Biomarker trajectories and health outcomes

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Overview

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

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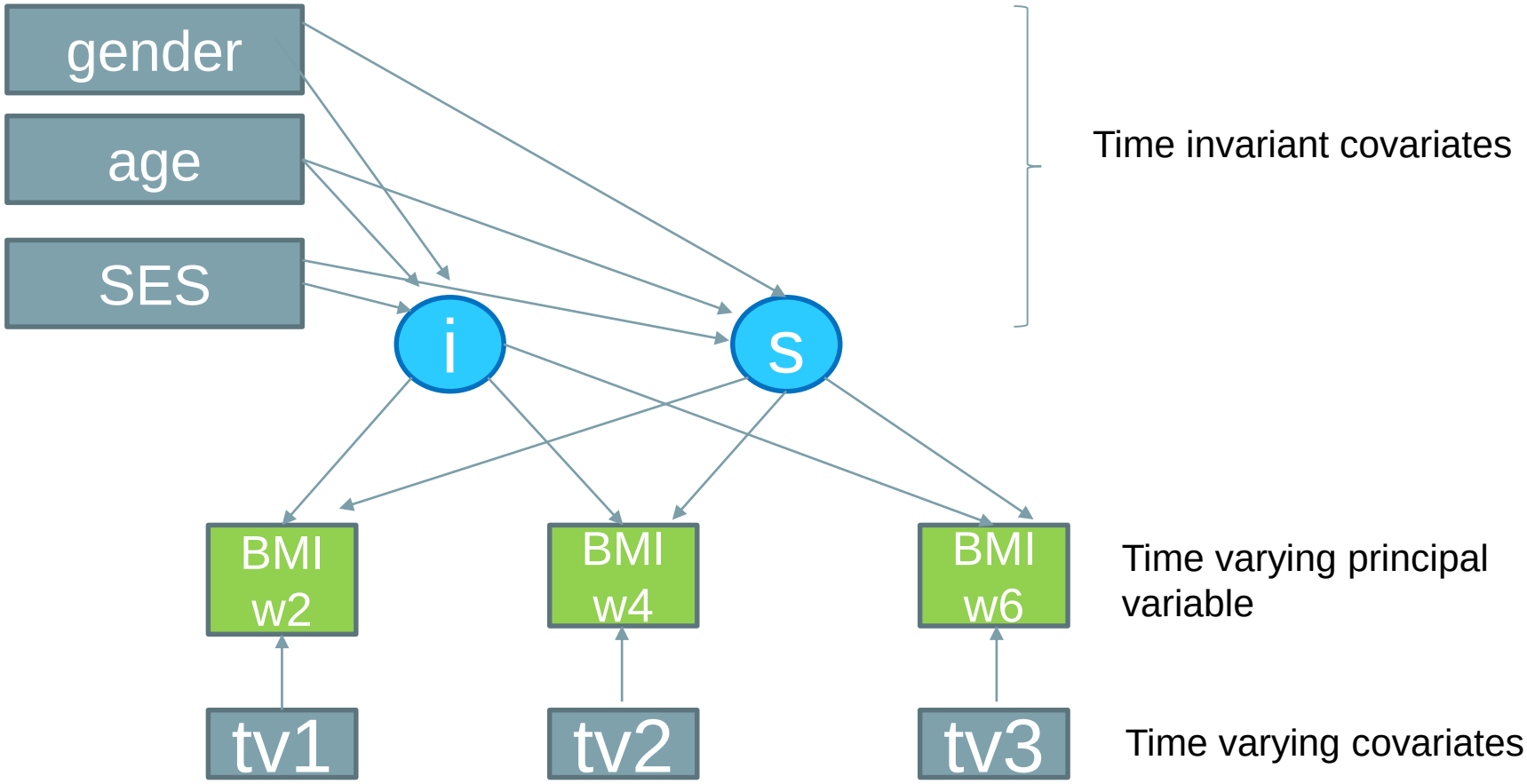
Growth curve modelling

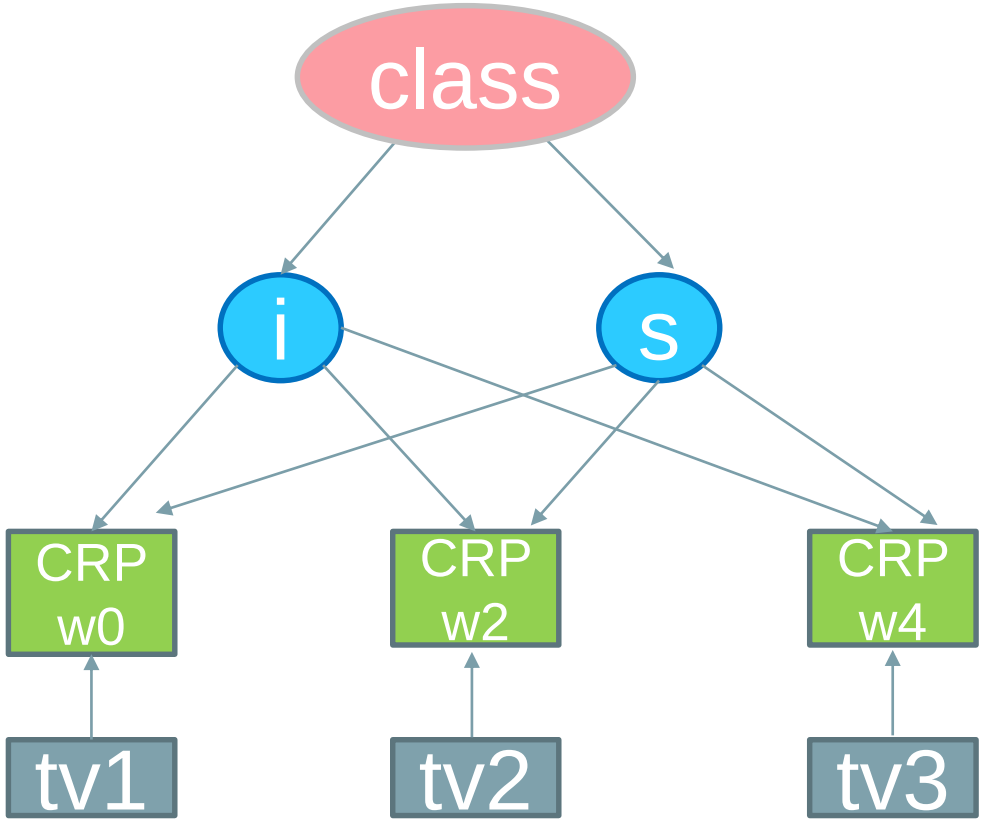
- Individual trajectories over time: Latent growth curve models
  - One trajectory for each person: Intercept and slope(s)
  - An average trajectory to characterize the entire sample
  - Variance trajectory = An indication of the extent to which individual trajectories deviate from the average trajectory

