THE TRANSLATION OF FRAILTY SCIENCE TO THE ASSESSMENT AND MANAGEMENT OF OLDER ADULTS

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Outline & Disclosures

- I. What has research taught us about the value of frailty to clinical care?
- II. How do we translate this frailty science into clinical practice?
- III. What might the future frailty assessment and management look like?

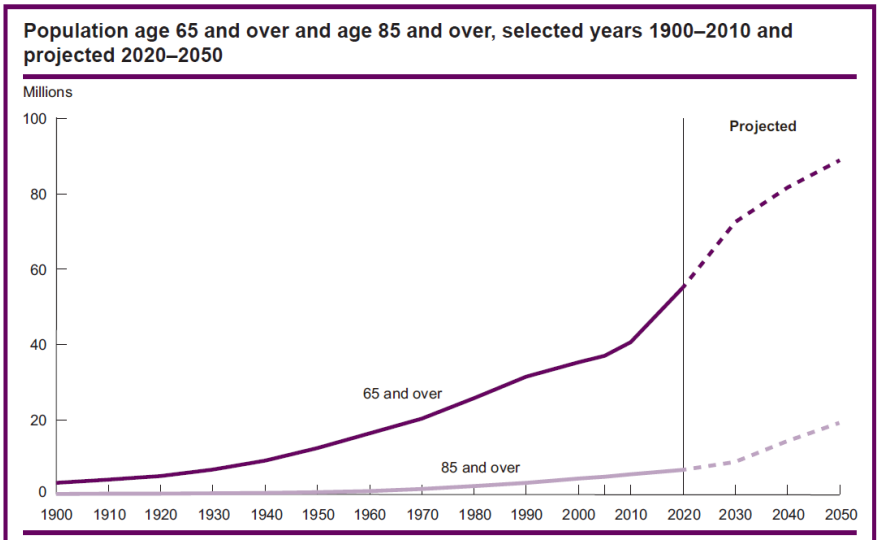
The work that will be presented today has been supported by:

- NIA 1K23AG049106 Huisingh-Scheetz (PI)
- NIA R01AG048511 Waite(PI)
- NIA R01AG04353 Waite(PI)

I. What has research taught us about frailty?

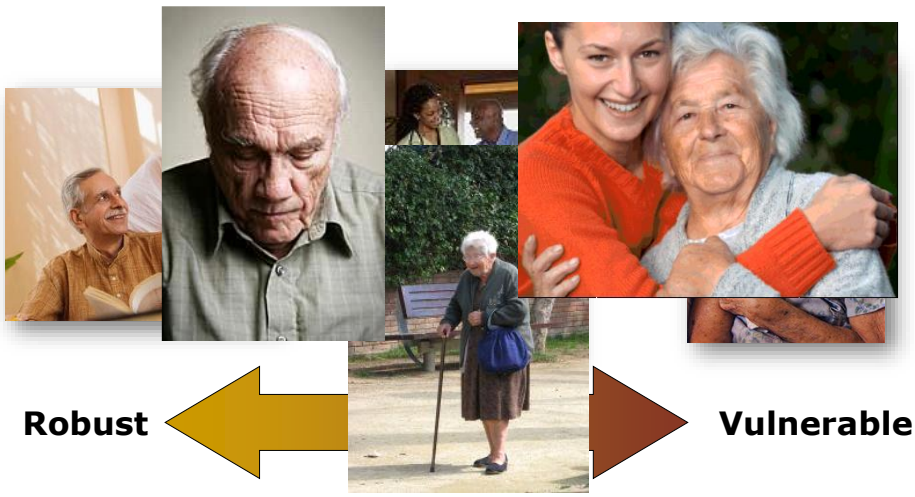
Esther

- 82 yo Female, Multiple falls, “tripped” on things.
- **PMH**: Osteopenia, glaucoma, HTN.
- **Soc Hx:** Widowed. Former smoker. No ETOH.
- **Meds**: 6 (BZD)
- **ROS**: Denied chest pain, SOB, palpitations. No loss of consciousness, no fractures.
- **PE**: Well groomed, no distress. HEENT: no nystagmus, ears normal, no sinus tenderness. CV, Lung, Abd exams normal. Neuro: CNs intact, romberg negative, no tremor. Extremities without edema.



Adapted from: "Older Americans 2012: Key Indicators of Well-Being," Federal Inter-Agency Forum on Aging-Related Statistics: http://agingstats.gov/agingstatsdotnet/Main_Site/Data/2012_Documents/Docs/EntireChartbook.pdf

80 Year Old Adults…



Trends in Survivorship Variability by Age

FIGURE 4a Trends in average age-specific standard deviations of the mortality distribution for females across countries, 1900–2006

