a significant knowledge gap centered on the relationship between OAB and cognitive function as well as the relationship between anticholinergic medication use and cognitive impairment. Pharmacologic management of urgency urinary incontinence has historically included the use of nonselective muscarinic antagonists. However, recent evidence has suggested an association of long-term anticholinergic use with Alzheimer's disease and related dementias (ADRD).<sup>44, 45</sup>

#### *Recommendations:*

- ✓ Assess the temporal relationship between overactive bladder and cognitive decline through large health

care databases and prospective studies or registries.

- ✓ Evaluate the safety and effectiveness of anticholinergics and beta-3 agonists related to ADRD.
- ✓ Identify the knowledge gaps of clinicians and patients as well as systematic barriers contributing to utilization of anticholinergic OAB medications in patients.

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## Section 2: Pelvic Organ Prolapse

### Background

Pelvic organ prolapse (POP) is the descent of one or more of the anterior, posterior, or apical pelvic floor compartments.<sup>1</sup> POP is thought to occur secondary to failure of the pelvic support structures including the levator ani muscle complex, cardinal and uterosacral ligaments, and endopelvic fascial connections.<sup>2</sup> POP can be identified anatomically on physical exam and by patient-reported symptoms. Approximately 50% of women have evidence of POP on physical examination.<sup>3-8</sup> Of these women, 3-6% will have descent of prolapse beyond the hymen, which is well-correlated with the onset of patient symptoms.<sup>9-11</sup> POP increases in prevalence and severity with increasing age;<sup>4,12</sup> it is projected that 9.2 million women will have POP by 2050.<sup>13</sup> Risk factors for the development of symptomatic POP include age, vaginal parity, and possibly some connective tissue disorders.<sup>3,5-7</sup> At the molecular level, cellular senescence, collagen loss/degradation, and connective tissue impairment have been associated with POP.<sup>14</sup> Overall, the pathophysiologic mechanisms underlying the development, progression, and severity of POP are inadequately understood.

Treatment options for bothersome symptomatic POP include pelvic floor physical therapy/pelvic muscle strengthening, pessary fitting, and surgical intervention. No effective preventative strategies for POP have been identified. Data on the effectiveness of existing interventions to improve pelvic floor strength are lacking and the development of novel preventative strategies is needed. Pessaries are a nonsurgical approach for treatment for prolapse. Although overall safe, complications including discomfort, local tissue devascularization and erosion can limit use.<sup>15</sup>

Surgical approaches include both native tissue and mesh-based reconstructive procedures and obliterative procedures. Optimal reconstructive surgical outcomes involve addressing all of the anterior, posterior, and apical compartments contributing to the pelvic organ prolapse.<sup>16</sup> Pelvic floor functional anatomic studies have demonstrated a correlation between apical failure and paravaginal defects;<sup>17</sup> this is corroborated by the finding of similar POP-Q point improvements and Patient Global Impression of Improvement (PGI-I) scores between cohorts undergoing robotic sacrocolpopexy with or without concurrent paravaginal defect repairs.<sup>18</sup> Both native tissue site-specific rectocele repair and posterior colporrhaphy provide improvements in symptoms and

quality of life parameters.<sup>19</sup> A recent systematic review of apical suspensions showed a higher risk of anatomic recurrence with native tissue based vaginal approach (sacrospinous and uterosacral ligament suspensions) compared with mesh sacrocolpopexy.<sup>20</sup> A meta-analysis comparing trans-vaginally placed anterior type I polypropylene mesh to native tissue demonstrated a lower subjective awareness of prolapse with mesh augmentation, but the composite risk of subsequent surgery for prolapse, incontinence, and mesh extrusion was significantly higher.<sup>21</sup> After a series of safety communications, in 2019 the FDA halted the sale and distribution of mesh surgical products for the transvaginal repair of pelvic organ prolapse.<sup>22, 23</sup> Postoperative prolapse recurrence ranges from 6-30%<sup>24</sup> highlighting the need to develop new strategies to the durability of surgical procedures by improvement of native tissue integrity or development of novel biomaterials.

Symptomatic POP is associated with urinary incontinence, depression, anxiety, sleep disturbance, sexual dysfunction, deteriorating physical function and diminished socialization.<sup>25-28</sup> It has a substantial negative impact on the physical function and quality of life of women.<sup>29</sup> Due to the severity of this condition, 1 in 7 women will undergo surgical correction of POP.<sup>30,31</sup> The lifetime risk of surgical intervention increases by age and by age 80, 20% of women will have undergone surgical correction of POP.<sup>32</sup> The number of women seeking treatment of POP is expected to increase as our population ages; by 2050, approximately 250,000 women are projected to undergo surgery for POP annually.<sup>13</sup>

The comprehensive economic burden of the condition is not well-defined<sup>33</sup> and extends far beyond the condition itself (e.g., caregiving needs, exacerbation of concomitant pelvic floor disorders, loss of work, and decreased societal productivity). Existing studies have focused either on direct surgical or ambulatory costs and are limited by inclusion of other pelvic floor disorders. The direct surgical cost of POP was estimated to be \$1 billion annually in studies from the 1990s.<sup>34</sup> Contemporary studies, which evaluate the broader economic impact of changes in management of POP (including the introduction of robotic sacrocolpopexy, uterine-sparing approaches, and ambulatory care specific to POP), are lacking.

## Research Priorities and Opportunities

### Normal and Abnormal Functional Anatomy/Biomechanics

*Research Gap:* The pelvic organ support system consists of multiple intact interconnected boney, muscular, and connective tissue structures whose complex 3D arrangement facilitates gastrointestinal and genitourinary function.<sup>35</sup> Prior work has focused on the contribution of levator ani impairment (avulsion and/or denervation) to POP development, but its relationship to anatomic measurement surrogates remains uncharacterized.<sup>36</sup> Additionally, the vectors of external forces applied to the pelvic floor and their contribution to POP development is unclear. Further investigations are needed to understand the occurrence, combination, and interaction of failures of other aspects of the support system to develop evidence-based prevention and rationally directed therapy. Finally, there is a limited understanding of how specific anatomical findings produce specific symptoms.

#### Recommendations:

- ✓ Develop prospective observational studies to correlate measurements of genital hiatus size, perineal body length and mobility, and vaginal axis to the degree of POP and/or degree of POP symptoms.
- ✓ Establish physiologic studies to identify conditions of external force that increase pelvic floor pressure and their correlation to POP.
- ✓ Expand research that investigates the association between specific types of anatomical failures and the symptoms they produce, with the goal of creating prolapse phenotypes based on objective and subjective findings.

### Molecular, Cellular, Genetic and Biomechanical Factors

*Research Gap:* The molecular, cellular, genetic and biomechanical factors that influence the development and/or progression of POP are poorly understood.<sup>37,38</sup> These factors include but are not limited to hormones, predisposing genetic/epigenetic factors, aging, metabolic disturbances (including obesity), and vaginal delivery.<sup>39-41</sup> A fundamental molecular, cellular, and tissue level understanding of POP pathophysiology is critical to identification of populations at risk, appropriate counseling, and personalized treatment strategies directed at the etiologies of POP.

