Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN)

Qualitative Assessment of Lower Urinary Tract Dysfunction Study Protocol (Protocol 1)

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Background

Dysfunctions of the lower urinary tract affect both men and women and have adverse effects on health-related quality-of-life and daily functioning, including work productivity.[1] There are many causes and risk factors for LUTD, such as malfunctioning bladder, sleep disorders, obesity, diabetes and genetic predisposition. Moreover, patients with LUTD can suffer from significant comorbidities, which complicate research and treatment decisions. To improve our understanding of the complex interrelationships among these variables, high quality tools are needed to fully characterize LUTD patients and to comprehensively measure treatment outcomes.[2] Self-report measurements are important tools to characterize patients and to effectively guide treatment.

There is an opportunity to improve the measurement of health for patients with LUTD. One deficiency in the field is that practice guidelines for male patients with LUTD are based on the AUA Symptom Index (AUA-SI), [3, 4] but since its development, newer questionnaires have been created with expanded content as well as differentiation of symptom severity versus bother.[5, 6] Although many questionnaires are currently available to assess urinary symptoms, each with different strengths and weaknesses, there is little guidance on how to use these questionnaires in clinical practice. In the case of the LUTS Tool [5, 6], for example, analyses have been conducted at the level of individual symptoms, but scoring algorithms to guide treatment and describe patient severity are not available. Thus, there is a need to examine the content of existing questionnaires to 1) determine what is missing and 2) identify questionnaires, items, and subscales and their application to research and clinical management.

Study Objectives

Statement of Purpose for the LURN Self-reported Measures Battery. This protocol is part of an overall effort to create a state-of-the-art resource for broadly measuring health for patients with lower urinary tract dysfunction (LUTD). The primary objective of this resource, known as the LURN Self-reported Measures Battery, is to comprehensively characterize the experiences of patients with LUTD for the purpose of identifying subtypes of patients with LUTD, as well as to describe a profile of symptoms that can be linked to other measurements in future research (e.g., biomarkers, genetics). In sum, the primary purpose of the LURN Self-reported Measures Battery will be characterization and description. Secondary objectives of the LURN Self-reported Measures Battery, for which additional development work will be required, include developing better patient-reported endpoints for clinical trials, monitoring symptoms in the course of clinical care. Future development work will also include possible short forms, which are brief questionnaires designed to efficiently measure targeted information.

Assessment Format. Because the LURN Self-reported Measures Battery will be designed to make use of existing state-of-the-art technology, the primary format of it will be computerized. Thus, respondents will complete it at computers and/or tablets. The final assessment tool will include features to ensure ease of use with patients, such as consistent time frames and response options for questions. In future protocols, we will test alternative assessment formats (e.g., interview-based methods for people who cannot read).

The specific objectives of Protocol 1 are:

1. To conduct qualitative interviews with clinical experts (Project 1A) to understand their perspectives on the concerns voiced by patients with LUTD as well as the experts' needs for self-report measures of LUTS.
2. To conduct qualitative interviews with patients (Project 1B) to understand the range of experiences of patients with LUTD related to their health.
3. To review existing self-report tools and identify gaps where important patient experiences are not reflected (Project 1C).
4. To develop new items to address any gaps in content (Project 1C).
5. To evaluate existing, revised, and new items to ensure understandability of the questions and appropriateness of the response options (Project 1D).
6. To conduct a translatability review of candidate items to identify and address English phrasings that might complicate translation to non-English languages (Project 1E).

At the conclusion of Protocol 1, we expect that items in the LURN Self-reported Measures Battery will demonstrate the following properties:

- Comprehensive in measuring each subcategory of the domain
- Clear and understandable, even to people with low literacy
- Relevant to respondents and clinicians
- Amenable to cultural and linguistic translation

Future LURN protocols will address the psychometric characteristics of our items and scales, the recall period of the items, and the responsiveness of the items to changes in clinical status over time.

Preliminary Conceptual Framework

Our preliminary conceptual framework includes two components: a disease-impact model describing the effects of unknown underlying LUTD disease processes on the experience of the person (Figure 1) and an initial list of symptoms associated with LUTD (Table 1). This overall conceptual framework was informed by a review of the literature and discussions among the LURN investigators. In the disease impact model, the underlying urologic disease process causes **bodily manifestations** that are known through **test results** (e.g., urodynamic findings, prostate specific antigen), clinical observation ("**signs**" such as urine leak with coughing or enlarged prostate) and patients' reports of their bodily

experiences ("**symptoms**" such as urgency or hesitancy). (Although not shown in Figure 1, the severity of the bodily manifestations can be modulated by a number of non-urologic factors, such as non-urologic disease, medications, and diet.) These bodily manifestations can affect the person's day-to-day **functioning**. Following the World Health Organization[7], PROMIS[8], and others, we divide functioning into **physical**, **mental**, and **social** components. The person evaluates his or her symptom experience and functioning to arrive at a feeling or judgment concerning how **bother**ed (s)he is by these. The person's experience of bother is determined in part by his/her **personal characteristics**, such as his coping skills, beliefs about what is "normal" for someone his age, etc. (In the figure, symptoms and functioning are seen through the lens of personal characteristics.) The more bothered a person is by his/her symptoms and/or the way their functioning has been impacted, the more likely he will be to engage in **coping behaviors** (e.g., reducing fluid intake). These behaviors could in turn affect the bodily manifestation of the disease (e.g., less frequent urination) and/or the person's functioning. Thus, symptoms and functioning can cause bother, but bother can also cause changes in symptoms and functioning through changes in coping behaviors.

The disease impact model and initial list of symptoms inform the initial qualitative inquiry described in Projects 1A and 1B and will be revised in light of the data collected.

