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

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

Outcome Measurement Properties

Property	Definition	Types
Reliability	Degree to which a measure yields reproducible and consistent results	• Internal consistency • Test-retest • Intra-rater • Inter-rater
Validity	Degree to which a measure assesses what it is intended to measure	• Face • Content • Criterion • Construct
Responsiveness	Degree to which measure can accurately detect change when it has occurred	• Internal • External

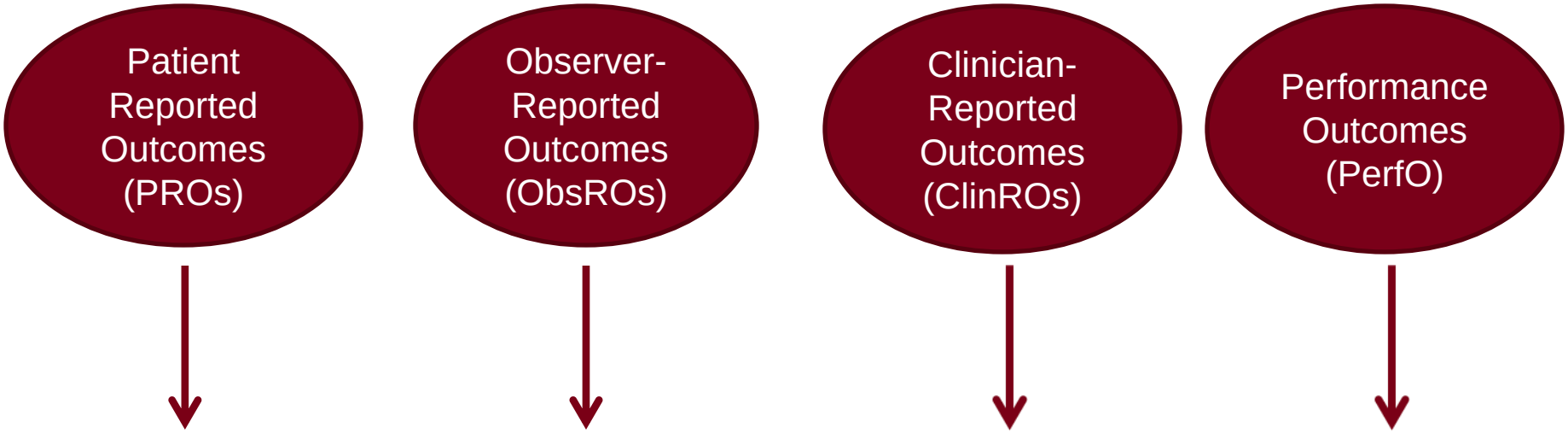
Minimal Clinically Important Difference (MCID)

- 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



- Symptoms
- Function
- Feelings
- Perspectives
- Adherence
- Falls

- UI severity
- Function
- Behavior
- Falls

- Delirium, falls
- UI severity (wet checks)
- Physical exam
- PVRs
- Urodynamic tests
- MRI or fMRI
- Polysomnography

- 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

Type	Comments
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)	
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

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

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]

[1]Dubeau CE et al. J Am Geriatr Soc, 1999; 47:989-94

[2]Talley, KMC et al. J Gerontol Nurs, 2016; Jun 3:1-5 [Epub ahead of print]

