Welcome and Introductions

Dr. Kirkali welcomed meeting participants. Following introductions, Dr. Kirkali reviewed the purpose of the urology interagency coordinating committee.

Symptoms of Lower Urinary Tract Dysfunction Network (LURN)

Dr. Kirkali noted that this funding opportunity announcement (FOA) is asking for added sites to join the current LURN investigators to expand on validating symptom-based instruments to measure early, late, transient, and persistent symptoms both in males and females, and to better define the phenotypes of men and women with symptoms of LUTD. The key responsibilities of the added research site (RS) and expanded data coordinating center (DCC) will be to adopt the study protocols developed by the LURN investigators, validate the developed patient reported outcome (PRO) measures, recruit study participants, and conduct extensive characterization (phenotyping) of them. Four Centers were awarded: one data coordinating center and three research sites. A goal of the LURN network is to develop patient-reported instruments.

Dr. Kirkali discussed the conceptual model of disease that begins with the underlying disease process that moves into body manifestation (symptom, sign, test) and concludes with how the patient functions (physical, mental, occupational, social). In addition to these factors, the patient’s expectation of treatment, bother symptoms, and ability to cope are products of how the patient functions. The current paradigm of treatment for lower urinary tract symptoms (LUTS) in men and for incontinence in women was discussed. Patients seeking treatment is determined by the severity of symptoms and level of bother to the patient.

The Network seeks to develop Patient-Reported Instruments that will:
- to capture all lower urinary tract dysfunction symptoms in both genders
- to assess bother & identify the most bothersome symptom
- to assess adaptation
- to assess coping behavior
- to identify the cause(s)
- to be used as a clinical outcome
As a result, the Network will advance this area of research with:

- FDA approved PROs for x, y, z
- Symptom change, bother, adaptation, coping are understood and well measured in patients
- Patients are extensively characterized and placed into informative bins

Participants offered the following feedback:

- Dr. Wiederhorn (Food and Drug Administration [FDA]) noted that patient symptoms may not be related to an organ due to referred pain, etc. It would be helpful to catalog the entire repertoire of how the urologic system works.
- Identification of biomarkers would be helpful
- Dr. Bavendam noted that development of a tool should be based on symptom inventory. This tool was never presented to the FDA because there was no product associated with it.
- Dr. Wiederhorn (FDA) noted that the FDA is stuck in a regulatory bind without a means to measure diseases such as interstitial cystitis (IC) and prostatitis. Bridging studies would be needed. For example, studies demonstrating that IC and overactive bladder (OAB) cause pain would have to be bridged. Concrete definitions would be needed to validate studies. However, NIDDK could redefine disease.
- Dr. Schwartz (Centers for Medicare & Medicaid Services [CMS]) suggested recruiting nursing home patients. Tools geared to general practitioners and geriatrics would be helpful.
- Dr. Begg (Office on Women’s Health [OWH]) noted that further clarification of OAB and IC would be helpful. OWH noted the women’s health unit in the FDA as well as the OWH are able to cofund studies.
- Dr. Lawrence (Agency for Healthcare Research and Quality [AHRQ]) noted that it would be important to differentiate patients who see urologists from patients who only see general practitioners. Also, he noted that they have evidence based practice centers are helpful. There may be a nursing home population.

Issues on Women` s Urology: How can we work together?

Dr. Bavendam noted a shift in focus from surgical intervention to other types of treatment for urological dysfunction. Very few patients that experience symptoms seek treatment and general practitioners are only trained in bladder dysfunction. Psychosocial factors have more influence over treatment than physiological factors. There are a number of benign conditions that affect bladder well-being: OAB, bladder infection, IC/painful bladder syndrome/chronic pelvic pain syndrome, bladder outlet obstruction, muscle and fascial weakness of pelvic floor support, and urethral incompetence.

