2018

A novel research definition of bladder health in women and girls: Implications for research and public health promotion

Emily S. Lukacz
University of California - San Diego

Tamara G. Bavendam
National Institutes of Health

Amanda Berry
The Children's Hospital of Philadelphia

Cynthia S. Fok
University of Minnesota - Minneapolis

Sheila Gahagan
University of California - San Diego

See next page for additional authors

Authors

Emily S. Lukacz, Tamara G. Bavendam, Amanda Berry, Cynthia S. Fok, Sheila Gahagan, Patricia S. Goode, Cecilia T. Hardacker, Jeni Herbert-Beirne, Cora E. Lewis, Jessica Lewis, Lisa Kane Low, Jerry L. Lowder, Mary H. Palmer, Ariana L. Smith, and Sonya S. Brady

JOURNAL OF WOMEN'S HEALTH
Volume 27, Number 8, 2018

DOI: 10.1089/jwh.2017.6786

A Novel Research Definition of Bladder Health in Women and Girls: Implications for Research and Public Health Promotion

Emily S. Lukacz, MD,[1] Tamara G. Bavendam, MD, MS,[2] Amanda Berry, MSN, CRNP, PhD,[3] Cynthia S. Fok, MD, MPH,[4] Sheila Gahagan, MD,[5] Patricia S. Goode, MSN, MD,[6,7] Cecilia T. Hardacker, MSN, RN, CNL,[8] Jeni Hebert-Beirne, PhD, MPH,[9] Cora E. Lewis, MD, MSPH,[10] Jessica Lewis, MFT,[11] Lisa Kane Low, PhD, CNM,[12] Jerry L. Lowder, MD, MSc,[13] Mary H. Palmer, PhD,[14] Ariana L. Smith, MD,[15] and Sonya S. Brady, PhD[16]; For the PLUS Consortium

Abstract

Background: Bladder health in women and girls is poorly understood, in part, due to absence of a definition for clinical or research purposes. This article describes the process used by a National Institutes of Health funded transdisciplinary research team (The Prevention of Lower Urinary Tract Symptoms [PLUS] Consortium) to develop a definition of bladder health.

Methods: The PLUS Consortium identified currently accepted lower urinary tract symptoms (LUTS) and outlined elements of storage and emptying functions of the bladder. Consistent with the World Health Organization's definition of health, PLUS concluded that absence of LUTS was insufficient and emphasizes the bladder's ability to adapt to short-term physical, psychosocial, and environmental challenges for the final definition. Definitions for subjective experiences and objective measures of bladder dysfunction and health were drafted. An additional bioregulatory function to protect against infection, neoplasia, chemical, or biologic threats was proposed.

Results: PLUS proposes that bladder health be defined as: ''A complete state of physical, mental, and social well-being related to bladder function and not merely the absence of LUTS. Healthy bladder function permits daily activities, adapts to short-term physical or environmental stressors, and allows optimal well-being (*e.g.*, travel, exercise, social, occupational, or other activities).'' Definitions for each element of bladder function are reported with suggested subjective and objective measures.

Conclusions: PLUS used a comprehensive transdisciplinary process to develop a bladder health definition. This will inform instrument development for evaluation of bladder health promotion and prevention of LUTS in research and public health initiatives.

Keywords: bladder, definition, health, urinary tract

[1]Division of Female Pelvic Medicine and Reconstructive Surgery, University of California San Diego, San Diego, California.
[2]National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland.
[3]Division of Urology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania.
[4]Department of Urology, University of Minnesota, Minneapolis, Minnesota.
[5]Division of Academic General Pediatrics, University of California San Diego, San Diego, California.
[6]Division of Gerontology, Geriatrics, and Palliative Care, University of Alabama at Birmingham, Birmingham, Alabama.
[7]Birmingham/Atlanta Veterans Affairs Geriatric Research, Education, and Clinical Center, Birmingham, Alabama.
[8]Howard Brown Health, Rush University College of Nursing, Chicago, Illinois.
[9]Division of Community Health Sciences, University of Illinois at Chicago, School of Public Health, Chicago, Illinois.
[10]Division of Preventive Medicine, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama.
[11]Yale School of Public Health, New Haven, Connecticut.
[12]University of Michigan School of Nursing, Ann Arbor, Michigan.
[13]Division of Female Pelvic Medicine and Reconstructive Surgery, Washington University in St. Louis School of Medicine, St. Louis, Missouri.
[14]School of Nursing, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.
[15]Division of Urology, University of Pennsylvania, Philadelphia, Pennsylvania.
[16]Division of Epidemiology and Community Health, University of Minnesota School of Public Health, Minneapolis, Minnesota.
PLUS Consortium' members are listed in the acknowledgments and were active participants in this work.