#### Recommendation:

- ✓ Create multi-disciplinary *in vitro*, *in vivo*, and translational studies of critical supportive tissues and their cell populations to identify cell signaling and metabolic pathways, extracellular matrix

modifications, and biomechanical alterations that may potentiate POP.

### Therapies for Prevention

*Research Gap:* To date, treatments have been focused on management of POP once symptomatic, and information is lacking concerning potential therapies to prevent pelvic floor and soft tissue injury and POP recurrence following surgical intervention. The current focus lies on vaginal birth parity as a risk factor for POP and cesarean delivery as a method of prevention, but additional data are required to elucidate alternate risk reduction modalities.<sup>42</sup>

#### Recommendations:

- ✓ Develop prospective studies to assess peripartum, intrapartum, and postpartum preventative strategies to decrease pelvic floor trauma/denervation (e.g., peripartum weight control, maternal positioning, perineal support, sequential pushing maneuvers, postpartum physical therapy), thus reducing risk of subsequent POP.
- ✓ Identify intra-operative and post-operative approaches to reduce the risk of POP recurrence (surgical approach, role and timing of topical estrogen, supportive devices, activity mobilization, pelvic floor physiotherapy).

### Treatment, Treatment Failure and Recurrence

*Research Gap:* Surgical treatment for POP has focused on the restoration of connective tissue support by compromised native tissue plication and the implantation of synthetic materials, most commonly polypropylene mesh. Native tissue plication appears to be associated with higher POP recurrence, but mesh has been associated with rare but serious complications including extrusion and chronic pain; complications have been particularly problematic when POP meshes are inserted via a transvaginal approach. Products designed to facilitate transvaginal insertion of mesh have therefore been reclassified and removed from market following a series of U.S. Food and Drug Administration (FDA) warnings.<sup>43</sup> Thus, novel and safer treatment options are needed for POP. Early work supports the use of softer implants with stable geometries under the conditions in which the implants are loaded.

#### Recommendations:

- ✓ Evaluate surgical outcomes in animal models using mesh with softer properties, stable geometries, and biologically active components that improve interaction with grafted tissues with the goal of restoring injured structures to the non-injured state.
- ✓ Engineer more biocompatible grafts and synthetic or non-synthetic regenerative materials to be used in prolapse surgery.

- ✓ Establish surgical algorithms that optimize prolapse repair outcomes based on patient POP characteristics as well as best practices in surgical repairs.

### Health Disparities

*Research Gap:* There is a relatively low representation of racial and ethnic minorities in POP research. Unknown factors in diverse populations may predispose or protect from the development of POP. Additionally, little is known regarding how POP symptoms are expressed across languages and cultures.

#### *Recommendations:*

- ✓ Develop epidemiologic studies to better understand disparities in care for diverse patients and identify risk factor clusters in geographic regions and within diverse populations, including studies with the framework that disparities in prolapse experience, treatment, and outcomes, such as those seen between different racial and ethnic groups, are not issues with a biological basis.
- ✓ Design population-based studies to assess the National Institutes of Health (NIH) initiative of health disparities in underserved groups seeking care for POP.

### Societal Impact and Financial Burden of Treatment Modalities

*Research Gap:* The financial burden of treatment modalities affects our ability to provide care to patients with POP as the likelihood of governmental support and outside funding may be reduced.

#### *Recommendation:*

- ✓ Create and explore cost-analysis studies in surgical techniques and devices in outpatient-based care of pelvic floor physiotherapy to treat POP.

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## Section 3: Fecal Incontinence

### Background

Accidental bowel leakage (ABL), or fecal incontinence (FI), is defined as unintentional leakage of mucous, liquid, or solid stool. This condition is further classified by either urge or passive incontinence. With urge FI there is awareness of the need to defecate but lack of ability to control the bowel contents. In contrast, passive FI is leakage without sensation that the bowel is full or ready to empty.

The prevalence of FI in women has been reported to be up to 24%.<sup>1</sup> There is increasing incidence of FI with age, as a longitudinal cohort study found adults older than 65 years had 2.79 higher odds of having weekly FI [95% CI 1.88, 4.14].<sup>2</sup> The true prevalence of FI is difficult to determine because the stigma associated with FI often prevents women from disclosing their symptoms to a medical provider, even when the symptoms have a negative impact on daily life.<sup>3</sup> Further, primary care and women's health care providers do not routinely screen for FI symptoms.<sup>4</sup>

Predictors of FI are independent of sex and gender and reported rates of FI are similar in men and women.<sup>2</sup> Patients who identify as non-Hispanic White and/or Hispanic have a higher incidence of FI than patients who identify as non-Hispanic Black and Asian. However, non-Hispanic Black and Hispanic women have been found to have greater symptom severity.<sup>2</sup> Although education level and marital status have no impact on FI incidence, adults with annual income greater than \$200,000 do have higher odds of weekly FI symptoms (OR 2.28, 95% CI 1.04,4.99).<sup>2</sup> Clinical characteristics significantly associated with FI include diarrhea, fecal urgency, constipation, and presence of inflammatory bowel diseases.<sup>2, 5</sup>

Current management options for FI include 1) conservative, non-surgical therapies such as supportive care (pads, diapers, barriers, diet modifications, behavioral), medical management (antidiarrheal agents, oral bulking agents), pelvic floor exercises ± biofeedback, devices (plugs, vaginal bowel control system), and injectable anal bulking agents; as well as 2) surgical management such as sacral nerve stimulation, anal sphincteroplasty, and fecal diversion requiring an ostomy in refractory cases.

Existing data, although limited, demonstrate a substantial economic burden associated with FI, both at the individual and health care system levels. Health care costs overall

are 55% greater for people with FI compared to those without.<sup>4</sup> The estimated financial cost of FI has been reported to be \$4,110 (2010) per person annually. Further, given its psychosocial burden, FI also leads to loss of household and work productivity, at an estimated cost of \$1,549 (2010) per person annually.<sup>6</sup> There is a significant association between FI symptom severity and economic burden.<sup>6, 7</sup> The financial burden on society, assessed by the cost of inpatient procedures alone for women with FI, was \$24.5 million (2003), nearly 2 decades ago,<sup>8</sup> and continues to rise. Globally, the value of the adult diaper market was estimated to be \$16.7 billion in 2021, which is projected to reach \$26.1 billion by 2027 <https://www.researchandmarkets.com/>.<sup>9</sup> There are additional data elaborating on the significant financial burden of FI.<sup>7,10-12</sup> As FI increases with age, paralleling the rapidly growing aging population, the economic impact on society will continue to expand.

### Research Priorities and Opportunities

Two broad themes to reduce the burden of FI were identified: 1) to optimize the effectiveness of existing treatments and to develop more effective treatments for FI through various research initiatives (basic science, translational, and clinical research), and 2) to better understand the psychosocial consequences of FI and provide support to alleviate the burden of living with FI.

### Pathogenesis

*Research Gap:* Working knowledge pertaining to the pathogenesis of FI is limited. The current understanding of the mechanism of fecal continence heavily focuses on the integrity of the anal sphincter complex to contain stool, which incompletely explains the mechanism of FI. The mechanism of fecal continence is complex and necessitates intact neuromuscular coordination within and beyond the anorectum and pelvic structures.