- 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



Group-based: Latent class growth analysis



Time varying principal variable

Time varying covariates

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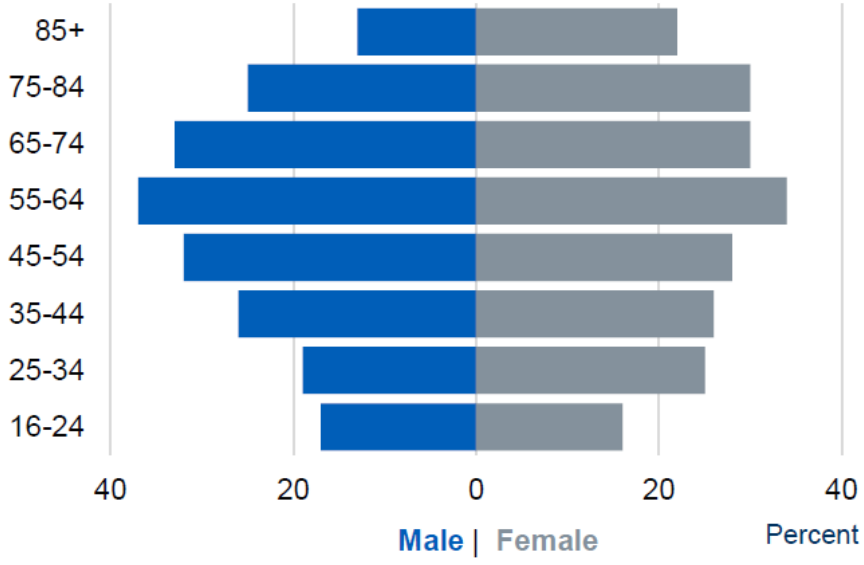
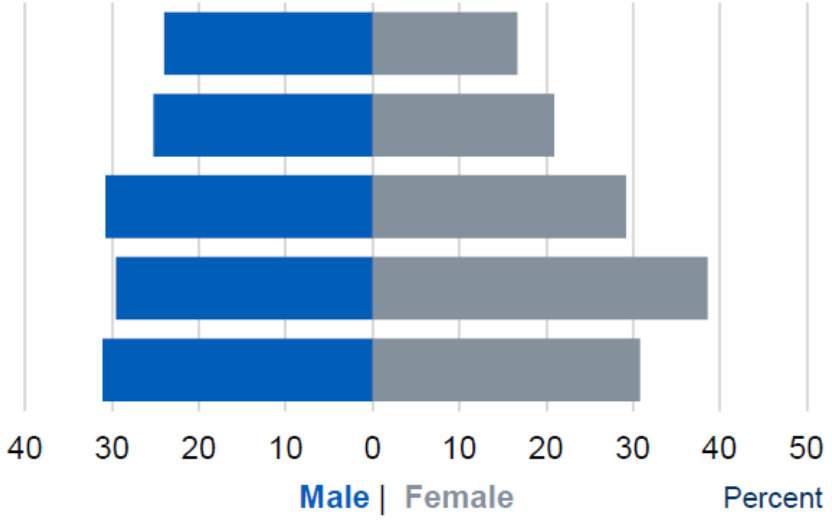
Body size and health consequences