Introduction

Lower urinary tract symptoms (LUTS) are highly prevalent affecting up to one in three women and girls and become increasingly common over the life course.[1,2] LUTS include patient-reported symptoms related to urine storage and emptying, which negatively impact quality of life.[3] Lower urinary tract dysfunctions such as urinary tract infections (UTIs, *i.e.*, bladder infections), urinary incontinence (UI), overactive bladder, bladder pain syndrome/interstitial cystitis, incomplete emptying, and bladder cancer are typically associated with LUTS. Certain medical conditions also contribute to LUTS (*e.g.*, neurologic disease, heart disease, diabetes, constipation, and autoimmune diseases).[4–6] Psychosocial, behavioral, and environmental conditions can have an impact on LUTS and bladder health, particularly in young girls.[7–10] Between 20 and 40% of children and adolescents with LUTS have associated mental health conditions such as anxiety, attention deficit hyperactivity disorder, or oppositional defiant disorder.[11] In addition, urinary symptoms have been reported in 65.7% of young athletes.[10] In adults, LUTS have been associated with decreased sexual enjoyment, poor sleep quality, lower productivity, depression, and poor health-related quality of life.[3,12–16] Alarmingly, more than 50% of seriously ill hospitalized patients >60 years of age reported that they considered death preferable to incontinence.[17]

While LUTS are common in women and have a negative impact on quality of life, most women do not seek treatment.[18,19] In a survey of working women, more than one in five had experienced UI at least monthly; however, fewer than half of those women sought care. A more recent epidemiologic study linked to electronic health records of 3316 women in Pennsylvania found that only 25% of women with UI sought care.[19,20] Stigma associated with LUTS may reduce treatment-seeking behaviors.[21] Many women cope with their symptoms through limiting fluids, scheduled urination, using absorbent products (*e.g.*, pads, panty liners), and other self-management strategies.[20] Some self-management strategies reduce symptom bother allowing normal activities, whereas others (*e.g.*, limiting social activities) can negatively affect quality of life. The growth of marketing campaigns for absorbent products for UI (an industry estimated to reach $2.7B by 2020) may contribute to reducing stigma and increasing treatment-seeking behaviors.[22,23] Alternatively, such campaigns may normalize LUTS and reinforce perceptions that LUTS are part of aging or being female.[19,24] An unintended consequence of this normalization of LUTS is potentially a lack of awareness of and motivation to pursue promising prevention and treatment options, leading instead to unhealthy self-management, including tolerating symptoms.[25]

While numerous effective treatment options for LUTS exist, there is sparse evidence informing optimal bladder health promotion and LUTS prevention strategies. Most primary prevention trials focus purely on one particular LUTS (*e.g.*, UI) and are targeted toward women at high risk of developing LUTS. Evidence supports the use of pelvic floor exercise programs for prevention of UI during pregnancy and in older populations, but outcomes for other LUTS such as urinary infections, voiding dysfunction, or pain are unknown.[26–29] Recent reviews of primary prevention of UTIs focus on nursing home and postmenopausal women with outcomes for UTIs, but do not describe the impact on other LUTS.[30,31] Although these prevention strategies appear to be effective, we cannot know if they truly promote overall bladder health. In part, this is because current research is not informed by a standardized definition of bladder health that guides the selection of measures used to evaluate prevention efforts. To accurately identify and promote optimal bladder health, a systematic, evidence-based approach to defining bladder health across the life course is first needed. A standardized definition of bladder health can aid in the identification of factors to promote health and modify risk factors for LUTS. We propose a new paradigm to define optimal bladder health extending beyond mere lack of symptoms to include concepts of well-being and resilience to short-term challenges to health.

The primary objectives of this work were twofold: (1) to describe the process used by our transdisciplinary consortium to develop a working research definition of bladder health and (2) to present the resulting bladder health definition that is proposed for use in research and public health.

Materials and Methods

Conceptualizing bladder health

The transdisciplinary Prevention of Lower Urinary Tract Symptoms (PLUS) Consortium is funded by the National Institutes of Health to advance research on LUTS prevention in women and girls. The purpose, organization, and function of the PLUS Consortium are described in detail by Harlow et al.[32] There was broad consensus across PLUS investigators that a definition of bladder health was a necessary first step to plan, perform, and evaluate the research required to advance LUTS prevention in women and girls. The absence of a commonly accepted definition of bladder health has hindered development of a comprehensive bladder health promotion and LUTS prevention agenda.[25,33] To date, bladder health has been framed in terms of absence of LUTS symptoms, an approach that ignores quality of life and the dynamic nature of health over the life course.[34,35] To this end, PLUS investigators acknowledged the need for a working definition of bladder health and adapted The World Health Organization's (WHO) definition of health as a framework. WHO asserts that "health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity."[36] In addition to the WHO definition, PLUS investigators considered more recent work by Huber et al., who contend that in the age of chronic disease, complete well-being may be an unattainable standard, particularly at later stages in the life course; they suggest redefining health as "the ability to adapt and to self-manage," recognizing the changing and multidimensional nature of health in a dynamic environment.[37] The deliberations of the PLUS investigators distinguished between two types of adaptations described by Huber et al. and others.[37–39] The first type of adaptation—*self-management*—includes compensatory behaviors in response to environmental constraints on timing of urination (*e.g.*, restricting fluid intake) and containment behaviors in response to symptoms (*e.g.*, wearing incontinence protection to fully engage in desired activities). For better or worse, terms have been developed to define and "medicalize" the latter self-management strategies (*i.e.*, contained incontinence—UI that is controlled by being contained with an

