Welcome

Health and Retirement Study
Biomarkers and Physical Measures Data

Webinar Agenda
- Part I: HRS Data Resources Overview
- Q&A
- Part II: Tour of the HRS Website
- Q&A
Webinar Speakers

Amanda Sonnega, PhD
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HRS | Health and Retirement Study

The Gerontological Society of America

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Quick Audience Poll

• Please tell us who you are:
  – Academia
  – Industry
  – Government
  – Medical Practice
  – Other
HEALTH AND RETIREMENT STUDY: BIOMARKERS AND PHYSICAL MEASURES DATA

Amanda Sonnega, PhD
Jessica Faul, MPH, PhD
GSA Webinar
April 24, 2018
BUILDING A BIOSOCIAL SURVEY: RATIONALE

- Validate self-reports of health status
- Identify health status information unknown to survey participants
- Enable richer modeling of pathways between socioeconomic determinants and physical outcomes
ADDING BIOLOGICAL MEASURES: IMPORTANT CONSIDERATIONS

• Change in mode (increase in face-to-face interviewing)
• Increased respondent burden
• Possible increased attrition
• Increased cost
• Preserving confidentiality of respondents
• Ethical issues
  • What to report back to respondents
• Preserve the integrity of a longitudinal observational study
  • Did not want it to be transformed into an intervention study
BIOLOGICAL MEASURES IN THE HRS

• Enhanced face-to-face (EFTF) interview
  • Physical measures (2006 and beyond)
  • Dried blood spot (DBS) biomarkers (2006-2016)
• Venous Blood Study (VBS) 2016
• We’ll review and show you where to find relevant documentation for each of these data sources
• In the second half of the webinar, we’ll tell you how to access the data
MEASURES IN THE EFTF INTERVIEW
DESIGN OF ENHANCED FACE-TO-FACE INTERVIEW

• 2006 and beyond
  ❑ Half of core sample is randomly assigned to face-to-face interview **enhanced** with physical and biological measures
  ❑ Other half sample assigned to telephone interview only
### DESIGN OF ENHANCED FACE-TO-FACE INTERVIEW

#### BIOLOGICAL MEASURES IN THE EFTF INTERVIEW

<table>
<thead>
<tr>
<th>Year</th>
<th>2006</th>
<th>2008</th>
<th>2010</th>
<th>2012</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFTF Sample</td>
<td>A</td>
<td>B</td>
<td>A</td>
<td>B</td>
<td>A</td>
</tr>
</tbody>
</table>

- **A** = First random half sample
- **B** = Second random half sample

- Alternate waves
- Physical measures and biomarker data available every wave on half of the full core sample – either A or B
- Longitudinal every 4 years
In the full sample:
- Blood pressure
- Breathing test (peak flow)
- Grip strength
- Balance tests
- Height and weight
- Waist circumference

Among those aged 65 and older:
- Timed walk (98.5 inches)

Public Release Data Core Section I
NEW PHYSICAL MEASURES IN 2016

• Hearing test (HRS Core 2016)
  • Siemens HearCheck devices
  • Same protocol as ELSA W7
  • Test 1 (1000 Hz)
  • Test 2 (3000 Hz)
  • Both ears (without hearing aids)

• Smelling test (HCAP)
  • Sniffin’ Sticks
  • Similar protocol to NSHAP

ELSA = English Longitudinal Study of Ageing
HCAP = Healthy Cognitive Aging Project
NSHAP = National Social Life, Health, and Aging Project
BIOMARKER: WHY DRIED BLOOD SPOT?

• Can obtain some high-value biomarkers
• Relatively easy and inexpensive
• Could be conducted by trained interviewers without a separate visit
DRIED BLOOD SPOT BIOMARKERS

• Assays 2006-2016
  • Important measures of metabolic syndrome and cardiovascular risk
    • HbA1c
    • Total and HDL cholesterol
    • C-reactive protein (CRP)
    • Cystatin C
  • One added in 2014 and 2016
    • IL-6 cytokine - related to immune response
• Released as sensitive health data
  • Requires additional step
DRIED BLOOD SPOT ASSAYS AND LABS