Dr. Bavendam reviewed the pathophysiology of the lower urinary tract (local [urological], nonurological, and systemic). OAB and urinary incontinence (UI) are associated with other major comorbidities such as: decreased cognition and estrogen, smoking, bowel function and, in particular, depression, obesity, diabetes, and cardiovascular disease. Dr. Bavendam discussed the challenges to bladder health throughout a woman’s lifespan. In early years, toilet training and menses can contribute to infections and voiding dysfunctions. The beginning of sexual activity and pregnancy and childbirth may lead to the development of other problems such as frequent urgency and incontinence, bladder infections, and IC. From approximately age 30 through the remainder of the lifespan, other potential risk factors include co-morbidities and the stress of career and being in caretaker roles. After age 40, menopause and estrogen decline may also contribute to frequent urgency and incontinence, bladder infections, and IC.

The goals of urologic research activities are to minimize impact of symptoms that cannot be eliminated, understand underlying pathophysiology broadly, improve treatment outcomes, and prevent (primary and secondary) urologic disease. Some challenges in women’s urologic research are that LUTS are not considered important from provider and payer standpoint – “lifestyle issue”, the primary researchers are surgeons, the best science demands a reductionist point of view, and it is hard to conceive of prevention from perspective of women with severe conditions.
Dr. Bavendam discussed the newest KUH initiative in urology: the Women’s Urology Prevention Network. The Network will examine women with and without LUTS. There are many opportunities for both individuals and clinicians within a LUTS prevention strategy including a heightened interest in treating these disorders by clinicians and promoting patient education among individuals. The visibility of these opportunities should ultimately move treatment efforts among the patient population to prevention.

In closing, Dr. Bavendam summarized the following new directions in women’s urology research:

- Investigate early in course of symptom evolution
- Adopt a holistic approach for aspects of the research
  - Profile our complex clinical trial subjects better
  - Explore impact of personality attributes and personal values on clinical trial participation and treatment outcome
- Diversify types of research methodology
- Support the assertion that UI is a important medical condition rather than a lifestyle issue – it is a barrier to achieving treatment goals for priority medical conditions
- Take current evidence about prevention and pilot targeted community based research initiatives that have measurable endpoints

Participants offered the following feedback:

- Dr. Wiederhorn noted that the term “LUTS” could be restrictive if the patient is experiencing unique symptoms.
- Dr. Begg noted the presence of a college health administrative network. One is based out of BWI airport. There is a director of research.
- Dr. Kranzfelder noted the bladder control for women campaign and clearinghouse efforts to educate patients.
- Dr. Lawrence noted a recently released report on surgical intervention for incontinence. Also, epidemiology and natural history data is needed for prevention studies. Quality of life measures should be added to prevention studies. Observational studies would be key for natural history.
- Dr. Huntley sees areas of overlap and would like to collaborative.
- Dr. Bavendam requested names for speakers and meeting participants for the meeting in February.
- Dr. Samad noted that the CDC has a small IC program and they are interested in provider education efforts. They have funded ICA. They will incorporate this group’s suggestions into the next RFA for IC. ANSER is another new initiative.

Agency Updates

- The OWH has an administrative supplement available for sex differences. Deadline is Jan 11. There is an R21 on women’s health and sex/gender differences. There is significant collaboration between OWH and NIDDK. Contacts for pain expertise and information about pain resources is available through OWH.
- The AHRQ noted evidence-based practice and systematic reviews have been completed. Another one on chronic urinary retention is ongoing. They receive PCORI funds for training. PIs interested in comparative effectiveness should be mindful of training grants available.
- The CDC noted an IC awareness education and partnerships initiative. There are no current research activities. Open to suggestions for IC awareness for provider education.
- The NCCAM noted efforts on pain and symptom management and promotion of healthy behaviors. An application hypnosis and urge incontinence and imaging was funded as well as neuroimaging studies on IBS. NCCAM also supports the PROMISE, PCORR network, and HMO common fund initiative.
- The FDA noted research on normal levels of testosterone. A paper will be published in a journal of urology in February. There is also work on patient reported outcomes.
- The NIA noted that NICHD formed a branch on gynecological health. This would be helpful for pelvic pain collaboration.
• CMS noted interest in partnering on initiatives.

**Topics for next meeting**

• AHRQ suggested speaking with PCORI on management opportunities.
• NIA noted that they will speak with the pelvic floor network.