84 **Figure 1: Conceptual Model of the Effects of Urologic Disease on the Person's Experience.**

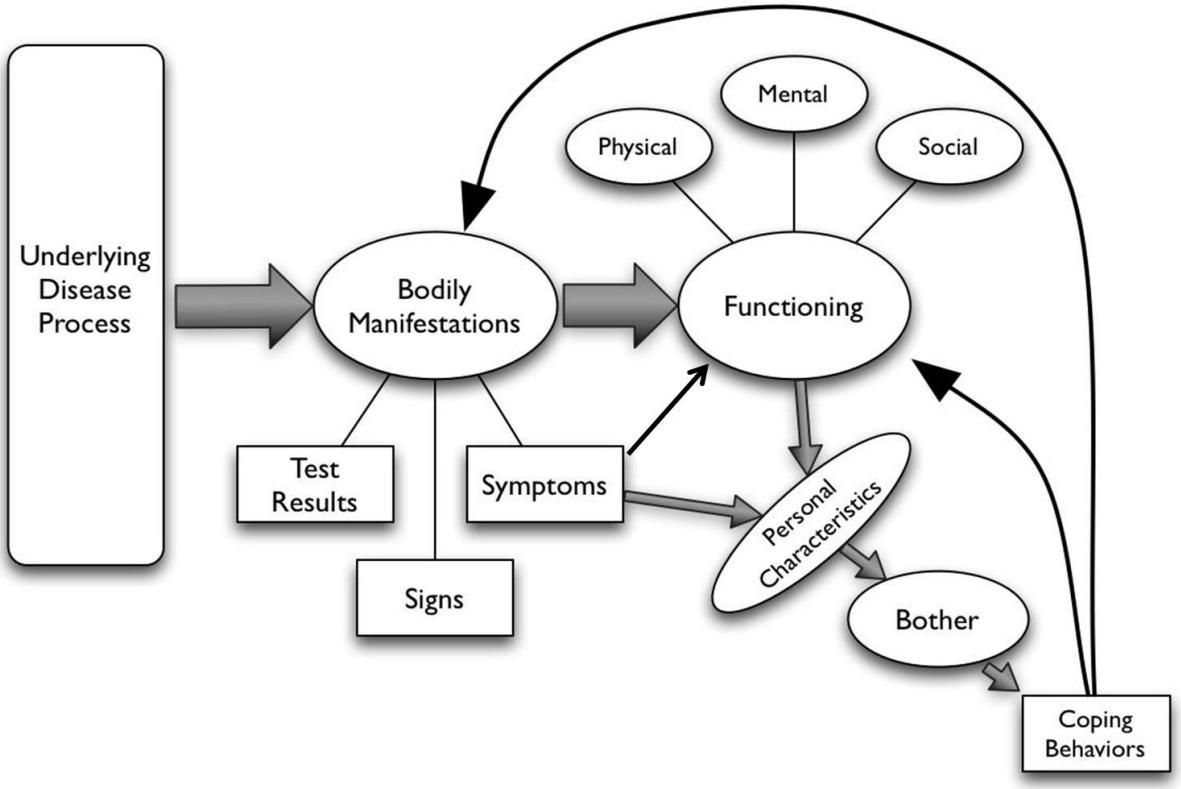

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Table 1: Initial Symptoms of LUTD	
Symptom Cluster	**Symptom**
Storage	Daytime frequency
	Nocturia
	Urgency
	Incontinence/Leakage (various types)
	Poor or absent sensation of bladder filling
	Pain/Discomfort/Pressure
Voiding	Slow/weak stream
	Splitting or spraying
	Intermittent stream/Double Voiding
	Hesitancy
	Straining
	Dribbling at the end of flow
	Dysuria
	Paruresis (i.e. shy bladder, shy bladder syndrome)
Post-micturition	Feeling of incomplete emptying
	Post-micturition dribble (delayed)
	Pain/discomfort/ pressure after urination
Other or Poorly Characterized	Confidence in warning signs of need to urinate soon
	Self-rating of overall bladder control
	Urgency with fear of leaking
	Abnormal bladder sensations
	Bother of symptoms

Study Design

Project 1A: Clinician Survey

We will interview physicians and healthcare providers about their clinical experience with LUTD patients to document the concerns voiced by patients. The sample will be 6 physicians with a urology-related specialty (e.g., urology, urogynecology), as well as 5 primary care physicians. All participating physicians must be Board Certified with more than 5 years of clinical experience. Additionally, eligible physicians must evaluate more than 5 patients with LUTS per week (including men and/or women). For the specialty clinicians, 3 will be clinicians who treat mostly men and the other 3 will be clinicians who treat mostly women. The clinicians needed for this phase will be recruited from the professional networks of the LURN investigators and will reflect geographic diversity. In addition to physicians, we

will interview 4 nurses or physician assistants who work in urology clinics, 2 who work mostly with men, 2 who work mostly with women. Interviews will be conducted either in person or over the telephone.

Clinicians will be asked to list and identify the most important and prevalent LUTD symptoms and concerns using open-ended queries. We will also ask healthcare providers to provide patient-friendly language for the symptoms in Table 1. An interviewer from Northwestern University or Duke University will conduct the Clinician interviews and document the results (Appendix A). Themes, symptoms and concerns provided by the clinical participants will be reviewed by LURN on the Self-reported Measures Working Group teleconferences to create new items that are not covered by existing tools (see Writing New Items below). Clinicians will be compensated $125 for their participation.

Project 1B: Qualitative Interviews with People Suffering from LUTD Symptoms

The purpose of the qualitative interviews is to ensure the completeness of the symptom framework of LUTD in existing self-report measures. In addition, these interviews may identify new content areas that may be missing from existing tools. Based on this research, we may identify new concepts to be assessed as part of LUTD, or along with LUTD assessment. Some participants will be drawn from the clinical practices of the Northwestern University, Duke University, and University of Iowa LURN investigators. Additional participants will be recruited from the communities of LURN sites. Interviews will be conducted by staff at Duke University, Northwestern University, or the University of Iowa. Participants will be interviewed in-person at his or her respective site. All participants will have an opportunity to ask questions about the study prior to agreeing to participate. Participants interviewed will provide written informed consent before beginning the study.

A trained research assistant will use a qualitative interview guide (Appendix B) to ask questions about LUTD as well as document responses. Interviews will also be audio-recorded and transcribed. Each interview is expected to take no more than 90 minutes. The draft interview guide may be modified based on clinician input. After participation, participants will be compensated $40. The recruitment strategy and eligibility criteria are described below.

Sample

The sampling plan was motivated by several considerations, the first being to sample adequate numbers of men and women; second, to include participants seeking care in clinics as well as community members who have LUTD symptoms but have not sought care, as research suggests these community members represent the majority of LUTS sufferers.[9] This sampling plan will ensure that we have a diversity of participants, including those who are naïve to treatment. Based on the experience of LURN clinicians, it is estimated that, overall, 25% of clinic participants recruited into this study will have little to no previous treatment for LUTD. Moreover, community-based participants will have not sought treatment for their symptoms, so will also be treatment naïve. The interview guide contains questions about care seeking, so the experience of our sample with regard to treatment will be recorded.