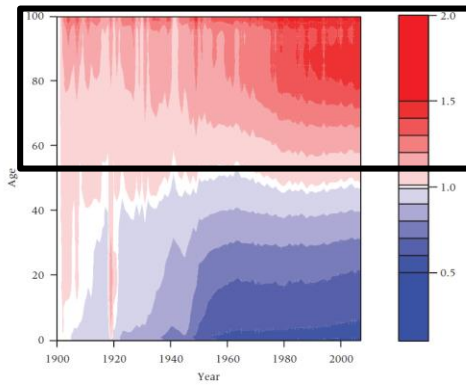
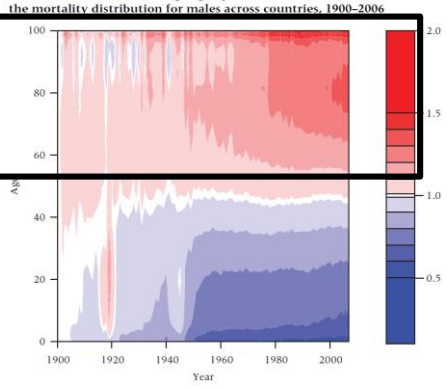
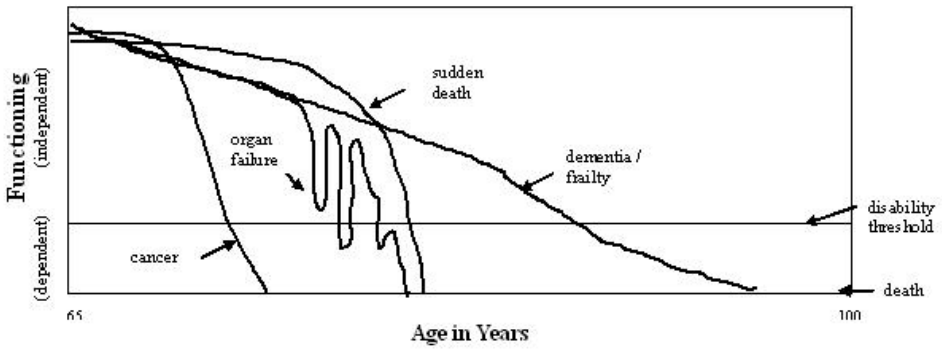


FIGURE 4b Trends in average age-specific standard deviations of the mortality distribution for males across countries, 1900–2006



Engelman et al. Implications for Increased Survivorship for Mortality Variation in Aging Populations. Population and Development Review. 36(3):511-539 (September 2010).

Potential Aging Trajectories



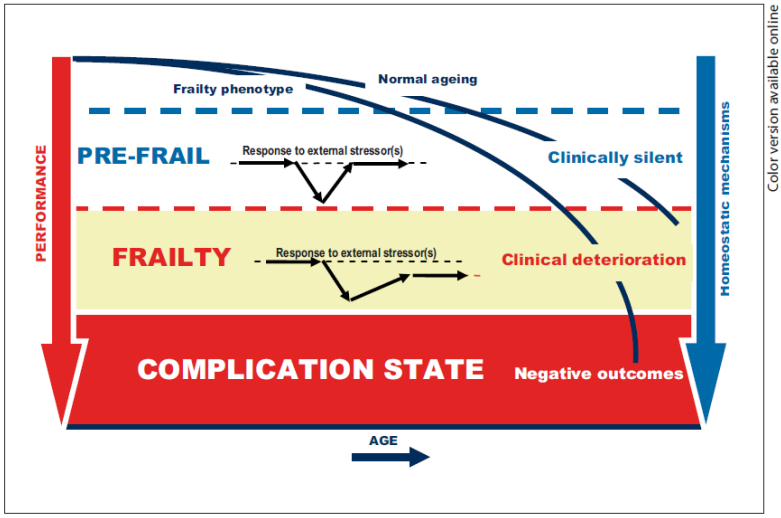
U.S. Department of Health and Human Services. A FRAMEWORK FOR IDENTIFYING HIGH-IMPACT INTERVENTIONS TO PROMOTE REDUCTIONS IN LATE-LIFE DISABILITY. VICKI A. FREEDMAN, NANCY HODGSON, JOANNE LYNN, BRENDA SPILLMAN, TIMOTHY WAIDMANN, ANNE WILKINSON, AND DOUGLAS A. WOLF. PROJECT TEAM. SEPTEMBER 27, 2006. PDF Version (90 PDF pages).

Health Status for Older Adults?

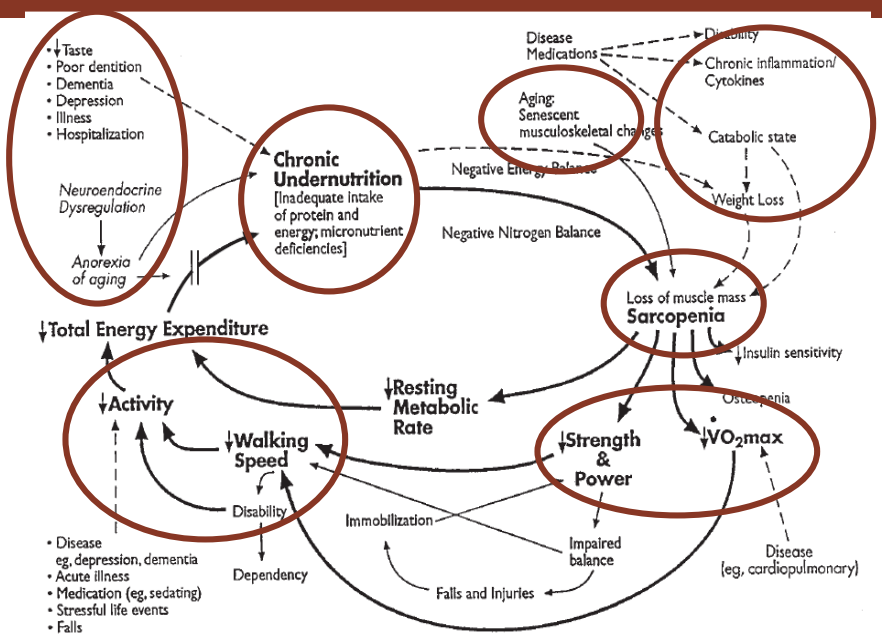
Age-related physiology breakdown

- Multisystem dysregulation
- ↓ Physiologic complexity
- ↓ Energetics and reserve
- ↓ Homeostatic capability

