Preliminary Dried Blood Spot Biomarker Data from the Study on global AGEing and adult health (SAGE)

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Talk outline

- Aging and chronic disease in LMICs
- Dried blood spots (DBS)
- WHO’s Study on global AGEing and adult health (SAGE)
- Preliminary biomarker data from SAGE Wave 1
- Ongoing and future biomarker research in SAGE
Aging and health in LMICs

- Population aging recognized as a global issue yet data primarily available for wealthy nations

- Yet, massive epi and demographic changes in LMICs, with population aging and increased NCDs

- Most international development not targeted on NCDs

- Much of NCD burden preventable or modifiable but data needed to inform health system responses
Dried blood spots (DBS) from finger prick

- Minimally invasive, field friendly tool for documenting health and physiology
- Unravel complex relationships between social and biological determinants of health
- Test models of aging

But, methodological issues need to be addressed in order to realize the potential of this powerful tool (DBS 2.0)

Shuar Health and Life History Project (Morona-Santiago, Ecuador)
Study on global AGEing and adult health (SAGE)

- Data collection platform on older adults (50+) with younger sample (18-49); n = >42,000
- Longitudinal study of 6 countries at different development levels
- W0 & W1 complete, W2 in process (2015), W3 planned (2017)
- Data designed for comparison with HRS, ELSA, CHARLS, LASI


See Kowal et al. 2012. *Int J Epidemiology* for data resource profile paper on SAGE
Today’s objectives

1. Present preliminary SAGE biomarker data from Wave 1

2. Discuss ongoing and planned work for SAGE Waves 2 & 3
Preliminary biomarker data – Methods

- DBS samples from ~38,000 Wave 1 respondents
- Transported to central national labs for storage and analysis
- Standard protocol and training
- Wave 1 DBS samples assayed for a core set of biomarkers
  - Hb
  - HbA1c
  - CRP
  - EBV antibodies
  - HIV

SAGE 2010 lab training (Durban, South Africa)
Preliminary biomarker data – Results

- Funding not available for all biomarkers in all countries but results from 5 countries and >70,000 analyses

<table>
<thead>
<tr>
<th>Country</th>
<th>CRP</th>
<th>Hb</th>
<th>HIV</th>
<th>HbA1c</th>
<th>EBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>7508</td>
<td>9581</td>
<td>Pending</td>
<td>5703</td>
<td>No</td>
</tr>
<tr>
<td>Ghana</td>
<td>Pending</td>
<td>2194</td>
<td>2634</td>
<td>Pending</td>
<td>Pending</td>
</tr>
<tr>
<td>India</td>
<td>5139</td>
<td>10,816</td>
<td>No</td>
<td>832</td>
<td>3406</td>
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<tr>
<td>Mexico</td>
<td>Pending</td>
<td>Pending</td>
<td>Pending</td>
<td>Pending</td>
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<tr>
<td>Russia</td>
<td>1431</td>
<td>1349</td>
<td>706</td>
<td>1001</td>
<td>1289</td>
</tr>
<tr>
<td>South Africa</td>
<td>3500</td>
<td>3600</td>
<td>2985</td>
<td>3160</td>
<td>3917</td>
</tr>
<tr>
<td><strong>Total, n</strong></td>
<td><strong>17,578</strong></td>
<td><strong>27,540</strong></td>
<td><strong>6325</strong></td>
<td><strong>10,696</strong></td>
<td><strong>8612</strong></td>
</tr>
</tbody>
</table>
Glycated hemoglobin (HbA1c) – Methods

- HbA1c results from DBS assay on Beckman Coulter Synchron platform developed in ZAF
  - Validation with 100 matched samples
  - Whole blood %A1c highly correlated to DBS %A1c (r=0.97)
  - Modest glycosylation over 3 months (<10%)
  - Inter-lab comparison with 57 DBS samples from LASI analyzed in SAGE ZAF lab. ZAF lab values showed excellent agreement with India (NARI) lab results (r=0.94)
  - Williams et al. in prep. *Am J Hum Biol.*
HbA1c – Select preliminary results

Diabetes underdiagnosis & disease management among older adults

Aim #1: Evaluate self-report diabetes status accuracy

- **India (n = 812)**: ~81% of men, 86% of women with no previous diabetes diagnosis had HbA1c levels ≥6.5%

