Biomarker trajectories and health outcomes

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ELSA Wave 8 Report Launch
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Overview

- Trajectories: methodology
- Individual trajectories of body size
- Group-based trajectories of an inflammation marker
- Association with ageing outcomes
Overview

- Trajectories: methodology
- Individual trajectories of body size
- Group-based trajectories of an inflammation marker
- Association with ageing outcomes
Growth curve modelling

- Individual trajectories over time: Latent growth curve models
  - One trajectory for each person: Intercept and slope(s)
  - An average trajectory to characterize the entire sample
  - Variance trajectory = An indication of the extent to which individual trajectories deviate from the average trajectory

- Group-based trajectories: Latent Class Growth Analysis
  - Multiple sub-groups in a population → for each group you get an intercept and slope(s)
  - Sub-groups are NOT known a priori, can emerge from the data → exploratory and descriptive analysis
  - Sub-groups are called classes
Individual: Latent growth curve model

- **Gender**
- **Age**
- **SES**

Time invariant covariates:
- **BMI w2**
- tv1

Time varying principal variable:
- **BMI w4**
- tv2

Time varying covariates:
- **BMI w6**
- tv3
Group-based: Latent class growth analysis

- Class
- i
- s

Time varying principal variable
Time varying covariates
Overview

- Trajectories: methodology
- **Individual trajectories of body size**
- Group-based trajectories of an inflammation marker
- Association with ageing outcomes
Body size and health consequences

- Global obesity epidemic → diabetes, CVD, some cancers, other chronic diseases
- Prevalence in the UK in 2015: 58% women and 68% men overweight or obese
- Obesity particularly prevalent 45-74y then decline
- Socioeconomic gradient
Body size and health consequences

- Both obesity and underweight are associated with higher mortality risk

Body size in relation to SES

- Higher obesity rates in lower SES groups
  - Compelling evidence in adults throughout midlife
  - Less studies and more conflicting evidence in older age
  - Decline in body size at older age: frailty / illness

Feng et al, Plos One 2015; Dugravot et al, AJCN 2010
Objective and Methods

Objective: Describe and compare BMI and waist circumference trajectories in ELSA and assess the effect of socioeconomic status

Population:
- Baseline year: 2004 (wave 2)
- Three time points: wave 2, wave 4, wave 6 (clinical examination)
  - N=3259 men, mean age at baseline 65.6 ± 9.2 y
  - N=3966 women, mean age 66.1 ± 9.6 y
- BMI and Waist Circumference measured by nurse
- SES measure: tertiles of wealth in 2004
- Covariates: smoking, physical activity, limiting longstanding illness, marital status
- 8-year period
- Linear and quadratic term of age on I and S to describe age-specific trajectories = aging vectors
Results (I)
Vector graph showing 8-year aging vectors of anthropometric markers, ELSA 2004-5 to 2012-13

BMI

Waist Circumference
Results (I)

Vector graph showing 8-year aging vectors of anthropometric markers, ELSA 2004-5 to 2012-13

- Less variations in men than women
- Increase in BMI and WC (gain) from 50 to ~70y
- Decrease after 70 y stronger for BMI than WC
- Cohort effect: younger cohort bigger
  E.g. a man who was 62 in 2004 has a lower BMI by 1kg/m² compared to a man who was 62 in 2012
Results (II)

Vector graph showing 8-year aging vectors of anthropometric markers according to wealth

- **BMI**
  - **Men**
    - Poorest wealth
    - Richest wealth
  - **Women**
    - Poorest wealth
    - Richest wealth

- **Waist Circumference**
  - **Men**
    - Poorest wealth
    - Richest wealth
  - **Women**
    - Poorest wealth
    - Richest wealth
Results (II)

Vector graph showing 8-year aging vectors of anthropometric markers according to wealth

- Strong effect of wealth on baseline BMI and WC
  - For men and women
  - For <70y and >70y
  - Poorer = greater body size

- No sig effect of wealth on slope
  - Men: parallel trajectories by SES group → the gap doesn’t close
  - Women: in poorest wealth group decline faster

→ Cumulative disadvantage
Conclusions (I)

- Identification of body size trajectories in ELSA:
  - Participants aged 50 to 70 tend to gain weight
  - Participants aged >70 tend to lose weight, likely to be lean mass
  - Cohort effect: younger cohort bigger

- Effect of wealth
  - At any given age, lower wealth associated with higher BMI and higher waist circumference
  - No significant effect of wealth on the change of body size: the gap doesn’t close or the decline in BMI tend to be stronger in older women

- Our results support the cumulative disadvantage theory: social disadvantage over the life course is associated with unfavourable body size

- Paper under review Zaninotto P & Lassale C “Socioeconomic trajectories of body mass index and waist circumference: results from the English Longitudinal Study of Ageing”
Overview

