The Epidemiology and Prevention of Frailty in Older Women

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Fast facts

- Average 80 y.o. 3-4 chronic diseases + 3 conditions (e.g. sleep, pain, allergy)

- Among 70+y.o. 60% take 5-9 medications; 20% take 10+ (Slone Survey)

- 65+ y.o. with ≥ 2 conditions →~ 80% Medicare costs
Universal, cross disease outcomes

- What is a universal outcome?
  - Health outcomes that are of importance to people
  - Outcomes on which ALL disease-specific outcomes exert their effect

- Common outcome metric for all diseases
- Useful for comparing treatments
- Targets for prevention of loss of independence
Universal, cross disease outcomes

- **Domains:**
  - Symptoms/impairments (e.g. dyspnea, pain, mobility, cognition, vision)
  - Function/disability (e.g. ADLs)
  - Survival
Positive Aging Model
(Adapted from Seeman 2001)

Demographic Characteristics
- Age
- Ethnicity
- Gender
- Socioeconomic Status

Personal Characteristics
- Efficacy
- Mastery
- Self-esteem
- Optimism
- Purpose in Life

Social Relationships
- e.g. Network Structure & Support

Social Challenges/Stressors
- Material
- Work
- Housing
- Relationships
- Neighborhood

Health Behavior Practices
- e.g. Physical activity participation and diet quality

Macro-Level Physical and Sociocultural Factors

Allostatic Resources/Physiologic Adaptive Capacity
- SAM-SNS/PNS
- HPA Axis

Physiologic Reserve Indicators
- (Newman*)
  - Immune
  - Metabolic
  - Hematologic
  - Cardiovascular
  - Thermoregulatory

Positive Aging
- * Perceived Health
- * Physiologic and Cognitive Function
  - Social Engagement
  - Maintaining Mobility
  - Avoiding frailty

Health Services Outcomes
- Years of independent living
- Number of hospitalizations
- Healthcare costs
- Survival/mortality

** (After MC Ewen Allostatic Load Concept)
Relationships among Frailty, Comorbidity and Disability

- Frailty: 1419 (21.4%)
- Comorbidity: 4822 (72.9%)
- Disability (≥1 ADL): 53 (0.8%)

17,303 with no disability, comorbidity, or frailty

16,367 w/ no disability, comorbidity, or frailty
Frailty Classification at Baseline and Year 3*

*Participants not classified as frail at baseline
# Odds Ratios/Hazards Ratios Relating Frailty at Baseline to Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Frail</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td><a href="#"><strong>Outcome</strong></a></td>
<td><strong>OR</strong></td>
<td><strong>95% CI</strong></td>
<td><strong>95% CI</strong></td>
</tr>
<tr>
<td>ADL Disability at Year 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partially adjusted</td>
<td>5.44</td>
<td>(4.54, 6.52)</td>
<td></td>
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<tr>
<td>Fully adjusted</td>
<td>3.13</td>
<td>(2.15, 4.56)</td>
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<tr>
<td>Avg # Hospitalizations during Follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ref=no hospitalizations)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partially adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.5 hosp./year</td>
<td>1.98</td>
<td>(1.85, 2.11)</td>
<td></td>
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<tr>
<td>&gt;0.5 hosp./year</td>
<td>4.21</td>
<td>(3.84, 4.63)</td>
<td></td>
</tr>
<tr>
<td>Fully adjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.5 hosp./year</td>
<td>1.46</td>
<td>(1.27, 1.68)</td>
<td></td>
</tr>
<tr>
<td>&gt;0.5 hosp./year</td>
<td>1.88</td>
<td>(1.53, 2.30)</td>
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<tr>
<td>Hip Fracture</td>
<td></td>
<td></td>
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<tr>
<td>Partially adjusted</td>
<td>1.74</td>
<td>(1.37, 2.22)</td>
<td></td>
</tr>
<tr>
<td>Fully adjusted</td>
<td>2.04</td>
<td>(1.24, 3.36)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partially adjusted</td>
<td>2.45</td>
<td>(2.21, 2.72)</td>
<td></td>
</tr>
<tr>
<td>Fully adjusted</td>
<td>1.83</td>
<td>(1.47, 2.30)</td>
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</table>
Aims of current R01 on Frailty

Study the inflammatory pathway and incident frailty among older women in WHI

- Drugs (statins, ace-inhibitors)
- Biomarkers (IL-6, CRP, TPA, D-dimer, Factor VIII, fibrinogen)
- Inflammation genes (1536 SNPs)
Inflammation and Frailty

Background

- Cross-sectional studies had shown associations between markers of coagulation, fibrinolysis and inflammation and disability or frailty.
- Mouse models of pro-inflammatory pathway activation due to deficiency of IL-10 showed development of muscle weakness and high IL-6 levels compared to control mice.
- Frail older adults were at increased risk of idiopathic VTE in CHS.
Table 3. Risk of frailty comparing levels of D-dimer and/or t-PA in the upper range of the distribution

<table>
<thead>
<tr>
<th>Biomarker Quartile</th>
<th>Model 1 Odds Ratio (95% CI)</th>
<th>Model 2 Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neither D-dimer nor t-PA in the upper quartile</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Only t-PA in the upper quartile</td>
<td>1.38 (1.05, 1.82)</td>
<td>1.29 (0.94, 1.76)</td>
</tr>
<tr>
<td>Only D-dimer in the upper quartile</td>
<td>1.30 (0.97, 1.74)</td>
<td>1.38 (0.99, 1.91)</td>
</tr>
<tr>
<td>Both D-dimer and t-PA in the upper quartile</td>
<td>1.90 (1.17, 3.08)</td>
<td>2.20 (1.29, 3.75)</td>
</tr>
<tr>
<td>Overall P-value (3-df test)</td>
<td>0.02</td>
<td>0.02</td>
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</tbody>
</table>

Model 1 adjusted for hypertension, hormone use, and BMI. Model 2 adjusted for model 1 covariates + education, alcohol consumption, hypertension, arthritis, and smoking.
Frailty: Adjusted minimum p-values for Inflammatory Pathway Genotypes

Adjusted Pmin

log2Beta(A,D,or R)

Colors indicate whether the adjusted minimum p value corresponds to the additive, dominant or recessive models. SNPs with excessive effect sizes, due to very small MAF, are not shown.
Evidence for Establishing Optimum Protein Intake in Older Adults

Jeannette Beasley, PhD, MPH, RD
Staff Scientist
Fred Hutchinson Cancer Research Center
Risk of Frailty by Quintile of Protein, (%kcal)
Associations between Dietary Protein and Lean Body Mass – Health ABC Study

*Adjusted for age, sex, race, study site, total energy intake, baseline LM, height, smoking, alcohol use, physical activity, oral steroid use, prevalent disease (diabetes, ischemic heart disease, congestive heart failure, cerebrovascular disease, lung disease, cancer), and interim hospitalizations.

Houston, D. K et al. Am J Clin Nutr 2008;87:150-155

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Evidence from Clinical Studies

- Nitrogen balance studies suggest RDA (0.8 g/kg) inadequate to maintain nitrogen balance in women >70 (Morse)

- Mid-thigh muscle area decreased among adults aged 55-77 years after 14-weeks on 0.8 g/kg protein diet (Campbell)

Association between dietary protein and protein synthesis

Paddon-Jones et al. JADA: 2009: 109 (9) pp 1582-1586
The End