Inclusion of UI and Geriatric Measures in Clinical Trials and Epidemiological Studies

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Disclosures

• Current funding:
  – NIDDK/NIH Prevention of Lower Urinary Tract Symptoms in Women
  – NIA/NIH Aerobic Exercise in Alzheimer’s Disease
  – NICHD/NIH Building Interdisciplinary Careers in Women’s Health

• Other financial relationships:
  – None

• Conflicts of interest:
  – None
Overview

• Significance of using validated measures in research
• Types of clinical outcome measures and their selection
• Summary of measures used in UI research
• Knowledge gaps and research opportunities
Significance

• Precise measures are important in understanding:
  – Characteristics of a patient subpopulation
  – Natural history of lower urinary tract symptoms
  – Patient and caregiver perspectives
  – Treatment effects

• Measures help define study eligibility criteria, sample size, and endpoints

• Valid measures help predict which patients are:
  – More likely to develop a condition
  – Benefit from a treatment
### Clinical Outcome Assessment

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Reported Outcomes (PRO)</td>
<td>• Direct report from the patient (study participant) about the status of his/her health condition or perspectives on functioning or activities</td>
</tr>
<tr>
<td>Observer Reported Outcomes (OBsRO)</td>
<td>• Observation by someone other than patient or health professional (e.g., caregiver, nursing assistant) that does not require medical judgment or interpretation</td>
</tr>
<tr>
<td>Clinician Reported Outcomes (ClinROs)</td>
<td>• Measurement by health care professional that involves clinical judgment or interpretation of observable signs, behaviors, or other physical manifestations related to the disease/condition</td>
</tr>
<tr>
<td>Performance Outcomes (PerfO)</td>
<td>• Based on a task(s) performed by a patient according to instructions that is administered by a health professional</td>
</tr>
</tbody>
</table>
## Outcome Measurement Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Definition</th>
<th>Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reliability</td>
<td>Degree to which a measure yields reproducible and consistent results</td>
<td>• Internal consistency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Test-retest</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Intra-rater</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Inter-rater</td>
</tr>
<tr>
<td>Validity</td>
<td>Degree to which a measure assesses what it is intended to measure</td>
<td>• Face</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Content</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Criterion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Construct</td>
</tr>
<tr>
<td>Responsiveness</td>
<td>Degree to which measure can accurately detect change when it has occurred</td>
<td>• Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• External</td>
</tr>
</tbody>
</table>
Minimal Clinically Important Difference (MCID)

- Important in studies evaluating treatments with patient-reported outcomes
  - Considers both statistical significance and whether observed change is meaningful to patients
- Used in sample size calculations and to facilitate interpretation of results
- Several methods available for calculating MCID, each with different results and limitations
- No consensus on MCID on different measures used in UI trials
Selecting an Outcome Measure

• Goals or aims of the study
• Characteristics of the population
• Focus of measurement, e.g., global, condition-specific, or performance-based
• Measurement properties (reliability, validity, responsiveness)
• Participant and administrative burden
• Ease of scoring and interpretation
• Costs of administration
Types of Outcomes in UI Research

**Patient Reported Outcomes (PROs)**
- Symptoms
- Function
- Feelings
- Perspectives
- Adherence
- Falls

**Observer-Reported Outcomes (ObsROs)**
- UI severity
- Function
- Behavior
- Falls

**Clinician-Reported Outcomes (ClinROs)**
- Delirium, falls
- UI severity (wet checks)
- Physical exam
- PVRs
- Urodynamic tests
- MRI or fMRI
- Polysomnography

**Performance Outcomes (PerfO)**
- Pelvic floor muscle strength
- Toileting ability
- Gait or wheelchair speed
- Cognitive test
International Consultation on Incontinence (ICI)

- Questionnaire modules:
  - Core modules: urinary, vaginal, & bowel symptoms, UI
  - Specialty conditions: nocturia, OAB, UAB, etc
    - Cognitively impaired elderly (in development)
  - Quality of life (QoL)
  - Sexual matters
  - Treatment satisfaction (in development)

- Recommends:
  - Use of ICIQ questionnaires in studies to standardize outcomes
  - Use of Grade A questionnaires in clinical trials

www.iciq.net
## PROs: Symptoms and Impact

*Most validated in white populations with broad age range; mean < 65 years*

<table>
<thead>
<tr>
<th>Type</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Symptom questionnaire (N=39) | • Many available, long and short forms, sex-specific, and symptom-specific  
• Clinically relevant  
• Combined scales measure all aspects of UI  
• May be difficult to interpret  
• Symptoms and impact may not correlate |
| Symptom + QoL questionnaire (N=25) | • Several available, long and short forms, and sex-specific  
• Condition-specific scales tend to be more clinically relevant and responsive  
• Prone to ceiling and floor effects  
• Generic QoL more easily converts to quality-adjusted utility measures, e.g., QALYs and DALYs |
| QoL questionnaire  
*Generic*  
*Condition-specific* (N=13) | • Several available, long and short forms, and sex-specific  
• Condition-specific scales tend to be more clinically relevant and responsive  
• Prone to ceiling and floor effects  
• Generic QoL more easily converts to quality-adjusted utility measures, e.g., QALYs and DALYs |