### Recommendations:

- ✓ Develop an understanding of the mechanisms of FI other than compromised anal sphincter complex trauma.
- ✓ Enhance understanding of indications for and utility of imaging and neuromuscular testing modalities and functional biomarkers.
- ✓ Investigate the role of the nervous system in the maintenance of continence.
- ✓ Delineate the roles of gut microbiota and metabolites on the pathophysiology of FI.

## Classifications of FI Types

*Research Gap:* An incomplete understanding of FI pathogenesis leads to a lack of consensus on the classification of FI types. The majority of FI patients suffer from “idiopathic” FI, which hinders investigative efforts.

### Recommendation:

- ✓ Improve the current FI classification system to address the spectrum of FI subtypes and standardize a pathogenesis-based disease classification system that corresponds to treatment algorithms.

## Treatments and Prevention

*Research Gap:* Effective long-term treatment options are limited, and there is a lack of a treatment algorithm that is based on FI mechanism (pathophysiology). There is limited understanding of how disturbances in the continence mechanism(s) impact treatment modalities.

### Recommendations:

- ✓ Identify optimal target populations and mechanism-based indications for various therapies, as well as develop mechanism-specific therapies that do not already exist.
- ✓ Develop therapies that either prevent fecal incontinence or directly target incontinence pathophysiology at the cellular and molecular levels.

## Reporting/Validated Measures:

*Research Gap:* FI is a multifactorial disorder with significant symptomatic burden. While multiple instruments exist, there is a lack of consensus among experts on how to optimally capture the condition burden of FI. Correlations among existing measures on treatment effectiveness are moderate at best, thus leading to inconsistent reports regarding the efficacies of various interventions.

### Recommendation:

- ✓ Develop an FI measurement tool that effectively captures the condition burden, reflects clinically significant change in a way that enables measurement of treatment efficacy, and achieves consensus for use amongst stakeholders (including patients).

## Psychosocial Consequences and Providing Support

*Research Gap:* Despite the tremendous burden of FI, there is little understanding of how to improve support for those living with FI.

### Recommendations:

- ✓ Investigate differential burdens among people living with FI, family/caregivers, and society overall.

- ✓ Conduct a needs assessment to develop an effective support system to alleviate the psychosocial burden of FI.
- ✓ Identify ways to reduce stigma and improve access to care, with an emphasis on reducing disparities and enhancing equitable care delivery.

## Research Inclusion/Diversity

*Research Gap:* Traditional research trials on FI have a narrow representation of people who suffer with FI.

### Recommendations:

- ✓ Engage a broader research population with intentional inclusion of participants from various backgrounds, thus ensuring representation across various social determinants of health.
- ✓ Consider eligibility criteria to allow a broader spectrum of condition severity to assess the impact and effectiveness of FI interventions.

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## Section 4: Recurrent Urinary Tract Infections

### Background

Urinary tract infections (UTIs) are some of the most common bacterial infections in the United States, and they disproportionately affect women.<sup>1</sup> “UTI” is often colloquially used to describe bacterial cystitis, an infection limited to the bladder rather than the upper urinary tract and kidneys. More than one half of women have one UTI in their lifetime, and approximately one third of these women develop recurrent UTI within 6 months.<sup>1-3</sup> Up to 10% of women will seek treatment for recurrent UTIs in their lifetime, with recurrent UTI defined as two or more culture proven UTIs in 6 months or three or more in 12 months.<sup>2</sup> *Escherichia coli* (*E. coli*) is the most common urinary tract pathogen and is found in 70-95% of UTIs detected with standard urine cultures.<sup>4</sup> However, *E. coli* is only seen in 66% of recurrent UTIs, with non-*E. coli* and resistant pathogens more commonly identified in women with recurrent UTIs (PMID: 29369839, PMID: 23055152).<sup>4, 5</sup> Risk factors for recurrent UTIs include behavioral, anatomic, biologic, and genetic factors, suggesting a complex interaction exists between host and pathogen. In addition, the emerging field of the urobiome has enhanced our understanding of the bladder’s non-sterile environment.

There is a vast body of evidence demonstrating the social and economic impact of recurrent UTIs. These infections negatively impact the quality of life of countless women, with studies of patients suffering from recurrent UTIs noting anxiety, depression, and significantly diminished quality of life.<sup>3,6,7</sup> Women suffering from recurrent UTIs experience burdens related to symptoms and treatment, including exposure to repeated courses of antibiotics. Repeated antibiotic exposure comes with additional side-effects and societal risks, including a predisposition to infections outside of the urinary tract and increased prevalence of multi-drug resistant bacteria. The rising prevalence of multi-drug resistant pathogens has paralleled increasing UTI rates and increased UTI-related hospital admissions over the last several decades.<sup>8-10</sup> As UTI rates continue to climb, the societal burden of recurrent UTI is expected to increase over the coming years.

Currently, the economic costs of UTIs, including health care costs and time missed from work, are approximately \$3.5 billion per year in the United States alone.<sup>11,12</sup> European studies have similarly shown the high annual patient cost for women suffering from recurrent UTIs that is mostly related to pharmacological therapies and

physician visits.<sup>6,13</sup> UTIs, specifically bacterial cystitis, account for nearly 1% of all outpatient clinic visits with approximately one fifth of these visits at the emergency department.<sup>11,14,15</sup> UTIs have been linked to 6.2% of infectious disease-related deaths,<sup>16</sup> and are responsible for 15.5% of hospital admissions amongst patients aged 65 years and older, second only to pneumonia.

Despite the profound social and economic impact of recurrent UTI, there is a paucity of information regarding pathophysiology, strategies to treat and prevent recurrent UTI, and non-antibiotic interventions to effectively prevent infection of the lower urinary tract. These persistent gaps in knowledge adversely impact the well-being of millions of women, who seek relief from emotional, physical, and economic burdens of their recurrent infections. In order to meet public health needs and progress towards a cure for recurrent UTI patients, the American Urogynecologic Society Scientific Committee recommends the following research priorities.

### Research Priorities and Opportunities

Three research areas are essential to the advancement of scientific knowledge related to UTI prevention and treatment: 1) characterization of healthy and disease states of the female bladder, 2) identification of biomarkers for rapid detection of UTI, and 3) investigation of patient-centered outcomes and disparities in UTI/recurrent UTI (rUTI) care.

#### Characterization of host-microbial interactions in the female bladder and with neighboring microbial niches

*Research Gap:* Throughout the body, health and function are dependent on a balance of the proper flora. It is believed that the genitourinary system is no exception. Currently, there is limited understanding of the microbial ecology of the lower urinary tract and neighboring microbial niches specifically the vagina. Pathogenic theories suggest that uropathogens invade the urothelium to cause UTIs, whereas other lower urinary tract symptoms are not associated with uropathogens. However, uropathogens are often present in the absence of UTI. To advance patient outcomes, we must understand the natural ecology of the genitourinary tract (bladder, vagina, and surrounding microbial niches) and its response to UTI-related treatments.

*Recommendations:*

- ✓ Conduct microbiome studies of the genitourinary tract to further the understanding UTI/rUTI and lay



the foundation for further investigation of ecological shifts associated with health and disease states.

