The Biosocial Life Course
Ageing
4th October 2018

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Projected global age profile in 2050
UN Population Fund, 2012

Projected UK population in 2033
Office for National Statistics
**Biosocial factors and ageing**

- Biogerontological and population perspectives on ageing
- Disease vs ageing processes
- Links between mental and physical health outcomes in ageing
- Psychobiological processes and the acceleration of ageing
- Concept of frailty as a pre-illness risk syndrome

**Hallmarks of ageing – biogerontology**

- Genomic instability
- Telomere attrition (telomere length)
- Epigenetic alterations
- Loss of proteostasis (heat shock proteins)
- Deregulated nutrient sensing (insulin, IGF-1, GH)
- Mitochondrial dysfunction (oxidative stress)
- Cellular senescence
- Stem cell exhaustion
- Altered intercellular communication (inflammation)

Lopez-Otin et al., Cell, 2013

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**Hallmarks of ageing - population**

- Sensory loss (sight, hearing, taste)
- Declining physical capability
- Disability and impaired activities of daily living
- Cognitive impairment
- Reductions in social / cultural participation

**English Longitudinal Study of Ageing**

<table>
<thead>
<tr>
<th>Sample</th>
<th>National representative sample 12,099 recruited in 2002 Currently around 9,000 in study (sample refreshed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50 to 100+</td>
</tr>
<tr>
<td>Genetics</td>
<td>GWAS on 7,400 Various candidate gene analyses</td>
</tr>
<tr>
<td>Funding</td>
<td>National Institute on Aging, ESRC, Government Departments</td>
</tr>
<tr>
<td>Contact</td>
<td>Andrew Steptoe (PI); Kate Coughlan (manager) <a href="http://www.elsa-project.ac.uk/">http://www.elsa-project.ac.uk/</a></td>
</tr>
</tbody>
</table>
Visual impairment by age - ELSA

Hand grip strength - ELSA

Social participation and age

Hallmarks of ageing - population

- Sensory loss (sight, hearing, taste)
- Declining physical capability
- Disability and impaired activities of daily living
- Cognitive impairment
- Reductions in social / cultural participation
- Increased risk of CHD, diabetes, cancers, arthritic conditions, frailty, and dementia
**'Successful' ageing**

Introduced by Rowe & Kahn (Science, 1987)
- Maintenance of high mental and physical function
- Sensory loss (sight, hearing)
- Low risk of disease and disability
- Continued engagement with life

105 operational definitions (Cosco et al, 2014)
- Most include physiological function, affective wellbeing, social engagement
- Prevalence is variable across studies (20-30%)

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Institute for Fiscal Studies, 2017

Fauja Singh, retired from marathon running at age 101

David Attenborough Aged 93
• Disease vs ageing processes
  - Long-term and life threatening conditions become more common with age (CHD, diabetes, cancers, arthritis, chronic lung disease, etc)
  - What changes at the functional and phenotypic levels are due to ageing per se and to the effects of age-related health problems?

Example of socioeconomic status

Wealth and mortality in ELSA

Men and women aged 50-64 at baseline, followed for 9.4 years
Adjusted for age, sex, marital status, smoking, physical activity, depressive symptoms and BMI
Demakakos et al, 2016, J Epidemiol Community Health
SES and age-related decline

- ELSA sample (4,566, mean age 64.4y) followed up over 8 years
- Wealth as an indicator of SES
- Outcome-wide analysis
- Does rate of decline in 6 domains - physical capability, sensory function, physiological function, cognitive performance, emotional wellbeing and social function – vary with SES?
  - Controlling for age, gender, ethnicity, education, long-term health conditions

Graphs showing trends in different domains across different wealth groups.
**Biosocial factors and ageing**

- **Disease vs ageing processes**
  - Long-term and life threatening conditions become more common with age (CHD, diabetes, cancers, arthritis, chronic lung disease, etc)
  - What changes at the functional and phenotypic levels are due to ageing per se and to the effects of age-related health problems?
  - Are age-related changes influenced by psychosocial factors?

