Special Article

Symptoms of Lower Urinary Tract Dysfunction Research Network

Claire C. Yang, Kevin P. Weinfurt, Robert M. Merion, Ziya Kirkali* and the LURN Study Group

From the Department of Urology, University of Washington, Seattle, Washington (CCY), Department of Psychiatry and Behavioral Sciences, Duke University, Durham, North Carolina (KPW), Arbor Research Collaborative for Health and the Department of Surgery, University of Michigan, Ann Arbor, Michigan (RMM), and National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland (ZK)

Abbreviations and Acronyms

DCC = data coordinating center

LUTD = lower urinary tract dysfunction

LUTS = lower urinary tract symptoms

NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases

PROM = patient reported outcome measure

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* Correspondence: Division of Kidney, Urology and Hematology, Two Democracy Plaza, Room #627, 6707 Democracy Blvd., MSC 5458, Bethesda, Maryland 20892 (telephone: 301-594-7718; FAX: 301-480-3510; e-mail: ziya.kirkali@nih.gov).

Purpose: To address gaps in understanding and treating lower urinary tract symptoms, the NIDDK created the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN). The goals of LURN are to work collaboratively to 1) identify and explain the important subtypes of lower urinary tract symptoms; 2) improve the measurement of patient experiences of lower urinary tract symptoms; 3) disseminate novel findings to researchers, clinicians and patients; and 4) generate data, research tools and biological samples for future studies.

Materials and Methods: As a first step in understanding subtypes of lower urinary tract symptoms, LURN will focus on disorders of urinary sensation (eg urgency) and their causes. These are being examined with respect to patient experience, organism or systemic factors, genitourinary organs and tissues, and cellular/molecular factors. This is being achieved via an observational cohort study that is currently enrolling patients with lower urinary tract symptoms (target number 1,000) and that will extensively characterize patients with lower urinary tract symptoms. Future studies embedded within the observational cohort study will focus on neuroimaging and sensory testing, biomarkers and organ based factors. To advance the science of measurement of lower urinary tract symptoms, LURN is also developing and evaluating a comprehensive set of self-report questions to provide more granular assessments of lower urinary tract symptoms.

Results: LURN has taken its first steps by developing a framework for studying lower urinary tract symptom subtypes.

Conclusions: In developing this framework, LURN is choosing an initial domain on which to focus (sensory experiences), and creating and executing protocols designed to improve measurement of self-reported symptoms and identify patient subtypes.

Key Words: lower urinary tract symptoms, research, government agencies

To hasten advances in assessing and treating lower urinary tract dysfunction, the NIDDK created the Symptoms of Lower Urinary Tract Dysfunction Research Network. In this article we introduce the motivation for LURN, its scientific objectives and study design, and lessons learned to date. The research and clinical communities are invited to

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provide comments, ideas and proposals to interact with LURN.

Motivation for LURN

Challenge of Understanding and Treating LUTS. Patients present with a wide variety of symptoms putatively but not uniformly related to the lower urinary tract, including LUTS associated with urine storage, voiding and post-micturition. Although symptoms are attributed to the lower urinary tract, their etiology may or may not have their source in the organs, structures and functions of the lower urinary tract. For example, urinary incontinence may be entirely due to anxiety disorder.[1] When the cause of LUTS is definitively linked to 1 or more structures and/or functions of the lower urinary tract, the term lower urinary tract dysfunction is appropriately applied. The distinction between LUTS and LUTD is important; improvements in the diagnosis and management of patients with LUTS are predicated on better understanding of all potential etiological and contributing factors, including but definitely not limited to LUTD alone.

LUTS are highly prevalent and occur in each gender to a similar extent, with 51.3% and 59.2% of men and women, respectively, exhibiting storage symptoms; 25.7% and 19.5%, respectively, exhibiting voiding symptoms; and 16.9% and 14.2%, respectively, exhibiting post-micturition symptoms.[2] Unfortunately, many patients who seek care for LUTS experience neither total nor permanent resolution of their symptoms with current management approaches.[3,4] The impact of LUTS is significant and wide-ranging.[5,6] LURN was developed to address the gaps in understanding and treating LUTS.

One of the barriers to improving diagnosis and management of patients with LUTS is incomplete knowledge and imprecise classification of subtypes of patients with LUTS and their associated etiologies. Effective treatments cannot be determined without identifying clinically meaningful clusters of patients and their corresponding causes. There has been a growing appreciation that the causes of LUTS are perhaps more numerous than once thought. The original use of the term LUTS attached symptoms to a specific urological organ, the prostate. In men older than age 50, LUTS are usually attributed to urinary obstruction caused by an enlarged prostate (ie benign prostatic hyperplasia). However, research suggests that common pathophysiological changes, such as inflammation and fibrosis, and connective tissue, vascular, or neurological factors in more than 1 urological organ may be responsible for a group of symptoms.[7–9] Moreover, involvement of adjacent nonurological organs (eg colon), remote organs (eg brain), other diseases or conditions (eg diabetes mellitus), medications (eg diuretics), or lifestyle factors (eg fluid consumption habits) also contribute to the development or severity of LUTS. While LUTS was used for male symptoms associated with an enlarged prostate in the past, today it has been expanded to include urinary symptoms of women. In the U.S. general population, women have a higher prevalence of urinary symptoms,[10] many of which are commonly considered a side effect of childbearing. But obesity, diabetes, metabolic syndrome, cardiovascular disease, sexual activity and aging are also associated with increased risk of LUTS.[11] Thus, research is needed to understand how these and other factors determine the symptoms and experiences of important clinical subtypes of patients with LUTS related to LUTD and other etiologies.

Opportunity for Improved Self-Reported Measurements of Health in Patients with LUTS. The effort to identify subtypes of patients and explain their variants of LUTS will benefit from high quality measurement of all patient characteristics. This is especially true of patient characteristics that are typically self-reported, such as symptoms, bother, approaches to adaptation/coping and functioning. Success in identifying and explaining important patient subtypes will rely on the comprehensiveness, validity, and precision of such self-reported concepts. In terms of comprehensiveness, the set of measures must address the symptoms and experiences deemed important by patients. Validity includes determination of the time period within which patients can accurately recall the measures being self-reported (eg prior 7 days vs prior month). For precision, the measures must have as little error as possible to allow sufficient distinctions between patients to define important clinical subtypes. Thus, improved self-reported measurements can advance person centered approaches to classifying and treating patients with LUTS.

Development of LURN. In recognition of these challenges and opportunities, NIDDK convened a Meeting on Measurement of Urinary Symptoms (MOMUS) in November 2011 to frame a discussion focused on identifying the research needed to advance the field of LUTS diagnosis and treatment (http://www.niddk.nih.gov/news/events-calendar/Pages/meeting-on-measurement-of-urinary-symptoms-momus.aspx). Based on the MOMUS recommendations the NIDDK developed and funded LURN as an interdisciplinary consortium based cooperative research network (RFA-DK-11-026) to catalyze the LUTS research community. Initially formed in 2012 and expanded in 2013 (RFA-DK-12-017), LURN is now a functioning research network (www.nih-lurn.org)