- ✓ Aim to further elucidate the impact of aging and hormones on UTI susceptibility, pathogenesis, and response to treatment.
- ✓ Investigate novel non-antibiotic approaches for prophylaxis and treatment of UTI/rUTI.
- ✓ Investigate neuro-immune changes associated with infection response to understand the development of uncomplicated UTI versus complicated UTI/rUTI.
- ✓ Develop microbiome studies of large, diverse populations to ascertain the efficacy, safety, and durability of treatment modalities over both the short and long term (minimum 1 year).

### Biomarker Rapid Detection

*Research Gap:* Women with rUTI can have episodes of bacteriuria that do not require antibiotics. Distinguishing disease states that would benefit from antibiotics from those that would not is especially important in patients with both bladder pain syndrome and rUTI. Accurate biomarkers will enhance diagnostic accuracy and improve clinical decision making. Some studies show that urinary markers (such as IL-6) can differentiate between asymptomatic bacteriuria (ASB) and UTI, but further investigation into biomarkers that can rapidly distinguish ASB from UTI are needed.

#### Recommendations:

- ✓ Design studies to identify specific biomarkers that characterize symptomatic UTI versus asymptomatic bacteriuria.
- ✓ Elucidate the role of the immune system with respect to UTIs and inflammation.
- ✓ Develop relevant animal models or ex-vivo human cell/tissue derived models (including bladder organoids or bladder on a chip) to facilitate development of rapid uropathogen or biomarker detection technologies.

### Patient-Centered Outcomes & Care Equity

*Research Gap:* There is inadequate data related to patients' experiences with UTI/rUTI and patient-centered goals related to care. Furthermore, equity in rUTI care has not been examined, and there is a paucity of data related to treatment access, efficacy, and long-term outcomes amongst non-White and Hispanic patients.

#### Recommendations:

- ✓ Capture the psychosocial burden of UTI/rUTI.
- ✓ Investigate health literacy related to UTI/rUTI and establish treatment goals for rUTI via large, multi-center, socio-economically diverse studies.
- ✓ Emphasize patient education tools and care pathways for UTI/rUTIs, patient-centered outcome measures, and equity in UTI/rUTI care.

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## Section 5: Sexual Health in Women with Pelvic Floor Disorders

### Background

Patients with pelvic floor disorders (PFD) consider sexual health important, feel that their sex lives are affected by their PFDs, and believe that PFD treatment improves their sex lives. Lack of improvement in sexual function after pelvic reconstructive surgery is viewed by patients as a serious complication.<sup>1</sup> Patients may be embarrassed by urine loss during sexual activity, how their genitalia look, and/or express concerns that their prolapse may prohibit sexual activity.<sup>2</sup> Patients with fecal incontinence are largely omitted from sexual function research, but limited evidence reveals accidental bowel leakage's profound impact on sexual function.<sup>3-6</sup> In addition, patients who undergo reconstructive surgery are often hesitant to resume sexual activity because they think that intercourse will harm the repair or their partner.<sup>7</sup> Despite its importance, data regarding sexual health in patients with PFDs are limited. Research has established sexual dysfunction prevalence among patients with PFDs, and there are questionnaires to assess these problems in research settings;<sup>8,9</sup> however, little has been done to improve the sexual lives of patients with PFDs.<sup>10</sup> In the clinical setting, health care providers do not feel prepared to discuss sexual concerns and, when they do, they have limited research to guide recommendations that are meaningful. Additionally, much of our research is limited to cisgender individuals and is not inclusive of women with different sexual orientations and those who do not have male partners. Although it is imperative that research in the context of sexual function and PFDs investigates treatments and solutions, the overall knowledge gaps first require better understanding and defining of these conditions. Finally, sexual function and dysfunction is multifactorial and requires expertise beyond just pelvic reconstructive surgeons.

Societal burden is high given that sexual dysfunction is common among women with pelvic floor symptoms. It is estimated that approximately 64% of women presenting to urogynecology practices suffer from some type of sexual dysfunction.<sup>11</sup> Women with PFDs are more likely to have decreased sexual arousal, decreased orgasm, and increased rates of dyspareunia compared to women without pelvic floor symptoms.<sup>12</sup> A more thorough understanding of the prevalence of sexual dysfunction among each of the individual pelvic floor disorders is essential.

The economic burden of male sexual dysfunction has been well described in the literature,<sup>13</sup> whereas that of female sexual dysfunction has not yet been clearly

defined. Preliminary work in cisgender women with sexual dysfunction presenting to a specialized sexual function clinic in the United Kingdom, found the average cost per patient in 2004 to be £472 (equivalent to £700 today or \$900 U.S. dollars).<sup>14</sup> A study in the United States found that the medical expenses for women with hypoactive sexual desire disorder (HSDD) were 27.9% higher than those without in the year before their diagnosis, and 19.5% higher in the year following diagnosis, with a difference of \$1,146 and \$897 per patient, respectively.<sup>15</sup> These differences were primarily related to a higher number of outpatient services and prescriptions in women with hypoactive sexual desire disorder (HSDD). Investigation into the impact of female sexual dysfunction on quality-adjusted life years has been recommended as this would offer a more comprehensive perspective on the true economic burden of the condition; however, this has not yet been completed.<sup>13</sup> The economic burden of sexual dysfunction related to pelvic floor disorders (PFDs) remains unknown. Given the strong association of sexual dysfunction with PFDs<sup>12</sup> and the estimated \$412 million direct annual costs associated with ambulatory care for PFDs, which continues to increase,<sup>16</sup> it can be safely concluded that the cost of sexual dysfunction due to PFDs is also unacceptably high.

### Research Priorities and Opportunities

#### Improve Overall Understanding of Basic Anatomy and Physiology and How They Relate to Sexual Function

*Research Gap:* Overall, there is lack of understanding of the female pelvic anatomy and physiology and how it contributes to the sexual response. This knowledge gap translates to complications decreasing sexual function following urogynecologic surgical procedures for incontinence and pelvic floor disorders.

#### *Recommendations:*

- ✓ Characterize the female pelvic anatomy and physiology to better understand the contribution and importance of all pelvic organs, glands, hormones, nerves, and vasculature to sexual function.
- ✓ Conduct descriptive and qualitative studies of pelvic anatomy in healthy, postpartum, and older (postmenopausal) individuals with and without pelvic floor disorders.

## Standardization in Terminology, Screening and Reporting

*Research Gap:* There is a lack of consistent reporting and lack of consensus on specific female sexual health outcomes in research trials for pelvic floor disorders, including validated sexual function questionnaires, domains of sexual function, and definitions of sexual function outcomes (persistent dyspareunia, de novo dyspareunia, sexual activity).

### Recommendations:

- ✓ Describe current validated questionnaires evaluating sexual function related to women with pelvic floor disorders and make recommendations on how they should be reported in research trials, including specific questions and domains.
- ✓ Determine the optimal screening questions for sexual health in the clinical setting and in research trials based on validation and qualitative research.
- ✓ Provide recommendations for sexual function outcome reporting for prospective trials in urogynecologic research (including baseline and postoperative data for sexual activity, dyspareunia, and de novo dyspareunia).
- ✓ Improve study robustness by recognizing that comparing a sexually active cohort at the beginning of a study to those active at the end of the study is not possible because of the fluidity of patients identifying as sexually active over time and develop methods to account for this fluidity.<sup>17</sup>

## Patient Centered Counseling and Changes with PFDs Surgery on Sexual Function

*Research Gap:* There are a lack of data on the effect of pelvic floor disorders and their treatment on sexual function, including lack of standardization of definitions, such as dyspareunia, inconsistent outcome reporting and not accounting for fluctuations in sexual activity. Advancing knowledge in this area would allow for a better understanding of the risks and benefits of surgical interventions, and help our patients make well informed decisions.