- **Biogerontological and population perspectives on ageing**
  - Disease vs ageing processes
  - Links between mental and physical health outcomes in ageing
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**Mental and physical health at older ages**

- Levels of depression and distress are raised in people with chronic diseases of older age

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**Depression in chronic illness**

<table>
<thead>
<tr>
<th>N studies</th>
<th>Health condition</th>
<th>Measure</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitchell 2011</td>
<td>Cancer</td>
<td>Int + quest</td>
<td>13-17%</td>
</tr>
<tr>
<td>Matte 2016</td>
<td>COPD</td>
<td>Int + quest</td>
<td>27%</td>
</tr>
<tr>
<td>Ali 2006</td>
<td>Type 2 diabetes</td>
<td>Int + quest</td>
<td>18%</td>
</tr>
<tr>
<td>Ciesla 2001</td>
<td>HIV+</td>
<td>Interview</td>
<td>9%</td>
</tr>
<tr>
<td>Thomsa 2008</td>
<td>Coronary heart disease</td>
<td>Interview</td>
<td>20%</td>
</tr>
<tr>
<td>Bar 2003</td>
<td>Chronic pain</td>
<td>Interview</td>
<td>52%</td>
</tr>
<tr>
<td>Stubbs 2016</td>
<td>Osteoarthritis</td>
<td>Int + quest</td>
<td>20%</td>
</tr>
<tr>
<td>Ayerba 2013</td>
<td>Stroke</td>
<td>Int + quest</td>
<td>29%</td>
</tr>
<tr>
<td>Warsch 2004</td>
<td>General population</td>
<td>Interview</td>
<td>4%</td>
</tr>
</tbody>
</table>

Steptoe, 2018, Handbook of Psychosocial Epidemiology
Mental and physical health at older ages

- Levels of depression and distress are raised in people with chronic diseases of older age
- Multimorbidity associated with higher levels of depression and distress

Mental and physical health at older ages

- Levels of depression and distress are raised in people with chronic diseases of older age
- Multimorbidity associated with higher levels of depression and distress
- Depression and distress can be both a predictor and a consequence of chronic disease

Depression and incident coronary heart disease

<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Number of studies</th>
<th>Number of participants</th>
<th>Odds ratio or relative risk (95% CI of CHD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rugalla et al. (2002)</td>
<td>11</td>
<td>35,540</td>
<td>1.64 (1.29–2.08)</td>
</tr>
<tr>
<td>Colquhoun et al. (2003)</td>
<td>25</td>
<td>100,428</td>
<td>1.31 (1.50–2.10)</td>
</tr>
<tr>
<td>Wachter-Sengers et al. (2003)</td>
<td>10</td>
<td>NR</td>
<td>1.04 (1.01–1.08)</td>
</tr>
<tr>
<td>Nobiletti et al. (2006)</td>
<td>21</td>
<td>34,956</td>
<td>1.33 (1.15–1.53)</td>
</tr>
<tr>
<td>Nielson et al. (2010)</td>
<td>11*</td>
<td>NR</td>
<td>1.10 (0.90–1.25) adjusted</td>
</tr>
<tr>
<td>Van der Kooij et al. (2007)</td>
<td>16</td>
<td>650,061</td>
<td>1.5 (1.36–1.68)</td>
</tr>
<tr>
<td>Gouveia et al. (2016)</td>
<td>50</td>
<td>803,560</td>
<td>1.30 (1.22–1.40)</td>
</tr>
</tbody>
</table>

Table 1: Depression as a risk factor for incident CHD

CHD, coronary heart disease. *Includes only those studies of participants without CHD at baseline.