ICI gave “A” grade to 36 instruments
PROs: Bladder Diaries

• Bladder or voiding diary
  – Paper and electronic versions available
  – Able to measures several outcomes: daytime/nighttime voids, voided volume, incontinent episodes, urgency, fluid intake, pad use
  – Reliable method; number of days kept may depend on UI severity and diagnosis
  – Easy to interpret
  – Risk of missing data based on outcomes measured
  – May alter behavior
# PROs: Function, Goals, Behavior, and Perceptions

<table>
<thead>
<tr>
<th>Type</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical function</td>
<td>• Vulnerable Elders Survey (VES-13)</td>
</tr>
<tr>
<td></td>
<td>• NHANES ADL Scale</td>
</tr>
<tr>
<td>Goal-attainment scale</td>
<td>• Goal Assessment Goal Achievement Questionnaire</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>• Geriatric Self-Efficacy Index for Urinary Incontinence</td>
</tr>
<tr>
<td></td>
<td>• Broome Pelvic Muscle Exercise Self-Efficacy Scale</td>
</tr>
<tr>
<td>Patient preference for</td>
<td>• Best-Worse Scaling</td>
</tr>
<tr>
<td>treatment (OAB)</td>
<td></td>
</tr>
<tr>
<td>Treatment adherence</td>
<td>• Exercise diaries (weekly, monthly)</td>
</tr>
<tr>
<td>Global impression of</td>
<td>• Estimated Percent Improvement</td>
</tr>
<tr>
<td>improvement</td>
<td>• Global Perception of Improvement</td>
</tr>
<tr>
<td>Treatment satisfaction</td>
<td>• OAB Satisfaction Questionnaire</td>
</tr>
<tr>
<td></td>
<td>• Patient Satisfaction Questionnaire</td>
</tr>
</tbody>
</table>

Either not graded by ICI or Grades ranged from A-C
Condition-Specific PROs Developed for Older Adults

- Quality of life
  - Urge Impact Questionnaire (URIS)\(^1\)

- Toileting ability
  - Minnesota Toileting Skills Questionnaire\(^2\)

\(^2\)Talley, KMC et al. J Gerontol Nurs, 2016; Jun 3:1-5 [Epub ahead of print]
PROs: Family Caregivers

• Condition-specific QOL
  – Overactive Bladder Family Impact Questionnaire (OAB-FIM)\(^1\)

• Generic burden scales
  – Zarit Caregiver Burden Interview\(^2\)
  – Caregiver Activity Survey\(^3\)

\(^1\)Coyne KS et al. *Neurol Urodyn*, 1998;46:683-92
Based on item response theory (IRT)

Advantage: uses standardized scores (T-score) that allows comparison across populations and conditions

Administered by paper, computer, or app

No UI measure

http://www.healthmeasures.net/explore-measurement-systems/promis
Challenges in Measuring UI in Frail Older Adults

**Older Adult**
- Cognition
- Vision
- Manual dexterity
- Literacy

**Caregiver**
- Availability/willingness
- Additional burden
- Adherence
Observer-Reported Outcomes (ObsROs)

- UI measures
  - Pad weights, 1 hr, 1-3 days
  - Pad counts
  - Wet checks\(^1\)
  - MDS Incontinence Scale\(^2\)

- QoL measures
  - MDS Social Engagement Scale\(^3\)

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\(^1\)Fogarty et al., *QRB Qual Revi Bull*, 1989:15:273-8
UI Measures Used in Nursing Homes

- Minimum Data Set (MDS) rating on UI severity (4 categories) by NH staff
- Wet checks by NH staff or research staff
- Challenges:
  - Reliability of MDS ratings may not discriminate UI severity at intermediate levels\(^1,2\)
  - Wide variability between MDS ratings and wet checks performed by NH staff vs research staff\(^2\)
- MDS may be useful in large secondary data analyses to answer policy questions

\(^1\)Resnick et al., Neurourol Urodyn 1996; 15:583-598
\(^2\)Crooks et al., J Am Geriatr Soc, 1995;43:1363-1369
Performance-Based Outcomes (PBOs)

• Toileting ability
  – Performance Oriented Timed Toileting Test (POTTI)

• Mobility measures
  – Gait or wheelchair speed
  – Timed Up and Go Test
  – 30 second Chair Stand Test
  – Short Physical Performance Battery

• Cognitive measures
  – Alzheimer’s Disease Assessment Scale for Cognition (ADAS-Cog)
  – Specific tests for different aspects of cognition, e.g., NIH Toolbox®
Knowledge Gaps

- Few PROs measures are validated in frail and oldest old elderly
- Few instruments validated for family caregiver impact (condition-specific) and bladder diary for care recipient, and none that measure treatment satisfaction
- Few, if any, UI studies have incorporated PROMIS measures, and there is no PROMIS measure for UI
- Limited information known about minimal clinically important difference (MCID) of current measures in older adults, frail elderly, and family caregivers
Research Opportunities

• PRO Instrument development and/or validation studies for in older populations, especially frail elderly and family caregivers

• Testing of strategies to increase efficiency and accuracy of measures in frail older adults and family caregivers

• Use of mHealth and other technology to measure UI outcomes

• Use of PROMIS measures in epidemiological studies and clinical trials to enable meta-analyses and comparisons across conditions

• Meta-analytic studies of UI and geriatric measures in incontinence studies