- Trajectories: methodology
- Individual trajectories of body size
- Group-based trajectories of inflammation markers
- Association with ageing outcomes
Inflammation and aging outcomes

- Compelling evidence of associations between elevated inflammation biomarkers (C-reactive protein, Inteleukin 6 and Fibrinogen mainly) with a range of age-related outcomes:
  - Cardiovascular, Diabetes, Cancer
  - Cognitive function and dementia
  - Sarcopenia and osteoporosis
  - Frailty
- Most studies used only one measurement of biomarker
- Few studies have used two measurements to define “chronic inflammation”
  - Akbaraly et al, CMAJ 2013: Whitehall II, 5 years apart
- Promising but partial evidence
- Little is known about long-term changes in inflammation as predictor
- No study on trajectories on more time points
Methods

Objective: Identify group-based trajectories of inflammation and assess the associations with ageing outcomes

- N=2,439
- Exposure: hsCRP (mgL) measured at wave 0, 2 and 4 in ELSA
- Exclusion of existing cardiometabolic disease: CHD, stroke, diabetes
- Adjustment for: age, sex, education, smoking, BMI and NSAID use at baseline
- Distal outcomes measured at wave 6:
  - Physical functioning
  - Cardiometabolic health
  - Lung function
  - Cognitive function
  - Depression CES-D
Methods

Core participants at baseline (wave 0, 1998) N=11,107

- Did not attend wave 6 visit n=5,564
  - Of whom died between wave 1 and 6 n=2,510

Core participants who attended wave 6 visit N=5,543

- Exclusion of chronic disease at wave 0 (n=452)
  - Coronary Heart Disease n=85
  - Stroke n=41
  - Diabetes n=69
  - Cancer n=279

- Missing CRP at 2 or 3 occasions (waves 0, 2, 4) n=2,665

Healthy core participants with 2 or 3 CRP measurements (waves 0; 2; 4) N=2,439

- Missing baseline smoking status n=1
- Missing education n=1

Analytical sample N=2,437
Results: trajectories of CRP

CRP (mg/L)

Stable-high (4.6%)
High-to-medium (9.9%)
Medium-to-high (14.3%)
Stable-low (71.3%)

Time (years)
Results: Association with physical functioning

<table>
<thead>
<tr>
<th>CRP trajectory</th>
<th>N</th>
<th>N cases</th>
<th>OR (95% CI) a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disability: ADL b</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1762</td>
<td>210</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>336</td>
<td>93</td>
<td>2.09 (1.51, 2.88)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>231</td>
<td>50</td>
<td>0.92 (0.60, 1.42)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>107</td>
<td>24</td>
<td>0.90 (0.50, 1.62)</td>
</tr>
</tbody>
</table>

| **Disability: IADL c** |    |         |               |
| Stable-Low    | 1762| 191     | 1.00 (ref)    |
| Medium-to-High| 336 | 67      | 1.62 (1.15, 2.30) |
| High-to-Medium| 231 | 47      | 1.20 (0.79, 1.82) |
| Stable-High   | 107 | 15      | 0.90 (0.48, 1.69) |

| **Balance impairment d** |    |         |               |
| Stable-Low    | 1762| 361     | 1.00 (ref)    |
| Medium-to-High| 337 | 112     | 1.59 (1.20, 2.11) |
| High-to-Medium| 231 | 79      | 1.31 (0.94, 1.83) |
| Stable-High   | 107 | 35      | 1.46 (0.91, 2.33) |
## Results: Association with physical functioning

### Lower body strength impairment: Chair rise

<table>
<thead>
<tr>
<th>Impairment Level</th>
<th>Cases</th>
<th>Progressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable-Low</td>
<td>1575</td>
<td>21</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>272</td>
<td>8</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>191</td>
<td>9</td>
</tr>
<tr>
<td>Stable-High</td>
<td>88</td>
<td>6</td>
</tr>
</tbody>
</table>

- **1.00 (ref)**
- **1.74 (0.73, 4.10)**
- **2.39 (1.02, 5.58)**
- **3.22 (1.14, 9.09)**

### Musculoskeletal impairment: Walking speed

<table>
<thead>
<tr>
<th>Impairment Level</th>
<th>Cases</th>
<th>Progressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable-Low</td>
<td>1637</td>
<td>202</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>290</td>
<td>67</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>199</td>
<td>38</td>
</tr>
<tr>
<td>Stable-High</td>
<td>94</td>
<td>25</td>
</tr>
</tbody>
</table>

- **1.00 (ref)**
- **1.61 (1.15, 2.24)**
- **1.05 (0.69, 1.59)**
- **1.44 (0.84, 2.45)**

