Study of Osteoporotic Fractures* and Cohorts for the Biology of Aging

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SOF
The Great Grandmother of Cohort Studies

• Since 1986, 10,000, ≥65 followed 30 years
Want to talk about SOF?

- Kris Ensrud, MD, MPH
- Jane Cauley, DrPH
- Peggy Cawthon, PhD

They also speak “MrOS”
What’s unique about SOF?

• Visits q 2-4 years – no more clinic site visits

• Many direct measurements of aging
  o BMD
  o Cognition, dementia (adjudicated)
  o Objective measures of sleep
  o Circadian activity rhythms
  o Vision, hearing
  o Performance tests (gait speed)
  o Expertise in trajectories of longitudinal data

• Serum at multiple time points and DNA
Aging outcomes

• Hip fracture (1,700), all (8,000), falls (>25K)
• Dementia
• Frailty
• Costs of health care
Value of direct measurements

• Determinants of survival
• Assumption free statistical mining of nearly 400 candidate age-related variables
• Index of aging
Components of the SOF Index direct measurements

<table>
<thead>
<tr>
<th>Component</th>
<th>Hazard Ratio</th>
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<tbody>
<tr>
<td>No. step-ups completed (10 Seconds)</td>
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<tr>
<td>Health compared to others of the same age?</td>
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<tr>
<td>Average Step Length</td>
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<td>Walking Speed</td>
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<td>Contrast Sensitivity</td>
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**Performance**
Contrast sensitivity
A window into the brain?

- Measures retinal atrophy
- Correlated with atrophy of the hippocampus
SOF Index: very strong predictor of 20 year mortality

![Graph showing survival over time with a p-value of less than 0.001](image)
Healthy Aging Index

From CHS (Anne Newman)

Physiologic index

- FVC (pulmonary function)
- Carotid wall thickness
- Cystatin-C (renal function)
- White matter grade (brain MRI)
- Fasting glucose

Tertiles: 0=best, 2=worst. Score: 0 to 100
Healthy Aging Index is a strong predictor of mortality
An Index of Biological Aging

- Very valuable for drug development
- Discovery of targets: the genetic and blood-based determinants of the rate of aging
- Testing potential drugs: a surrogate marker for proof of concept, phase 2 dose selection
Billionaires With Big Ideas Are Privatizing American Science

By WILLIAM J. BROAD  MARCH 15, 2014
Private funding

• Companies with very large budgets are investing
  o New measurements in current cohorts
  o New cohorts with next gen biology, devices
Google X, Life Sciences

Google's New Moonshot Project: the Human Body
Baseline Study to Try to Create Picture From the Project's Findings

“Baseline” Cohort Study
- Cohort of 10,000 and growing
- Intensive measurement and sample collection
Potential linked trajectories of measurements (knitting)

Measurements also linked to outcomes in existing longitudinal studies.

Years of active follow-up!

Marker level

"Baseline"

Make new measures
(You can only knit what you measure)

Health ABC, SOF
We need new cohorts for the study of the human biology of aging

- Go beyond the limits of current cohorts
- “EMR Epidemiology” will have very limited phenotyping
- Examine human cells
- Include laboratory scientists
New cohorts for human aging

• Measure key pathways of cell biology
  Mitochondria       Autophagy      Senescence

• Needs cells (muscle, fat, sorted blood cells) for functional studies, advanced imaging, physiology and performance tests

• Needs large size for key outcomes: healthy longevity, mobility disability, falls, frailty
Summary
Cohorts for Translational Study of Aging

• Talk with SOF and MrOS about studies of aging and bone

• Private groups might invest in cohorts, to aid develop and test treatments and devices