absorbent product or a collecting device).[40] The second type of adaptation—*resilience*—occurs throughout the life course and is consistent with the concept of allostasis, the body's capability of regaining homeostasis after physical, psychosocial, or environmental challenges to the organ system (*e.g.*, complete recovery after a UTI).[38,41] Resilience throughout the life course may prevent the development of LUTS and therefore the need for self-management strategies (*e.g.*, wearing incontinence protection). The PLUS Consortium emphasized the concept of resilience in developing a definition of bladder health to capture the concept as not merely the absence of LUTS, but also the bladder's ability to adapt to short-term physical, psychosocial, and environmental stressors without lasting harm to the system.[36–38,41] This requires a definition that addresses the concepts of well-being and resilience to stressors and is distinct from ''self-management'' strategies to cope with LUTS.

Considering bladder health in women and girls across the life course

Although overall prevalence of LUTS may be similar in men and women, the mechanisms by which LUTS affect females differ from that of males.[13,42] Females are disproportionately affected by some LUTS, with women having nearly thrice higher prevalence of UI and bladder pain syndrome than men.[43,44] Therefore, the work of the PLUS Consortium is focused exclusively on women and girls, which are an understudied population with unique needs for bladder health promotion research. To understand bladder health across the life course in women and girls, it is also important to recognize biologic changes in development and exposures to risk and protective factors that occur over time. PLUS investigators intended for the proposed definition of bladder health to be used across a wide age spectrum, acknowledging changes that occur at the various stages of life and that well-being, resilience, and risk may vary over the life course.[45,46] The Consortium proposed five developmental stages important in the study of bladder health across the life course: Childhood (≤10 years), Adolescence (11–17 years), Emerging Adulthood (18–25 years), Adulthood (26–64 years), and Older Adulthood (≥65 years). Using these proposed life stages, researchers can expand understanding of risk factors for LUTS and protective factors for bladder health by identifying populations across the life course with varying degrees of bladder health. For example, novel prevention opportunities may exist for children, adolescents, and young women at various developmental time points (*e.g.*, toilet training, school entry, puberty, sexual debut, and pregnancy).

The PLUS process

The process began with exploration of lessons learned from other health promotion campaigns (*e.g.*, cardiovascular health); however, the lack of evidence for bladder health risk and protective factors prohibited use of a similar mode to that used in cardiovascular health. Thus, PLUS investigators used an iterative process to define bladder health and formed a transdisciplinary Terminology, Conceptual Frameworks and Models (TCFM) group to lead the activity. The TCFM group included two co-chairs (one with clinical and another with public health expertise) and 12 investigators with expertise in urogynecology, obstetrics and gynecology, nursing, pediatrics, geriatrics, public health, and behavioral sciences. The priority for the TCFM group was to establish a common language for PLUS, think conceptually about bladder health, and to propose a bladder health definition to the PLUS Consortium for consideration, refinement, and approval. The consortium and TCFM group's approach was consistent with Mohammed and Dumville's integrative framework of team knowledge.[47] This framework includes the processes of information sharing (*i.e.*, group discussion and information exchange), transactive memory (*i.e.*, utilizing group members as memory aids), group learning (*i.e.*, construction of new knowledge by the group), and cognitive consensus (*i.e.*, reconciling different perspectives to define and conceptualize key issues). These processes guided taskwork, teamwork, and representation of key issues. The PLUS approach to developing a bladder health definition was also similar to how another transdisciplinary group of experts studied healthcare delivery in low- and middle-income countries.[48]

A framework table of bladder storage and emptying functions was initially drafted, and with collaboration from other PLUS investigators, the TCFM group mapped accepted LUTS definitions associated with various bladder dysfunctions to a list of elements of bladder function.[40,49–53] Consideration of the elements of bladder function was a useful bridge in developing definitions for healthy bladder functions. In addition, we took the novel step of including a bioregulatory function of the bladder to acknowledge the roles of the bladder lining and urine composition in bladder health and dysfunction. ''Bladder Health'' and ''Bladder Dysfunction'' definitions were proposed for each bladder function: storage, emptying, and bioregulatory. The definitions took into account the known variation across the life course (*e.g.* development of continence in children is reliant on bladder maturation and appropriate neurodevelopmental function, while storage capacity and emptying efficiency may change with advanced age).