- 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

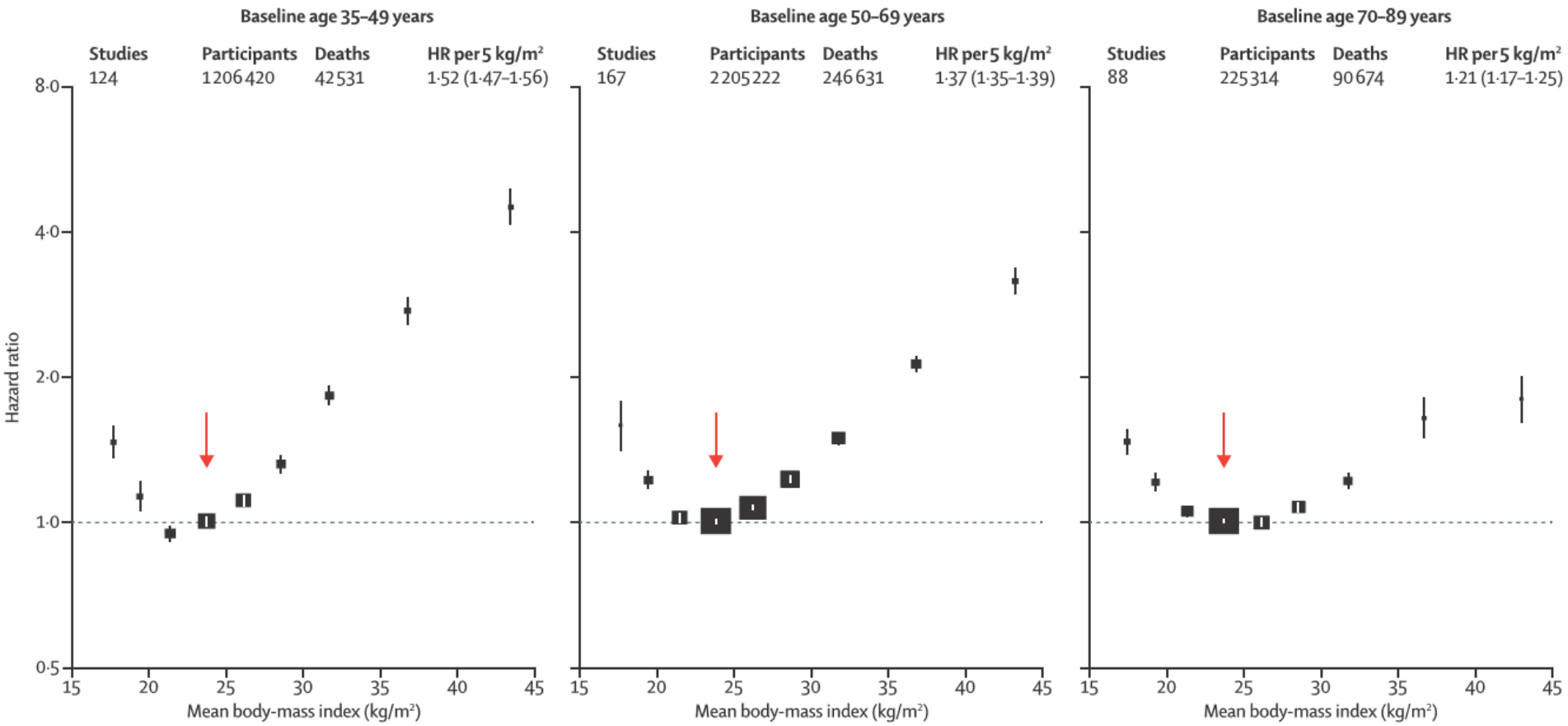




Health Survey for England 2015

Body size and health consequences

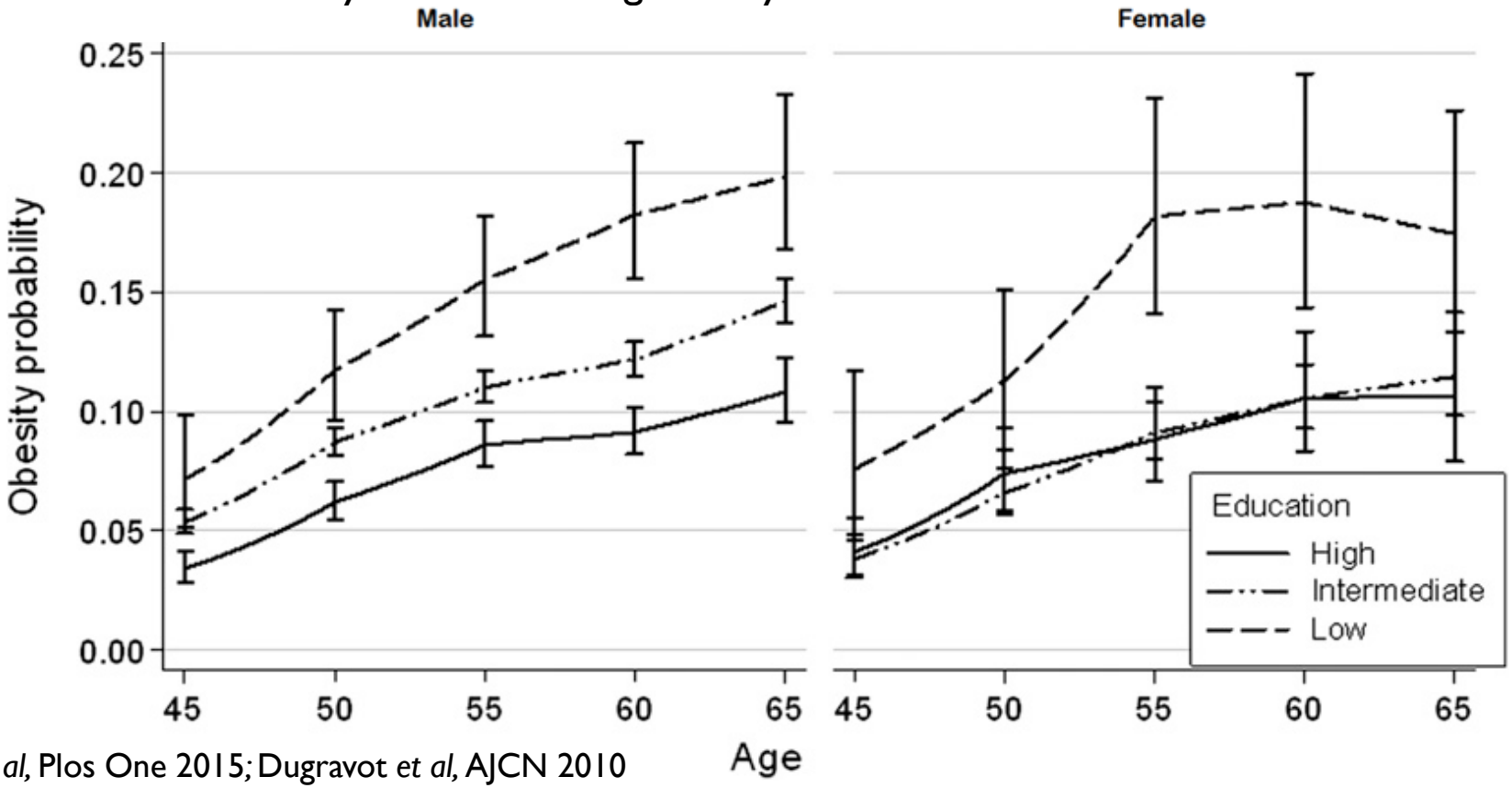
- Both obesity and underweight are associated with higher mortality risk



