Aging and Physical Function

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WHI Steering Committee, May 5, 2011
Today’s Discussion

- Goals of Aging Research
- Areas of Interest of High Potential Relevance / Interest to WHI
  - Trajectories
  - Multimorbidity
  - Successful Aging
The Limits of Longevity

- Longest life: 122 yrs
- Oldest living person: 114 yrs
- Only 2 have broken 120 yrs
- Men take just 5 of the top 50 spots

Jean Calment 1875-1997
Expression of a physical or mental limitation in a social context

The gap between a person’s capabilities and the demands of the environment

IOM, 1991
Activities of Daily Living

- Eating
- Dressing
- Bathing
- Transferring from bed to chair
- Using the toilet

Instrumental ADLs

- Preparing meals
- Shopping
- Housekeeping
- Managing money
- Taking medications
- Using the telephone
The Shape of Disability

Functional Independence → Limitation → Disability

- Independence
- Aging, Disease
- Successful compensation
- Difficulty in task performance. Compensation partly successful
- 1 ADL dependence
- 1-2 ADLs dependence
- ≥3 ADLs institutionalization

Time
Specific Concerns of Aging Research

- **Outcomes**
  - Falls, delerium, dementia, incontinence, syncope, vision problems, mobility problems, osteoporosis

- **Signs, Symptoms and Complaints**
  - Frailty, unexplained weight loss, sleep problems, slowing, pain, fatigue, weakness
<table>
<thead>
<tr>
<th>Condition</th>
<th>PAR % 65-74</th>
<th>PAR % 75-84</th>
<th>PAR % ≥ 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot Problems</td>
<td>33.8</td>
<td>24.8</td>
<td>15.7</td>
</tr>
<tr>
<td>Arthritis</td>
<td>18.9</td>
<td>21.3</td>
<td>7.9</td>
</tr>
<tr>
<td>Cognitive Imp</td>
<td>10.9</td>
<td>9.9</td>
<td>21.3</td>
</tr>
<tr>
<td>Heart Problems</td>
<td>24.1</td>
<td>7.9</td>
<td>7.8</td>
</tr>
</tbody>
</table>

Age-related changes in physiologic systems
Physiologic Aging and Functional Health

- Function
- Reserve
- Rate of Aging
- Limitation
- Disability
- Death

Age

[Diagram showing the relationship between age, reserve, rate of aging, limitation, disability, and death.]
Sarcopenia – *The age-related loss in skeletal muscle mass.*

*Sarco = flesh, penia = poverty*

- Muscle mass is lost progressively after mid-adulthood.
- Muscle mass correlates with strength.
- Low strength is a hallmark of disability.
- Many disabling conditions are associated with accelerated lean mass loss.
Adjusted Lean Mass Loss by Levels of Energy-Adjusted Total Protein Intake

N = 2,066  Houston DK et al AJCN 2008
24,417 women 65-79

Diet Measure – FFQ

Intake Calibrated based on Nitrogen Excretion & DLW

3 years of follow-up

Frailty: 3 of 5
- Exhaustion
- Weight Loss
- ↓ Physical Function
- ↓ Physical Activity
- (Weakness)

<table>
<thead>
<tr>
<th>Frailty Risk, per 20% increase in intake (Odds ratio &amp; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein intake, %kcal/d</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Protein intake, g/kg body weight/d</td>
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</table>

A 20% higher protein intake was associated with between a 23-35% lower risk of frailty onset.

Beasley JM et al. JAGS 58:1063-71, 2010
### RR of Incident Mobility Limitations in Later Life by Weight from Age 50: The Health ABC Study

<table>
<thead>
<tr>
<th>Weight Change</th>
<th>Women RR (95% CI)</th>
<th>Men RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5% Loss</td>
<td>1.30 (1.00-1.69)</td>
<td>1.43 (1.12-1.83)</td>
</tr>
<tr>
<td>±5%</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>&gt;5 - 10% Gain</td>
<td>1.08 (0.83-1.39)</td>
<td>1.16 (0.88-1.54)</td>
</tr>
<tr>
<td>&gt;10 - 20% Gain</td>
<td>1.22 (0.96-1.54)</td>
<td>1.48 (1.13-1.94)</td>
</tr>
<tr>
<td>&gt;20% Gain</td>
<td>2.24 (1.78-2.81)</td>
<td>2.08 (1.54-2.81)</td>
</tr>
</tbody>
</table>

Adjusted for: age, race, field site, education, smoking status, drinking status, physical activity, and self-rated health

Houston DK et al. Am J Epidemiol 2009;169:927
Race and Gender and the Onset of Mobility Limitation

The Health ABC Study

- White Men
- White Women
- Black Men
- Black Women

- p-value (gender) = 0.0003
- p-value (race) < 0.0001
- p-value (race X gender) < 0.0001

Follow-Up Days

Mobility Limitation Free
The death rate decreases 12% for every 0.1 m/s increase in gait speed.
Sub-Clinical Disease and Frailty
Among those without prior CVD history
Cardiovascular Health Study*

Not Frail
Intermediate
Frail

EKG ABI Cerebral MRI

Disease Prevalence

Newman, J Gerontol Series A, 2001
While there is a ‘normal’ loss of physiologic function with age – the pattern of change between individuals is striking.