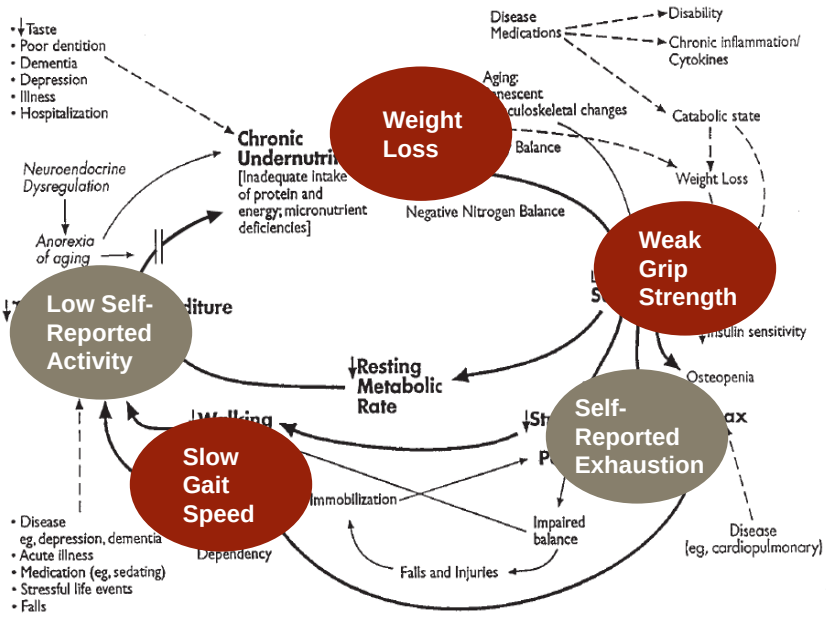
Frailty



- Frailty Syndrome: A Tranisitional State in a Dynamic Process.Gerontology 2009: 55:539-549



Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-56. Epub 2001/03/17. PubMed PMID: 11253156.



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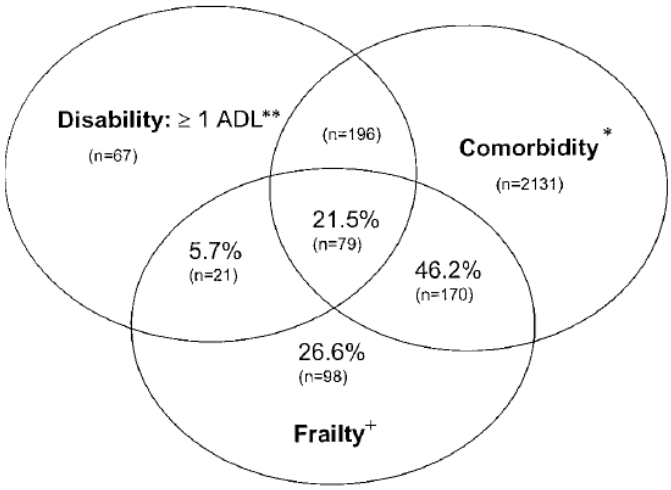
Frailty vs. Disability vs. Comorbidity



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Frailty and Biomarkers

- **inflammatory markers (CRP, IL-6)**
- **osteopenia/porosis**
- **CRI**
- **insulin resistance**
- **cortisol**
- **blood clotting markers**

- **androgens/estrogens**
- **DHEA-S**
- **IGF-1**
- **Micronutrients (total carotenoids, retinol, Vit D, Vit B6, folate)**
- **diurnal cortisol variation**
- **immune function**
- **hemoglobin**
- **heart rate variability**

(Hubbard 2009 J Cell Mol Med; Travison 2011 J Clin Endocrinol Metab.; Michelon 2006 J Gerontol A Biol Sci Med Sci.; Frisoli 2011 Bone.; Shlipak 2004; Collerton 2012 Mech Aging Dev, Mitnisky 2015 BMC, Johar 2014 J Clin Endocrinol Metab, Parvaneh 2015 Gerontology)

	Clinical Outcomes
Frailty	Re-Hospitalization
	Procedural morbidity and mortality
	Disability
	Falls
	Fracture
	Institutionalization
	Delayed recovery from acute illness
	High healthcare utilization
	Iatrogenesis
	Medication side effects
	High-Risk Biomarkers

