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Consensus Committee
C/O Rachel Riley
National Academies of Sciences, Engineering and Medicine
500 5th Street NW
Washington, DC 20001

WomensHealthResearch@nas.edu

RE: NASEM Assessment of NIH Research on Women's Health

Dear Consensus Committee Members,

On behalf of the American Urogynecologic Society (AUGS), we write to offer our perspective and to commend the committee for its due diligence and commitment to assessing NIH research as it relates to women's health. We also thank you for the opportunity to provide public comment both via written letter and verbally during the January 25th public meeting.

AUGS is a national medical society whose mission is to promote the highest quality of care in female pelvic medicine and reconstructive surgery through excellence in education, research, and advocacy. AUGS represents more than 2,000 members, including practicing physicians, nurse practitioners, physical therapists, nurses and health care professionals, and researchers from many disciplines studying pelvic floor disorders.

AUGS recently completed the attached National Urogynecology Research Agenda for advancing the treatment and management of pelvic floor disorders. This agenda is also supported by 14 other national societies with an interest in women's health and Pelvic Floor Disorders. The research agenda identifies knowledge gaps and research priorities across six topic areas further outlined below and incorporates important cross-cutting themes related to health disparities, multidisciplinary research, and training future scientists.

We want to emphasize the importance of understanding and evaluating the conditions that women face throughout their lives, including conditions that become more prevalent in the post-reproductive years. One in 4 women will struggle with some kind of pelvic floor disorder, and so our society and our members continually advocate for advancements in research and education for these issues.

We recognize that research in female-specific conditions is woefully underfunded, and that much of the limited funding goes to research involving reproductive-aged women. However, women's health care encompasses the full life span, including conditions that worsen with the menopausal transition and those affecting post-reproductive and older women, which are the fastest growing segment of the U.S. population. The CDC reports that over 50% of women aged sixty-five and older suffer from incontinence.

About one third of postmenopausal women will struggle with recurrent urinary tract infections. Because these non-cancerous conditions are referred to as "benign", they are often deprioritized for funding or emphasis. And yet, these common conditions are especially prevalent in post-reproductive aged women and can lead to substantial sequential events such as falls, increased utilization of health care and hospitalizations, and significantly impact daily life for potentially up to half of a woman's lifetime. This takes an enormous economic and emotional toll on individuals and has a significant fiscal impact on our society. This burden is also differentially borne by women compared to men as several of the disorders mentioned are much more prevalent in female populations.

AUGS sought the input of our Research & Quality Improvement Council including members of our Scientific Committee and Basic Science Sub-Committee in drafting the following responses to the committee's questions.

- **What does "women's health" mean to you? What are important considerations for how to define women's health and women's health research?**

  Women's health reflects matters of pathophysiology and psychosocial issues and encompasses the full life span of women, including conditions affecting post-reproductive and geriatric women, the fastest growing segment of the U.S. population.

  Scientific research beyond the reproductive phase should be prioritized, as the role that women play in society extends far beyond that of reproduction. The average woman spends more than half of her life outside the reproductive years, yet much of women's health research funding focuses on pregnancy and childbirth.

- **What are the knowledge and research gaps in women's health and women's health research? What are the barriers to filling these gaps?**

  The American Urogynecologic Society (AUGS) has developed a National Urogynecology Research Agenda (https://www.augs.org/research-agenda/) which serves the urogynecology research community by synthesizing and presenting key gaps and research priorities for a variety of Pelvic Floor Disorders. 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.

  Six conditions were prioritized for inclusion in the Research Agenda, including pelvic organ prolapse; lower urinary tract symptoms; recurrent urinary tract infections; bladder pain syndrome/interstitial cystitis and myofascial pelvic pain; female sexual health; and fecal incontinence. A high-level review of the findings and gaps in each of these areas is outlined below.

  The largest barrier to filling these research gaps is the overall lack of research funding as outlined in our response to the next question.

