

## Ageing: the Biosocial Perspective

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#### Our World in Data

#### Median age, 1990

The median age divides the population into two parts of equal size; that is, there are as many people with ages above the median age as there are with ages below.



Source: United Nations - Population Division (2022)

OurWorldInData.org/age-structure • CC BY

Note: 1950 to 2021 show historical estimates. From 2022 the UN projections (medium variant) are shown.

#### Our World in Data

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Note: 1950 to 2021 show historical estimates. From 2022 the UN projections (medium variant) are shown.

#### **Biosocial factors and ageing**

- Biogerontological and population perspectives on ageing
- Disease vs ageing processes; 'biological ageing'
- Biosocial processes at older ages methods of study
- Positive emotional wellbeing and health at older ages



Lopez-Ortin et al *Cell*, 2023

### Characteristics 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

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- Sensory loss (sight, hearing, taste)
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- Reductions in social / cultural participation
- Increased risk of CHD, diabetes, cancers, arthritic conditions, frailty, and dementia

### Ageing and long-term health conditions



MacNee et al. Eur Respir J 2014;44:1332-1352



Fauja Singh, retired from marathon running at age 101

David Attenborough Aged 97



## Challenges in ageing

- Health issues
  - Living with long-term conditions; increased prevalence of dementia; socioeconomic inequalities; terminal care
- Economic issues
  - Ensuring adequate incomes; costs of health and social care; employment at older ages; transport and access



Figure 5.8. Age profile of public health spending in the UK (relative to 30-year-olds)

Institute for Fiscal Studies, 2017

#### Old-age dependency ratio, 2021

Our World in Data

The ratio of the number of people older than 64 relative to the number of people in the working age population (15-64 years). Data are shown as the number of dependents per 100 working-age population.



# Challenges in ageing

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- Economic issues
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- Social and psychological issues
  - Maintenance of psychological wellbeing; loneliness and isolation; age discrimination; social / cultural engagement

#### Population ageing longitudinal cohorts

- English Longitudinal Study of Ageing (ELSA)
  - Nationally representative sample of men and women aged 50+ living in the community
  - Started in 2002, typically assessed every 2 years
  - Four sets of biomarker assessment so far
  - Sample periodically refreshed (c19,000)
- Health and Retirement Study (HRS)
  - Nationally representative sample of men and women aged 50+ living in the USA
  - Started in 1992, typically assessed every 2 years
  - Biomarkers assessed once so far
  - Sample periodically refreshed (c43,000)

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#### Prevalence of multimorbidity by age and deprivation



#### JAMA Internal Medicine | Original Investigation

#### Comparison of Health Outcomes Among High- and Low-Income Adults Aged 55 to 64 Years in the US vs England

HwaJung Choi, PhD; Andrew Steptoe, DSc; Michele Heisler, MD, MPH; Philippa Clarke, PhD; Robert F. Schoeni, PhD; Stephen Jivraj, PhD; Tsai-Chin Cho, MSc; Kenneth M. Langa, MD, PhD

JAMA Internal Medicine September 2020 Volume 180, Number 9

Comparison of adults aged 55-64 from the HRS and ELSA in 2008-2016 46,887 person-years of observations

Annual income divided into deciles

Adjusted for age, sex, country of birth, race, household size and marital status

#### Income and health outcomes



#### Income and health outcomes

A Functional limitation



B High risk of diabetes (HbA<sub>1c</sub> >6.5%)



Adjusted for age, sex, country of birth, race, household size and marital status Choi et al, *JAMA Intern Med*, 2020



- Lower SES related to earlier onset of agerelated health problems
- Is SES also associated with aging processes independently of health?

## Chronological vs biological ageing

#### Chronological age

Age in years since birth

#### **Biological age**

- Age based on changes in biological processes
  - Telomere length
  - Epigenetic biological clocks
  - Phenotypic indices

## Cellular ageing and telomeres





at the ends of the chromosomes.

University of California San Francisco President of Salk Institute, San Diego Nobel laureate in physiology or medicine, 2009

## **Cellular ageing and telomeres**



Blackburn et al, Science, 2015

#### Education and leukocyte telomere length



Model 2: + smoking, BMI, physical activity Model 3: + household income Steptoe et al, 2011 BBI

## Phenotypic biological ageing

- Measures of biological ageing based on changes in multiple biomarkers of diverse bodily systems
- Individual biomarkers regressed on age, then combined using principal components analysis (PCA) or similar
- Differences from chronological age reflect biological age
- Derived measures depend on biomarkers available.
   A lot of variability (e.g. Crimmins et al, *Geroscience*, 2021)

#### Phenotypic ageing and childhood adversity



Analysis of UK Biobank, mean age 56.4, sd 7.7 Yang et al, JAMA Network Open, 2022

## **Epigenetic clocks**

- Measures of biological ageing based on DNA methylation (methylation of CpG sites)
- Calibrated against phenotypes
- Correlated with chronological age, but discrepancies reflect biological age
- Multiple clocks: GrimAge, PhenoAge, DunedinPACE, Horvath, Hannum

#### **Epigenetic clocks and SES**



McCrory et al, 2021, J Gerontol A Biol Sci Med Sci

# Socioeconomic indicators

Birth / Childhood	Adolescence	Early adult life	Mid adult life	Older age
Parental education and occupation	Own education, Parental education and occupation	Own education, Occupational status, income	Occupational status, Income	Accumulated wealth, Income