Mortality

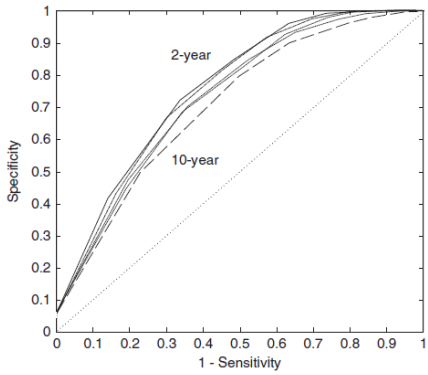


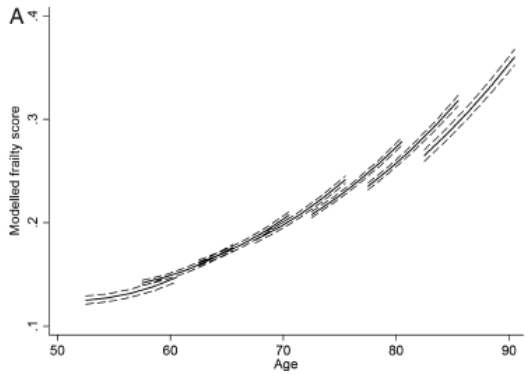
Figure 3. The receiver operating characteristic (ROC) curves for the Frailty Index in the prediction of individual death within various periods of followup (2, 4, 6, 8, and 10 years). The values show the areas under the ROC curve (AUC). The solid and thicker dashed lines show the ROC curves for individual death prediction of 2 years (AUC = 0.78) and 10 years (AUC = 0.72), respectively; thinner dashed lines represent ROC curves for 8 (AUC = 0.73), 6 (AUC = 0.75), and 4 (AUC = 0.76) years. The diagonal indicates AUC = 0.5.

Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. J Am Geriatr Soc 2010;58:681-7

Frailty Course

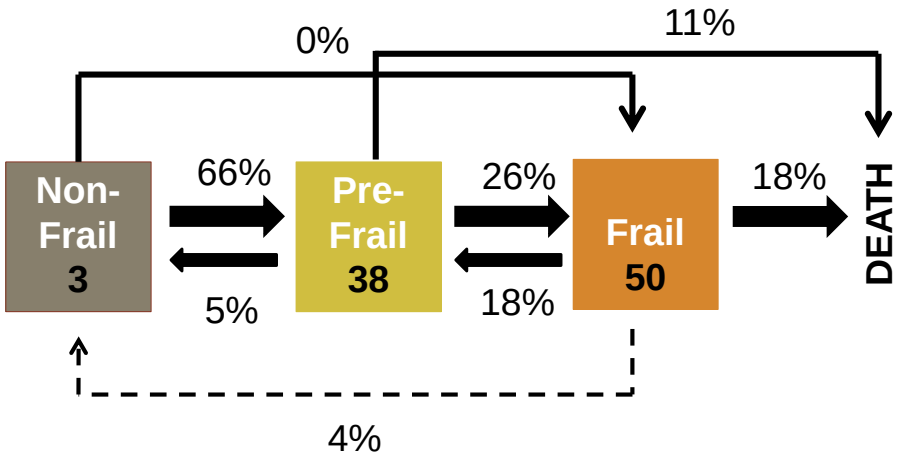
- Chronic
- Progressive

(5-yr follow-up intervals)



Marshall A, Nazroo J, Tampubolon G, Vanhoutte B. Cohort differences in the levels and trajectories of frailty among older people in England. J Epidemiol Community Health 2015;69:316-21

Short-Term Frailty Course: 1 Year Frailty Transitions



Frailty may be modifiable.

Managing Frailty: Interventional RCTs

Treatment	Effects on frailty	Considerations
Exercise Various (resistance/strength, aerobic)	↑↑↑	Sustainability
Nutrition (protein, caloric, amino acids)	↑	Best paired with exercise
Pharmacotherapy Synbiotics, Estrogen + progesterone, Atamestane, DHEA, Topical testosterone, SARM, rhGH	⊘	Side Effects
Multidimensional / Home-based programs	↑↑	Labor-intensive

On-Going Trials
Gherlin, allopurinol, Bimagrumab, BYM338, Vitamin D….

Bibas L, Levi M, Bendayan M, Mullie L, Forman DE, Afilalo J. Therapeutic interventions for frail elderly patients: part I. Published randomized trials. Prog Cardiovasc Dis 2014;57:134-43. Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392-7. Bendayan M, Bendayan M, Bibas L, Levi M, Mullie L, Forman DE, Afilalo J. Therapeutic interventions for frail elderly patients: part II. Ongoing and unpublished randomized trials. Prog Cardiovasc Dis 2014;57:144-51.

Screening Recommendations

All adults:

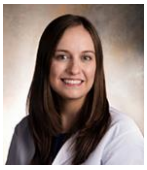
- ≥ 70 years
- ≥ 5% weight loss in prior year

Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392-7.