An iterative process was used to develop and refine terminology and the proposed definitions for health and dysfunction. Beginning in September 2015, PLUS TCFM members engaged in biweekly organized web-based discussions about definition development. Based on expertise, investigators were assigned to subgroups to advance work on each element of bladder function pertaining to the definition. Clinical experts shared existing knowledge of LUTS, while other experts broadened that knowledge to improve understanding for nonclinical audiences. To obtain input and refine the emerging definition, the TCFM investigators regularly shared progress with and received input from the entire PLUS Consortium through webinars and during in-person PLUS meetings. In addition, during in-person meetings, TCFM members led small group activities for all PLUS investigators to identify gaps in the definition and assess areas of uncertainty. By July 2017, the PLUS Consortium achieved consensus and approved the definitions for the elements of bladder function for use in development of a bladder health measurement questionnaire.

Results

The PLUS definition of bladder health

The working PLUS Definition of Bladder Health is as follows:

Table 1. Overview of Prevention of Lower Urinary Tract Symptoms Consortium Bladder Dysfunction and Health in Women and Girls

		Bladder dysfunction		*Bladder health*	
Bladder function	*Elements of function*	*LUTS/subjective experience(s)*	*Objective measure(s)*	*Subjective, experience(s)*	*Objective, measure(s)*
Storage	Capacity - Day/waking - Night/sleeping Continence - Day/waking - Night/sleeping Sensation - Urge - Comfort	Bothersome LUTS that occur during storage—*e.g.*, increased daytime frequency, nocturia, urinary incontinence, enuresis, nocturnal enuresis, postvoid dribble, urgency, absence of urge, bladder pain	Physical finding or measure related to LUTS during storage—*e.g.*, small bladder capacity, decreased time between voids, detrusor overactivity, urinary leakage	Ability to hold urine for a reasonable duration of time and sense bladder fullness without fear of or concern about urgency, discomfort, or leakage[a]	Physical finding or measure related to healthy storage—*e.g.*, healthy first sensation, strong desire to void, maximum capacity, functional capacity, duration of time between urge and void, duration of time between voids
Emptying	Initiation Stream flow - Speed - Character - Continuity Efficacy Sensation - Relief of urge - Completeness - Comfort	Symptoms that occur during emptying—*e.g.*, hesitancy, straining (at initiation and to completely empty), slow stream, interrupted stream, spraying/splitting, feeling of incomplete emptying, postvoid dribble, inability to sense when flow is complete, or dysuria	Measurable findings or signs related to LUTS that occur during the emptying of the bladder—*e.g.*, premature or delayed initiation of stream, flow pattern, flow rate, elevated postvoid residual	The ability to empty the bladder completely in a timely, efficient, effortless, comfortable manner and resume continence[a] - Time to go from urge (delay in initiation of flow) - Duration of emptying - Completeness of emptying - Urine flow stops when desired	Physical finding or measure related to healthy emptying—*e.g.*, time to initiation of stream, duration of total void, character of stream, minimal to no postvoid residual urine volume
Bioregulatory	Biosis barrier Physical/chemical barrier Cancer barrier	NA	Measurable findings related to the breakdown in the protective and communication functions of the bladder resulting in LUTS—*e.g.*, infection, inflammation, collagen degradation, malignancy	NA	Measurable findings related to define healthy bioregulatory measures—*e.g.*, biomarkers, microbiome, proteins that are adaptable to short-term physical or environmental stressors, able to completely recover from disruption, without long-term or persistent sequelae

[a]Function does not impact daily activities on a routine basis, is adaptable to short term physical or environmental stressors, and allows a woman to pursue her optimal well-being (e.g. travel, exercise, social, occupational or other activities).

LUTS, lower urinary tract symptoms; NA, not applicable.

> "A complete state of physical, mental, and social well-being related to bladder function and not merely the absence of LUTS. Healthy bladder function permits daily activities, adapts to short-term physical or environmental stressors, and allows optimal well-being (*e.g.*, travel, exercise, social, occupational, or other activities)."

Underlying this overall definition, PLUS developed definitions for each of the three functions of the bladder (Table 1). The storage function of the bladder requires that the bladder acts as a low-pressure reservoir with a competent urethra that maintains pressure against increased abdominal pressure and communicates the state of bladder fullness *via* an intact nervous system. The defined elements of storage include: capacity (as measured by frequency of urination and storage volume), continence, and sensation (including comfort and urge). The emptying function of the bladder requires a sustained bladder contraction with relaxation of the urethra until urine is emptied completely, with an intact nervous system to communicate the state of bladder emptiness. The defined elements of emptying include: stream initiation, stream flow characteristics, efficacy of urination, and sensation (*i.e.*, relief of urge, completeness, and comfort). We acknowledged that the elements of storage and emptying functions may be different during daytime (waking) and nighttime (sleeping) hours, which are reflected in the symptoms of dysfunction as defined by current International Continence Society (ICS) and International Children's Continence Society (ICCS) terminology.[40,49–53] For each element of storage and emptying we identified subjective experience and objective features of bladder function and dysfunction (Table 1).