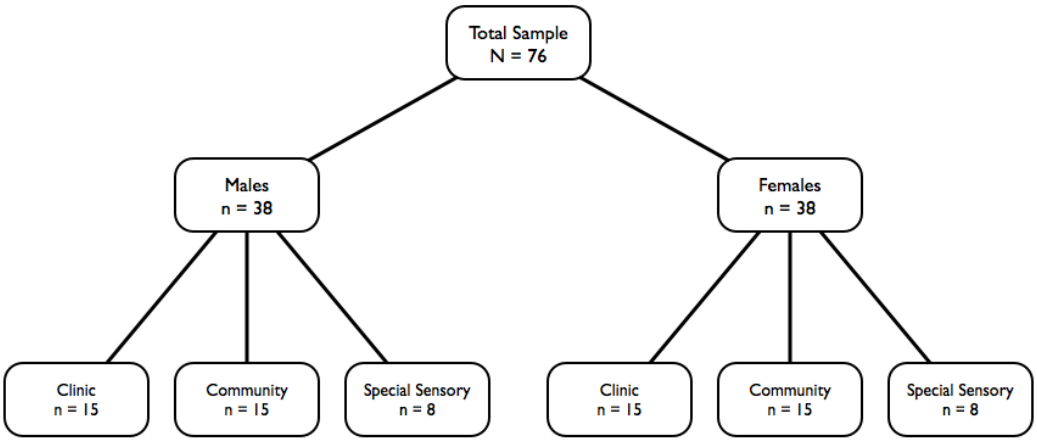
We hypothesize that individuals who do not seek care may differ from clinic patients in terms of symptom profile and level of severity. For example, it is possible that their symptoms are less severe; providing an opportunity to ensure that low-level, possibly prodromal symptoms can be measured. Third, we seek to oversample participants who have experienced abnormal bladder sensation, including lack of bladder sensation. These phenomena are not currently assessed with existing instruments and thus are not well understood. These symptoms may help to subtype patients and may be prodromal signs of later, more serious symptoms. Fourth, we wish to sample enough participants to allow us to document a wide range of experiences and symptoms, as well as factors that improve or aggravate symptoms (i.e., non-urologic factors). Finally, we desire a sample that is diverse with respect to race and ethnicity, education level, and symptom severity. Figure 1 displays the sampling framework for the qualitative interviews, leading to a total sample size of 76. We will recruit at least 16 participants (50% men, 50% women) who are likely to have abnormal bladder sensations, or lack of sensation. These participants will include people with a recent lower spinal cord injury, recent lower back surgery, women with a recent difficult vaginal child delivery, women with a recent radical hysterectomy, underactive bladder, people with uncontrolled diabetes, as well as older individuals (age 65+).

Our sample size was selected to provide a reasonable chance of reaching thematic saturation (i.e., no new and substantial themes emerge with additional interviews) based on our experience conducting qualitative interviews with other patient groups. We anticipate that saturation will be reached by the time we have interviewed 76 participants. However, we will plan to interview up to 100 participants if saturation has not been reached. Alternatively, if saturation is reached (see Analysis below) within any subgroup (see Figure 2) before all people are interviewed, recruitment within that subgroup will be considered complete.

Overall recruitment and recruitment of sub-groups will be monitored weekly. We will review descriptive statistics for age, gender, ethnicity, and LUTD symptom within clinic- and community-recruited participants. We aim to have an overall sample that is at least 25% non-white. If we are not able to reach our recruitment target for non-white participants, we will continue adding recruitment strategies to enrich the sample for this sub-group (e.g., using marketing campaigns or community outreach).

To aid in characterizing the sample, each participant will complete the LUTS Tool at the end of the qualitative assessment. We will use quantitative data from the LUTS Tool to report on symptoms and bother that are present in the sample. In addition, participants will be asked to review the LUTS Tool and our symptom list and indicate to the research assistant what they feel is missing. This will help us to identify any content that may be missing from assessment tools in LUTD.

Figure 2: Sample Composition for Qualitative Interviews of Participants with Symptoms



Eligibility Criteria – Qualitative Interviews

1. 50% men, 50% women currently experiencing one or more LUTD symptoms based on screening.
2. Within gender, 50% of patients will be clinic referred, 50% will be drawn from the community by advertising.
3. Participants from the community must not have sought care for their LUTD symptoms.
4. Participants must be:
    - currently experiencing any LUTD symptom
    - willing and able to provide written informed consent
    - ≥ 18 years of age
    - willing and able to consent and actively participate
    - able to speak and read English
5. To ensure racial and ethnic diversity, at least 25% will be either non-white race or Hispanic/Latino ethnicity.

Recruitment Plan

The objective of the recruitment plan is to collect a diverse sample of participants with regard to symptoms and demographic characteristics. Thus, participants will be recruited from both clinics and local communities of LURN sites.

For community recruitment, we will use flyers (e.g., in clinics, shopping centers, subways), advertisements on websites. We will also advertise the LURN studies at local health fairs. Interested participants will call or email the LURN study coordinators for additional information about the study. As potential participants call in, they will speak with a research assistant who will provide an explanation of the study, screen participants, and enroll participants as they agree to be in the study. As part of the

screening interview, participants will be asked to spontaneously list their urologic complaints. Their open-ended reports will be compared to our symptom list to ensure that one or more symptoms are present (see Table 1). These responses will be used to ensure that our total sample includes the breadth of symptoms identified in our initial list (Table 1), as well as to help characterize the sample. Representation of different symptoms will be monitored throughout the study so that the research assistants conducting the screening interviews will know which types of symptoms are needed and which are no longer needed. Because participants will complete the LUTS tool, there will be an ongoing tally of which symptoms are present in our sample. Patients who are found to be ineligible for the study or who report symptoms for which minimum representation (see Sample) has been reached will be told that they do not meet the criteria.

For in-clinic recruitment, clinicians will refer potential participants to the research coordinator. The research coordinator can then, on-site, administer the screening interview to confirm eligibility and to obtain informed consent. The screening process for both in-clinic and community participants will be identical. The participant can then participate in the qualitative study or arrange to return at his or her convenience. Potentially eligible participants can also be identified via electronic medical records. These procedures may vary across sites, so a detailed manual of operations is being created to address site-specific issues. Some in-clinic participants may be sent invitation letters about the study (see Appendix D).