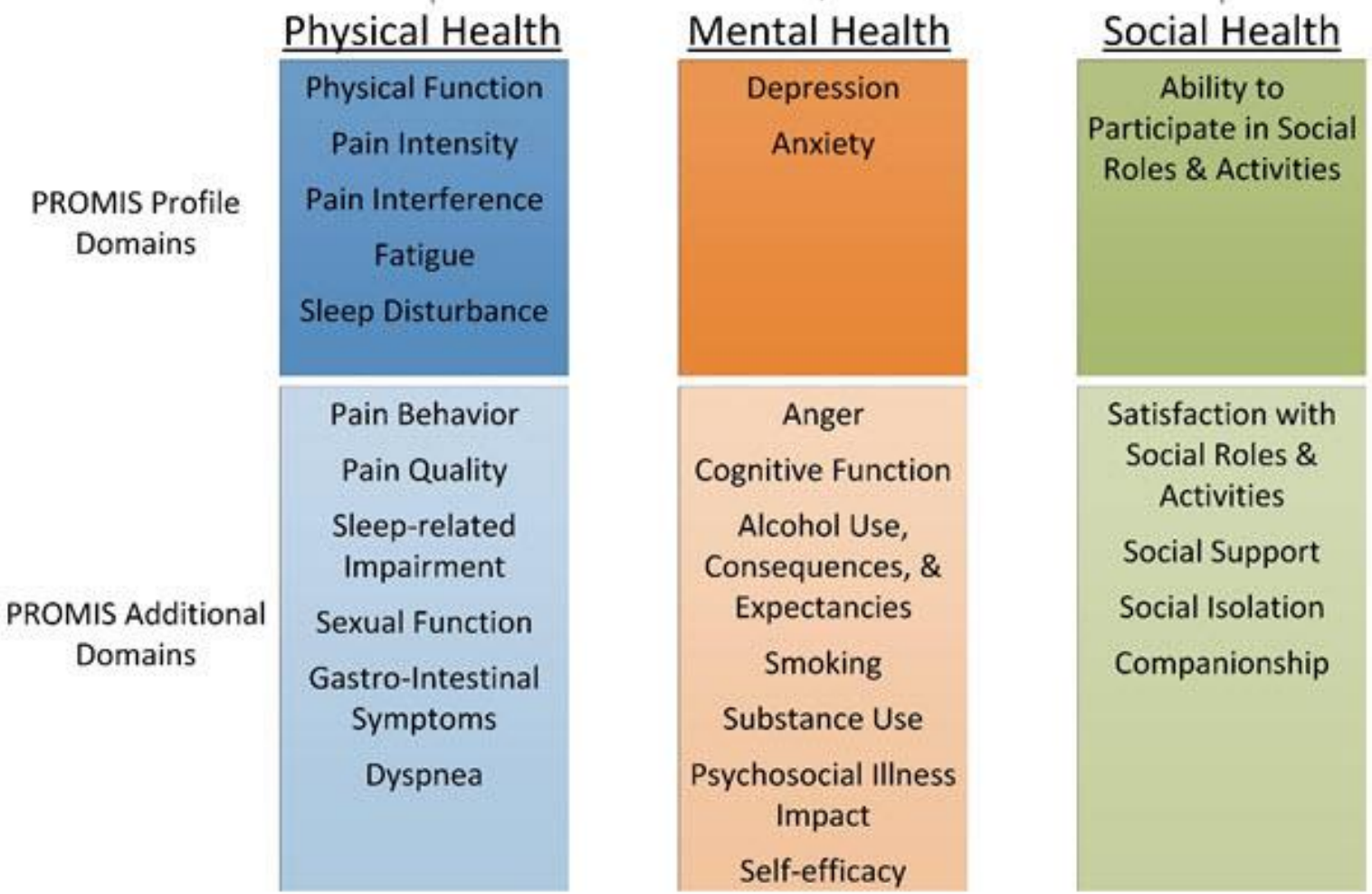
PROs: Family Caregivers

- 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. *Neurourol Urodyn,* 1998;46:683-92
[2]Zarit SH et al. *The Gerontologist,*1980;20:649-55
[3]Davis KL, et al. *Int J Geriatr Psychiatry,* 1997; 12:978-88

PROMIS Adult Self-Reported Health

Global Health



- 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

http://www.healthmeasures.net/explore-measurement-systems/promis

No UI measure

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]

[1]Fogarty et al., *QRB Qual Revi Bull,* 1989:15:273-8
[2]Resnick, NM et al. *Neurourol Urodyn* 1996;15:583-98
[3]Mor V et al. *J Gerontol B Psychol Sci Soc Sci, 1995;50B:P1-P8*

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