II. How do we extend frailty science into clinical practice?

Successful Aging and Frailty Evaluation (SAFE) Clinic

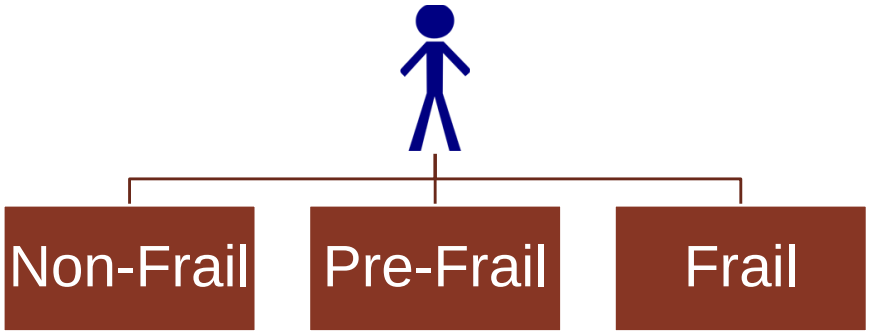
- *UNIQUE* model supporting care for frail and vulnerable patients
  - 1st in U.S.
  - 2nd Worldwide
- Consultative and longitudinal care
- Evidence-based comprehensive geriatric and frailty assessment
  - Inter-professional team: MD, APN, SW, nursing
  - Treatment plan tailored to frailty status


SAFE Clinic Assessment

Domain	Tool
Frailty	Phenotypic Frailty Criteria
Disability and Vulnerability	Vulnerable Elders Survey-13
Cognition	Montreal Cognitive Assessment
Physical Function	Short Physical Performance Battery
Depression Screen	Patient Health Questionnaire-2
Multimorbidity	Charlson Comorbidity Index / Chart Review
Pain	Pain Thermometer
Medications	Focused History
Hospitalization/Emergency Room Visits	
Social & Financial Support	
Home Service Utilization	
Geriatric Review of Systems and Syndromes	

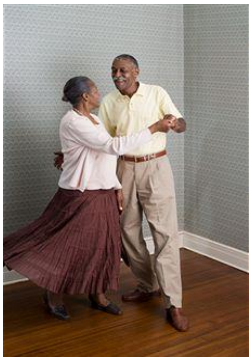
Framing the care plan



Treatment Goals

- Improve core manifestations of **frailty**:
- Exclude modifiable **precipitating factors**
- Minimize **consequences** of vulnerability
- Provide **individualized** education, resources

Tailored Care Plans



Non-Frail: VIGOROUS

- Physical activity routine: Moderate-Vigorous, Strength, Balance, Flexibility
- Healthy eating
- Maintain socialization / social engagement
- Social & functional support planning
- Preventive evaluations
- Vision / Hearing Screening
- Tighter control of medical conditions (HTN, DM)
- Smoking cessation
- Advance Care Planning

Tailored Care Plans

Pre-frail: OPPORTUNITY

- Physical activity routine: strength and balance
- Pre-habilitation for planned interventions
- Fall prevention and home safety
- Polypharmacy reduction
- Nutrition assessment, boost protein intake
- Driving safety
- Social & functional support needs
- Monitor for mood , cognitive , disability changes
- Support sleep
- Regular medical follow-up
- Smoking cessation
- Advance Care Planning
- Anticipate future social support needs

Tailored Care Plans

Frail: FRAGILE

- Hospitalization and invasive intervention avoidance
- Fall prevention and home safety
- Review benefits/burdens carefully for all treatments in light of limited remaining life expectancy
- Advance Care Planning
- Polypharmacy reduction: # meds, # doses, high SEs.
- Anticipate and manage caregiver stress
- Physical activity routine: sedentary behavior reduction, strength, balance, flexibility
- Nutritional assessment, boost protein intake
- Family / Patient Education
- Planning For Care Transitions
- Frequent Outpatient Monitoring

Esther

- 82 yo Female, Multiple falls, "tripped" on things. Now afraid of falling.
- **PMH**: Osteopenia, glaucoma, HTN.
- **Meds**: 6 (BZD)
- **Soc Hx:** Widowed. Former smoker. No ETOH. Lives alone. Children live out of town. Homemaker 2 days / month.
- **ROS**: Denied chest pain, SOB, palpitations. No loss of consciousness, no fractures. (+) impaired sleep, unintentional wt loss in last year (-) Exhaustion.
- **Fxnl Hx**: Declining physical activity, but still doing a few household chores daily. Early IADL difficulty. – getting in/out of tub, heavy house cleaning, lifting. Wears bifocals. "Carries" her husband's old cane when outside.
- **PE**: Well groomed, no distress. HEENT: no nystagmus, ears normal, no sinus tenderness. CV, Lung, Abd exams normal. Neuro: CNs intact, romberg negative, no tremor. Extremities without edema. (-) Orthostatics. Gait: Brisk, Balance: Tandem pose difficult, Grip strength: Weak grip strength, Cognition: MOCA 18/30 (calculation, naming, delayed recall)

Esther

82 year old female

- **Pre-frailty:** Increase home exercise (strength → endurance), PT/OT with focus on balance, small/frequent meals, increase protein
- **Falls:** DEXA, better use of cane, single vision lenses, safety educ, look for Vit D deficiency, shower bar / non-slip tub mat
- **Polypharmacy:** Minimize BZD
- **Advance Planning:** Update HCPOA, POLST, financial POA
- **Cognitive impairment**: rule out reversible causes, engage family in finance and medication oversight, consider pharmacotherapy, sleep hygiene / diary.

III. What might future frailty assessments look like?

Frailty is an essential marker of older adult health.

- **Challenging to implement in clinical practice**.
  - Self-reported items including physical activity are inherently biased.
  - Cognitive impairment makes recall challenging.
  - Time consuming.
- **Question: Can we use accelerometry to assess frailty and predict frailty-related outcomes in the free-living environment?**



What is accelerometry?