Lower Urinary Tract Symptoms/Urinary Incontinence

Stress urinary incontinence (SUI) affects 14-41% of biologic females between the ages of 30 years and 60 years. Overactive bladder (OAB) in women has been estimated to affect millions with its greatest prevalence (over 50%) in adults ≥60 years old. Numerous studies have demonstrated the negative impact of OAB and SUI on independence, self-esteem, mental health conditions, and interpersonal relationships. Voiding dysfunction is described using a variety of symptoms that depart from normal voiding sensation and function. 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. 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. This condition can severely impact quality of life, prompting 1 in 7 women in the United States to undergo surgical correction of POP. Worsening POP has also been associated with deteriorating physical function, anxiety, depression, fatigue, sleep disturbance, and lower satisfaction with participation in social roles. 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.

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. 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.

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. 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.

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. 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. MFPP can be acute; however the chronic syndrome is characterized by pain originating from the pelvic floor muscles. 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. 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.

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.

- **What should be the most important considerations NIH should use in prioritizing the research on women's health it supports?**

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. 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). 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). 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. AUGS urges the NIH to consider increasing the amount of research funding directed towards women's health beyond maternity and reproductive care.

In summary, reproductive sciences and non-cancerous gynecologic disorders receive far less attention and funding than they deserve based on their prevalence and impact on women in society.

- **From an equity perspective, what improvements can be made to NIH processes to advance health and gender equity in its research investments?**

As outlined in section 7 of the attached research agenda, health disparities in the care of pelvic floor disorders (PFD) is a prevalent issue worldwide, notably affecting specific racial and ethnic groups. 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. The research agenda highlights several recommendations related to research design and types of studies that should be prioritized to improve health disparities.

- ✓ Promote racial/ethnic representation in research studies through directing efforts towards diverse recruitment and retention in large studies that will inform clinical guideline development.
- ✓ 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.

- **How can NIH training and education systems and programs be improved to build and maintain a robust women's health research workforce? What were the barriers and opportunities within the current programs?**

According to a recent article published in *JAMA* titled "National Institutes of Health Funding for Surgeon-Scientists in the US—An Update and an Expanded Landscape" the surgeon-scientist phenotype is significantly threatened. In 2020, only 0.7% of surgeons in the workforce were funded by the NIH. (*JAMA Surg.* Published online January 24, 2024. doi:10.1001/jamasurg.2023.7167)

Training and education programs should include strategies to actively retain clinician-scientists in the field of women's health research, as well as recognize and overcome barriers to independence.

Barriers: Physicians who choose to specialize in OBGYN will always have an interest in women's health and addressing gaps in research. Yet, because we are a surgical subspecialty, competing demands are a force to be reckoned with. The protected time afforded by K award programs is instrumental for surgeon scientists. Far too many capable junior researchers fall away because of the lack of time to pursue important research questions, and because the clinical mission is what is emphasized.

Recommendations:
- ✓ Expand funding and mentorship opportunities to support early- and mid-career researchers.
- ✓ Promote formalized research training during post-graduate medical education.

- ✓ 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.

- **How do the structure, systems, and review processes of NIH affect the type of and level of investments in women's health research? How could these systems be strengthened and improved to better support advances in women's health?**

  A major barrier for the physician scientists represented by AUGS is not having a "home" institute dedicated to pelvic floor disorders (PFDs). PFD research is split across 3 institutes depending upon its focus (NIA, NICHD and NIDDK) which puts urogynecology research in competition with other fields that have significantly more resources.

  One major system change that could significantly strengthen the NIH's ability to support advances in women's health is to explore ways to expand the pool of reviewers who are experts in various women's health topics and to ensure appropriate study section assignment.

Thank you for your work on the NASEM Assessment of NIH Research on Women's Health and please consider AUGS as a partner to collaborate with on this important endeavor to advance women's health research. Please do not hesitate to reach out to Stacey Barnes, AUGS CEO, at 301-273-0570, ext. 116 or email Stacey@augs.org for any additional comments or support needed.

Sincerely,

Stacey Barnes
AUGS Chief Executive Officer

Nazema Y. Siddiqui, MD, MHS
AUGS Research & Quality Improvement Council Board Liaison

Attachments: AUGS National Urogynecology Research Agenda