## Urinary Incontinence in the Elderly: A Translational Research Agenda for a Complex Geriatric Syndrome

# Current State of the Art: What We Think We Want to Know

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## **State of the Art Process**

- Process developed at U13 Sleep conference M. Vitiello
- Need for consensus building involving all participants
- Must result in a few actionable items addressing issues within even fewer overarching priority domains

#### **Priority Domains is Sleep and Aging Research**

Relationship between SCR (Sleep Circadian Rhythm) and aging

Relationship between SCR, health conditions and function, and health services in individuals, their caregivers, and their bedpartners

Treatment of SCR disturbances and disorders and implementation of treatments

Disparities in SCR, other clinical outcomes, functional, quality of life, and health services

The SCR research workforce and funding

## **State of the Art Process**

- "List the 2-4 most important questions you believe need to be addressed within the next 5 years for the optimal advancement of urinary incontinence research/medicine in the context of UI and aging"
- Responses summarized at the beginning of the meeting
- Discussed in small group sessions
- Revisited in the last session after all presentations
- Groups report out on highest priorities
- Summarized in consensus paper

# Responses from UI Conference Participants

- 36 Respondents
  - –4 Program Committee members
  - -10 Presenters/moderators
  - -1 NIH staff
  - -21 other attendees
- 108 research questions generated

# **Approach to Summary**

- General review and identification of topics
- Cluster responses
- Synthesize responses within cluster
- Review for potential gaps or omissions
- Generate overarching research questions
- For prioritization during our conference

## Clusters

- 1. Causes, mechanism, and pathways (23)
- 2. Relationships among syndromes (13)
- 3. Translational work (4)
- 4. Testing treatments (28)
- 5. Implementation issues (12)
- 6. Predictors, progression and prevention (18)
- 7. Research methods and approaches (10)

# Causes, Mechanisms & Pathways

- Impact of aging and chronic diseases on pathways regulating normal lower urinary tract (LUT) function
- Impact of aging and chronic diseases on the capacity of the LUT to maintain or restore normal function (resilience) when confronted with common challenges:
  - -mechanistic stressors (e.g. bladder filling, ischemia, oxidative stress, infection, altered microbiome) or
  - -symptom-based stressors (e.g. urgency)
- Better understanding of associations and links between specific stimuli at the level of urine constituents, bladder wall, and receptors AND associated symptoms

## Relationships among Syndromes

#### Mechanisms

- -Relationships between UI and other geriatric syndromes (cognitive impairment, falls)
- Relationships between UI/nocturia and sleep quality/disorders and night-time falls
- -Relationships with physical activity, depression

#### Treatment Effects

- Treatment of sleep disorders (apnea) impact UI?
- Treatment of UI impact sleep?

#### Impact on treatment of other conditions

- Barriers to cardiovascular medication compliance?
- Barrier to treatment of depression?

## **Translational Work**

- Identify therapeutic targets within regulatory pathways
  - Individual molecules
  - Networks of molecules
  - Defined pathophysiologic mechanisms
- Develop Treatments
  - Single and multi-component
  - Phenotype-specific treatment protocols
  - –Urgency, DO

# **Testing Treatments**

#### Efficacy

- Testing of single or multiple component interventions in complex older adults
- Specific populations: men, nursing home, oldest old, dementia, neurological conditions, refractory OAB, mild UI
- Specific treatments: Vitamin D, DDAVP, deep brain stimulation, Rx for SUI, novel therapies, education/self-help

#### Impacts

- -What are the impacts of Tx on cognition?
- Do programs with other targets improve UI? (physical function, physical activity, falls, vascular risk factors)
- Adherence predictors, facilitators, barriers
- Predicting outcomes aging, absorbent products

# Implementation Issues

#### Help-seeking

- -What factors influence help-seeking (age? ethnicity? social factors?)
- -Impact of absorbent products (delay help-seeking?)
- -How often do providers ask about UI?

## Adoption/uptake of behavioral intervention

- -What is the incidence of referral for conservative therapy
- -What are the facilitators & barriers?
- What strategies can optimize uptake?

#### Awareness

- Education for providers
- Education for general public

## Predictors, Progression & Prevention

### Predictors (risk & protective factors)

- -Behaviors (toileting, voiding habits, lifestyle)
- -Early symptoms, phenotypes
- Biomarkers
- -Vascular health, frailty

#### Interventions

- Individual level prevention strategies (behavioral, OAB)
- Programs to promote physical activity or reduce falls

### Target populations

- At-risk (diabetes, neurodegenerative disease, multiparous)
- People with early symptoms
- Hospitalized patients

# Research Methods & Approaches

#### Measurement

- -What are the best measures?
- -What are meaningful outcomes?
- -What constitutes "quality" of continence care?
- Develop clinically-relevant geriatric outcome measures

#### Methods

- Comprehensive characterization
- Compare with healthy age matched controls
- Recruiting frail older adults and caregivers to research

#### Approach

- Entice researchers from other fields to include UI
- How to support models of UI in older animals

- 1. How do aging and chronic diseases affect regulatory pathways involved in lower urinary tract homeostasis, voiding, and continence in the elderly, and what is their capacity to respond to common stressors?
- 2. What are the mechanisms that link UI and other lower urinary tract symptoms to other geriatric syndromes, including cognitive impairment, falls, and sleep disorders?

- 3. How do we translate our evolving understanding of the mechanisms of aging and disease into the design of effective treatments?
- 4. How do we determine the most effective and appropriate single or multi-component treatment approaches for individual older adults, especially in the context of frailty or multi-morbidity?

- 5. How can we promote help-seeking and optimize the availability and uptake of conservative treatments for UI, including strategies for the patient and provider level?
- 6. What modifiable factors, including individual behaviors, increase the risk of developing or worsening UI?

- 7. What lifestyle behaviors or intervention strategies promote sustained continence in the context of aging
- 8. What are the most clinically-relevant and meaningful outcome measures for incontinence trials in older adults?