The Global BMI Mortality Collaboration, *Lancet* 2016

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

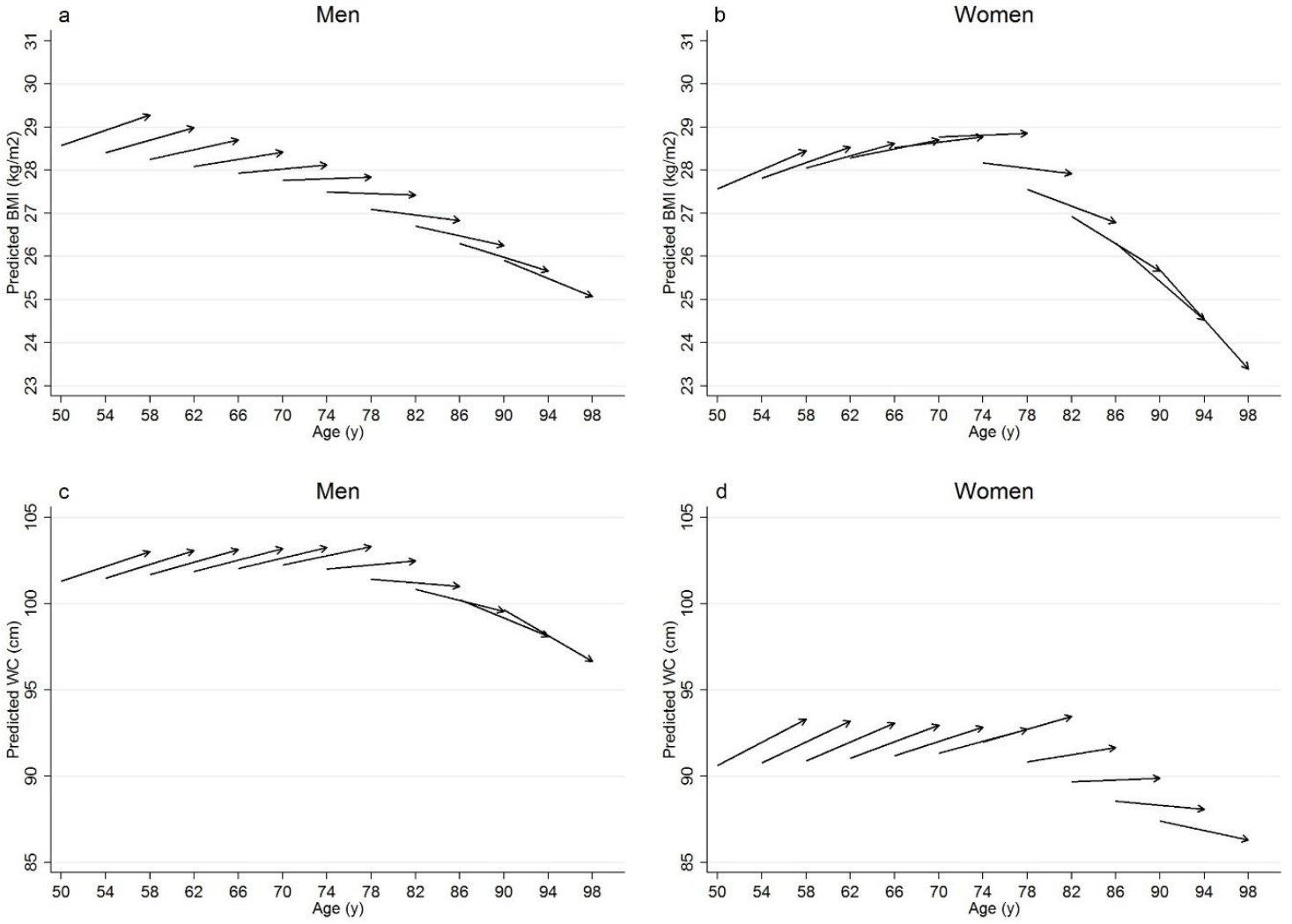
- Population:
  - Baseline year: 2004 (wave 2)
  - Three time points : wave 2, wave 4, wave 6 (clinical examination)
    - N=3259 men, mean age at baseline 65.6 ± 9.2 y
    - N=3966 women, mean age 66.1 ± 9.6 y
  - BMI and Waist Circumference measured by nurse
  - SES measure: tertiles of wealth in 2004
  - 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



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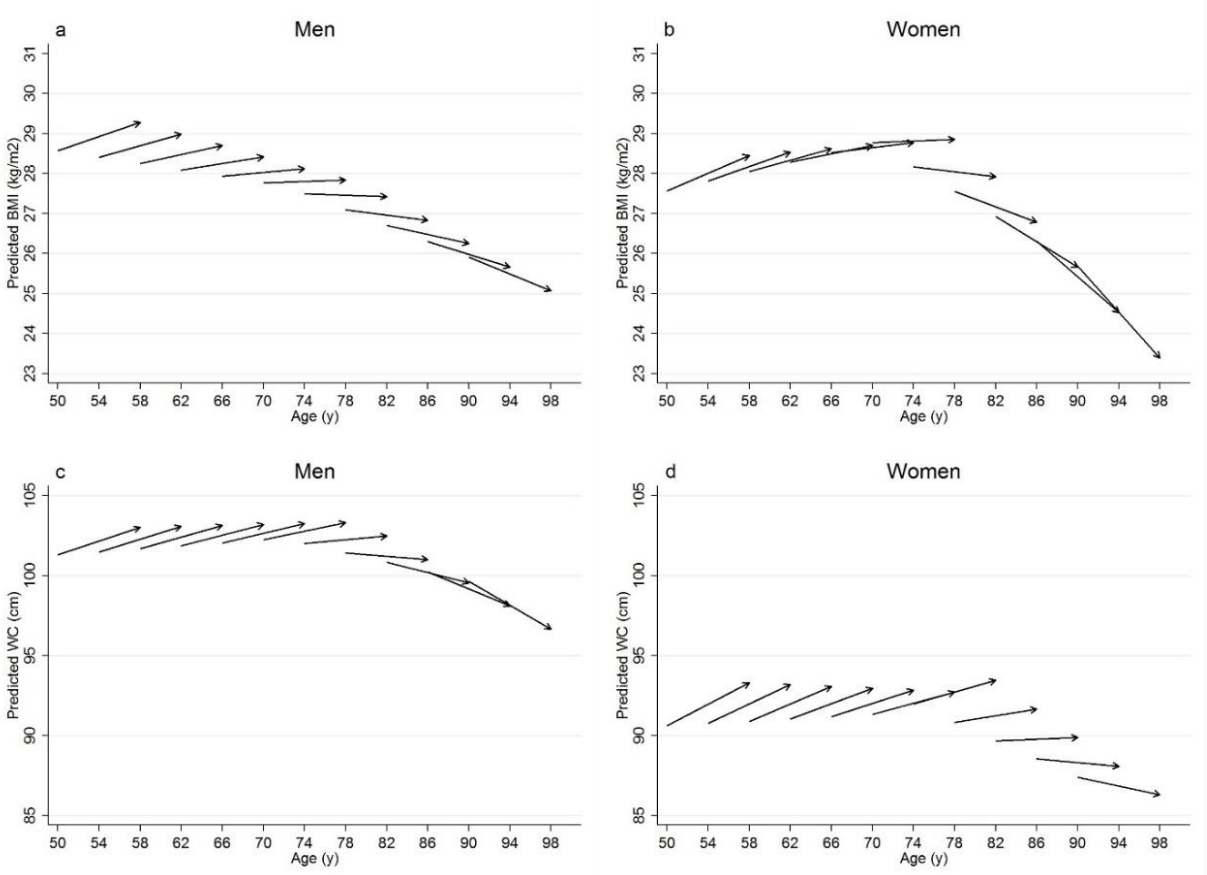