### Musculoskeletal impairment: Grip strength

<table>
<thead>
<tr>
<th>Impairment Level</th>
<th>Cases</th>
<th>Progressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable-Low</td>
<td>1725</td>
<td>274</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>329</td>
<td>60</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>224</td>
<td>40</td>
</tr>
<tr>
<td>Stable-High</td>
<td>104</td>
<td>26</td>
</tr>
</tbody>
</table>

- **1.00 (ref)**
- **1.12 (0.81, 1.55)**
- **1.05 (0.71, 1.55)**
- **1.57 (0.95, 2.57)**

### Arthritis

<table>
<thead>
<tr>
<th>Impairment Level</th>
<th>Cases</th>
<th>Progressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable-Low</td>
<td>1762</td>
<td>697</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>337</td>
<td>175</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>231</td>
<td>109</td>
</tr>
<tr>
<td>Stable-High</td>
<td>107</td>
<td>58</td>
</tr>
</tbody>
</table>

- **1.00 (ref)**
- **1.55 (1.16, 2.06)**
- **0.72 (0.49, 1.04)**
- **1.02 (0.60, 1.72)**
## Results: Association with CVD risk factors

<table>
<thead>
<tr>
<th>CRP trajectory</th>
<th>N total</th>
<th>N cases</th>
<th>OR (95% CI) $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypertension</strong> $^b$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1691</td>
<td>808</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>321</td>
<td>205</td>
<td>1.57 (1.21, 2.04)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>223</td>
<td>127</td>
<td>1.06 (0.78, 1.44)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>104</td>
<td>58</td>
<td>1.02 (0.67, 1.57)</td>
</tr>
<tr>
<td><strong>Low HDL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1493</td>
<td>143</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>282</td>
<td>45</td>
<td>1.41 (0.97, 2.06)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>183</td>
<td>27</td>
<td>1.24 (0.77, 1.99)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>92</td>
<td>12</td>
<td>0.88 (0.45, 1.72)</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1761</td>
<td>145</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>337</td>
<td>51</td>
<td>1.29 (0.89, 1.86)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>231</td>
<td>31</td>
<td>1.03 (0.66, 1.63)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>107</td>
<td>21</td>
<td>1.42 (0.81, 2.47)</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1708</td>
<td>349</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>318</td>
<td>148</td>
<td>1.95 (1.36, 2.80)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>220</td>
<td>90</td>
<td>0.97 (0.63, 1.49)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>102</td>
<td>60</td>
<td>1.82 (0.95, 3.49)</td>
</tr>
<tr>
<td><strong>Low FEV1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1512</td>
<td>283</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>282</td>
<td>86</td>
<td>1.84 (1.36, 2.50)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>191</td>
<td>58</td>
<td>1.75 (1.22, 2.52)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>92</td>
<td>29</td>
<td>2.16 (1.32, 3.55)</td>
</tr>
</tbody>
</table>
### Results: Association with mental health

<table>
<thead>
<tr>
<th>CRP trajectory</th>
<th>N total</th>
<th>N cases</th>
<th>OR (95% CI) a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depression</strong> b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1755</td>
<td>248</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>336</td>
<td>78</td>
<td>1.55 (1.13, 2.12)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>228</td>
<td>50</td>
<td>1.16 (0.79, 1.70)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>107</td>
<td>19</td>
<td>0.79 (0.44, 1.40)</td>
</tr>
<tr>
<td><strong>Memory impairment</strong> c</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable-Low</td>
<td>1762</td>
<td>283</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>Medium-to-High</td>
<td>337</td>
<td>70</td>
<td>1.05 (0.76, 1.44)</td>
</tr>
<tr>
<td>High-to-Medium</td>
<td>231</td>
<td>49</td>
<td>1.12 (0.78, 1.63)</td>
</tr>
<tr>
<td>Stable-High</td>
<td>107</td>
<td>22</td>
<td>1.00 (0.58, 1.70)</td>
</tr>
</tbody>
</table>
Conclusions (II)

- Identified 4 long-term trajectories of CRP over a 10 year period
- Increasing CRP from medium to high levels associated with most adverse ageing outcomes:
  - poor cardiometabolic health
  - lower physical functioning and increased arthritis
  - Lower respiratory functioning
  - increased depressive symptoms
- Maintaining high levels of CRP associated with some outcomes
- Independent of health behaviours, SES, BMI, anti-inflammatory drugs
- Monitor inflammation levels over time can help prevent adverse ageing outcomes

General conclusions

- ELSA rich study with repeated measurements
- Latent growth curve modelling useful to identify both individual and group-based trajectories
- Useful to describe evolution of health markers over time and relate it to contextual factors
- Interesting to group individuals that follow similar pattern of trajectories over time and relate this to disease risk or any aspect of ageing
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