### Recommendations:

- ✓ Investigate sexual function and changes to sexual health as caused by pelvic floor disorders and its treatments.
- ✓ Improve patient understanding and counseling on sexual health and the anticipated impact of sexual health with PFD treatment.

## Explore Sexual Health and Dysfunction in Understudied Populations with PFDs

*Research Gap:* There is an overall paucity of data and poor understanding related to sexual function and key understudied populations, including all women who have sex, women in the postpartum period, women who have sex with women, and transgendered individuals.

### Recommendations:

- ✓ Describe and understand the impact of pelvic floor disorders on women who have sex, including women who have sex with women and transgendered individuals, as the impact of pelvic floor disorders on sexual function is not well studied.
- ✓ Develop rigorous prospective data regarding changes in sexual function before, during, and after pregnancy.

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## Section 6: Bladder Pain Syndrome/Interstitial Cystitis and Myofascial Pelvic Pain

### Background

Bladder pain syndrome/interstitial cystitis (BPS/IC) and myofascial pelvic pain (MFPP) are two chronic pain conditions that are commonly assessed and treated within the specialty of urogynecology.

#### Bladder Pain Syndrome/Interstitial Cystitis

BPS/IC is characterized by pain perceived to emanate from the bladder with associated urinary urgency, frequency, and nocturia lasting more than 6 weeks in the absence of other identifiable causes.<sup>1</sup> BPS/IC symptoms are common, yet the condition is often underdiagnosed and undertreated, largely due to considerable phenotypic heterogeneity of the syndrome. Further complicating the diagnosis and treatment of BPS/IC, is a lack of understanding of disease pathogenesis. The etiology of BPS/IC is thought to be multifactorial with interactions between autoimmune, neuroendocrine, allergic, and infectious pathways.<sup>2,3</sup> Despite this complex pathogenesis, the current dominant clinical paradigm is entrenched in the concept that the urothelial glycosaminoglycan layer, composed of hyaluronic acid, a non-sulfated glycosaminoglycan, and three sulfated-glycosaminoglycans (chondroitin sulfate, heparan sulfate, and dermatan sulfate), serves as a permeability barrier to prevent penetration of urinary toxins and pathogens into bladder tissues.<sup>4</sup> Many experts believe that the root cause of BPS/IC is disruption of the permeability barrier integrity due to deficiency of the glycosaminoglycan layer. Although several treatments focus on glycosaminoglycan replenishment, these therapies are not universally effective, thereby reinforcing the need for a better understanding of the BPS/IC pathophysiology to enable identification of novel therapeutic targets.

The health burden of BPS/IC is immense and disproportionately affects women at a 5:1 female to male ratio.<sup>5</sup> Per the Research and Development (RAND) Interstitial Cystitis Epidemiology (RICE) study, 6.5% of U.S. cisgender women 18 years or older meet BPS/IC criteria, translating to approximately 8 million women.<sup>6</sup> Although 87% of study participants meeting diagnostic criteria consulted a physician about their symptoms, only 40% had seen a lower urinary tract specialist and fewer than 10% reported a diagnosis of BPS/IC.<sup>6</sup> Disability from BPS/IC has been compared to other chronic illnesses, and quality of life for patients with BPS/IC is rated subjectively worse than that of patients with end-stage renal disease on dialysis.<sup>7</sup> These patients have increased rates of concurrent chronic pain disorders (e.g., irritable bowel syndrome, vulvodynia, fibromyalgia), sleep and

sexual dysfunction, and psychosocial difficulties, including higher acute and chronic stress levels, more anxiety and depression, worse coping skills, and more self-reported cognitive deficits.<sup>8-10</sup> Furthermore, in comparison to men, women with BPS/IC report higher levels of early life trauma, greater symptoms of pain, and poorer quality of life with regard to physical activity.<sup>10</sup>

A recent systematic review, evaluating the cost of chronic pelvic pain management, estimated an annual expense of \$2.8 billion in the United States, with highly varied results from across the world including Japan at ¥191,680 to ¥246,488 (\$1,514 to \$1,947 U.S. dollars) and Australia at \$16,970 to \$20,898 (\$12,488 to \$15,379 U.S. dollars) per woman per year.<sup>11</sup> The diagnosis and prevalence of BPS/IC is likely underestimated; thus, it is difficult to gauge this condition's true economic impact.<sup>12</sup> The annual cost of BPS/IC in the United States was estimated at \$750 million in 2000.<sup>12</sup> Two claims-based studies evaluating data from 1998 to 2003 involving insurance plan-specific and managed care populations demonstrated between \$3,000 and \$4,000 additional annual costs for patients with BPS/IC compared to those without the diagnosis.<sup>13,14</sup> A study spanning 2009-2014 that included both payer and patient costs, revealed an estimated expense of \$7,223 annually for patients with BPS/IC, with approximately 71% being spent on outpatient visits and medication costs.<sup>15,16</sup> This economic burden is comparable to other gynecologic conditions, such as leiomyomas and gynecologic malignancy (estimated annual expenses in the United States of \$2 billion and \$3.8 billion, respectively),<sup>11</sup> without accounting for additional costs such as absenteeism and missed days of work, reduced productivity, long-term unemployment, and societal issues such as opioid use/dependence associated with BPS/IC.<sup>17</sup>

#### Myofascial Pelvic Pain

Myofascial pelvic pain (MFPP) is a pelvic floor disorder (PFD) characterized by pain originating from the pelvic floor muscles<sup>†</sup> and can involve increased muscle tone<sup>‡</sup>.<sup>18</sup> Chronic MFPP syndrome is persistent or episodic pain (in the absence of a local pathological condition with symptoms suggestive of lower urinary tract, sexual, bowel or gynecological dysfunction), and often is associated with negative cognitive, behavioral, sexual or emotional consequences.<sup>19-23</sup> The etiology of MFPP is not well understood and is likely multifactorial in many patients. MFPP can be present without concomitant medical pathology or as a precursor or sequela to urologic, gynecologic, or musculoskeletal conditions.<sup>24</sup> Several theories have been proposed and include metabolic imbalance at the motor end plate in peripheral tissue, central sensitization of pain, and neuromuscular

microtrauma related to the specific muscular demands of these muscles.<sup>25-28</sup> MFPP is an underrecognized and notable source of pelvic pain and other PFD symptoms that merits substantial research attention.