- Less variations in men than women
- Increase in BMI and WC (gain) from 50 to ~70y
- Decrease after 70 y stronger for BMI than WC
- Cohort effect: younger cohort bigger

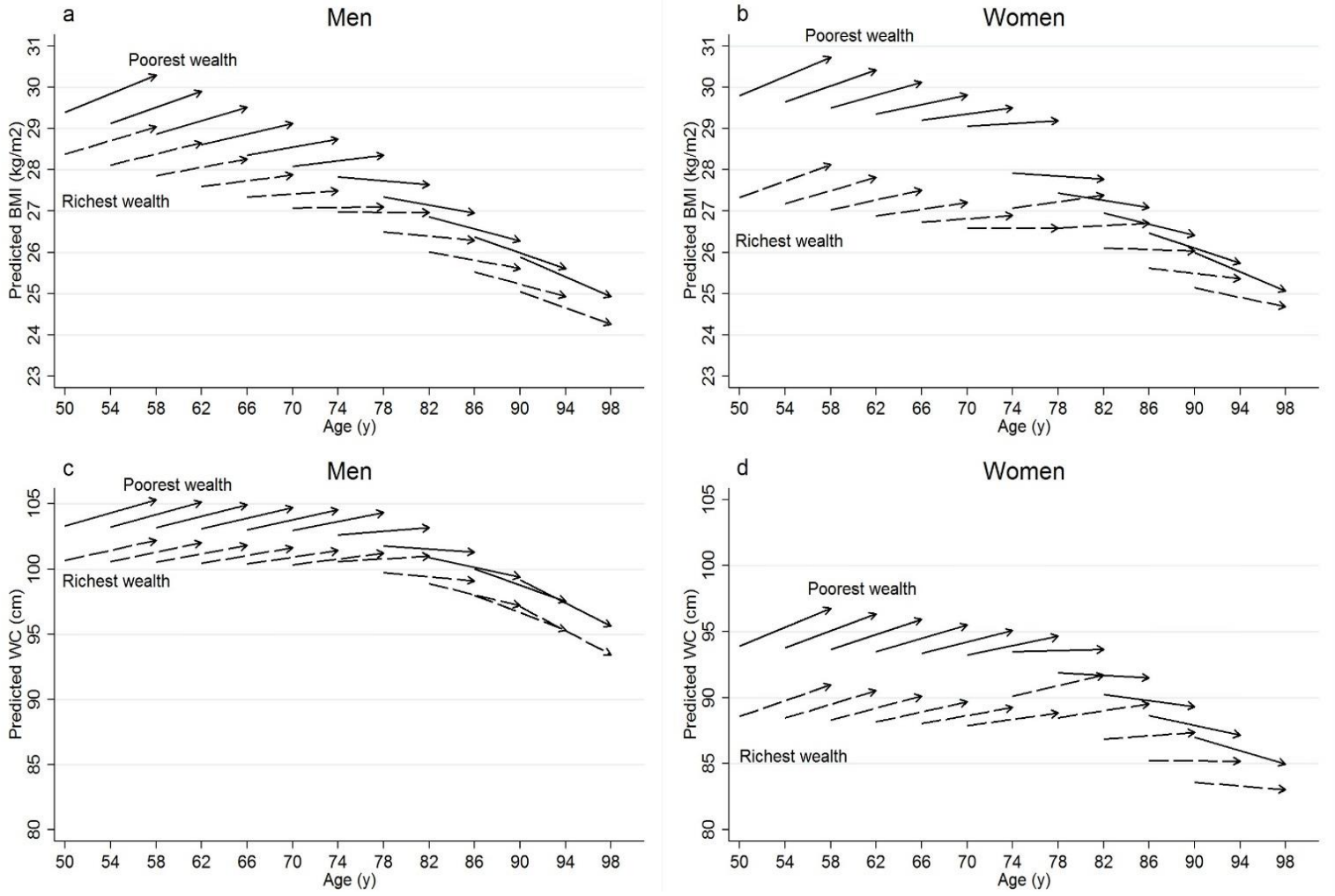
E.g. a man who was 62 in 2004 has a lower BMI by 1kg/m^2 compared to a man who was 62 in 2012

Results (II)

