The Baltimore Longitudinal Study of Aging (BLSA)

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Agenda

• What is the BLSA?
• How can I work with BLSA?
The Baltimore Longitudinal Study of Aging (1953)

The Gerontology Branch at the Baltimore City Hospital
What is the Baltimore Longitudinal Study of Aging?

Established in 1958 as a continuous enrollment “life-long” cohort to study normative aging (NIA was established in 1962)

Overhauled in 2003/04 by Luigi Ferrucci with a new paradigm to identify multifactorial sources of aging processes, including frailty, loss of mobility and cognitive impairment

Expanded in 2008 and 2011 “IDEAL”; targeted enrollment of healthy elders to promote research on healthy aging
# BLSA Study Population: total 3218

<table>
<thead>
<tr>
<th>Age at entry</th>
<th>MEN</th>
<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>&lt;30</td>
<td>245</td>
<td>11</td>
</tr>
<tr>
<td>30-39</td>
<td>251</td>
<td>35</td>
</tr>
<tr>
<td>40-49</td>
<td>251</td>
<td>57</td>
</tr>
<tr>
<td>50-59</td>
<td>215</td>
<td>50</td>
</tr>
<tr>
<td>60-69</td>
<td>238</td>
<td>45</td>
</tr>
<tr>
<td>70-79</td>
<td>313</td>
<td>15</td>
</tr>
<tr>
<td>80-89</td>
<td>118</td>
<td>1</td>
</tr>
<tr>
<td>90+</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1640</td>
<td>214</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of visits</th>
<th>men</th>
<th>women</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>741</td>
<td>655</td>
</tr>
<tr>
<td>5-9</td>
<td>508</td>
<td>423</td>
</tr>
<tr>
<td>10-19</td>
<td>541</td>
<td>212</td>
</tr>
<tr>
<td>20+</td>
<td>127</td>
<td>11</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1917</td>
<td>1301</td>
</tr>
</tbody>
</table>
The Goals of BLSA

**Characterize** multiple aspects of the aging process and their interaction:

- **Describe** longitudinal physical and cognitive changes that define aging
- **Identify** genetic, physical, behavioral and environmental factors that affect the rate of physical and cognitive aging
- **Understand** interrelationships between aging and chronic disease and other conditions and their independent and joint impact on age-related decline
- **Identify** strategies for successful adaptation to aging
- **Develop** hypotheses concerning possible targets for intervention that may positively affect several aspects of the aging process and prevent age-related diseases

**Endpoints** include life expectancy, healthy longevity, mobility limitation, cognitive impairment and frailty
# Measures in the Baltimore Longitudinal Study of Aging

## BLSA Paradigm

A Hierarchical Network of Measures

### Homeostatic Network/Behavioral Factors

<table>
<thead>
<tr>
<th>Category</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormones</strong></td>
<td>Insulin, Ghrelin, Leptin, Adiponectin, Glucose, Testosterone, Estradiol, DHEAs, Cortisol, TSH</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td>PCR, IL-6, sIL-6R, gp130, TNF-α, TNF-1, TNF-2, IL-18, IL-15, Homocysteine</td>
</tr>
<tr>
<td><strong>Immune Function</strong></td>
<td>WBC and Differentials, Cytopheresis</td>
</tr>
<tr>
<td><strong>Sleep and Rest</strong></td>
<td>Sleep Duration and Quality, Autonomic Function and Heart Rate Variability</td>
</tr>
<tr>
<td><strong>Nutrition</strong></td>
<td>Dietary Intake, VitD, VitB12, Folate, VitE, Albumin</td>
</tr>
<tr>
<td><strong>Activity and Engagement</strong></td>
<td>Exercise, Accelerometry, Recreation, Social Interaction</td>
</tr>
</tbody>
</table>