The prevalence of MFPP varies widely from 18% to 78%.<sup>29-31</sup> MFPP may be involved in an estimated 22% to 94% of cases of chronic pelvic pain (CPP) and found in 87% in patients with BPS/IC.<sup>29, 32-36</sup> A recent retrospective cohort study from patients that underwent uncomplicated minimally invasive hysterectomy demonstrated that the prevalence of MFPP was 42.7%.<sup>37</sup> More recently, MFPP has been recognized in patients with non-pain PFDs with prevalence estimates ranging from 24% to 85%.<sup>20-23</sup> Severity of MFPP has been independently correlated with worsening PFDs, including pain in the lower abdomen and difficulty emptying the bladder, as well as with defecatory dysfunction.<sup>23</sup> In patients with urinary incontinence, the prevalence of MFPP may be as high as 51.7% and within those, an inverse relationship between pain and muscle strength has been demonstrated.<sup>38</sup> It has also been shown that in cisgender women with both urinary incontinence and MFPP there is a significantly greater anterior pelvic tilt and posterior displacement of the body than in those with urinary incontinence but without MFPP.<sup>39</sup> In patients with a diagnosis of constipation, MFPP has been shown to be highly associated with a diagnosis of rectal evacuation disorder.<sup>40</sup> Severity of MFPP has also been correlated with subjective symptoms of prolapse, such as pelvic pressure and heaviness, but not with objective findings of prolapse.<sup>23</sup> Women with MFPP are also at high risk of sexual dysfunction (91.5%) and painful intercourse (88.4%),<sup>41</sup> and have a higher prevalence of anxiety.<sup>42</sup>

MFPP represents a significant economic burden on society, but data on the economic burden of MFPP are limited.<sup>43</sup> Worldwide, the economic burden of chronic pelvic pain conditions, including BPS/IC, is substantial with overall cost estimates exceeding \$6 billion per year.<sup>11</sup> Health care costs, including outpatient and inpatient care, laboratory tests and procedures, complementary therapies, and pharmacy costs range from \$1,367 to \$7,043 per woman per year, and prescription costs alone are estimated between \$193 and \$2,457 per woman per year.<sup>11</sup> Considering MFPP is estimated to be present in up to 94% of cisgender women with CPP<sup>29,34,36</sup> and up to 87% of cisgender women with BPS/IC,<sup>33,35</sup> MFPP likely represents a substantial economic burden on women and health care systems worldwide, although further work is needed to understand the attributable costs.

[†pelvic floor myalgia, MFPP syndrome, ‡pelvic floor tension myalgia].

## Research Priorities and Opportunities

### Bladder Pain Syndrome/Interstitial Cystitis

#### **Diagnosis**

*Research Gap:* BPS/IC is a clinical diagnosis of exclusion and is primarily based on subjective findings.<sup>1</sup> There is a poor understanding of the disease etiology, a variety of condition phenotypes, and an absence of non-invasive diagnostic tests or established biomarkers.

#### *Recommendation:*

- ✓ Develop and validate molecular<sup>44</sup> and imaging<sup>45, 46</sup> biomarkers to facilitate accurate diagnosis and help to discriminate between the BPS/IC phenotypes.

#### **Disease Phenotypes**

*Research Gap:* BPS/IC has phenotypic distinctions, most notably those with “classic” Hunner lesions (HL) and those without. Until the most recent 2022 AUA guideline amendment, all patients with BPS/IC were generally evaluated and treated in a similar tiered and sequential fashion.<sup>47,48</sup> Patients with HL benefit from bladder-targeted therapies, whereas patients without HL represent a more heterogenous cohort, overlapping significantly with other somatoform disorders.

#### *Recommendation:*

- ✓ Develop additional prospective studies to evaluate differential management of these clinical BPS/IC phenotypes with application to current treatment guidelines in attempt to enable more personalized and effective treatments.<sup>48-50</sup>

#### **Current Treatments**

#### *Research Gaps:*

- ✓ There are numerous strategies for the treatment of BPS/IC, yet rigorous clinical trials that directly compare different therapeutic modalities are limited.<sup>51</sup>
- ✓ Many experts attribute BPS/IC symptoms to a deficiency of the urothelial glycosaminoglycan (GAG) permeability barrier, and various therapies (i.e., intravesical heparin, dimethyl sulfoxide; oral pentosan polysulfate) are believed to yield therapeutic benefit by restoring the GAG layer;<sup>4,52</sup> however, the precise role of the urothelial GAG layer in BPS/IC etiology has never been established. Further complicating this, the literature on bladder instillations aimed at GAG repletion is limited and demonstrates considerable variability in instillation ingredients, tools used to assess clinical

improvement after treatment, and methods to monitor long-term efficacy.<sup>30, 53, 54</sup>

- ✓ Despite high rates of co-morbidity between mental health disturbances and BPS/IC, as well as the inclusion of amitriptyline as a common oral therapy, there is a gross deficiency in prospective data on bladder pain symptoms reported by patients with anxiety and depression. Additionally, most studies looking at these associations have failed to adjust for antidepressant use (i.e., selective serotonin reuptake inhibitors), which can inherently impact bladder symptoms.
- ✓ Most studies have used doses of intradetrusor botulinum toxin established for overactive bladder rather than assessing alternative doses and administration frequencies specific to BPS/IC.

#### *Recommendations:*

- ✓ Create and carry out, large, high-quality randomized clinical trials that directly compare therapeutic effectiveness of different BPS/IC treatments using standardized outcome measures, while also considering pharmacokinetic and pharmacodynamic drug parameters that impact treatment success.
- ✓ Generate quality data to inform standardization of bladder instillation formulations. Furthermore, given evidence of a vision-threatening maculopathy as a potential long-term side effect of oral pentosan polysulfate therapy,<sup>55,56</sup> a better mechanistic understanding of the role, if any, of urothelial GAGs in BPS/IC pathogenesis and the suitability of GAG replenishment in BPS/IC treatment is necessary.
- ✓ Improve the understanding of the relationship between BPS/IC and mental health disturbances.<sup>57-59</sup> Develop a national registry or other large and representative cohort study that collect mental health information, including antidepressant medication use, across a range of health care visits.
- ✓ To determine if botulinum toxin is truly beneficial in this condition, large multicenter randomized trials with standardized patient phenotyping, botulinum toxin dosage, treatment frequency, and outcome reporting are warranted.<sup>60</sup>

#### **Treatments on the Horizon**

##### *Research Gaps:*

- ✓ Emerging evidence suggests that an altered microbiome and the use of a vaccine that targets uropathogenic microbes could play a role in diagnosing and treating BPS/IC, respectively.<sup>61</sup>
- ✓ There has been an increasing body of literature investigating the use of cannabis for various chronic

pelvic pain conditions, including BPS/IC, with disparate results.<sup>62, 63</sup>

- ✓ There is mounting evidence that hyperbaric oxygen therapy (HBOT) may be beneficial in the treatment of BPS/IC; however, the effect of HBOT according to patient phenotype and in conjunction with other BPS/IC treatments has not been evaluated.<sup>2,3,64,65</sup>

##### *Recommendations:*

- ✓ Examine the impact of the host microbiome on BPS/IC pathogenesis.
- ✓ Investigate the use of cannabinoids and compounds that affect the endocannabinoid system compared to both placebo and current BPS/IC treatments to help determine whether cannabinoids are a safe and viable treatment option in this patient population.<sup>62, 63</sup>
- ✓ Evaluate the potential role of HBOT in BPS/IC treatment, particularly as an adjuvant to conventional therapy, via large multicenter randomized trials with standardized outcome measures.