Analysis

We will analyze our qualitative data using a combination of pre-specified themes and a grounded theory approach, [10, 11] allowing participants to define important concepts. Qualitative interviews will be immediately sent electronically for transcription. All transcripts will be transcribed and imported into NVivo. We will develop a codebook to capture symptoms and themes mentioned by patients. Two trained research assistants will independently code one transcript to develop an initial code book that will guide subsequent coding. The codebook will be updated throughout the data collection process as new information arises from interviews. Coders will read through each transcript to 1) flag adjectives that are used to describe symptoms, and 2) code for the presence of symptoms, concerns, and themes that could be used as content for a questionnaire. This information will be compiled into a table for review by the LURN investigators to determine what content might need to be included in a prototype questionnaire. At regular supervision meetings, interview notes and transcripts will be reviewed by Dr. Griffith and Dr. Flynn. This will serve to monitor the emergence of new themes and determine what, if any, changes should be made to the interview guide to follow-up on interesting findings.

We anticipate our codebook will be structured similarly to our working conceptual model (Figure 1), however we will retain flexibility and allow patient and clinician responses to help us modify and adapt this schema. The field note summaries from the interviewers will be used in tandem with the

transcripts for analysis. The summaries provide additional information about the flow and tone of the interview that greatly aids interpretation of results. The Self-reported Measures Working Group will generate alternative explanations and perspectives on the data. We anticipate that no new themes will emerge after 76 interviews (i.e., saturation), but we will add interviews if necessary. Several LURN investigators (e.g., Dr. Griffith, Dr. Cella) have experience with specialized software that facilitates the organization of qualitative content to help determine whether saturation has been met. Themes and symptoms from the qualitative interview will be reviewed each week on LURN teleconferences with a focus on new themes. When a small number of new themes emerges – fewer than five – on any particular teleconference, the team will review the importance of these themes as well as their overlap with previously-identified themes. Based on this review, the research team will reach consensus regarding whether saturation has been reached.

We expect that new areas of importance will be identified via these interviews, including the ways in which patients adapt to their urinary symptoms, and the factors that modulate their symptoms (see Appendix B: Qualitative Interview Guide). Although many symptoms of LUTD are known (see Table 1), some are not covered by existing questionnaires (see "other" section of Table 1). We also expect that community participants will differ from clinic participants in terms of symptom profiles (type and severity of symptoms), non-urologic factors, and adaptation strategies.

Project 1C: Initial Item Creation and Revision

Writing New Items

Prior to writing new items, members of our team will create an item library (demarcated by measure name, item ID, item context, item stem, response options, and sub-domain thematic area) which will consist of all existing questionnaires and items for which LURN has been given permission to use, or items that are free of intellectual property concerns. These items will be derived from a variety of tools (e.g., the LUTS tool, the AUA-SI). This database will be in the form of an "item matrix," which can be used to keep track of items, changes to items, and the rationale for any changes to items. The team of people writing new items will consist of LURN investigators. All members of LURN will be invited to contribute, and the team will seek guidance from specific members as needed. During working group teleconferences, potential new items identified from clinician surveys and patient qualitative interviews will be presented for review.

Items will be binned (i.e., organized into dimensions) via discussion during working group meetings. The proposed dimensional framework will be circulated and approved by the working group. For each dimension, two working group members will be assigned to write new items, as well as flag items that are potentially irrelevant or redundant (i.e., winnowing). Via drafting and discussion, these two-member teams are expected to generate lists of new items. These lists will be reviewed by a third person before presentation to the entire working group. If more changes are needed, the three team members will continue to redraft and review until the items are ready. The entire working group will be

involved in the last phase of reaching consensus on all items. The final set will be submitted to the team members who are conducting cognitive interviews for further refinement. Dr. Weinfurt will guide the discussions to resolve discrepancies and to reach consensus on item wording.

Rewriting Existing Items

We anticipate that many items will need to be rewritten in order to synchronize wording and format of items. Because many items will be derived from existing, high-quality tools, we do not anticipate that many items will be winnowed out during the review progress. The principle for rewriting items will be to preserve as much as possible of the original item, but to help the item fit within the broader administration framework, and to clarify items when needed.

Reasons for Rewriting or Revising Items

The reasons for item revision will be documented. The following are reasons for items to be revised:

1. Clarity: Items that are unclear will be revised to aim for (a) clarity of instructions to respondent, and (b) clarity of the item text, including singularity of concept. Some items may be too long, written at a high literacy level, or written with poor grammar. All aspects of the items (e.g., item context, stem, response options) will be subject to scrutiny and possible revision.
2. Precision: If an item measures more than one concept, we will rewrite it obtain one concept per item. Ambiguous items that can be interpreted in multiple ways will also be rewritten.
3. Acceptability to respondents: Items will be revised to maximize one's ability and willingness to provide an informative answer.
4. Adaptation to a standard data collection format: Items will be revised and reworded so that all LURN items have a similar format, as well as a similar "look and feel".

Project 1D: Cognitive Interviews

Rationale

The purpose of the cognitive interviews is to examine each item in detail with diverse participants with and without LUTS.[12, 13] Based on cognitive interviews, we may refine and reword items. Cognitive interviews will occur after completion of the open-ended, qualitative phase, as well as after we add new items to the pool. Cognitive interviews rely on intensive verbal probing of participants by a trained interviewer. The process generally consists of questions to ascertain: (1) comprehension of the question (e.g., what does the respondent believe the question is asking? What do specific words and phrases in the question mean to the respondent?), (2) the processes used by the respondent to answer the question (e.g., what information does the respondent need to recall to answer the question? What strategies does the respondent use to answer the question?), (3) decision processes, such as motivation and social desirability (e.g., is the respondent motivated to thoughtfully answer the question? Is the respondent influenced by social desirability in answering the question?), and (4) response processes

(e.g., Can the respondent match his or her response to the question's response options?) Some of these processes may be conscious, whereas other processes may be unconscious (i.e., outside the respondent's awareness). The LURN cognitive interviews will use a verbal probing technique in which respondents are queried by a trained interviewer after they complete each item on a paper-and-pencil version of the questionnaire of interest.