Mid-life health characteristics determine health, function and disability in old age. Most of this information is from studies of men.

The greater the reserve, the greater the expected delay in disability onset. What, if anything, can slow the rate of decline is unclear but disease processes can accelerate it.
Most older adults have more than one chronic condition. Clinically, the failure to consider these conditions collectively leads to fragmented, burdensome, contradictory and sometimes dangerous care. Epidemiologically, multimorbidity has been considered a nuisance dealt with by adjustment using comorbidity scales of varying sophistication. Conversation is starting in which multimorbidity is an object of study in its own right.
Which chronic diseases and disease combinations are specific to multimorbidity in the elderly?

- German insurance claims data in 2004 – age 65+
- Multimorbidity – at least 3 of a possible 46 chronic diseases w/in a year -- 62% of the sample was multimorbid
- Chronic conditions w/ high and low RR for multimorbidity

**Top 4**
- Renal insufficiency
- Obesity
- Liver Disease
- Chronic cholecystitis

**Bottom 4**
- Hypertension
- Dementias
- Cancers
- Low Vision

Despite positive evidence for the metabolic benefits of weight loss, there is reluctance to recommend weight loss in older adults because it may:

- Exacerbate age-related losses in bone mineral content and skeletal muscle
- Initiate or worsen functional decline
- Unintentional weight loss:
  - Associated with more severe disease or unrecognized health problems
  - Predicts higher hospitalization, disability, and mortality rates
Two studies of randomization to weight-loss and total mortality: Combined Data

<table>
<thead>
<tr>
<th>Study</th>
<th>Group Size</th>
<th>Deaths</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TONE</td>
<td>n=585, 101 deaths</td>
<td>0.82 (0.55-1.22)(^a)</td>
<td></td>
</tr>
<tr>
<td>ADAPT</td>
<td>n=316, 43 deaths</td>
<td>0.49 (0.26-0.93)(^b)</td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>n=901, 144 deaths</td>
<td>0.62 (0.40-0.98)(^c)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) adjusted for age, gender, race, study site, CVD history, DBP, smoking status, randomization to low sodium intervention
\(^b\) adjusted for age, gender, CVD history, randomization to exercise intervention
\(^c\) adjusted for age, gender, race, CVD history, study (TONE or ADAPT)

Shea MK et al. 2010 & Shea MK et al., submitted.
Development of a Physiological Profile of Exceptional Health in Old Age: Observations from Eleanor M. Simonsick, Anne B. Newman, Tamara B. Harris, Stephen B. Kritchevsky, Susan Rubin, and Steven R. Cummings
Procedure

1. Select 20 candidate markers of exceptional health, including measures of physiologic capacity as well as low levels of traditional risk factors

2. Determine those that best discriminate high from average functioning 70-79 year-olds (concurrent validity)

3. Identify those that best predict maintained high function 4 years later (predictive validity)
Odds Ratios* Associated with the “Best” Candidate Markers of Exceptional Health

<table>
<thead>
<tr>
<th>Marker</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSST ≥ 40</td>
<td>2.31</td>
<td>1.95 – 2.72</td>
</tr>
<tr>
<td>400 M &lt; 5:00/5:20 m</td>
<td>2.04</td>
<td>1.68 – 2.46</td>
</tr>
<tr>
<td>5 Chair rises &lt; 12.5 s</td>
<td>1.49</td>
<td>1.26 – 1.77</td>
</tr>
<tr>
<td>Gait speed ≥ 1.25m/s</td>
<td>1.35</td>
<td>1.13 – 1.62</td>
</tr>
<tr>
<td>IL-6 ≤ 1.6 pg/mL</td>
<td>1.32</td>
<td>1.12 – 1.55</td>
</tr>
<tr>
<td>&gt; 60 Finger taps</td>
<td>1.22</td>
<td>1.03 – 1.43</td>
</tr>
</tbody>
</table>

*adjusted for age, sex, and other markers listed
Some Questions for WHI to Consider

1. What should a woman do NOW to minimize her chance of future disability?
   a) What would have the greatest impact?
   b) Is the answer the same for minority women?

2. What predicts trajectories of physiologic/functional parameters in women?

3. What are the patterns of morbidity in WHI? What do these patterns suggest for intervention priorities?

4. What are the mid-life predictors of ‘exceptional’ aging?
   a) Can ‘exceptional’ aging be promoted?