#### **Myofascial Pelvic Pain Research**

##### ***Prevalence***

*Research Gap:* Current prevalence studies for MFPP are wide ranging, have small sample sizes, vary by associated condition, and have not been quantified using standardized instruments.<sup>24,66</sup>

##### *Recommendations:*

- ✓ Determine prevalence estimates of MFPP in females across their lifespan.
- ✓ Develop studies where different groups of patients are screened for MFPP using a standardized pelvic examination tool.<sup>66</sup> These groups should include asymptomatic participants, those with chronic pelvic pain syndromes, and those with symptoms of pelvic floor disorders without pain.

##### ***Etiology***

##### *Research Gaps:*

- ✓ MFPP is commonly identified in women with chronic pelvic pain<sup>30,67,68</sup> who present for evaluation of pelvic floor disorders,<sup>22,23,69</sup> yet our understanding of the risk and protective factors for development of MFPP is limited.
- ✓ Existing studies are either conducted in populations already diagnosed with chronic pelvic pain related to a specific disease entity (i.e., bladder pain syndrome/interstitial cystitis, endometriosis) or are retrospective or case-control studies designed to explore potential associations in women found to



have pelvic floor disorder symptoms and/or MFPP on examination.<sup>23,32</sup>

*Recommendations:*

- ✓ Develop longitudinal, population-based studies designed to identify and define the risk and protective factors for developing MFPP.
- ✓ Evaluate the effects of lifestyle (i.e., physical activity, sedentarism, chronic stress), general activity levels (i.e., frequency, intensity, timing of onset), and medical disorders (i.e., constipation, obesity, airway disease) in people with and without chronic pain or pelvic floor disorders are warranted.

**Diagnosis**

*Research Gaps:*

- ✓ There are no patient-reported outcome surveys, imaging studies, or laboratory tests to assist with the diagnosis of MFPP.
- ✓ A simple and standardized pelvic examination that screens for MFPP has been developed but has not been used in broader studies.<sup>66</sup>
- ✓ Imaging of skeletal muscle in other parts of the body (i.e., neck muscles) has identified changes termed “trigger points” in patients with myofascial pain, and while “trigger points” in the pelvic floor muscles have been identified primarily by digital palpation, these areas have not been confirmed via imaging.<sup>70</sup>

*Recommendations:*

- ✓ Develop validated, patient-reported outcomes surveys specific for MFPP to determine population prevalence rates, identify patients at risk prior to an initial internal examination, and give an objective measure of response to treatment.
- ✓ Research the reproducibility of the validated screening pelvic examination tools in different patient populations to improve reportable research outcomes in this condition.
- ✓ Advances in imaging modalities, such as magnetic resonance elastography and optical spectroscopy, to characterize skeletal muscle changes in MFPP and determine if these are consistent with trigger points identified on physical examination may help determine underlying pathophysiology and direct targeted treatment to these areas.<sup>71</sup>

**Treatments**

*Research Gaps:*

- ✓ The evidence supporting adjunctive therapies for MFPP is limited and greatly impacted by variation in dose, route, timing, and duration. There is some evidence, however, to suggest that oral and intravaginal muscle relaxants, anticonvulsants, and

neuropathic pain medications may provide benefit in women with MFPP symptoms based on small studies and clinical experience with data extrapolated from chronic pain conditions.<sup>72-74</sup>

- ✓ The current literature around pelvic physical therapy with and without biofeedback, electrical stimulation, and relaxation training is limited by significant methodological flaws, including small sample size, short follow-up, poor statistical analyses, and lack of standardization of protocols and outcome reporting.<sup>75-79</sup> In addition, trials assessing other types of physiotherapy that include education, exercise, and group programming are lacking. There is some evidence to support the use of pelvic floor botulinum toxin injections for the treatment of MFPP and levator hypertonicity, but high-quality studies are lacking. Current studies are limited by small sample sizes, non-standardization in dosage and number of sites injected, route of injection (transvaginal, transperineal), and needle guidance methods (by electromyography, ultrasonography, or by palpation).<sup>80-85</sup>

*Recommendations:*

- ✓ Develop well-designed mechanistic, dose/route finding, and efficacy studies for oral and vaginal medications used as adjunctive therapies in MFPP patients.
- ✓ Utilize randomized trials involving pelvic physical therapy in MFPP patients that are phenotype-based, with longer periods of follow-up and detailed intervention parameters.
- ✓ Prioritize well-designed studies to determine the optimal dosage, route of injection, and needle guidance techniques for pelvic floor botulinum toxin.

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## Section 7: Health Disparities

### Health Disparities

#### Background

Health disparities are differences in health in defined groups of people who experience social, economic, demographic, or geographic disadvantage and experience greater health risks or worse health outcomes compared to groups that are positioned in society to have greater advantage.<sup>1-4</sup> Examples of groups who have endured health inequities include those with low socioeconomic status, those from racial/ethnic minority groups, and women and other groups who have collectively experienced disadvantage or systemic discrimination.<sup>1-4</sup> Numerous studies have demonstrated that health disparities directly lead to significant personal burden (including morbidity and mortality) as well as increased economic burden on a population level.<sup>5-10</sup>

Health disparities in the care of pelvic floor disorders (PFD) is a prevalent issue worldwide, notably affecting specific racial and ethnic groups. Racial/ethnic health inequities in PFD care are specific to barriers to care, care-seeking behaviors, and treatment/management of PFDs.<sup>11-28</sup>

While we know these disparities exist, the understanding of these inequities remains poor given small cohort study sizes, lack of data collection on race/ethnicity and social and structural determinants of health, and the vast differences in research methodologies limiting opportunities for pooled analyses of existing data. Without a sound understanding of the disparities that drive health inequity, development and utilization of interventions to eliminate disparities will be ineffective.

#### Research Priorities and Opportunities

##### Research Gaps:

- ✓ A major contributor to the perpetuation of racial/ethnic minority health disparities is the lack of diverse racial/ethnic representation in research; both with subjects and investigators. Multiple studies demonstrate the severe lack of diversity in participant cohorts for federally funded research studies which are often used to shape and generate the development of clinical guideline recommendations.<sup>11,25, 29-31</sup> The absence of diversity in research subjects may result in findings from a

narrow population being mis-applied to a broader, more diverse population. Health inequities may lead to worse outcomes which will be missed if diverse populations are not included in research.

- ✓ Race is a social construct and a rough proxy for several conditions and policies that determine allocation of resources and opportunities that inevitably impact health. Race/ethnicity are often recorded using the categories assigned by the United States Census Bureau. This categorization may not be representative of how a participant views oneself, and this limits interpretation of what these constructs mean given the broad inclusion into each racial/ethnic category. The majority of health disparities research focuses on recording the disparity, and there is an absence of research regarding the way to bring about health equity for PFDs.