- **ZAF (n = 3356)**: Using ≥6.5% cutoff, drastic underestimation of diabetes prevalence based on SR
  - SR: 7% in men and 10% in women
  - HbA1c: 85% for both sexes
  - With modified cutoff (>7% HbA1c): >50% prevalence for both men and women
Aim #2: Consider whether childhood socioeconomic position affects HbA1c among older adults in China

- **Methods**: Participants with elevated HbA1c (≥6.5%) age-and sex-matched 1:4 to controls with normal HbA1c (688:2752)

- **Results**: High adult education had a higher risk for abnormal HbA1c (OR=1.23[95%CI: 1.09-1.39]), and physical inactivity (OR=1.38[95%CI: 1.11-1.71]) and high BMI (OR=1.11[95%CI: 1.02-1.22])

- High parental education and adult education were risk factors of elevated HbA1c in older adults in China independent of adult health conditions.
Hemoglobin (Hb)

- DBS results based on modified Drabkin’s method
- Evaluate anemia in Ghana; 1265 participants, ~76% high risk, especially elevated in women (80% vs. 71%)

- Highest two wealth quintiles have the lowest burden but still extremely high overall

![Graph showing % Older Ghanaians At Higher Anemia Health Risk by wealth quintile and gender.](image)

*Evaluated using a 12 g/dL total Hb cutoff*
C-reactive protein (CRP)

CRP used modified hsCRP DBS assay from McDade et al., 2004. *Clin Chem*.


**Aim:** Evaluate elevated CRP in ZAF and Russia

<table>
<thead>
<tr>
<th></th>
<th>% Low Risk (&lt;1 mg/L CRP)</th>
<th>% Average Risk (1-3 mg/L CRP)</th>
<th>% High Risk (&gt;3 mg/L CRP)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>44.4</td>
<td>28.8</td>
<td>26.8</td>
<td>1968</td>
</tr>
<tr>
<td>Men</td>
<td>43.2</td>
<td>29.1</td>
<td>27.7</td>
<td>1464</td>
</tr>
<tr>
<td>Russia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>5.3</td>
<td>53.8</td>
<td>40.9</td>
<td>171</td>
</tr>
<tr>
<td>Men</td>
<td>6.9</td>
<td>52.8</td>
<td>40.3</td>
<td>159</td>
</tr>
</tbody>
</table>

~27% in ZAF with high risk CRP, and ~40% in the small Russian sample
HIV

Analysis using DBS ELISA method from ZAF, with confirmation using alternate measure

**Aim:** HIV prevalence and risk factors in Ghanaian older adults

- N = 1669
- HIV+ rate for adults aged 50-plus is ~2.3%, with higher rates in women and urban dwellers
- Provides much needed prevalence data for older adults

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV-positive (%)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.9</td>
<td>830</td>
</tr>
<tr>
<td>Female</td>
<td>2.4</td>
<td>839</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>2.3</td>
<td>663</td>
</tr>
<tr>
<td>60–69</td>
<td>3.0</td>
<td>463</td>
</tr>
<tr>
<td>70+</td>
<td>1.3</td>
<td>543</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>2.6</td>
<td>764</td>
</tr>
<tr>
<td>Rural</td>
<td>1.8</td>
<td>905</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Currently married</td>
<td>2.3</td>
<td>873</td>
</tr>
<tr>
<td>Cohabitating</td>
<td>5.0</td>
<td>20</td>
</tr>
<tr>
<td>Separated or divorced</td>
<td>2.4</td>
<td>292</td>
</tr>
<tr>
<td>Widowed</td>
<td>1.7</td>
<td>458</td>
</tr>
</tbody>
</table>
HIV

Aim: Prevalence of HIV among older ZAF adults

- ZAF data available for 3839 older adults (findings published in Negin et al. 2012. *AIDS*)
- Results: HIV prevalence was 6.4% and was particularly elevated among women aged 50–59 and those living in rural areas

HIV-infected older adults in South Africa have high rates of chronic disease and weakness

Considerably higher than in previous studies
Ongoing and future SAGE biomarker studies

- Clean W1 data and publish
- Wave 2 collection ongoing – NIH funding request pending for W2 & W3 analyses
- Cross-lab harmonization & methods development—New and revised DBS assays
- Allostatic load: Multi-system dysregulation (HbA1c, apoB, IL-6, CRP, CyC, TL)

Filming CRP video assay protocol (http://www.bonesandbehavior.org/sage/)
Acknowledgments

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