- Accelerometer → Wearable devices: hip, wrist, ankle, thigh, chest…
- Continuously collect acceleration data, 3-7 days, data recorded every second or more.
- Traditionally, data are summarized into a single measure for study.


Hip


Wrist


Thigh


Chest

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Accelerometry provides high resolution logs of mobility, a central component of frailty measurement.

Forest View

24 hours of data

1 hour of data

Tree View

1-mintue of data

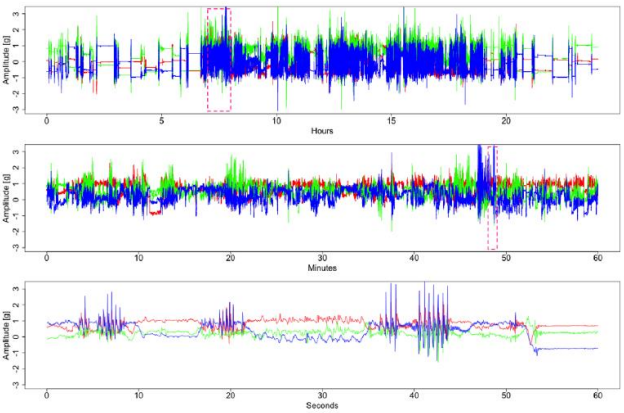

Fig. 1 Accelerometry data from three orthogonal axes of an accelerometer located on the left wrist. Each axis data is shown in a different color. The top panel displays 24 h of data collected between 12 a.m. and 12 a.m. The middle panel displays a 1-h interval from 8:40 a.m. to 9:40 a.m. (indicated in the top panel as a dashed-line rectangle). The bottom panel displays a 1-min interval from 8:51 a.m. to 8:52 a.m. marked as a dashed-line rectangle in the middle panel. The signal was acquired at a sampling frequency of $f_s = 80$Hz (Color figure online)

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Karas M, Bai J, Straczkiewicz M, et al. Accelerometry data in health research: challenges and opportunities. *Stat Biosci.* 2019;11(2):210-237.

Traditional Accelerometry Measures

- **Average % time spent in sedentary, light, moderate-vigorous activity**
  - Proportion of time spent above a count threshold, specific to device, location, population, person
- **Total activity**
  - Sum of activity counts per day
- **Bout length** (eg, 30 minute sedentary bouts)
  - Various measures including average or total number of bouts of activity meeting certain count threshold criteria

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Average accelerometry-measured activity is significantly related to older adult health.

Accelerometry + Covariates = Health Outcome

- **3-Meter Gait Speed (p<0.001)**
- **Chair Stands (p=0.002)**
- **Self-Rated Physical Health (p<0.001)**
- **Self-Rated Mental Health (p=0.009)**
- **Diastolic Blood Pressure (p=0.01)**
- **Hgb A1c (p=0.01)**
- **C-Reactive Protein (p=0.02)**
- **Heart Problems (p=0.01)**
- **Diabetes (p<0.001)**
- **Any ADL Difficulty (p=0.04)**
- **Any IADL Difficulty (p=0.02)**

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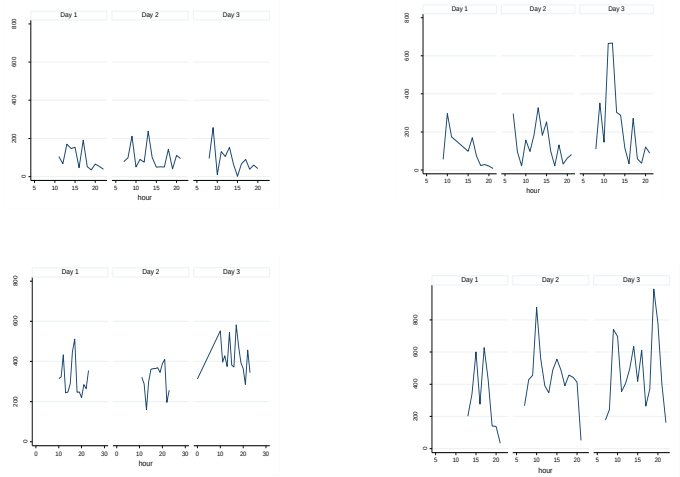
Huisingh-Scheetz M, J of Gerontology: Series B Psychological Sciences and Social Science 2014.
Huisingh-Scheetz M, Archives of Gerontology and Geriatrics., 2016.
Huisingh-Scheetz M, J of the Amer Geriatrics Society, 2016

Summarizing accelerometry data "looses" a lot of information.