During development of these definitions, PLUS investigators acknowledged that the proposed categorization of bladder functions differs slightly from previously described bladder phases of storage, emptying, and postmicturition.[42,54,55] In health, we did not consider "postmicturition" as a bladder function; rather we acknowledged it as a time interval whereby dysfunction in emptying or storage could occur. The healthy bladder should transition from emptying to storage without a defined "postmicturition" health state. In contrast, postvoid dribble is a LUTS that can be manifest in either storage or emptying dysfunctions. To acknowledge that postvoid dribble is likely a multifactorial condition, we present this dysfunction in both storage and emptying dysfunction.

The bladder bioregulatory function focuses more broadly on lower urinary tract dysfunction. Bioregulation was considered as bidirectional communication between the bladder and the environment that prevents systemic or local infection, transmits appropriate physiologic signals, or regulates cellular function. In health, the bladder barrier protects the individual from pathogens, chemicals, and malignancy; it is adaptable to short-term physical, psychosocial, or environmental stressors; and it is able to recover from disruption without long-term or persistent sequela. A breakdown of the protective barrier may lead to infection, inflammation, malignancy, or other maladies. The bioregulatory function is subdivided into three main functions as follows: (1) Biosis barrier (representing the host-defense system), (2) physical/chemical barrier (preventing toxins from penetrating beyond the mucosal layer), and (3) cancer barrier (preventing malignant expression of bladder tissues). These functions include many biomarkers and "-nomics" (*e.g.* genomics, proteomics, and metabolomics) related to lower urinary tract dysfunction. The list is intended to acknowledge the breadth of markers being studied, rather than serving as an exhaustive list that represents all known mechanisms for LUTS or bladder health. Biological markers of this sort may be identified in the healthy bladder, and they will be considered when measuring bladder health and outcomes in prevention studies.

The PLUS Consortium bladder health and dysfunction working table serves as a repository of working terminology and as a resource to help develop an instrument to measure bladder health, identify gaps in knowledge regarding health and dysfunction, and highlight areas for future bladder health research. A distillation of this work is presented in Table 1.

Discussion

The PLUS definition of bladder health has been systematically created to guide the selection of measures and develop an evidence base for LUTS prevention and bladder health promotion. This foundational work will further the efforts of the PLUS Consortium and the broader research community in the development of cross-sectional and longitudinal studies. This definition provides a starting point for the PLUS research agenda designed to describe the spectrum of bladder health in women and girls and to enable the exploration of risk and protective factors for LUTS and bladder health. Refinements to this first PLUS bladder health definition will undoubtedly occur as PLUS investigators incorporate new information from emerging scientific evidence, including qualitative research. The importance of community engagement, with broad stakeholders, is essential to this effort, and key stakeholders will provide input to further evolve the PLUS bladder health definition. This description of our process and transdisciplinary approach may inform others studying conditions with similar needs and challenges in expanding beyond a focus on symptoms (*e.g.*, bowel health, mental health, and so on).

PLUS investigators have already begun the work of developing and validating bladder health measurement tools for use in various research endeavors, including basic, clinical, and translational science and public health; these tools will be used to assess the spectrum of bladder health. Existing LUTS measurement tools are being evaluated to determine those that can be modified to measure bladder health. In addition, measures are being developed to capture elements of health-related factors, including full participation in desired activities and to resilience to short-term physical, psychosocial, and environmental stressors without lasting harm to the system. The PLUS Consortium plans to collect normative objective data for proposed bladder functions (*e.g.*, storage, emptying, and bioregulatory), study the prevalence of bladder health in the population, and to identify risk and protective factors associated with incidence of LUTS and maintenance of bladder health in women and girls. Establishment of a biobank for biological samples, including serial samples in women and girls with healthy bladders, will also advance our understanding of bladder health and incident of LUTS.

Conclusions

As a key initiative of the PLUS Research Consortium, investigators offer this description of the process for developing a bladder health definition in women and girls. This

critical first step is essential to support research activities to measure and influence bladder health and LUTS prevention on a population level.