# Low socioeconomic status and the acceleration of aging

- Does lower socioeconomic status promote more rapid decline in age-related processes independent of health status?
- Wealth as indicator of SES
- Adjustment for age, gender, ethnicity, education and longterm health conditions
- 'Outcome-wide' epidemiological analysis
  - Physical capability
  - Sensory function
  - Physiological function
  - Cognitive function
  - Emotional wellbeing
  - Social functioning

Steptoe & Zaninotto Proc Nat Acad Sci USA, 2020



#### Changes in walking speed

3

Lowest



2

Highest

0

**Changes in physical activity** 

Adjusted for age, gender, ethnicity, education and long-term conditions



#### **Changes in lung function**



Adjusted for age, gender, ethnicity, education and long-term conditions





education and long-term conditions



education and long-term conditions



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#### Psychosocial determinants of health: pathways

Lifestyle	<ul> <li>Smoking, food choice, physical exercise, alcohol consumption, healthy weight, adherence to treatment</li> </ul>
Biology	<ul> <li>Modifications in neuroendocrine, cardiovascular, inflammatory, immunological and other physiological responses</li> </ul>

#### Social – Biological Interface

- Autonomic nervous system
   > Blood pressure, heart rate, heart rate variability
- Neuroendocrine pathways
   Cortisol, adrenaline/noradrenaline
- Psychoneuroimmunological (PNI) pathways
  - Innate immunity (inflammatory cytokines), humoral immunity (immunoglobulins), immune cell expression



#### Otte et al, 2016, *Nat Rev Disease Primers*

#### Allostatic load



- Short-term fluctuations are necessary for responding to the environment
- 2. Excessive fluctuations can impair regulatory systems
- 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

# 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
- Telomere length and epigenetic alterations

### Psychosocial factors and inflammation

C-reactive protein, Interleukin (IL) 6, tumor necrosis factor (TNF $\alpha$ ), fibrinogen

Coronary heart disease, depression, frailty, adiposity, autoimmune diseases, diabetes, trauma, infection

### Psychosocial factors and inflammation

- C-reactive protein, Interleukin (IL) 6, tumor necrosis factor (TNF $\alpha$ ), fibrinogen
  - Coronary heart disease, depression, frailty, adiposity, autoimmune diseases, diabetes, trauma, infection
- Heightened inflammation associated with
- Low socioeconomic status, chronic work stress, childhood adversity, social isolation, loneliness, depression

# Psychobiological processes and health risk

#### Levels of study

- Psychophysiological stress testing
- Naturalistic monitoring
- Epidemiological studies





#### **Trier Social Stress Test (TSST)**



## Saliva sampling



#### Cortisol and Trier Social Stress Test



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#### Cortisol profile over the day



#### Cortisol waking response



#### Social isolation and cortisol over the day



Adjusted for age, gender, grade of employment, smoking, BMI and time of waking (Grant et al, 2009, Ann Behav Med)

# 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

# Cortisol responses and leukocyte telomere length



# Telomere length and biological responses to stress



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## **Psychosocial factors**

#### **Risk factors**

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

#### Depression in chronic illness



#### Depression and mortality in chronic illness

	N studies	Health condition	Hazard ratio / relative risk (95% Cl)
Pinquart, 2010	76	Cancer	1.22 (1.14 – 1.30)
Atlantis, 2013	7	COPD	1.83 (1.00 – 3.36)
van Dooren, 2013	16	Type 2 diabetes	1.46 (1.29 – 1.66)
Sokoreli, 2016	26	Heart failure	1.40 (1.22 – 1.60)
Meijer, 2011	29	Coronary heart disease	2.25 (1.73 – 2.93)
Pan, 2011	8	Stroke	1.55 (1.25 – 1.93)

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#### **Protective factors**

- Social connectedness
- Social support
- Positive wellbeing
- Optimism
- Purpose in life

## Positive psychological wellbeing

Hedonic / affective	<ul> <li>Feelings or moods such as happiness, sadness, and pleasure</li> </ul>		
Evaluative	<ul> <li>Evaluations of how satisfied people are with their lives</li> </ul>		
Eudaimonic	<ul> <li>Judgements about meaning and purpose in life</li> </ul>		

Steptoe, Deaton, and Stone *Lancet*, 2015

#### Different types of positive wellbeing and mortality

- 6,028 publications screened, 113 evaluated in detail
- 90 studies of initially 'healthy' populations included in meta-analysis
- Follow-up periods of 2 to 20+ years 52% had follow-up >10 years
- Protective association
   Pooled hazard ratio:
   Affective/experienced:
   Eudaimonic:
   Evaluative:
- 0.92 (95% CI 0.91-0.93) 0.91 (95% CI 0.86-0.98) 0.93 (95% CI 0.91-0.95) 0.88 (95% CI 0.83-0.94)

Martín-María et al *Psychosom Med,* 2017

## 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%

Age, sex: HR 0.25 (.21 - .31)

Demographics: HR 0.29 (.24 - .35)

Baseline health and mobility HR 0.35 (0.29 - 0.43)

Emotional distress and health behaviour HR 0.37 (0.31 – 0.46)

#### **Biosocial factors and ageing**

- Biogerontological and population perspectives on ageing are complementary
- Changes in physiology and psychosocial experience with advancing age are not only due to disease. Research on links between psychosocial factors and ageing is very active
- Biosocial processes at older ages can be studied with multiple methods
- Not just the negative; positive psychosocial factors such as emotional wellbeing are relevant to health at older ages