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

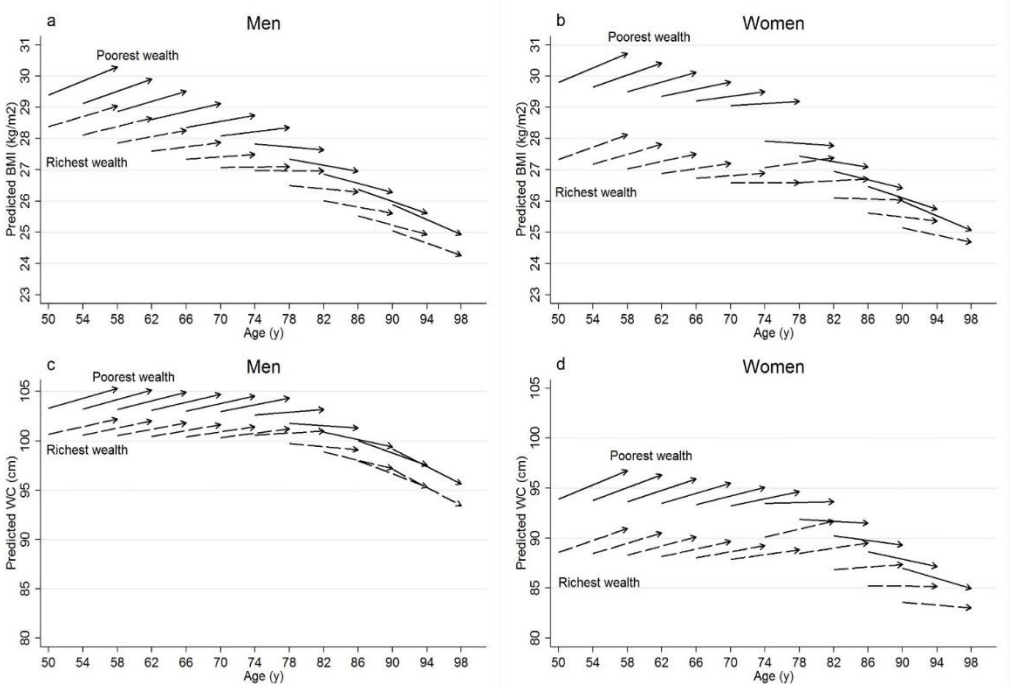
BMI

Waist Circumference



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"

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Inflammation and aging outcomes

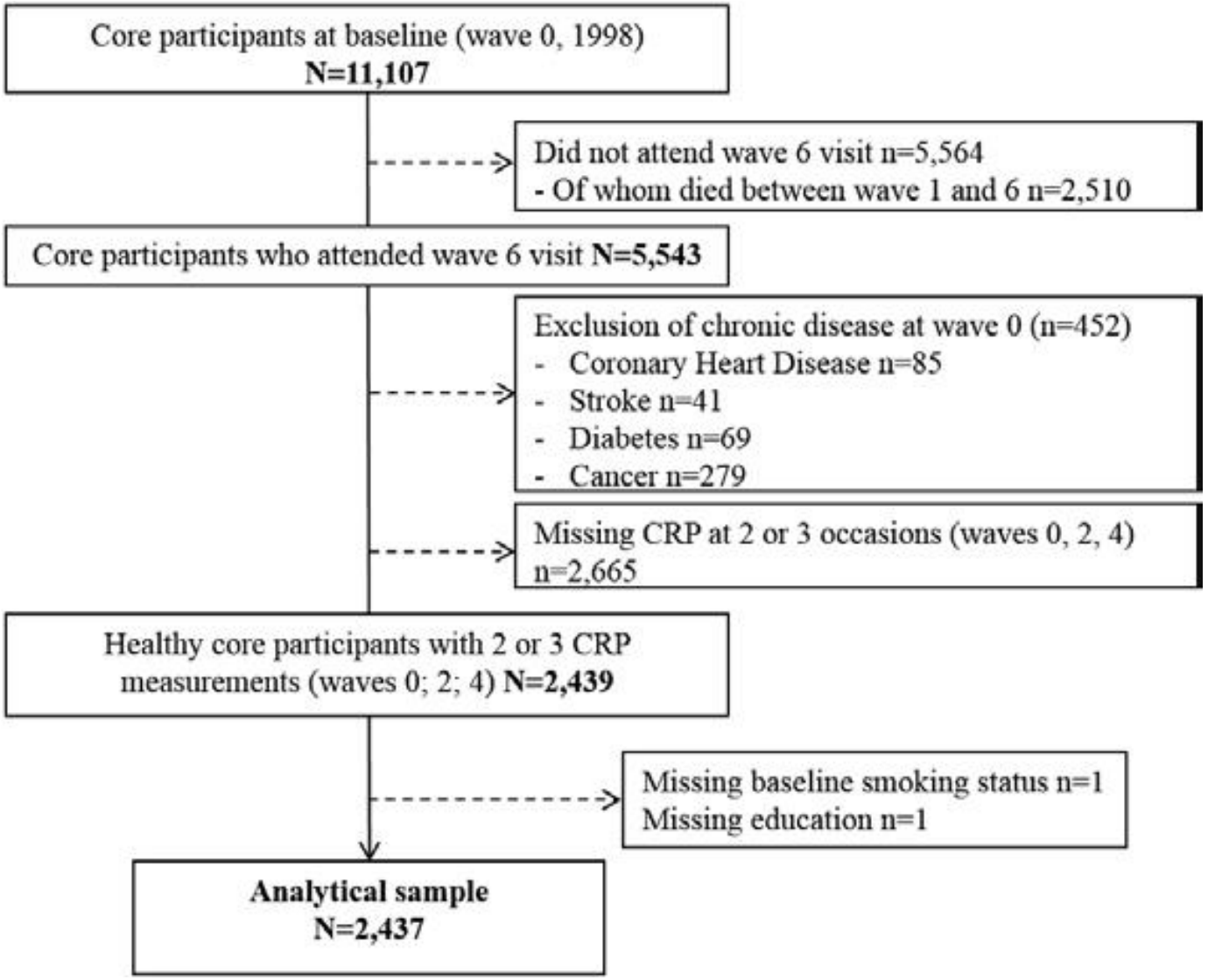
- Compelling evidence of associations between elevated inflammation biomarkers (C-reactive protein, Inteleukin 6 and Fibrinogen mainly) with a range of age-related outcomes:
  - Cardioascular, Diabetes, Cancer
  - Cognitive function and dementia
  - Sarcopenia and osteoporosis
  - Frailty
- Most studies 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
  - Jenny *et al*, J Gerontol A Biol Sci Med Sci 2012: Cardiovascular Healthy Study All Stars, 9 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