A number of different labs were used for the dried blood spot assays

• 2006
  • Biosafe Laboratories (HbA1c, HDL & Total Cholesterol)
  • University of Vermont (CRP & Cystatin C)

• 2008
  • Biosafe & Flexsite (HbA1c)
  • Biosafe & University of Washington (Cholesterol)
  • University of Vermont (CRP & Cystatin C)

• 2010
  • Heritage Labs (HbA1c, HDL & Total Cholesterol)
  • University of Washington (CRP & Cystatin C)

• 2012-2016
  • University of Washington

<table>
<thead>
<tr>
<th>HbA1C (%)</th>
<th>N</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>% High HbA1c (≥ 6.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006 HbA1c (Biosafe) KA1CBIOS</td>
<td>6102</td>
<td>5.81</td>
<td>0.87</td>
<td>13.59</td>
</tr>
<tr>
<td>2008 HbA1c (Biosafe) LA1CBIOS</td>
<td>4102</td>
<td>5.76</td>
<td>0.92</td>
<td>12.91</td>
</tr>
<tr>
<td>2008 HbA1c (FlexSite) LA1CFLEX</td>
<td>1748</td>
<td>5.97</td>
<td>0.92</td>
<td><strong>18.92</strong></td>
</tr>
<tr>
<td>2005-2008 NHANES HbA1c</td>
<td>4791</td>
<td>5.81</td>
<td>0.99</td>
<td>13.89</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Cholesterol (mg/dL)</th>
<th>N</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>% High Risk (≥ 240 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006 HRS (Biosafe) KTCBIOS</td>
<td>5797</td>
<td>195.44</td>
<td>40.85</td>
<td>14.92</td>
</tr>
<tr>
<td>2008 HRS (Biosafe) LTCBIOS</td>
<td>3917</td>
<td>197.07</td>
<td>50.29</td>
<td>20.81</td>
</tr>
<tr>
<td>2008 HRS (Univ Wash) LTCUW</td>
<td>1718</td>
<td>220.48</td>
<td>66.42</td>
<td>33.00</td>
</tr>
<tr>
<td>2005-2008 NHANES</td>
<td>4759</td>
<td>202.93</td>
<td>43.47</td>
<td>16.00</td>
</tr>
</tbody>
</table>
THE UPSHOT

• Resulting biomarker values based on DBS vary across assays and laboratories
• Results across waves and labs were not comparable
• Analysts would want to make comparisons to standard whole blood assays
• Needed a correction method...
CONSTRUCTION OF NHANES EQUIVALENT ASSAY VALUES

• National Health and Nutrition Examination Survey (NHANES)
• Both NHANES and HRS are population-based studies and they are intended to represent the non-institutionalized US population when sampling weights are used
• For some purposes, it may be advantageous to adjust the HRS DBS values to levels consistent with NHANES, exploiting the fact that the population distributions should be the same
CONSTRUCTION OF NHANES EQUIVALENT ASSAY VALUES

• These variables were constructed by assuming that the distribution of the DBS assays is similar to that in NHANES
  • We determine the value of both assays at each percentile
  • Then transform the DBS assays into the NHANES scale after adjusting for any between-lab differences

• This conversion to equivalent values makes the percentage at high-risk levels in HRS similar to that in NHANES
CONSTRUCTION OF NHANES EQUIVALENT ASSAY VALUES

Total Cholesterol before Adjustment

Total Cholesterol after Adjustment
CONSTRUCTION OF NHANES EQUIVALENT ASSAY VALUES

• We recommend using the NHANES equivalent values for any analyses using the DBS data

BUT

• Because the same NHANES data used to standardize across HRS waves, you cannot make statements about population-level trends between 2006 to 2008 or 2010 to 2012
PHYSICAL MEASURES AND BIOMARKERS ELIGIBILITY VARIABLES

• EFTFASSIGN indicator of when the R was in EFTF sample

• KPMELIG – Eligibility for 2006 physical measures
• LPMELIG – Eligibility for 2008 physical measures
• MPMELIG – Eligibility for 2010 physical measures
• NPMELIG – Eligibility for 2012 physical measures
• OPMELIG – Eligibility for 2014 physical measures
• PPMELIG – Eligibility for 2016 physical measures
SAMPLE-SPECIFIC WEIGHTS