Acknowledgments

The PLUS Research Consortium

Research Centers (alphabetically): **Loyola University Chicago Stritch School of Medicine, Chicago, Illinois**, Linda Brubaker, MD, MS and Elizabeth Mueller, MD, MSME, Co-Principal Investigators; *Key Investigators*: Colleen Fitzgerald, MD, MS; Cecilla Hardacker, RN, MSN; Jenifer Hebert-Beirne, PhD; Missy Lavender, MBA; David Shoham, PhD; **University of Alabama at Birmingham, Birmingham, Alabama,** Kathryn L. Burgio, PhD, Principal Investigator; *Key Investigators*: Patricia S. Goode, MD; Cora Beth Lewis, MD; Alayne Markland, DO, MSc; Gerald McGwin, PhD; Beverly Williams, PhD; **University of California at San Diego, San Diego, CA,** Emily S. Lukacz, MD, Principal Investigator; *Key Investigators*: Sheila Gahagan, MD, MPH; Daphne LaCoursiere, MD, MPH; Sarah E. Linke, PhD; Bess Marcus, PhD, MS; Jesse Nodora, DrPH; **University of Michigan, Ann Arbor, MI,** Janis M. Miller, PhD, MSN, Principal Investigator; *Key Investigators*: Lawrence Chin-I An, MD; Lisa Kane Low, PhD, MS, CNM; **University of Pennsylvania, Perlman School of Medicine**,: Diane K. Newman, DNP, CRNP, Principal Investigator; *Key Investigators*: Amanda Berry, CRNP; C. Neill Epperson, MD; Kathryn Schmitz, PhD; Ariana Smith, MD; Ann Stapleton, MD; Jean Wyman, PhD; **Washington University School of Medicine, St. Louis, MO**, Siobhan Sutcliff, PhD, Principal Investigator; *Key Investigators*: Aimee James, PhD; Jerry Lowder, MD, MSc; Colleen McNicholas, DO, *MSCI*; Mary Townsend, ScD; **Yale University School of Medicine, New Haven, CT**, Leslie M. Rickey, MD, Principle Investigator; *Key Investigators*: Deepa Camenga, MD, MS; Toby Chai, MD; Jessica Lewis, PhD.

NIH Program Office: National Institute of Diabetes and Digestive and Kidney Diseases, Division of Kidney, Urology and Hematologic Diseases, Bethesda, MD; Project Scientist: Tamara G. Bavendam MD, MS; Project Officer: John W. Kusek, PhD, NIH Personnel: Ziya Kirkali, MD, Chris Mullins, PhD, Robert Star, MD, Jenna Norton, MPH.

Scientific and Data Coordinating Center: University of Minnesota, Minneapolis, MN, Bernard L. Harlow, PhD, and Kyle Rudser, PhD, Co-Principal Investigators; *Key Investigators*: Sonya S Brady, PhD; John Connett, PhD; Haitao Chu, MD, PhD; Cynthia Fok, MD; Todd Rockwood, PhD; Keith Vargo, MPA.

Steering Committee: Chair: Mary H. Palmer, PhD, University of North Carolina at Chapel Hill; Chair (now retired): Denise Simons-Morton, MD, MPH, PhD.

Author Disclosure Statement

There are no financial conflicts directly related to this work. The PLUS Research Consortium is supported by the National Institutes of Health (NIH) through cooperative agreements (DK106786, DK106853, DK106858, DK106898, DK106893, DK106827, DK106908, DK106892).

Financial Disclosures: Past 5 years.

E.S.L.: Has received consulting fees from: Renew Medical, Inc. (a company that manufactures a device for management of accidental bowel leakage), AMS/Astora (a company that manufactured products to treat prolapse and incontinence), Axonics (a company that manufactures neuromodulation device for incontinence). She has also received research supplies and/or funding from Pfizer (a pharmaceutical company that manufactures drugs for treatment of incontinence), Boston Scientific (a company that manufactures products to treat prolapse and incontinence), and Uroplasty (a company that manufactures products to treat incontinence) and author royalties from UpToDate (an online medical reference site) and honoraria from MedEdicus (a medical publishing company); T.B., A.B., S.G., P.G., C.T.H., J. H.-B., J.L., L.K.L., J.L., M.H.P., and S.B.: none; C.S.F.: Author royalties from UpToDate (an online medical reference site); C.E.L.: Grant support from Novo Nordisk for clinical trials in obesity and type 2 diabetes mellitus (a pharmaceutical company that manufactures drugs to treat these conditions); A.L.S.: Has received research supplies from Allergan (a pharmaceutical company that manufactures drugs for the treatment of incontinence).

References

1. Coyne KS, Sexton CC, Bell JA, et al. The prevalence of lower urinary tract symptoms (LUTS) and overactive bladder (OAB) by racial/ethnic group and age: Results from OAB-POLL. Neurourol Urodyn 2013;237:230–237.
2. Minassian VA, Bazi T, Stewart WF. Clinical epidemiological insights into urinary incontinence. Int Urogynecol J 2017;28:687–696.
3. Coyne KS, Sexton CC, Irwin DE, Kopp ZS, Kelleher CJ, Milsom I. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: Results from the EPIC study. BJU Int 2008;101:1388–1395.
4. Kupelian V, Rosen RC, Link CL, et al. Association of urological symptoms and chronic illness in men and women: Contributions of symptom severity and duration-results from the BACH survey. J Urol 2009;181:694–700.
5. Yu C, Hsu C, Lee W, Chiang P, Chuang Y. Medical diseases affecting lower urinary tract function. Urol Sci 2013; 24:41–45.
6. Rechberger T, Nowakowski Ł, Rechberger E, Ziętek A, Winkler I, Miotła P. Prevalence of common comorbidities among urogynaecological patients. Ginekol Pol 2016;87: 342–346.
7. Vasconcelos MMA, East P, Blanco E, et al. Early behavioral risks of childhood and adolescent daytime urinary incontinence and nocturnal enuresis. J Dev Behav Pediatr 2017;38:736–742.
8. Joinson C, Heron J, Von Gontard A, Butler U, Golding J, Emond A. Early childhood risk factors associated with daytime wetting and soiling in school-age children. J Pediatr Psychol 2008;33:739–750.
9. Joinson C, Sullivan S, von Gontard A, Heron J. Early childhood psychological factors and risk for bedwetting at school age in a UK cohort. Eur Child Adolesc Psychiatry 2016;25:519–528.
10. Schettino MT, Mainini G, Ercolano S, et al. Risk of pelvic floor dysfunctions in young athletes. Clin Exp Obstet Gynecol 2014;41:671–676.