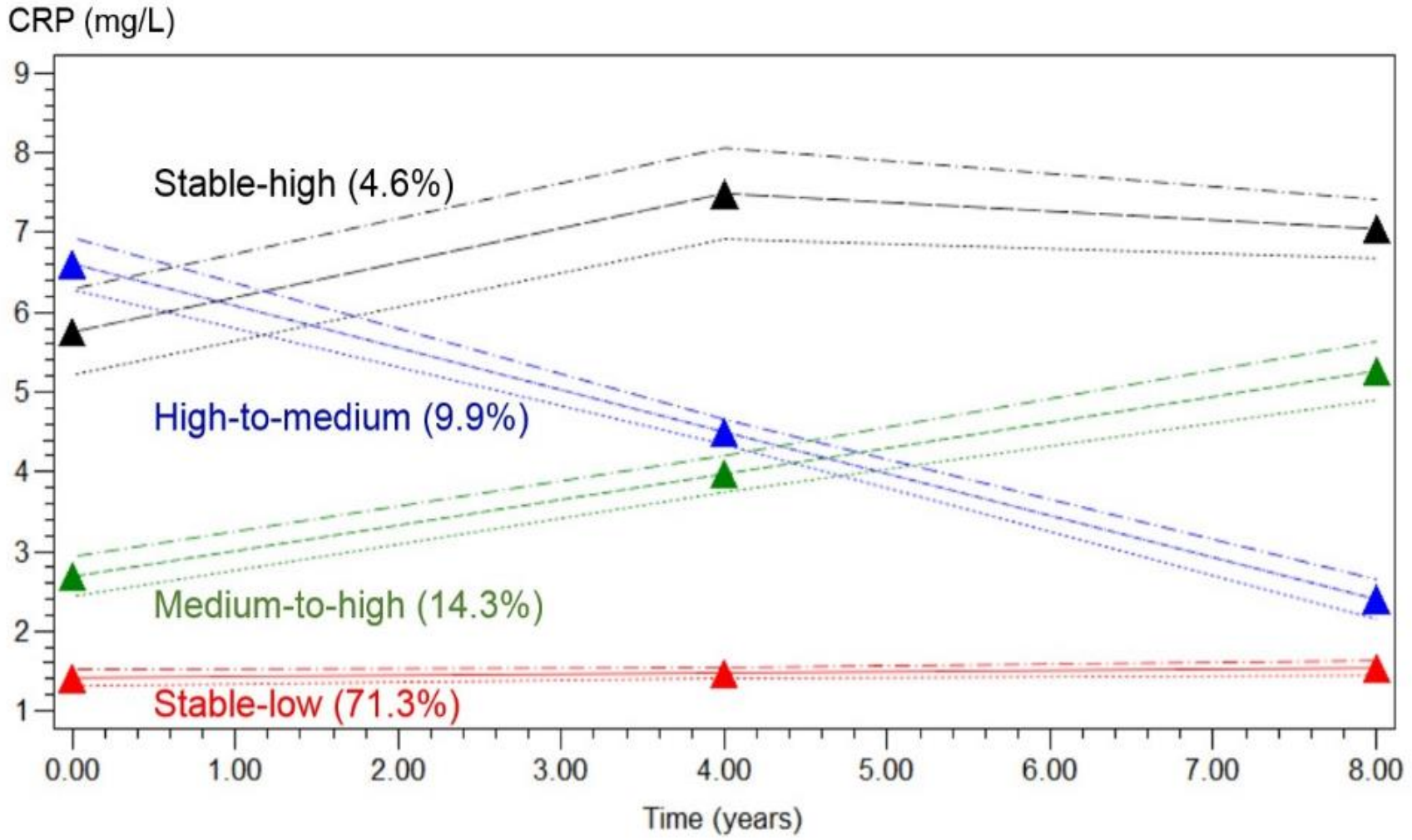
Objective: Identify group-based trajectories of inflammation and assess the associations with ageing outcomes

- 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

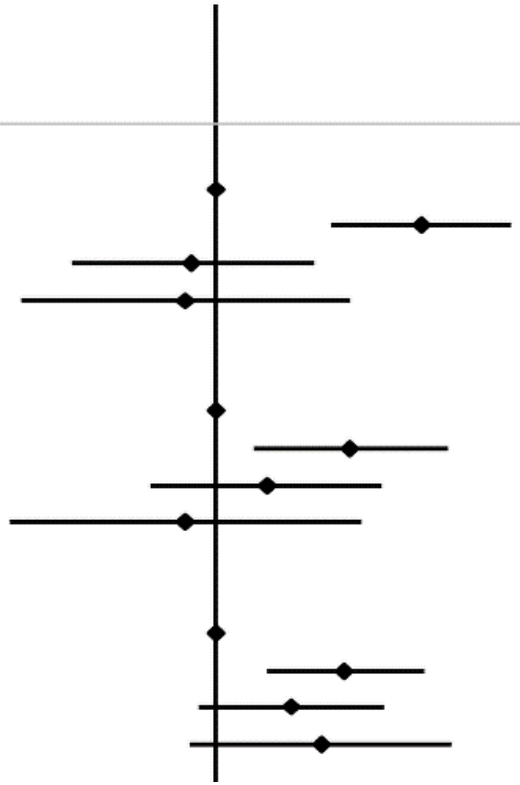

Core participants at baseline (wave 0, 1998)
N=11,107
Did not attend wave 6 visit n=5,564
- Of whom died between wave 1 and 6 n=2,510
Core participants who attended wave 6 visit N=5,543
Exclusion of chronic disease at wave 0 (n=452)
- Coronary Heart Disease n=85
- Stroke n=41
- Diabetes n=69
- Cancer 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