Sample and Procedures

As with Project 1B, recruitment for this project will rely on in-clinic participants and participants recruited from the community. For this phase of the protocol, recruitment and screening for participants will be identical to the qualitative interview phase. After obtaining informed consent, the research assistant will present items from the LURN item pool to patients. These will include a pool of items, some of which will be new and likely others from the AUA-SI, the MLUTS/FLUTS (long versions), and the LUTS Tool. After the cognitive interview has been completed, the research assistant will administer the Wide Range Achievement Test (WRAT) Reading Subtest to the participant.[14] In order for participants to complete the literacy assessment, interviews will need to be face-to-face and not by phone, because the WRAT cannot be administered by phone. Each item that is part of the cognitive interview will be reviewed by at least two individuals with low literacy, defined as a reading level less than ninth grade using the WRAT-4 Reading subtest or less than a twelfth grade education or equivalent (e.g., GED).

We will require that every item be reviewed by at least 1 White and 1 non-White person with LUTS, as well as at least 1 White and 1 non-White person without LUTS. We anticipate that each interview will include approximately 35 items. Participants will read and answer one item at a time, after which they will be asked to provide feedback on response categories, time frame, item interpretation, applicability, and overall impression of the items. The draft cognitive interview guide is presented in Appendix C. We expect most cognitive interviews to last approximately 90 minutes. Interviewers will summarize their findings from each interview. Interviews will be audiotaped, transcribed, and stored electronically, facilitating access to these data across LURN. Participants will receive $40 for this study. Because cognitive interview are iterative, the exact sample size is a projection, but we anticipate 50 interviews will be required.

Eligibility Criteria – Cognitive Interviews

Participants with LUTS must be:

- currently experiencing any LUTS,
- willing and able to provide informed consent,
- $\geq$ 18 years of age,
- willing and able to consent and actively participate, and
- able to speak and read English.

Half of the participants with LUTS will be male and half will be female. In addition, within gender, 50% of patients will be clinic referred and 50% will be drawn from the community by advertising.

Participants without LUTS must be:

- willing and able to provide informed consent,
- ≥ 18 years of age,
- willing and able to consent and actively participate,
- able to speak and read English, and
- free of significant LUTS. Their responses on the LUTS Tool 1-month version administered during screening will include:
    - "1-3 times a day" or "4-7 times a day" on question 2 ("during a typical day in the past month, how many times did you urinate during waking hours?"),
    - "None" or "1 time a night" on question 3 ("during a typical night in the past month, how many times did you wake up because you needed to urinate?"), and
    - "Never" or "Rarely" for every other LUTS Tool item.

Half of the participants without LUTS will be male and half will be female. At least two women and two men without LUTS will be over age 60 and at least two women and two men will be under age 40.

In addition:

1. To ensure ethnic and racial diversity, at least 25% of participants with and without LUT will be non-White.
2. Among the participants with and without LUTS, each item must be reviewed by at least two individuals with low literacy, defined as follows:
    - a reading level less than ninth grade using the WRAT- 4 Reading subtest
    - or less than a twelfth grade education or equivalent (e.g., GED).
3. Participants who complete cognitive interviews cannot be the same individuals as those in the qualitative interview phase.

Analysis and Revision

Each item will be seen initially by 5 men and 5 women with LUTS, and 5 men and 5 women without LUTS. Of the 10 men and 10 women viewing each item, 2-3 men and women will have low literacy. At minimum, we require that each item be reviewed by at least 2 participants with LUTS endorsing the target symptom. Three team members from the Self-reported Measures Working Group will decide, on an item-by-item basis, whether the item needs to be revised based on the results of the cognitive interviews. Problematic items will be revised by smaller domain groups with input from the Self-reported Measures Working Group as needed. Items are defined as being "substantially revised" if their revision involved more than (1) adding or removing a supportive word or other word that did not

change the meaning of a phrase, (2) word substitutions that are not more than a semantic simplification, or (3) changing the order of words.

For substantially revised items, we will test them again in a second round of cognitive interviews. We project that 50% of the items will require a second round of cognitive interviewing after being modified. For the second round, each item will be seen by 3 people, with 1-2 being of low literacy. Returning participants will be contacted by phone to review the revised items. Participants for this second (and third) review phases may be the original reviewers, new reviewers, or a mixture of both.

The Self-reported Measures Working Group will review the revised items and participants' responses from the second round of interviews. If an item is no longer considered problematic, it will be retained in the item bank and moved forward for testing. If an item does not appear to be comprehensible or relevant in the second review, this item will likely be dropped, but the group can opt for a third round of cognitive interviews if the item is deemed important. We project that 15% of the original pool of items may require a third round of cognitive interviewing. Like the second round, for the third round, each item will be seen by 3 people, with 1-2 being of low literacy. The intent of this methodology is to reach a point of diminished returns wherein we have addressed most of the concerns that might arise with the understandability of a question.

Project 1E: Translatability Review

Translation into additional languages is beyond the scope of LURN during this funding period. However, our plan is to create items that can be clearly translated into non-English languages. Items that have gone through cognitive interviewing will be submitted to a *translatability review* by experts from Northwestern University. They will review the items and identify words or phrases that might be difficult to translate into a wide variety of languages. If any items require substantial rewriting as a result of this review, we will conduct another round of cognitive interviews to ensure that they remain understandable to English-speaking persons with LUTD.

389 **Project Timeline**

Activity	**Projected time of completion**
Approval of Protocol by Steering Committee and NIDDK	Time Zero
IRB Submission	+1 month
IRB Approval	+ 2 months
Site orientation	+ 0.5 months
1A: Recruit and interview clinicians	+ 1 month
1A: Analyze data from clinician input	+ 0.5 months (assuming analyses are occurring as data come in)
1B: Recruit for and conduct qualitative interviews	+ 5 months (6 per week = 3 months)
1B: Analyze qualitative interview data	+ 1 month (assuming analyses are occurring as data come in)
1C: Write new items	+ 1 month (but can be going on while data are collected)
1D: Recruit for and conduct cognitive interviews	+ 2 months (Assume 66 items, 33 items/person, 10 people per item = 30 interviews)
Analyze cognitive interview data	+ 1 month
Convene LURN team and consultants to finalize self-report battery	+ 1 month
1E: Translatability review	+ 1 month
Prepare manuscripts for submission	+ 1 month (will be ongoing throughout)
Total Time	**18 months**

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Appendix A: Clinician Interview

[Note: Italics denote comments for the interviewer.]