11. von Gontard A, Baeyens D, Van Hoecke E, Warzak WJ, Bachmann C. Psychological and psychiatric issues in urinary and fecal incontinence. J Urol 2011;185:1432–1437.
12. Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. World J Urol 2003;20:327–336.
13. Kupelian V, Wei JT, O'Leary MP, et al. Prevalence of lower urinary tract symptoms and effect on quality of life in a racially and ethnically diverse random sample: The Boston Area Community Health (BACH) Survey. Arch Intern Med 2006;166:2381–2387.
14. Sexton CC, Coyne KS, Vats V, Kopp ZS, Irwin DE, Wagner TH. Impact of overactive bladder on work productivity in the United States: Results from EpiLUTS. Am J Manag Care 2009;15(4 Suppl):S98–S107.
15. Mishra GD, Barker MS, Herber-Gast G-C, Hillard T. Depression and the incidence of urinary incontinence symptoms among young women: Results from a prospective cohort study. Maturitas 2015;81:456–461.
16. Melville JL, Delaney K, Newton K, Katon W. Incontinence severity and major depression in incontinent women. Obstet Gynecol 2005;106:585–592.
17. Rubin EB, Buehler AE, Halpern SD. States worse than death among hospitalized patients with serious illnesses. JAMA Intern Med 2016;176:1557–1559.
18. Fritel X, Panjo H, Varnoux N, Ringa V. The individual determinants of care-seeking among middle-aged women reporting urinary incontinence: Analysis of a 2273-woman cohort. Neurourol Urodyn 2014;33:1116–1122.
19. Minassian VA, Yan X, Lichtenfeld MJ, et al. The iceberg of health care utilization in women with urinary incontinence. Int Urogynecol J 2012;23:1087–1093.
20. Palmer MH, Fitzgerald S. Urinary incontinence in working women: A comparison study. J Womens Health 2002;11:879–888.
21. Norton JM, Dodson JL, Newman DK, et al. Nonbiologic factors that impact management in women with urinary incontinence: Review of the literature and findings from a National Institute of Diabetes and Digestive and Kidney Diseases workshop. Int Urogynecol J 2017;28:1295–1307.
22. Tannenbaum C, van den Heuvel E, Fritel X, et al. Continence across continents to upend stigma and dependency (CACTUS-D): Study protocol for a cluster randomized controlled trial. Trials 2015;16:565.
23. Carol Hymowitz LC-L. The adult diaper market is about to take off—bloomberg. Bloomberg Businessweek, 2016. Available at: https://www.bloomberg.com/news/articles/2016-02-11/the-adult-diaper-market-is-about-to-take-off Accessed July 2, 2017.
24. Melville JL, Wagner LE, Fan M-Y, Katon WJ, Newton KM. Women's perceptions about the etiology of urinary incontinence. J Womens Health (Larchmt) 2008;17:1093–1098.
25. Palmer MH, Athanasopoulos A, Lee KS, Takeda M, Wyndaele JJ. Sociocultural and environmental influences on bladder health. Int J Clin Pract 2012;66:1132–1138.
26. Boyle R, Hay-Smith EJ, Cody JD, Morkved S. Pelvic floor muscle training for prevention and treatment of urinary and fecal incontinence in antenatal and postnatal women: A short version Cochrane review. Neurourol Urodyn 2014;33:269–276.
27. Kissler K, Yount SM, Rendeiro M, Zeidenstein L. Primary prevention of urinary incontinence: A case study of prenatal and intrapartum interventions. J Midwifery Womens Health 2016;61:507–511.
28. Diokno AC, Sampselle CM, Herzog AR, et al. Prevention of urinary incontinence by behavioral modification program: A randomized, controlled trial among older women in the community. J Urol 2004;171:1165–1171.
29. Sampselle CM, Newman DK, Miller JM, et al. A randomized controlled trial to compare 2 scalable interventions for lower urinary tract symptom prevention: Main outcomes of the TULIP study. J Urol 2017;197:1480–1486.
30. Caretto M, Giannini A, Russo E, Simoncini T. Preventing urinary tract infections after menopause without antibiotics. Maturitas 2017;99:43–46.
31. Meddings J, Saint S, Krein SL, et al. Systematic review of interventions to reduce urinary tract infection in nursing home residents. J Hosp Med 2017;12:356–368.
32. Harlow BL, Bavendam TG, Palmer MH, et al. The prevention of lower urinary tract symptoms (PLUS) research consortium: A transdisciplinary approach toward promoting bladder health and preventing lower urinary tract symptoms in women across the life course. J Womens Health 2017 [Epub ahead of print]; DOI: 10.1089/jwh.2017.6566.
33. Lukacz ES, Sampselle C, Gray M, et al. A healthy bladder: A consensus statement. Int J Clin Pract 2011;65:1026–1036.
34. Rortveit G, Daltveit AK, Hannestad YS, Hunskaar S. Urinary incontinence after vaginal delivery or cesarean section. N Engl J Med 2003;348:900–907.
35. Stenström Bohlin K, Ankardal M, Lindkvist H, Milsom I. Factors influencing the incidence and remission of urinary incontinence after hysterectomy. Am J Obstet Gynecol 2017;216:53.e1–53.e9.
36. World Health Organization. Constitution of the World Health Organization. Basic Documents, Forth-fifth edition, 2006:1–18.
37. Huber M, Knottnerus JA, Green L, et al. How should we define health? BMJ 2011;343:d4163.
38. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. Ann N Y Acad Sci 1998;840:33–44.
39. Sterling P, Eyer J. Allostasis: A new paradigm to explain arousal pathology. In: Fisher S, Reason JT, eds. Handbook of life stress, cognition and health. NY: John Wiley and Sons Ltd., 1988:631–651.
40. Abrams P, Artibani W, Cardozo L, Dmochowski R, van Kerrebroeck P, Sand P. Reviewing the ICS 2002 terminology report: The ongoing debate. Neurourol Urodyn 2009;28:287.
41. Reason J. Stress and cognitive failure. In: S. Fisher, J. Reason (eds.). Handbook of Life Stress, Cognition and Health. Hoboken, NJ: John Wiley and Sons, 1988, p. 629.
42. Irwin DE, Milsom I, Hunskaar S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: Results of the EPIC study. Eur Urol 2006;50:1305–1306.
43. Wu JM, Matthews CA, Vaughan CP, Markland AD. Urinary, fecal, and dual incontinence in older U.S. adults. J Am Geriatr Soc 2015;63:947–953.
44. Clemens JQ, Meenan RT, O'Keeffe Rosetti MC, Brown SO, Gao SY, Calhoun EA. Prevalence of interstitial cystitis symptoms in a managed care population. J Urol 2005;174:576–580.
45. Halfon N, Larson K, Lu M, Tullis E, Russ S. Lifecourse health development: Past, present and future. Matern Child Health J 2014;18:344–365.
46. Alwin DF. Integrating varieties of life course concepts. J Gerontol B Psychol Sci Soc Sci 2012;67 B:206–220.