• Sample weights for the Physical Measure/Biomarker subsamples in Tracker file
• Separate weights for:
  Physical Measures (e.g., KPMWGTR)
  Biomarkers (e.g., KBIOWGTR)
• Important determinants of participation: race, sex, age, education, marital status, overall health status, health conditions, mobility, and functional limitations (IADLs)

If your analysis uses physical measure or biomarker data – use these weights not core weights!
VENOUS BLOOD STUDY
EXPANSION OF BIOLOGICAL CONTENT

- Biomarkers already in HRS contribute, but much more to be done with whole blood
- For behavioral science, biological measurement is primarily aimed at studying pathways linking lifetime social and environmental experience to health...
- ...and secondarily to enhance the measurement of population health itself
- For aging, we are interested in biological markers of the pace of aging and how they connect social experience to healthy aging
VENOUS BLOOD STUDY (VBS)

- Project collected venous blood from all panel HRS respondents in 2016-2017
- Verbal consent at the end of the core survey
- Blood draw contracted to Hooper Holmes
  - Scheduled and conducted separate in-home visit for blood collection
  - Attempted to be within 4 weeks of core interview
- 79% consented and 83% who consented completed
- N=9,934
HEMATOLOGICAL ANALYSIS (50.5 mL Venous Blood)

Collection

Lab Processing and Assaying

Storage

Field Centrifugation

Cryopreservation

Flow Cytometry

Lab Centrifugation

Assays

3 X 10 mL SST

8 mL CPT

10 mL EDTA

2.5 mL PAXgene RNA

7 mL Serum

3.5 mL Plasma & DNA

Aliquots of Cryopreserved Cells

Stabilized RNA

Serum

Assays

Cryopreservation

CBC

3.5 mL Plasma & DNA

Stabilized RNA

HRS
CONSIDERATIONS IN SELECTING ASSAYS

- Age-related biomarkers
  - Related to age-related clinical change, disease, disability, cognitive loss, mortality
  - Aging processes at the cellular or molecular level
  - Harmonize with other studies
- Socially influenced
  - Some evidence of a relationship with age, gender, race/ethnicity, socioeconomic status, stress, life circumstances
- Feasible
  - Given our collection, shipping, and assay ability
  - Cost effective
## Assays and Estimated Storage by Tube

<table>
<thead>
<tr>
<th>Tube Type and Blood Volume</th>
<th>Assay</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mL SST (Serum) - 1</td>
<td>Total cholesterol, HDL and LDL cholesterol, Triglycerides, High-sensitivity CRP (hsCRP), Vitamin D (25 Hydroxy), Ferritin (FRTN), IGF-1, DHEAs, Cytokine Panel (IL-6, IL-1RA, IL-10, TNF-alpha, sTNFR-I, and TGF beta [activated form]), B-type natriuretic peptide (NT-proBNP)</td>
<td>7 mL Serum</td>
</tr>
<tr>
<td>10 mL SST (Serum) - 2</td>
<td>Comprehensive Metabolic Panel ([CMP]: Albumin, Alk Phos, ALT, AST, Bili, Ca, Cl, CO2, Creat, Gluc, K, Total protein, Na, BUN), Cystatin C, Clusterin, BDNF, Homocysteine (methylation cases only)</td>
<td></td>
</tr>
<tr>
<td>10 mL SST (Serum) - 3</td>
<td>Repository only</td>
<td></td>
</tr>
<tr>
<td>8 mL CPT (Cells)</td>
<td>Cryopreservation/Flow Cytometry</td>
<td>9 aliquots of cryopreserved cells</td>
</tr>
<tr>
<td>10 mL EDTA (Whole Blood)</td>
<td>Complete blood count ([CBC]: White blood cell [WBC, leukocyte] count, WBC types [WBC differential], Red blood cell [RBC] count, Hematocrit [HCT, packed cell volume, PCV], Hemoglobin, RBC indices: mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], and mean corpuscular hemoglobin concentration [MCHC], Platelet [thrombocyte] count, Mean platelet volume [MPV]), CMV seroprevalence, mtDNA copy number, telomere length, DNA methylation</td>
<td>3.5 mL Plasma Extracted DNA</td>
</tr>
<tr>
<td>2.5 mL PAXgene RNA</td>
<td>RNA-seq</td>
<td>Stabilized RNA</td>
</tr>
</tbody>
</table>
### Panel Sample