##### Recommendations:

- ✓ Promote racial/ethnic representation in research studies through directing efforts towards diverse recruitment and retention in large studies that will inform clinical guideline development.
- ✓ Strengthen relationships/collaborations with community partners that will in turn optimize education on PFDs to the public, increase access for community members to PFD providers and, ultimately, create partnerships that provide opportunity to engage in collaborative, inclusive research.
- ✓ Craft research questions and select research methodologies that center populations of interest and allow for investigations of structural determinants of health that can become targets of policy interventions.
- ✓ Emphasize research that centers the voices and perspectives of groups that experience health inequities.
- ✓ Utilize a framework within research design that comprehensively captures a broad spectrum of variables (inclusive of social determinants of health as well as biologic, physical, environmental, and demographic factors) that influence health outcomes and policy interventions; this will enrich data used for analyses that can better address research questions aimed to narrow health disparities and achieve health equity. With respect to racial/health inequities in particular, frameworks should acknowledge and explore the contribution of racism in health care settings and the lives of people from racial/ethnic groups of interest.

- ✓ Prioritize research that seeks paths to improve and achieve health equity over projects with a primary aim to categorize or describe disparity.

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## Section 8: Moving Beyond Multidisciplinary Research

### Background

Groundbreaking solutions to the problems challenging women with pelvic floor disorders are exceedingly complex, requiring sophisticated and still yet undiscovered novel approaches to study design, measurement tools, and data analysis that exceed the capabilities of a single discipline. In this way, the future of foundational mechanistic discoveries as well as pragmatic solutions to pelvic floor disorders requires integrating the expertise and perspectives of individuals from a broad range of disciplines. The value of a team with multiple experts from different fields who collaborate to answer critical questions is a clear path to having the greatest impact on the field; however, the approach to do this is not straightforward and requires understanding differences between three commonly used terms.<sup>1</sup> The first, “multidisciplinary research,” describes an approach that brings together individuals from different disciplines to solve a problem with each contributing knowledge from their respective disciplines in an additive fashion but not moving beyond respective disciplines. The second, “interdisciplinary research,” similarly integrates information, data, techniques, and tools from two or more disciplines, but moves to advance understanding beyond the scope and boundaries of any single discipline or practice to explain more complex phenomena and generate novel therapeutic approaches and solutions in an integrative (as opposed to additive) fashion. The third, “transdisciplinary research,” considered the most transformational, elevates interdisciplinary studies to an even higher level by creating a new discipline with a novel conceptual framework. Transdisciplinary research enables innovations that pave the path to paradigm-shifting discoveries. Conceptually, the field of urogynecology is an example of a transdisciplinary subspecialty as it is defined by the core principles of gynecology and urology, and supplemented by input from gastroenterology, colorectal surgery, geriatrics, neurology, biomechanics, radiology, and physical rehabilitation. A similar approach to research in urogynecology would necessitate collaborations between scientists and clinicians via a multi-scalar “team science” approach, originating at the molecular level, extending up

to cells, tissues, organs, and individuals, while taking into account environmental and psychosocial determinants of health. Capitalizing on the skills of multiple experts from various areas of science and medicine would allow our field to make substantial leaps forward, while potentially affecting policy changes relevant to women's health.

### Research Priorities and Opportunities

#### Encourage Collaborations

*Research Gap:* The field of urogynecology, and our patients, continue to suffer from significant scientific disparities compared to many other disciplines. In this era of rapidly evolving sophisticated techniques, the transdisciplinary research is urgently needed to improve our understanding of the mechanisms responsible for pathogenesis of pelvic floor disorders.

#### *Recommendations:*

- ✓ Elevate the science to a transdisciplinary platform and step out of a siloed research model, which arguably has put us far behind other fields.
- ✓ Encourage collaborations from experts outside of our field, adapt their measurement tools and methods to develop novel ones, and then validate them in our system(s).
- ✓ Prioritize national meetings' content from experts in outside fields and shift from a high emphasis on clinical outcomes to placing an equal value on translational and basic research.
- ✓ Publish outside of specialty journals and obtain joint appointments in other schools within their academic centers.
- ✓ Encourage national societies to use their internal funding mechanisms and partner with outside funding agencies and science policy experts to foster inter- and trans-disciplinary approaches to research.<sup>2</sup>
- ✓ Generate support from national societies and funding agencies to achieve the potential value of inter- and trans-disciplinarity.<sup>3</sup>
- ✓ Disseminate information that affords wide-spread awareness of these critical processes



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## Section 9: Training Future Scientists

### Background

Concerns around the physician-scientist workforce arose as early as the 1970s, when the director of the National Institutes of Health (NIH) characterized physician-scientists with an MD degree as an “endangered species.”<sup>1</sup> Over subsequent decades, efforts were made to foster the development and retention of physician-scientists. Despite these efforts, in 2014 the NIH Physician-Scientist Workforce Working Group reported persistent deficits in the workforce, with particular concerns related to the aging population of physician-scientists and persistent inequities related to grants awarded to researchers from backgrounds traditionally underrepresented in medicine.<sup>1</sup> Given that developing and retaining physician-scientists from diverse backgrounds is critical in fulfilling AUGS' vision of eliminating the impact of pelvic floor disorders on women's quality of life, identifying and eliminating barriers along the physician-scientist training pathway is integral to our mission.

### Research Priorities and Opportunities

#### Aging Workforce

*Training Gap:* The average age of the physician-scientist workforce has increased over the past several decades, with there being 1.6 more physician-scientists over the age of 61 years compared to those under the age of 50 years.<sup>2</sup>

#### *Recommendations:*

- ✓ Expand funding and mentorship opportunities to support early- and mid-career researchers.
- ✓ Promote formalized research training during post-graduate medical education, as prior studies have found an association with the presence of research education and pursuit of a career in research.<sup>3</sup>
- ✓ Strengthen advocacy efforts to ensure ample investment in a physician-scientist workforce with expertise in pelvic floor disorders.
- ✓ Quantify and recognize the time and effort invested by mentors, such that junior investigators can benefit from their insight and expertise.

#### Diversity, Equity, and Inclusion

*Representation Gap:* Investigators from backgrounds traditionally underrepresented in medicine continue to face disproportionate barriers to advancement in physician-scientist career pathways. There is persistent underrepresentation of researchers who self-identify as African American and Indigenous American among recipients of federal research funding.<sup>1</sup> Furthermore, there is inadequate reporting on the representation of sexual and gender minorities, and those from economically disadvantaged backgrounds.

#### *Recommendations:*

- ✓ Create equity-centered mentorship and funding opportunities.
- ✓ Implement outreach and pipeline efforts in communities to increase awareness and accessibility of physician-scientist career pathways.
- ✓ Generate networking opportunities and infrastructure to support underrepresented colleagues.
- ✓ Improve socioeconomic data collection from training program and grant applicants and awardees.

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## About AUGS

The American Urogynecologic Society (AUGS) is the premier non-profit organization representing professionals dedicated to treating female pelvic floor disorders. Founded in 1979, AUGS represents more than 2,000 members, including practicing physicians, nurse practitioners, physical therapists, nurses and health care professionals, and researchers from many disciplines.

### Mission Statement

As the leader in urogynecology, AUGS drives excellence in comprehensive care for women with pelvic floor disorders.

### Vision Statement

To eliminate the impact of pelvic floor disorders on a woman's quality of life.

### Contact

To learn more, visit [www.augs.org](http://www.augs.org). Please direct all inquiries to AUGS Interim Chief Executive Officer, Stacey Barnes, at [board@augs.org](mailto:board@augs.org).