World Population Ageing: 1950-2050

Population ageing is unprecedented, without parallel in human history—and the twenty-first century will witness even more rapid ageing than did the century just past. Population ageing is pervasive, a global phenomenon affecting every man, woman and child. Population ageing is enduring: we will not return to the young populations that our ancestors knew. Population ageing has profound implications for many facets of human life.
Ageing is the most important risk factor for many common diseases.
LLHW Centre for Ageing and Vitality

Molecular mechanisms of ageing
- Mitochondrial dysfunction
- Inflammation

Animal models
- Human and mouse tissue resource
- Epigenetics and transcriptomics
- Capacity building
- Public and policy engagement

Interventions to promote healthy ageing
- Nutrition
- Physical activity
LLHW Centre for Ageing and Vitality

Molecular mechanisms of ageing

Interventions to promote healthy ageing
LLHW Centre for Ageing and Vitality

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- Nutrition
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To realise our objectives

Build on our achievements

Mitochondria

Inflammation

Dietary Antioxidant (BHA)

Control diet $nfb1^{-/-}$
24.52 +/- 1.02

BHA diet $nfb1^{-/-}$
1.62 +/- 0.44 ***
To realise our objectives

Build on our achievements

Nutrition

Physical activity

Data Management: Cloud internet

Security

Processing
Storage
Provenance / Audit

eScience Central

Newcastle University
LLHW Centre for Ageing and Vitality

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Epigenetics and transcriptomics

Capacity building

Nutrition

Physical activity
Links with other Centres in Newcastle

Newcastle Biomedical Research Centre

LLHW Centre for Ageing and Vitality

CIMA: The Centre for Integrated research into Musculoskeletal Ageing

Wellcome Trust Centre for Mitochondrial Research

MRC Centre for Neuromuscular Diseases
Research is focussed on three of major disease areas of direct relevance to the older person:
the **ageing brain** (dementia and stroke)
the **ageing body** (chronic liver disease, diabetes and cardiovascular disease)
the **ageing limbs** (musculoskeletal disease)
Links with other Centres in Newcastle

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CIMA
The Centre for Integrated research into Musculoskeletal Ageing

Wellcome Trust Centre for Mitochondrial Research

MRC Centre for Neuromuscular Diseases
Links with other UK Centres and Units

MRC Unit for Lifelong Health and Ageing
MRC National Survey for Health and Development
Links with other UK Centres and Units

MRC Genome Damage and Stability Centre

School of Life Sciences
El-Khamisy Lab

MRC Human Genetics Unit

the forefront of research into human genetics

MRC Medical Research Council

Mitochondrial Biology Unit
Importance and mechanisms of mitochondrial changes in human ageing?
The Hertfordshire Cohort Studies are a group of unique studies of men and women born in the English county of Hertfordshire between 1911 and 1939.
Table 1: Participant characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>79</td>
<td>72.6 (2.4)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>79</td>
<td>173.9 (6.3)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79</td>
<td>82.1 (13.0)</td>
</tr>
<tr>
<td>DXA Lean mass (kg)</td>
<td>79</td>
<td>56.3 (6.8)</td>
</tr>
<tr>
<td>Grip strength (kg)</td>
<td>79</td>
<td>37.7 (8.0)</td>
</tr>
<tr>
<td>Mid upper arm circumference (cm)</td>
<td>78</td>
<td>31.8 (2.8)</td>
</tr>
<tr>
<td>Walking speed (m/s)</td>
<td>77</td>
<td>1.1 (0.2)</td>
</tr>
<tr>
<td>6m timed up and go (secs)*</td>
<td>77</td>
<td>10.5 (9.4, 11.7)</td>
</tr>
<tr>
<td>Chair rise time (secs)*</td>
<td>76</td>
<td>16.5 (14.7, 18.6)</td>
</tr>
<tr>
<td>Fibres deficient in COX/SDH (%)</td>
<td>79</td>
<td>1.1 (0.0, 2.1)</td>
</tr>
<tr>
<td>VO2 max (ml/kg/min)*</td>
<td>61</td>
<td>8.5 (7.3, 11.1)</td>
</tr>
<tr>
<td>Flamingo stands (&lt; 5 secs)+</td>
<td>78</td>
<td>48 (61.5%)</td>
</tr>
<tr>
<td>Low** SF36 physical functioning score+</td>
<td>79</td>
<td>24 (30.4%)</td>
</tr>
<tr>
<td>Any EWGSOP sarcopenia+</td>
<td>77</td>
<td>6 (7.8%)</td>
</tr>
<tr>
<td>Graded EWGSOP sarcopenia+: None</td>
<td>77</td>
<td>50 (64.9%)</td>
</tr>
<tr>
<td>Pre Sarc (FFM)</td>
<td>21</td>
<td>27.3%</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>4</td>
<td>5.2%</td>
</tr>
<tr>
<td>Severe sarcopenia</td>
<td>2</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

+ n(%)  
*Median (lower quartile, upper quartile)  
**Bottom fifth of the SF-36 physical functioning score i.e. ≤90
COX/SDH histochemistry

- **COX reaction**
  - Oxidation of Diaminobenzidine (DAB)
  - Complex IV

- **SDH reaction**
  - Reduction of Nitrobluetetrazolium
  - Complex II

Combined COX/SDH reaction
COX/SDH – representative images

No COX deficiency – HSS 005/5917 (0%)
COX/SDH – representative images

Medium COX deficiency – HSS 059/6778 (2.3%)
COX/SDH – representative images

High COX deficiency – HSS 093/5276 (14.2%)
Mitochondrial dysfunction underestimation

COX/SDH

6 abnormal fibres

cl-20

12 abnormal fibres

COX-deficient fibres (1) = 6
COX-normal but cl-20 deficient fibres (2) = 6
Tool to assess mitochondrial complexes in single cells

Accurate
Reproducible
Reliable
Automatic

Complex IV
Complex I
Quadrupule immunofluorescence (IF)
Software detection (IMARIS)
Software detection (IMARIS)
Classification of fibres based on COX-I and cl-20 expression
Sarcopenia cohort

HSS 140_6284

% of fibres

COX-I expression

cl-20 expression

Neg
Int(-)
Int(+)
Pos

COX OR Cl neg
COX and Cl: int
COX normal / Cl int
COX int / Cl normal
COX and Cl normal
Sarcopenia cohort

HSS 033_5029
- % of fibres
- COX-I expression vs. cl-20 expression
- Neg, Int(-), Int(+), Pos

HSS 093_5765
- % of fibres
- COX-I expression vs. cl-20 expression
- Neg, Int(-), Int(+), Pos

COX OR Cl neg
COX and Cl: int
COX normal / Cl int
COX int / Cl normal
COX and Cl normal