Reminder: All participating physicians must be Board Certified with more than 5 years of clinical experience. Additionally, eligible physicians must evaluate more than 5 patients with LUTS per week (including men and/or women). Clinicians can be physicians, nurses, or physician assistants.

Interviewer name: _____

Interviewer site: _____

Date: _____

Years in practice: _____

Years treating patients with symptoms of the lower urinary tract: _____

How many LUTD patients do you treat per week? _____

Opening: Thank you for agreeing to share your perspectives on patients with lower urinary tract dysfunction. Your input today will help us to develop better ways to measure experiences of patients with LUTD. Specifically, we are interested in knowing your thoughts about the most important symptoms experienced by these patients.

1. *Open-ended input:* Please consider anything and everything that relates to patients with lower urinary tract dysfunction. What do you think are some of the most important symptoms and concerns of patients with LUTD?

[Interviewer should use the table below to document the results of questions 1, 2, and 3 in the guide.]

Symptom		***Clinician Mentioned***	***Importance (Scale of 0-10)***
Storage	Daytime frequency		
	Nocturia		
	Urgency		
	Incontinence/Leakage (various types)		
	Poor or absent sensation of bladder filling		
	Pain		
	Discomfort		
	Pressure		
Voiding	Slow/weak stream		
	Splitting or spraying		
	Intermittent stream/Double Voiding		
	Hesitancy		
	Straining		
	Dribbling at the end of flow		
	Dysuria		
Post-micturition	Feeling of incomplete emptying		
	Post-micturition dribble (delayed)		
Other	Confidence in warning signs of need to urinate soon		
	Self-rating of overall bladder control		
	Urgency with fear of leaking		
	Paruresis (i.e. shy bladder, shy bladder syndrome)		
	Abnormal bladder sensations		
	Bother of symptoms		

[Additional symptoms]			

2. *Elicit importance ratings for symptoms that the clinician has listed:* Let's talk about the symptoms you just mentioned. For each one, I would like you to rate the importance of the symptom to your typical patient with LUTD. Please use a 0 to 10 scale, where 0 is "Not at All Important" and 10 is "Extremely Important."

3. *Elicit importance ratings for the symptoms from LURN's initial list (Table 1) the clinician did NOT mention.* Now I'd like to ask you to rate the importance of some other symptoms that patients with LUTD might report.

4. *Gather information about bother.* Thinking about the symptoms of lower urinary tract dysfunction, what do you think is the most bothersome part of the experience for the patient?

   Probes:

   1. The intensity/severity symptom (how strong it is)
   2. The frequency (how often it happens)
   3. The duration (how long it lasts)
   4. The unpredictability (how easily one can anticipate a symptom)
   5. The variability (how much the symptom can fluctuate over time)
   6. Something else (describe)

5. *Patient-friendly language.* We would like to have patient-friendly language for these symptoms (Table 1 and any new symptoms). Can you suggest ways to describe these that are understandable to most patients?

6. *Open-ended Closing*: Are there symptoms, concerns, or comorbidities associated with lower urinary tract dysfunction that we have not covered today? *Make a numbered list of any new concerns.*

1. _____

2. _____

3. _____

4. _____

5. _____

6. _____

7. _____

8. _____

9. _____

10. _____

7. *Assess measurement needs:* We are also interested in understanding your needs for questionnaires in your practice.

1. As a practicing clinician, do you have any needs for a questionnaire about LUTD?

2. What questionnaires do you currently use?

i. What are their strengths?

ii. What are their weaknesses?

3. What would like to see in a new questionnaire about LUTD?

4. What are the biggest problems with existing questionnaires?

Interviewer Comments:

When the interview is complete, turn off the recording. Thank them for participating.

Verify that it is OK to contact them again with future questions.

Appendix B: Qualitative Interview Guide

Verifying and Augmenting the Proposed Symptom Structure

Participant ID Number:

Date of Interview: ____/____/_____
mm / dd / yyyy

1. Open-ended opening:

We are interested in your experience with urinary symptoms. There are no right or wrong answers to these questions. We just want to hear about your thoughts, opinions, and experiences.

Can you please describe the urinary symptoms that you experience? Also tell me about any concerns you have that are associated with these symptoms. This can include other symptoms that you have, concerns you have about the symptoms, or any other things that may impact your daily activities or quality of life.

Interviewer lists all symptoms and concerns provided by the patient:

The interviewer makes a list here (to keep track of them, number them 1, 2, 3, etc.).

Ask about onset of symptoms

How did your symptoms begin?

What did you first notice?

Duration

For each symptom, ask "How long have you had this symptom"; *document the response.*

Bother

I'm going to ask you to rate how much each symptom bother you on a 0-10 scale with 0 being no bother and 10 being the highest possible bother.

After all symptoms are listed, collect a 0-10 bother rating; ask "On a scale of 0-10, how much does [*symptom*] bother you?"

2. Non-urologic Factors

How do your symptoms change over time?

What things make your symptoms worse?

What things make your symptoms better?

3. Adaptive behaviors

What things do you do or have you done in the past to improve/reduce your symptoms?

Are there other ways in which you cope with your symptoms? *If yes,* tell me more about them.

Do you ever delay going to the bathroom to urinate? *If yes,* tell me more about this.

Do you ever go to the bathroom to urinate more often than usual? *If yes,* tell me more about this.

Do you ever go to the bathroom to urinate even when you do not feel the need to go?
If yes, tell me more about this

Since you began experiencing symptoms, have you made any changes to your life to help you cope with these symptoms? If so, what changes have you made?

4. Querying about care seeking

Have you sought care or treatment for any of the symptoms that we have discussed today (*give examples if needed)*?

Depending on response, query about why or why not. Document all of the reasons.

5. Normal functioning

In your own words, how would you describe normal bladder functioning?

What do you think is important for normal bladder function?

6. Open-ended closing

Are there any other concerns that we have not covered today? *Make a numbered list and collect a 0-10 importance rating.*

7. Feedback (after completion of LUTS Tool)

Please think about the questionnaire that you just completed. Is there anything that this questionnaire is missing? Are there any other questions that you think are important to ask?

(After presenting symptom list)

Please look at this list of symptoms. Can you think of any other symptoms of bladder or urinary function that we should add to this list?

Thanks for participating in this study!