<table>
<thead>
<tr>
<th>Metabolic Panel</th>
<th>Innovative Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid Panel</td>
<td>N=4000</td>
</tr>
<tr>
<td>CBC</td>
<td></td>
</tr>
<tr>
<td>Ferritin (FRTN)</td>
<td></td>
</tr>
<tr>
<td>IGF-1</td>
<td></td>
</tr>
<tr>
<td>DHEA-S</td>
<td></td>
</tr>
<tr>
<td>Cystatin C</td>
<td></td>
</tr>
<tr>
<td>Vitamin D (25 Hydroxy)</td>
<td></td>
</tr>
<tr>
<td>High-sensitivity CRP (hsCRP)</td>
<td></td>
</tr>
<tr>
<td>Cytokine panel (IL-6, IL-1RA, IL-10, TNF-alpha, sTNFR-I, and TGF beta (activated form))</td>
<td></td>
</tr>
<tr>
<td>Flow cytometry (cryopreserved cells)</td>
<td></td>
</tr>
<tr>
<td>CMV seroprevalence</td>
<td></td>
</tr>
<tr>
<td>B-type natriuretic peptide (NT-proBNP)</td>
<td></td>
</tr>
</tbody>
</table>

### Innovative Sample

1. **Traditional biochemical/harmonized marker**
2. **Immune system and inflammation marker**
3. **Innovative aging/cognitive marker**

<table>
<thead>
<tr>
<th>DNA Methylation</th>
<th>Homocysteine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telomere length</td>
<td>RNA-seq</td>
</tr>
<tr>
<td>mtDNA copy number</td>
<td>Clusterin</td>
</tr>
</tbody>
</table>
JF1 850 (EPIC) Chip
Jessica Faul, 5/4/2017

JF2 Single end, 50bp reads ~ 40 million reads/sample
Jessica Faul, 5/4/2017
INTERNATIONAL COMPARISONS
Several other HRS family studies collect physical measures and biomarkers, which provide the opportunity for cross-national comparison

- English Longitudinal Study of Ageing (ELSA)
- The Irish Longitudinal Study on Ageing (TILDA)
- China Health and Retirement Longitudinal Study (CHARLS)
- Indonesian Family Life Survey (IFLS)
- Longitudinal Aging Study in India (LASI)
- Survey of Health, Ageing and Retirement in Europe (SHARE)
- Study on Global AGEing and Adult Health (SAGE)
- Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA)
RELEVANT USER GUIDES


Crimmins, Faul, Kim et al. (2013) Documentation of Biomarkers in the 2006 and 2008 Health and Retirement Study


Crimmins, Faul, Kim & Weir (2017) Documentation of Blood-Based Biomarkers in the 2014 Health and Retirement Study


And a published paper:

Part I Clarifying Questions?

- We will not be using the raised hand feature today.
- Please use the questions feature accessible on the right hand side of your screen.
- If we do not get to all of the questions today, we will email responses after the webinar.
Part II: Tour of the HRS Website

- http://hrsonline.isr.umich.edu/
Health and Retirement Study

• Archived recordings on GSA’s YouTube
  – Introduction to the Health and Retirement Study
  – Data on Cognition
  – Biomarkers and Physical Measures Data

hrsquestions@umich.edu

www.geron.org/webinar
In an effort for continual improvement, we would like to hear your thoughts. Please provide feedback by clicking the survey link at the end of the webinar.

Thank you again—we hope you enjoyed the program!
Part II Clarifying Questions?

- We will not be using the raised hand feature today.
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- If we do not get to all of the questions today, we will email responses after the webinar.
Thank you

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• The nation’s oldest and largest interdisciplinary organization devoted to research, education, and practice in the field of aging
  – 5,500+ interdisciplinary members around the world touching all facets of aging

• Mission
  – Promote multi- and interdisciplinary research in aging
  – Translate and disseminate research findings
  – Promote/advocate for education/awareness on aging across disciplines
  – Foster application of research into policy development

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