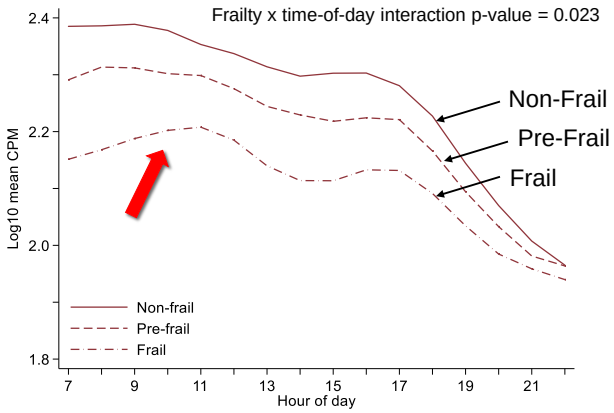


Mean Hourly Counts Per Minute Across Hour of Day for Four Older Adults

Newer Accelerometry Measures

- **Wavelet Analysis**
  - Comparison of a 'prototype signal' to all accelerometry signals to detect specific activities (eg, fall)
    - (Palmerini 2015 A Wavelet-Based Approach to Fall Detection)
- **Functional Data Analysis**
  - Assess diurnal activity patterns as regression outcome
    - (Goldsmith 2017 New Insights into Activity Patterns in Children)
- **Sustained Harmonic Walking**
  - Detection of 10 s periods of walking, not device specific, harmonic is individualized
    - (Urbanek 2015 Prediction of sustained harmonic walking in the free-living environment using raw accelerometry data)
- **Machine Learning**

Timing: Frailty can be identified, in part, by reduced accelerometry-measured activity, particularly in the morning.



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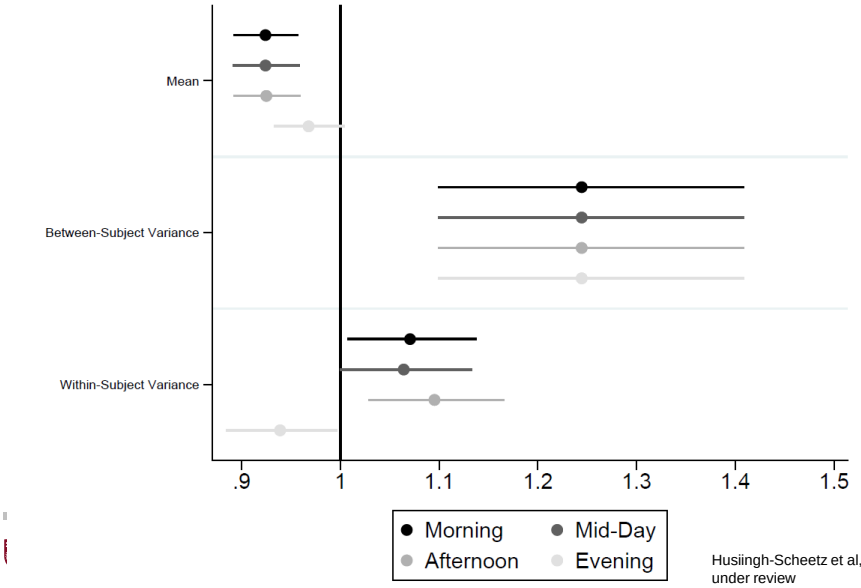
Huisingh-Scheetz M 2018 J of Gerontology Med Sci. (*Editor's Choice Article), 2018.*

Variance: Frail adults have more variable activity patterns across the day



Husiingh-Scheetz et al, 2020, under review

Gait Characteristics: Left wrist accelerometry output during walk

Sustained Harmonic Walking

↓

Amplitude

Periodicity

Stride-to-stride variability

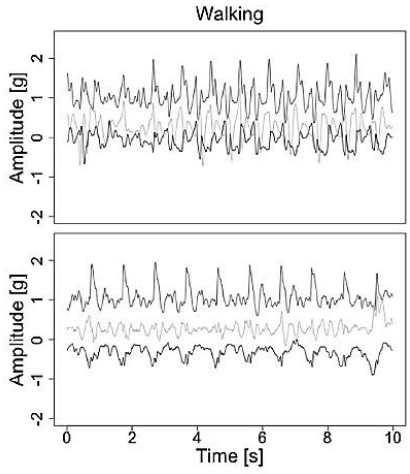


Figure from: Karas M, Bai J, Straczkiewicz M, *et al.* Accelerometry data in health research: challenges and opportunities. *Stat Biosci.* 2019;**11**: 210-237.
Urbanek JK, Zipunnikov V, Harris T, *et al.* Prediction of sustained harmonic walking in the free-living environment using raw accelerometry data. *Physiol Meas.* 2018;**39**: 02NT02.
Urbanek JK, Zipunnikov V, Harris T, Crainiceanu C, Harezlak J, Glynn NW. Validation of Gait Characteristics Extracted From Raw Accelerometry During Walking Against Measures of Physical Function, Mobility, Fatigability, and Fitness. *J Gerontol A Biol Sci Med Sci.* 2018;**73**: 676-681.

Active-to-Sedentary Transition Probability is associated with physical function.

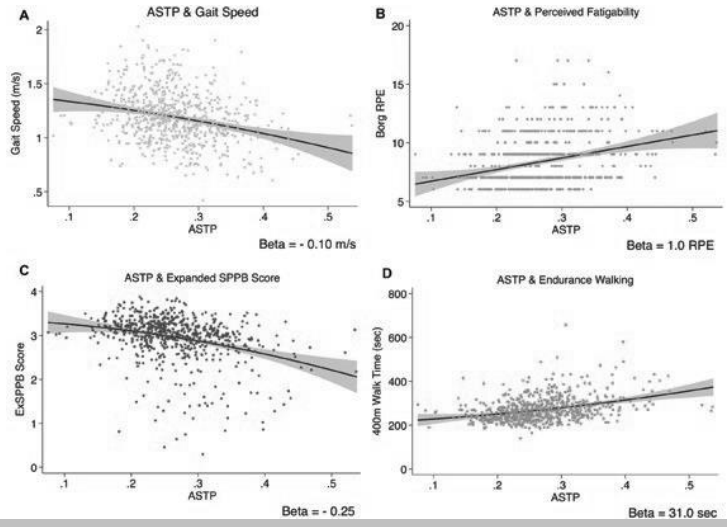


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Figure from: Schrack JA, Kuo PL, Wanigatunga AA, *et al.* Active-to-Sedentary Behavior Transitions, Fatigability, and Physical Functioning in Older Adults. *J Gerontol A Biol Sci Med Sci*. 2019;**74**: 560-567.

