CLIN-STAR WEBINAR

Application Frailty Research to the Clinical World: Four Case Studies

April 19, 2022
1-2pm ET (10-11am PT)

Moderators:

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Mara McAdams DeMarco, PhD
Sara E. Espinoza, MD, MSc

Presenters:

Abdulla A. Damluji, MD, PhD
Jennifer Lai, MD, MBA
Megan J. Huisingh-Scheutz, MD

Co-Sponsor:

OAIC National Coordinating Center
Claude D Pepper Older Americans Independence Center

NIH National Institute on Aging
afa American Federation for Aging Research
A few housekeeping items…

- All lines are muted
- Have a question?
  Enter in the Q&A box at the bottom of screen
- Rolling—we will be recording…
Jeremy D. Walston, MD; Johns Hopkins University

Raymond and Anna Lublin Professor of Geriatric Medicine and Gerontology

Director, Johns Hopkins Human Aging Project

Multiple PI of Clin-STAR, Chair of Research Core

Co-PI of the Frailty-Focused Johns Hopkins Older American Independence Center
INITIATIVES on Website  https://clin-star.org/

- Research Database
- Pilot Grants connecting early career and senior investigators from different disciplines and institutions
- Special Interest Groups
- Mentoring Office Hours
- Webinars, Peer Support, Outreach Funds
- Funding, Research, and Career Development Resources

A NATIONAL PLATFORM TO ADVANCE AGING RESEARCH ACROSS SPECIALTIES AND DISCIPLINES
WEBINAR OBJECTIVES:

➢ Learn about frailty, its importance in clinical practice, and how research in this field has evolved over the past decades

➢ Appreciate the importance for patient care that frailty be better integrated into treatment and care plans of older adults.

➢ Learn from four clinician-investigators how they’ve applied frailty principles in their transdisciplinary work.
Older Adults Want to Prevent Frailty and Preserve Resiliency

➢ High energy levels
➢ Good health
➢ Live independently
➢ Clear thinking
➢ Enjoyable social contacts and meaningful activities
Goals for Frailty and Resiliency Research

- Prevent iatrogenic complications in the most vulnerable subset of older adults
- Promote resiliency, function, cognition and quality of life in older adults
- Reduce frailty and the accumulation of chronic disease states
Figure. Age Distribution of Life Table Deaths for Women in the United States, per 100,000 People, 1900 and 2016

The red zone represents a period in life when the risk of frailty and disability begins to increase rapidly. The goal of aging science is to delay and compress the red zone, which may extend healthy life. Sources: 1900 data from Bell and Miller; 2016 data from Human Mortality Database.

Source: Olshansky SJ. From Lifespan to Healthspan. JAMA. Published online September 17, 2018. doi:10.1001/jama.2018.12621
Conceptualizing Frailty:

Disability / Physical Impairment?
Comorbidity / Diseases?
Cognitive Impairment?
Old Age?
Conceptualizing frailty: different measurements

➢ No agreed upon operational definition of frailty; many assessment instruments developed

![Diagram](image-url)

Figure 1. Representation of conceptual framework of two major theories on frailty. (A) Physical frailty, also termed phenotypic or syndromic frailty, is hypothesized to have a specific age-related biological basis that drives the appearance of signs and symptoms (outward pointing arrows). (B) Cumulative deficit frailty is hypothesized to be driven by cumulative nonspecific health, functional, psychological, and cognitive deficits (inward pointing arrows). Both concepts of frailty predict vulnerability to adverse outcomes and have led to multiple derivative frailty detection tools.

6 Buta 2016 7 Figure: Walston 2019
Physical Frailty Vs. Frailty Index Measures

- Frailty Index captures comorbidity and can be easily developed in electronic medical record by adding together conditions.
- Can be used in non-ambulatory and hospitalized patients.
- Good at finding those at high risk of pending mortality.
- Not always clear that there is any specific intervention that is common across populations.
Physical Frailty Vs. Frailty Index Measures

➢ Frailty phenotype is best captured in ambulatory populations, not during acute illnesses

➢ Good at finding those at high risk of mortality and other adverse health outcomes

➢ Needs specific measurements of grip strength and walking speed which may be difficult to obtain in some settings

➢ Hypothesized to have deep biological basis involve multisystemic decline

➢ Biology may allow the development of more specific diagnostic, preventive, and treatment strategies
Is Physical Frailty also a Platform for Other Geriatric Syndromes?