Depression and incident stroke

Li et al. 2015, Int J Cardiology

Carney & Freedland 2017, Nature Rev Cardiology
Mental and physical health at older ages

- Levels of depression and distress are raised in people with chronic diseases of older age
- Multimorbidity associated with higher levels of depression and distress
- Depression and distress can be both a predictor and a consequence of chronic disease
- Depression and distress predict adverse outcomes in chronic diseases of older age

Impact on:
- Psychological wellbeing
- Quality of life
- Health service utilisation
  - Emergency care
  - Outpatient visits
  - Medication costs

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Depression and mortality in chronic illness

<table>
<thead>
<tr>
<th>Study</th>
<th>N studies</th>
<th>Health condition</th>
<th>Hazard ratio / relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinquart, 2010</td>
<td>76</td>
<td>Cancer</td>
<td>1.22 (1.14 – 1.30)</td>
</tr>
<tr>
<td>Atlantis, 2013</td>
<td>7</td>
<td>COPD</td>
<td>1.83 (1.60 – 3.36)</td>
</tr>
<tr>
<td>van Dooren, 2013</td>
<td>16</td>
<td>Type 2 diabetes</td>
<td>1.46 (1.29 – 1.66)</td>
</tr>
<tr>
<td>Sokonel, 2016</td>
<td>26</td>
<td>Heart failure</td>
<td>1.40 (1.22 – 1.60)</td>
</tr>
<tr>
<td>Majer, 2011</td>
<td>29</td>
<td>Coronary heart disease</td>
<td>2.25 (1.73 – 2.93)</td>
</tr>
<tr>
<td>Pan, 2011</td>
<td>8</td>
<td>Stroke</td>
<td>1.55 (1.25 – 1.93)</td>
</tr>
</tbody>
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Mental and physical health at older ages

- Levels of depression and distress are raised in people with chronic diseases of older age
- Multimorbidity associated with higher levels of depression and distress
- Depression and distress can be both a predictor and a consequence of chronic disease
- Depression and distress predict adverse outcomes in chronic diseases of older ages
- Depression and distress predict disability, while subjective wellbeing may be protective
Enjoyment of life and survival in ELSA

- 9,387 core members of ELSA (aged 50+)
  followed for 10 years, 7 months
- 2,045 dated fatalities
- Enjoyment of life from CASP19
  ➢ I enjoy the things that I do
  ➢ I enjoy being in the company of others
- Division into quartiles of enjoyment
- Cox proportional hazards regression

Update of Steptoe & Wardle
Archives of Internal Medicine 2012

Enjoyment of life and survival in ELSA

- Deaths
  - Lowest enjoyment: 31.1%
  - Second: 23.7%
  - Third: 18.8%
  - Highest enjoyment: 10.9%

Psychosocial factors

Risk factors
- Low socioeconomic status
- Work stress
- Life events
- Chronic adversity
- Early life adversity
- Social isolation
- Depression, anxiety
- Hostility
- Loneliness
- Maladaptive coping

Protective factors
- Social connectedness
- Social support
- Positive wellbeing
- Optimism
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Psychosocial determinants of health: pathways

**Lifestyle**
- Smoking, food choice, physical exercise, alcohol consumption, healthy weight, adherence to treatment

**Biology**
- Modifications in neuroendocrine, cardiovascular, inflammatory, immunological and other physiological responses

**Neuroendocrine**
- Cortisol, adrenaline, testosterone, noradrenaline

**Cardiovascular**
- Blood pressure, heart rate, heart rate variability

**Immune**
- Lymphocyte counts and activity, natural killer cells, immunoglobulins

**Inflammatory**
- C-reactive protein, interleukin (IL) 6, fibrinogen

**Metabolic**
- Lipids (cholesterol), glucose, insulin
Psychosocial determinants of health: pathways

- Autonomic nervous system
- Neuroendocrine pathways
- Psychoneuroimmunological (PNI) pathways

Psychobiological processes and health

A question of balance:

- Reduced activation
- Optimal activation
- Heightened activation

Some effects of cortisol

- Stimulation of glucose production in the liver
- Release of free fatty acids from fat stores
- Regulation of water balance
- Stimulation of anti-inflammatory responses
- Immune regulation

Otte et al, 2016, Nat Rev Disease Primers
Some effects of high cortisol

Potentially damaging effects
• Increased lipid (LDL-cholesterol) in the blood
• Suppression of immune function
• Decalcification of bone
• Deposition of abdominal fat
• Damage to the hippocampus
• Muscle wasting
• Impaired reproductive function

Age-related biomarkers relevant to Soc-B programme

• Cortisol (saliva and hair)
• Inflammatory markers: C-reactive protein, IL-6, fibrinogen, white blood cell counts (blood)
• Metabolic markers: HbA1c, fasting glucose (blood)
• Cardiovascular markers: blood pressure, heart rate, heart rate variability

When are psychobiological responses hazardous?