Appendix C: Cognitive Interview Guide

Instructions: The participant is given each LURN item one item at a time. After reading and responding to an item, record their answer and query the participant using the following:

Participant ID Number: Date of Interview (mm/dd/yyyy): ____/____/_____

Question #: Record Answer _____

1. How did you come up with that answer?

2. In your own words, could you tell me what this question is asking?

3. What did you think of how the question was asked?

Was the question confusing?

Was the question clear? – or – Was anything about the question unclear?

Was the question too long?

What did you think of the response options? Would other response options have been better?

4. How easy or difficult was it to recall over the past XX days?

Would it be better to ask about a different length of time?

5. Can you recommend any changes to make it better?

Do you have any other feedback? Anything else?

Appendix D: Sample Invitation Letter

[Date]

[Name]

[Address]

Invitation to participate in an interview study

Dear [Patient]:

The [*site name*] is participating in a study to learn more about the experience and impact of having [condition]. To do this, [*site name*] will be conducting interviews to discuss experiences with urinary symptoms. This will help healthcare researchers to better understand the experience and impact of having urinary and bladder symptoms.

Participation is entirely voluntary. If you are at least 18 years of age, have been diagnosed with… from [*condition*] and are currently [*enrollment criteria*], then you could be invited to participate in an interview that will last 60-90 minutes. The discussions will be held in a location near our clinic and arranged at a time convenient for most people to attend. Alternatively, these interviews can be completed by phone. You will receive $40 for your participation in this study.

If you wish to be part of this study, please call us at *[number*] or email us at [address]. When you call, one of our staff members will ask you a few questions to confirm your eligibility for this project. If you are eligible to participate, you will be contacted soon afterwards to set up a time for the interview.

We hope that you will be interested in being part of this study. This opportunity to discuss your experience with urinary symptoms may help others in the future.

Sincerely,

[*Site PI or Clinic Investigator*]

Appendix E: Data acquisition, quality control, and analysis plan for LURN Protocol 1

Definitions

Analyst – A person who will be using NVivo software to assign codes to relevant sections of interview transcriptions. We propose two analysts for Protocol 1, one of whom will be from Northwestern University and one of whom will be from the DCC. Both analysts will code each interview.

Code (noun) – A word or phrase used to group similar sections of interview text. An example for the qualitative interviews might be "Incontinence" to capture all interview text about incontinence symptoms, or "Impact of stress incontinence" to capture all interview text about the way stress incontinence influences participants' behaviors, attitudes, etc.

Code (verb) – To assign codes to interview text.

Members of the Self-reported Measures Workgroup – Any site investigators, study coordinators, NIDDK staff, and DCC staff who are interested in participating in collaborative activities regarding quality control, data analysis, and the interpretation and application of results.

Project 1A – Clinician Interviews

Data acquisition:

1. Dr. James Griffith, and a second trained interviewer, will conduct audio-recorded interviews of clinicians. During the interview, the interviewer will fill out the table of symptoms based on issues described by the clinician and the importance of each symptom to patients.
2. Following each interview, audio recordings, and scanned copies of the interview form (with interviewer notes) will be sent to the DCC.
3. Audio-recorded interviews will be transcribed at the DCC.

Quality control:

4. The DCC analyst will audit at least one entire interview for transcription quality. The audit will involve listening to the audio recording of the interview while reading the transcript, to compare the written text to the audio. Additional audits of either portions of interviews or entire interviews will be performed intermittently.
5. Before analysis, analysts will search transcripts for markers of unintelligible text (if a transcriptionist cannot understand something, s/he will note it in the transcription file), and listen to the recordings to try to provide missing details.
6. During analysis, analysts will use interviewer notes and the recordings of interviews to aid the interpretation of the transcript. (This helps distinguish sarcasm or other verbal elements that could be misinterpreted by relying on the text of the transcript alone.)

7. Analysts and members of the Self-reported Measures Workgroup will discuss alternative explanations and perspectives.
8. Analysts will use transcripts, and recordings if necessary, to verify which symptoms in the symptom table were mentioned by the clinician, and how important clinicians think the symptoms are to patients.

Analysis:

9. Prior to the start of coding, members of the Self-reported Measures Workgroup will develop a preliminary coding scheme for the analysis of the interview data. This preliminary scheme will be developed based on existing questionnaire items, expected participant responses to interview questions, and Steering Committee discussions.
10. Analyze the transcriptions using NVivo software.
    a. Two trained analysts will use the preliminary coding scheme developed in #9 above to independently code one transcript.
    b. Codes assigned by each analyst will be compared to assess inter-rater agreement. Additional training and assessment will occur as necessary to ensure adequate reliability.
    c. The analysts will work together to develop a codebook to capture symptoms, concerns, and other topics mentioned by clinicians, both those in the original symptom table and new topics. The codebook will also include examples from interviews and will be updated as interviews continue and new codes emerge.
    d. As additional transcripts become available, analysts will continue to code and update the codebook as new information arises.
    e. Throughout the process, members of the Self-reported Measures Workgroup will review interview notes, transcripts, codes, and preliminary results. Collaborative discussions will facilitate quality control (see #9 above) as well as analysis.
11. Northwestern will send a copy of the final Northwestern NVivo project file to the DCC.
12. The DCC will use NVivo to compile analyst-assigned codes (including new symptoms or concerns, patient-friendly language, and themes regarding assessment needs) into tables for review by members of the Self-reported Measures Workgroup.
13. The DCC will perform quantitative analyses, such as average importance rating of symptoms, as needed.
14. Members of the Self-reported Measures Workgroup will use the analysis of clinician interviews to modify or augment items during Project 1C.

Project 1B – Qualitative Interviews

Data acquisition:

1. Two interviewers at each of Northwestern University, Duke University, and University of Iowa will conduct audio-recorded interviews of patients with symptoms of LUTD seeking care at one of the clinical centers and individuals with symptoms of LUTD from communities near the clinical centers.

2. Following each interview, audio recordings, scanned copies of interview notes, and scanned copies of the LUTS Tool will be sent to the DCC.
3. Audio recordings will be transcribed at the DCC.

Quality control:

4. The DCC analyst will audit at least one entire interview for transcription quality. The audit will involve listening to the audio recording of the interview while reading the transcript, to compare the written text to the audio. Additional audits, of portions of interviews or entire interviews, will be performed intermittently.
5. Before analysis, analysts will search transcripts for markers of unintelligible text, and listen to the recordings to try to provide missing details as in the procedure for Protocol 1A.
6. During analysis, analysts will use interviewer notes and the recordings of interviews to aid the interpretation of the transcript as in the procedure for Protocol 1A.
7. Analysts and members of the Self-reported Measures Workgroup will discuss alternative explanations and perspectives.