### Physiological Domains Relevant to Function

<table>
<thead>
<tr>
<th>Domain</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central Nervous System</strong></td>
<td>Cognition, Motivation, Motor Control, Coordination, Executive Function</td>
</tr>
<tr>
<td><strong>Peripheral Nervous System</strong></td>
<td>Nerve Conduction of Sensory and Motor Nerves</td>
</tr>
<tr>
<td><strong>Muscle Quality and Body Composition</strong></td>
<td>Isokinetic and Isometric Strength, Muscle Spectroscopy and Biopsy</td>
</tr>
<tr>
<td><strong>Bone and Joints</strong></td>
<td>Pain, ROM, Bone Density-Quality-3D Distribution (DXA and pQCT),</td>
</tr>
<tr>
<td><strong>Energetic Cost and Availability</strong></td>
<td>RMR, Cardiac Structure and Function, Arterial Compliance and IMT, Exercise Tolerance, Respiratory Function, Energetic Cost of Walking, Fatigue</td>
</tr>
<tr>
<td><strong>Sensory Feedback</strong></td>
<td>Visual Acuity, Contrast, Visual Field, Proprioception, Tactile Sensation, Hearing and Sound Discrimination, Taste Buds</td>
</tr>
</tbody>
</table>

### Outcomes

- **Mobility**
  - Self-Report Performance
  - Gait Laboratory
- **Cognition**
  - Performance Neuroimaging
What are the mechanisms by which aging and disease affect aging phenotypes and longevity?

**AGING and DISEASES**

- Changes in Body Composition
- Energy Imbalance Production/Utilization
- Homeostatic Dysregulation
- Neurodegeneration

**Aging Phenotypes**

- Stem Cells Exhaustion
- Altered Intercellular Communication
- Genomic Instability
- Telomere Attrition
- Epigenetic Alterations
- Loss of Proteostasis
- Deregulated Nutrient Sensing
- Mitochondrial Dysfunction
- Cellular Senescence

**Disease Susceptibility**

- Reduced Functional Reserve
- Reduced Healing Capacity and Stress Resistance
- Unstable Health
- Failure to Thrive

**Physical and Cognitive FRAILTY**

Ferrucci L, Studenski S. Clinical Problems of Aging. In: Harrison’s Principles of Internal Medicine, 18th Ed. – 2011

The Hallmarks of Aging
The BLSA aims to be responsive to:

- Emerging research questions in aging
- New discoveries and technologies
- Opportunities for translational studies
- Emphasis on extra- and intramural collaboration
  - Well-characterized human population
  - Continuous systematic follow-up
  - Extensive bio-specimen bank
  - Targeted recruitment of exceptionally healthy (IDEAL)
Participant Visit Timeline

Visit frequency: age <60 every 4 years, age 60-79 biannually; age ≥80 annually

- Due Letter
- Pre-Visit Questionnaire
- Visit Confirmation Letter
- BLSA Clinic Visit 2 to 4 days
- Visit Summary Packet
Core and Core+ Measures*

**CORE**
- Physical Examination + EKG
- Medical Interview
- Medications
- Vitals and Anthropometry
- General Interview
- Clinical Labs
- Core Cognitive Battery
- Physical Performance Testing
- Strength

**CORE+**
- Gait Lab
- Exercise Tolerance/Spirometry
- Resting Metabolic Rate
- Holter Monitor
- Echocardiography/Cardiovascular
- DXA and CT
- Early Markers Battery
- MRI, fMRI and MRS
- Nerve Conduction/Sensitivity
- Vision and Strip Meniscometry
- Auditory and Vestibular Function
- Ankle Proprioception
- Research Labs and 24Hr Urine
- Oral Glucose Tolerance Test
- Saliva/Other Biospecimens
- Taste Bud Photography
- FFQ, Fatigability, Accelerometry
- Personality

*All eligible participants every visit
Special and Special+ Measures*

**SPECIAL**
- Core Body Temperature
- Deuterated Creatine
- Muscle Biopsy
- Cytapheresis

**SPECIAL+**
- Energy Expenditure (DLW)
- Lumbar Puncture
- Skin Biopsy

**OPTIONAL STUDIES**
- Regional Adiposity
- VALIDATE
- Autopsy
- Neuroimaging (PET)

*Phased implementation or administered to selected participants and/or at selected or limited visits

Special and special+ measures are implemented to test new state of the art technology, verify new hypotheses that emerged in the BLSA and/or open the study to new hypotheses proposed by an intramural or extramural collaborator.
How to work with BLSA: research partnerships

- [www.blsa.nih.gov](http://www.blsa.nih.gov)
- Application process: new website mechanism for letter of intent, approval, full proposal
- Variable lists
- Interaction with BLSA investigators

“Researchers at NIH and at other academic and research institutions in the United States and internationally are welcome—and encouraged—to use BLSA data and specimens for scientific projects and grant applications.”