- Common biological change drives geriatric syndromes and functional and cognitive declines
- Physical frailty, Falls, Delirium, Incontinence, Sarcopenia
- Mild cognitive impairment, accumulating and accelerating chronic disease states
Physical Frailty as Biologic Construct

- Age-related changes in multiple molecular physiological systems provide a platform for vulnerability
- Persists for years before manifesting in clinical signs or symptoms
- Same systems hypothesized to impact resiliency to stressors
Complex Pathway to Frailty and Adverse Outcomes in Human Subjects

Potential Triggers
- Molecular Aging
- Mitochondrial decline
- DNA Methylation
- Apop/Necroptosis
- ↑ Senescent Cells
- ↑ Altered autophagy
- Genetic Variation
- Environment
- Diseases
- Depression
- Cognitive Decline
- Cancer
- Chronic Infection
- Cardiovascular
- Diabetes/Obesity

Physiology
- ↑ Inflammation
- ↑ HPA Axis
- ↑ Sympathetic nervous system
- ↑ Angiotensin system action
- ↓ Energy production
- • Altered Anabolic Hormones

Clinically Apparent
- Weakness
- Fatigue
- Weight loss
- Slowness

Outcomes
- Dependence
- Disability
- Chronic Diseases
- Cognitive Decline
- Mortality

Walston J, 2016
Clinically Apparent vs. Invisible

Molecular and Cellular Changes
- Mitochondrial dysfunction
- Stem cell exhaustion
- Dynamic physical property declines
- Epigenetic alterations
- Renin angiotensin system

Altered Energy Metabolism & Endocrine Systems
- Altered stress response systems
- Low DHEA-S
- Low IFG-1
- Glucose intolerance
- HPA axis

Immune/Inflammation
- Fatigue
- Increased clotting factors
- Anemia

Clinically Apparent
- Weakness
- Low activity
- Slow gait
- Fatigue
- Weight loss
- Mild cognitive impairment

Low albumin & cholesterol

Low activity
- Fatigue
- Increased clotting factors

Low DHEA-S
- Fatigue
- Glucose intolerance

Low IFG-1
- Glucose intolerance

Fatigue
- Increased clotting factors

Anemia
- HPA axis

Advanced changes
- Immune/Inflammation
- Ageing
- Mitochondrial dysfunction
- Stem cell exhaustion
- Dynamic physical property declines
- Epigenetic alterations
- Renin angiotensin system
- Low albumin
- Low cholesterol
- Low DHEA-S
- Low IFG-1
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Co-Director, San Antonio Claude D. Pepper Older Americans Independence Center
UT Health San Antonio
Director, San Antonio GRECC
Co-Chair, Clin-STAR Leadership Core
RESOURCES

JOHNS HOPKINS UNIVERSITY
https://frailtyscience.org/
https://coah.jhu.edu/research-programs-and-resources/frailty-and-resiliency/
https://www.johnshopkinssolutions.com/solution/frailty/

Frailty Science - A state-of-the-art online resource for researchers and clinicians on frailty-related science and how it might impact health and wellness for older adults. Our goal is to improve the understanding of how frailty develops, how to best assess it, and how to best treat and prevent frailty-related decline. https://frailtyscience.org/

Frailty Assessment Calculator - A standardized, evidenced-based method to assess frailty across clinical and research settings (free trial and licenses available) https://www.johnshopkinssolutions.com/purchasefrailty/

Geriatric Research Instrument Library (GRIL) - A web-based repository of information and resources about measurement instruments commonly used in gerontological research. Researchers can use GRIL to identify, compare and select instruments for their research investigations. https://www.peppercenter.org/public/gril.cfm

NIA Research Resources - Use the NIA Research Resources database to find NIA-supported scientific resources, datasets, informatics resources, and more. Search by keyword, resource type, or NIA Division or IRP. https://www.nia.nih.gov/research/resources

NIA Clinical Research Study Investigators' Toolbox - This is a web-based informational repository for investigators and staff involved in clinical research. The Toolbox contains templates, sample forms, guidelines, regulations and informational materials to assist investigators in the development and conduct of high-quality clinical research studies. https://www.nia.nih.gov/research/clinical-research-study-investigators-toolbox

Research Algorithms & Statistical Programs (GRASP) - A curated list of statistical analysis programs useful to biostatisticians engaged in studies of human aging. https://www.peppercenter.org/public/grasp.cfm

Recruiting Older Adults into Research (ROAR) Toolkit - This toolkit can be used to encourage older adults and their family caregivers, including underrepresented populations, to consider participating in research. https://www.nia.nih.gov/health/recruiting-older-adults-research-roar-toolkit

Research Fundamentals: Preparing You to Successfully Contribute to Research - Free comprehensive training from PCORI offers different ways to learn about the health research process and be involved in patient-centered outcomes research. https://www.pcori.org/engagement/research-fundamentals
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THANK YOU for joining us and for completing our brief SURVEY

(Survey will appear when you exit the webinar.)