Time to perform a 3-meter usual walk and a 5-repeated chair stands test

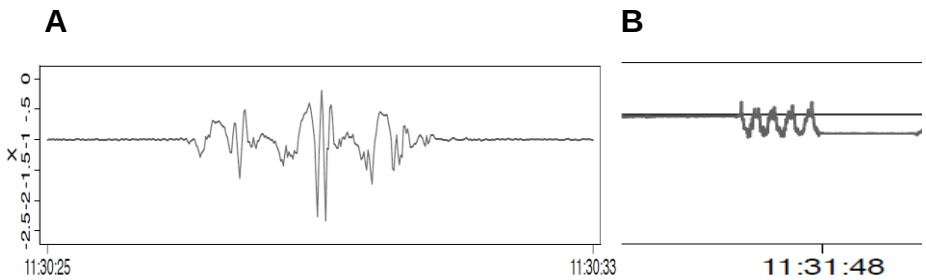

Figure. X-axis GENEActiv output worn adhered to the right thigh during self-administration of 3-meter timed walk (A) and 5 repeated chair stands (B). Five-second pauses in activity prior to and following the tests allow accurate identification of start and stop times. Calculation of the time required to complete these activities allows test scoring using previously established scales.

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III. What might future frailty management look like?

Engage

Promoting long-term mobility & socialization among older adults.

Photo by rawpixel on Unsplash

Website & Mobile App

Smart Voice

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EngAGE: Three access portals

Website

Web App

Smart Voice

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orbita

Set-Up

Older Adults

Caregivers

Intervention for Older Adults

Mon / Wed / Friday

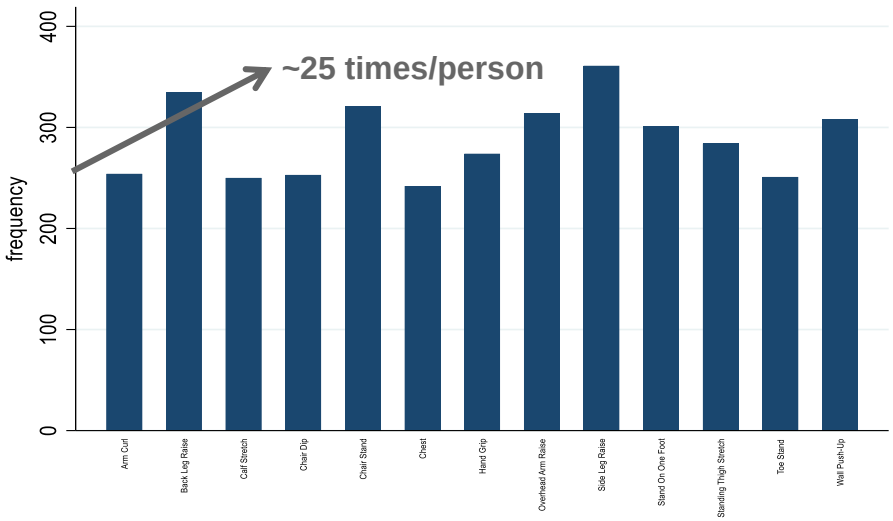
- Warm up
- Hand grip
- Arm curl
- Chair dip
- Toe stand
- Chest stretch
- Calf stretch

Tue / Thu / Sat / Sun

- Warm up
- Side leg raise
- Back leg raise
- Chair stand
- Overhead arm raise
- Wall push-up
- Stand on one foot
- Standing thigh stretch

Go4Life

Cumulative Exercise Completion Over 12 Weeks



Frailty Measures (unadjusted)

	Older Adults (n=10)		
	Pre-Intervention	**Post-Intervention**	**% Improved**
Grip Strength	26.3 kg	27.6 kg	70%
15-Foot Usual Walk Time (Average of 3 attempts)*	4.2 s	4.2 s	56%
8-Foot Usual Walk Time (Faster of 2 attempts)*	2.1 s	2.0 s	56%
5-Repeated Chair Stands*	12.0 s	9.7 s	89%
Semi-Tandem Balance*	10 s	10 s	No change
Tandem Balance*	5.9 s	6.5 s	56%

*Denominator = 9 (1 wheelchair-bound participant)

Take Home Points

- Older adulthood marked by high variability of health.
- Research has helped us better understand:
  - Frailty → aging physiology.
  - Frailty → assessment and management
- Translating research into clinical practice can improve clinical care AND inform clinical questions.
- The future of the frailty assessment and management is to be determined! Ambulatory monitoring? Voice Assistant care management?

Questions?