ELSA Biomarkers

Andrew Steptoe and Jessica Gong
Department of Epidemiology and Public Health
University College London

ELSA: Biomarker objectives

- To assemble a longitudinal dataset of biomarkers and physical capability measures in the ageing population

- To measure biomarkers relevant to major health outcomes at older ages, including cardiometabolic disease, frailty, dementia, and anemia

- To explore novel biomarkers potentially relevant to healthy ageing

Biomarkers and physical performance in ELSA

Wave 2 (2004/5) (7,666)	Wave 4 (2008/9) (8,218)	Wave 6 (2012/13) (7,730)	Wave 8/9 (2016/19) (6,594)
Weight, height, waist	Weight, height, waist	Weight, height, waist	Weight (in main interview) Waist (nurse visit)
Grip, balance, chair rise, tandem stand, leg raise, timed walk	Grip, balance, chair rise, tandem stand, leg raise, timed walk	Grip, balance, chair rise, tandem stand, leg raise, timed walk	Grip Timed walk
Blood pressure, lung function	Blood pressure, lung function	Blood pressure, lung function	Blood pressure
Lipids, triglycerides, HbA1c, glucose	Lipids, triglycerides, HbA1c, glucose	Lipids, triglycerides, HbA1c, glucose	Lipids, triglycerides HbA1c, glucose
C-reactive protein, fibrinogen	C-reactive protein, fibrinogen, white cell count	C-reactive protein, fibrinogen, white cell count	C-reactive protein, fibrinogen, white cell count
Haemoglobin, ferritin	Haemoglobin, ferritin	Haemoglobin, ferritin	Haemoglobin, ferritin
DNA	(DNA)	(DNA)	
	IGF-1, DHEAS	IGF-1, Vitamin D	IGF-1, Vitamin D
Apolipoprotein E		Cortisol, DHEA, cortisone, testosterone, progesterone (hair)	PAXgene tubes

Wave 11 (2023/24) Biomarkers

Physical function

➢ Grip strength, balance tests, leg raise, timed walk

Physiological measures

➢ Blood pressure, peak expiratory flow

Blood measures

➢ Lipid profile, triglycerides, fasting glucose, HbA1c
➢ C-reactive protein, fibrinogen, white blood cell count
➢ Ferritin, haemoglobin, vitamin D

Hair measures

➢ Cortisol, cortisone, progesterone, testosterone, DHEA

Stored aliquots of plasma and serum

Proteomics in ELSA

❖ Aim:
  ➢ Identify protein signatures relevant to ADRD risk

❖ Olink proteomic platform:
  ➢ Multiplexed antibody-based immunoassays with quantitative PCR
  ➢ PEA (proximity extension assay) technology
    ➢ High sensitivity and specificity
    ➢ Simultaneously measuring numerous proteins

Olink® Target panel selection

1. **Cardiovascular disease II (CVD II)**: cardiovascular and inflammatory markers for CVD and dementia
2. **Neurology (NEU I)**: markers relevant to neurobiological processes and neurological diseases including ADRD
3. **Neurology Exploratory (NEX):**
   - Includes exploratory and established markers for neurological diseases and biological processes such as axon development, neurogenesis and synapse assembly
   - Includes Neurofilament light polypeptide, important marker for degenerative neurological diseases and traumatic brain injury

92 proteins in each panel

ELSA participant selection

➤ Plasma samples collected from Wave 4 nurse visit (2008)

➤ Exclusion criteria:
  ❖ Died within 2 years of Wave 4
  ❖ Lost to follow-up (missing at ≥2 waves)
  ❖ Diagnosis of dementia at baseline

➤ Available plasma samples sent to Olink **(N=3,305)**

➤ ~ 96% of samples passed quality control

Dementia case identification

Combination of

➤ Reported physician diagnoses of dementia and AD

➤ Hospital Episode Statistics (Feb 1997 – Jan 2018) based on ICD-10 codes

➤ Mortality records up to April 2018

➤ Medication records (e.g. Donepezil, Rivastigmine)

➤ 239 incident cases up to early 2018

Volcano plot (T-test) illustrating Normalized Protein eXpression (NPX) difference in dementia versus no dementia from CVD II and NEU I Olink panels.