Analysis:

8. Prior to the start of coding, members of the Self-reported Measures Workgroup will develop a preliminary coding scheme for the analysis of the interview data. This preliminary scheme will be developed based on existing questionnaire items, expected participant responses to interview questions, and codes that emerged during the analysis of clinician interviews.
9. Analyze the transcriptions using NVivo software.
    a. Two trained analysts will use the preliminary coding scheme developed in #8 above and independently code one transcript.
    b. Codes assigned by each analyst will be compared to assess inter-rater agreement. Additional training and assessment will occur as necessary to ensure adequate reliability.
    c. The analysts will work together to develop a codebook to capture symptoms, concerns, and other topics mentioned by participants. The codebook will also include examples from interviews and will be updated as interviews continue and new codes emerge.
    d. As additional transcripts become available, analysts will continue to code and update the codebook as new information arises.
    e. Throughout the process, members of the Self-reported Measures Workgroup will review interview notes, transcripts, codes, and preliminary results. Collaborative discussions will facilitate quality control (see #7 above) as well as analysis.
10. Northwestern will send a copy of the final Northwestern NVivo project file to the DCC.
11. The DCC will use NVivo to compile analyst-assigned codes (including adjectives used to describe symptoms and the presence of symptoms, concerns, and other themes) into a table for review by the Self-reported Measures Workgroup.
12. Members of the Self-Reported Measures Workgroup will determine whether data saturation has been met by the initial 76 interviews. This will involve examining whether new information has been obtained by the most recent interviews. If data saturation has not been met (that is, if

the last interview participants provided information that earlier participants did not), the sites will schedule additional interviews.

13. The DCC will compare community participants and clinic participants in terms of symptom profiles (type and severity of symptoms), non-urologic factors, and adaptation strategies. The DCC will also perform quantitative analyses, such as average LUTS Tool scores within clinic, community, and special sensory samples, and other comparisons as needed.
14. Members of the Self-reported Measures Workgroup will use the analysis of qualitative interviews to modify or augment items during Project 1C.

Project 1C – Initial Item Creation and Revision

Data acquisition:

1. No additional data will be collected for Project 1C. Relevant information will be gathered from existing questionnaires that LURN has permission to use, and results from the clinician and qualitative interviews.

Quality control:

2. Creation of an item matrix or library, detailing:
    a. The name of the measure from which the item is derived (not applicable to new items)
    b. Item ID
    c. Item context
    d. Item stem
    e. Response options
    f. Sub-domain thematic area
    g. Changes to items
    h. Rationale for changes to items
    i. Bin (dimension)
    j. Final recommendation for the item (moving it to cognitive testing, or winnowing)

Analysis and other tasks:

3. Creation of a dimensional framework, or binning schema.
4. Bin existing items into dimensions.
5. Write new items.
6. Winnow items that are irrelevant or redundant.

Project 1D – Cognitive Interviews

Data acquisition:

1. Two interviewers at each of Northwestern University, Duke University, and University of Iowa will conduct interviews of patients with symptoms of LUTD seeking care at one of the clinical centers and individuals with symptoms of LUTD from communities near the clinical centers.
2. Following each interview, audio recordings and scanned copies of interview notes will be sent to the DCC.
3. Audio recordings will be transcribed at the DCC.

Quality control:

4. The DCC analyst will audit at least one entire interview for transcription quality. The audit will involve listening to the audio recording of the interview while reading the transcript, to compare the written text to the audio. Additional audits, of portions of interviews or entire interviews, will be performed intermittently.
5. Before analysis, analysts will search transcripts for markers of unintelligible text, and listen to the recordings to try to provide missing details as in the procedure for Protocol 1A.
6. During analysis, analysts will use interviewer notes and the recordings of interviews to aid the interpretation of the transcript as in the procedure for Protocol 1A.
7. Analysts and members of the Self-reported Measures Workgroup discuss alternative explanations and perspectives.

Analysis:

8. Prior to the start of coding, members of the Self-reported Measures Workgroup will develop a preliminary coding scheme for the analysis of the interview data. This preliminary scheme will be developed based on expected participant responses to interview questions.
9. Analyze the transcriptions using NVivo software.
    a. Two trained analysts will use the preliminary coding scheme developed in #8 above and independently code one transcript.
    b. Codes assigned by each analyst will be compared to assess inter-rater agreement. Additional training and assessment will occur as necessary to ensure adequate reliability.
    c. The analysts will work together to develop a codebook to capture misunderstanding, ideal recall periods, and other topics mentioned by participants. The codebook will also include examples from interviews and will be updated as interviews continue and new codes emerge.
    d. As additional transcripts become available, analysts will continue to code and update the codebook as new information arises.
    e. Throughout the process, members of the Self-reported Measures Workgroup will review interview notes, transcripts, codes, and preliminary results. Collaborative discussions will facilitate quality control (see #7 above) as well as analysis.
10. Northwestern will send a copy of the final Northwestern NVivo project file to the DCC.

11. The DCC will use NVivo to compile analyst-assigned codes for each item, across multiple interviews (Item 1, Participant A, B and C, then Item 2 Participant A, B, and C, etc.) for review by members of the Self-reported Measures Workgroup.
12. Domain Groups of the Self-reported Measures Workgroup will determine whether items need to be revised. Sites will schedule additional interviews for items that are substantially revised, and the process of analysis will be repeated.
13. After the second cognitive interviews of items that have been revised, Domain Groups of the Self-reported Measures Workgroup will determine whether the item should be excluded from the item bank or revised again.

Data acquisition:

1. Throughout the process of item writing, revision, and cognitive testing, the DCC will assist the Self-reported Measures Workgroup in tracking the status of each item. Once items are deemed relevant and comprehensible by patients, finalized items will be sent to translatability review experts at Northwestern University.
2. After their review, the experts at Northwestern University will send comments about words and phrases that may be difficult to translate.

Quality control:

3. The individuals conducting the review are trained and experienced in performing translatability reviews of items.

Analysis and other tasks:

4. Members of the Self-reported Measures Workgroup will discuss the results of the translatability review.
5. Items deemed too difficult to translate will require revision into an acceptably translatable version, and then undergo additional testing in cognitive interviews.