47. Mohammed S, Dumville BC. Team mental models in a team knowledge framework: Expanding theory and measurement across disciplinary boundaries. J Organ Behav 2001;22:89–106.
48. Veillard J, Cowling K, Bitton A, et al. Better measurement for performance improvement in low- and middle-income countries: The primary Health Care performance initiative (PHCPI) experience of conceptual framework development and indicator selection. Milbank Q 2017;95:836–883.
49. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology in lower urinary tract function: Report from the standardisation sub-committee of the International Continence Society. Urology 2003;61:37–49.
50. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. Neurourol Urodyn 2010;29:4–20.
51. Austin PF, Bauer SB, Bower W, et al. The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the standardization committee of the International Children's Continence Society. Neurourol Urodyn 2016;35:471–481.
52. Van Kerrebroeck P, Abrams P, Chaikin D, et al. The standardization of terminology in nocturia: Report from the standardization subcommittee of the International Continence Society. BJU Int 2002;90 Suppl 3:11–15.
53. Nevéus T, von Gontard A, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: Report from the Standardisation Committee of the International Children's Continence Society. J Urol 2006;176:314–324.
54. Sexton CC, Coyne KS, Kopp ZS, et al. The overlap of storage, voiding and postmicturition symptoms and implications for treatment seeking in the USA, UK and Sweden: EpiLUTS. BJU Int 2009;103 Suppl:12–23.
55. Wein AJ. Normal and abnormal function: An overview. In: Wein AJ, Andersson KE, Drake MJ, et al. (eds.). Bladder Dysfunction in the Adult: The Basis for Clinical Management. New York, NY: Humana Press, 2014, pp. 19–24.

Address correspondence to:
Emily S. Lukacz, MD
Division of Female Pelvic Medicine
and Reconstructive Surgery
University of California San Diego
9500 Gilman Dr. #0971
La Jolla, CA 9093

E-mail: elukacz@ucsd.edu