• Heightened reactions or failure of post-stress adaptation
• Sustained or repeated exposure may lead to chronic allostatic load

Allostatic load

1. Short-term fluctuations are necessary for responding to the environment
2. Excessive fluctuations can impair regulatory systems
3. This is manifest in progressive failure to maintain levels within normal operating ranges (both resting levels and response patterns)
4. Allostatic load is the cumulative physiological toll across multiple systems
**Stress and Allostasis**

Manifestations of chronic allostatic load:
- Failure of adaptation
- Impaired recovery
- Blunted reactivity

Effects on:
- Neuroendocrine function
- Autonomic NS activity
- Immune function
- Metabolism, adiposity
- Brain structure
- Reproductive function

- **Systolic BP by SES – heart scan study**

- **Social isolation and cortisol over the day**

- **Cellular ageing and telomeres**
Cellular ageing and telomeres

Psychosocial factors and telomere length

Shorter telomere length associated with:
- Perceived stress (Epel, 2004; Parks 2009)
- Mood disorders (Simon, 2006)
- Childhood adversity (Price, 2013)
- Hostility (Brydon, 2012)
- Pessimism (O’Donovan, 2009)
- Low social support (Carroll, 2013)
- Lower education (Steptoe, 2011)
- Experience of racial discrimination (Chae, 2014)

Telomere length and biological responses to stress

- Do individual differences in stress-related responses predict greater telomere attrition over time?
- 493 healthy men and women aged 53-76 years
- Cortisol responses to standardized mental stress tests
- Leukocyte telomere length measured at baseline and 3 years later
- Cortisol ‘responders’ and ‘non-responders’ compared

Telomere length and biological responses to stress
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Frailty

• A syndrome of vulnerability to sudden health changes triggered by minor stressors

Frailty

• Multisystem dysregulation – immune, endocrine, skeletal muscle, brain
• Clinical manifestation: fatigue, unexplained weight loss, falls, delirium, fluctuating disability

Clegg et al, 2013
Lancet
Frailty

- A syndrome of vulnerability to sudden health changes triggered by minor stressors
- Multisystem dysregulation – immune, endocrine, skeletal muscle, brain
- Clinical manifestation: fatigue, unexplained weight loss, falls, delirium, fluctuating disability
- Different models – Fried and Rockwood

Frailty and adverse outcomes

- Fried model
  - Recent weight loss; Exhaustion; Low energy expenditure; Slow gait speed; Weak grip strength
  - 3-5 Frail
  - 1-2 Pre-frail

- Rockwood index
  - Cumulative deficits across multiple systems (mood, physical signs, biomarkers, disabilities, illnesses)
  - The more people have wrong with them, the more likely they are to be frail

Frailty is a risk factor for

- Mortality
- Falls
- Care home admission
- Hospitalisation
- Dementia

Clegg et al, 2013
Lancet
Frailty and dementia risk

Frailty and adverse outcomes

Frailty is a risk factor for

- Mortality
- Falls
- Care home admission
- Hospitalisation
- Dementia

Risk factors for frailty

- Smoking
- Low physical activity
- Inflammation
- Vision and hearing impairment
- Loneliness

- Cultural engagement appears to be protective
Cultural engagement and frailty

Adjusted for age, sex, wealth, education, living alone, physical activity, organizational membership, and social activity.

Rogers & Fancourt, J Gerontol Psychol Sci, 2019

Ferrucci et al, 2018, Circulation Res