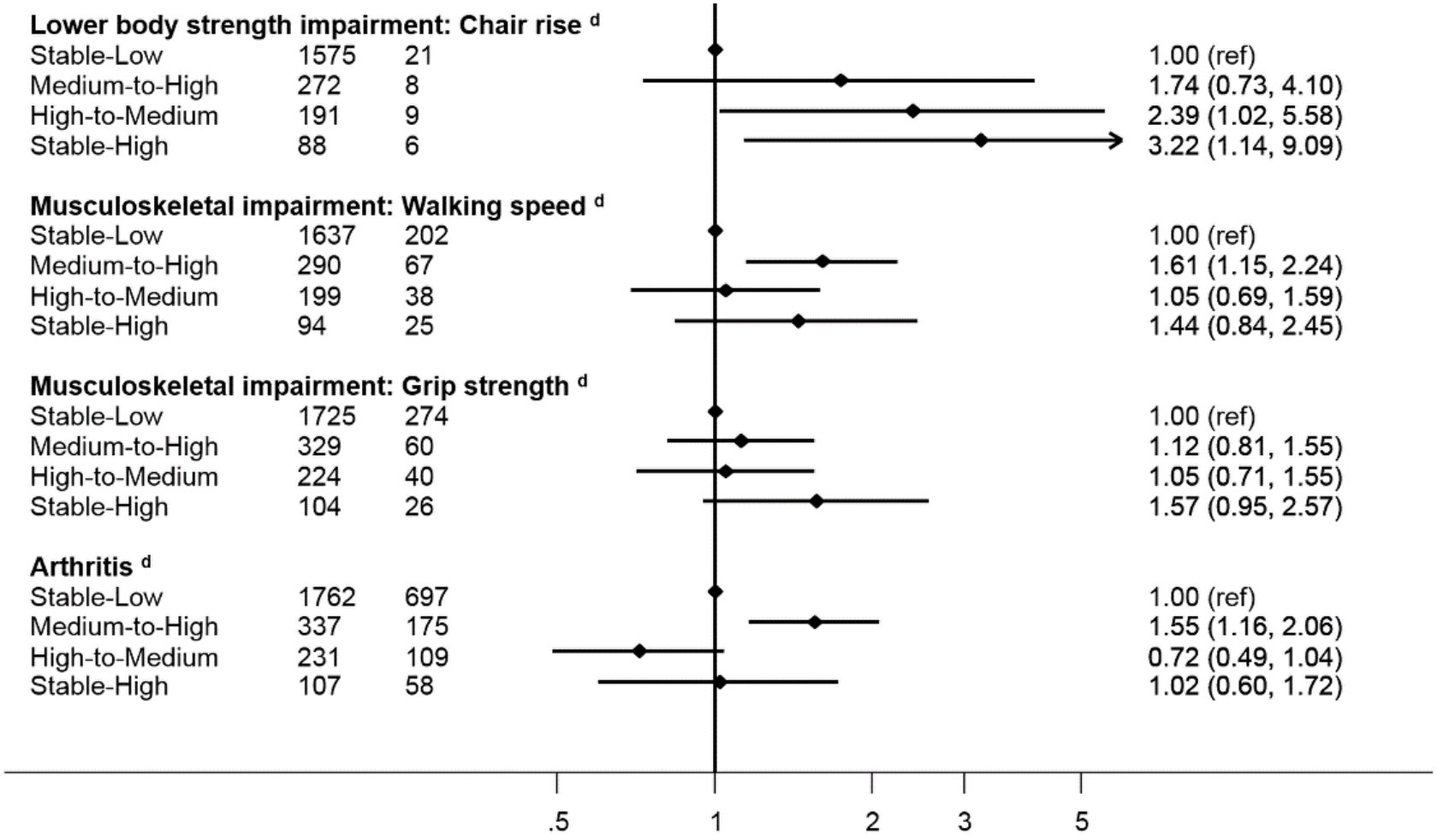


Results: Association with physical functioning

CRP trajectory	N total	N cases	OR (95% CI) [a]
Disability: ADL [b]			
Stable-Low	1762	210	1.00 (ref)
Medium-to-High	336	93	2.09 (1.51, 2.88)
High-to-Medium	231	50	0.92 (0.60, 1.42)
Stable-High	107	24	0.90 (0.50, 1.62)
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)

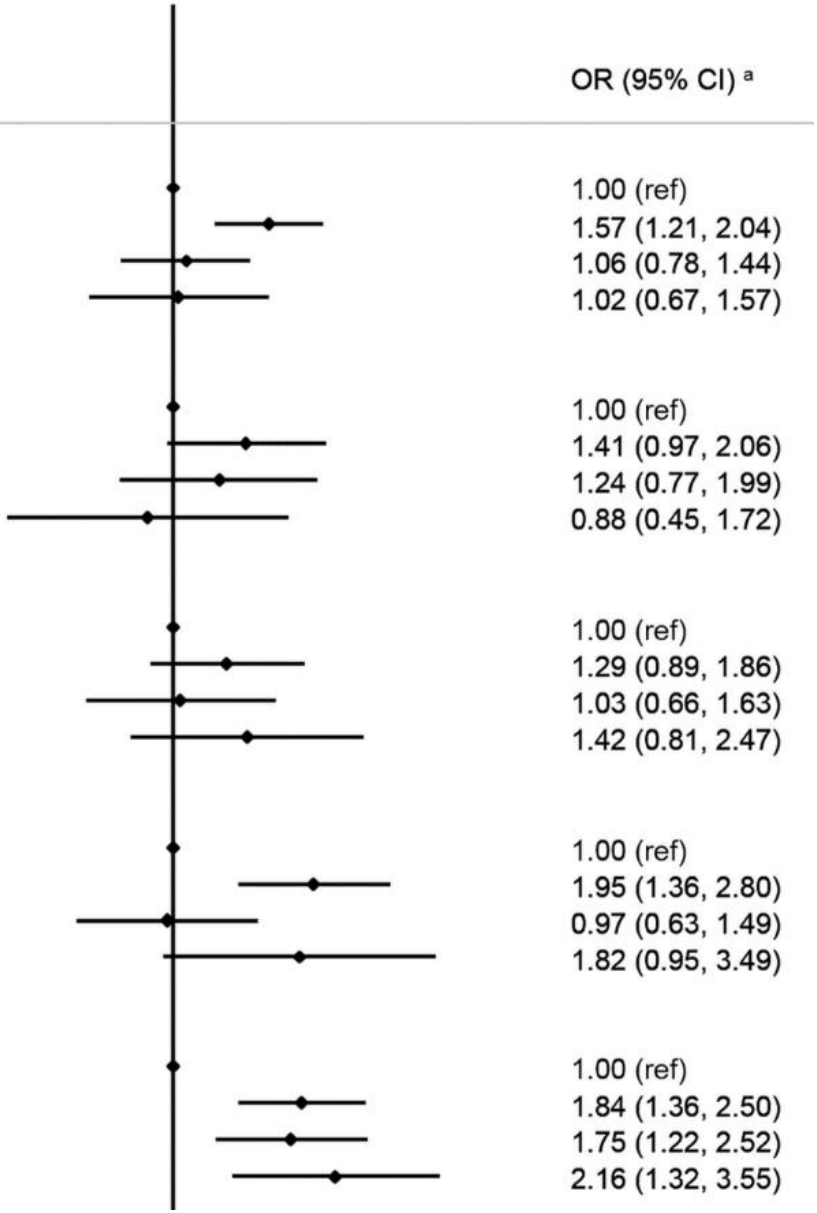


Results: Association with physical functioning

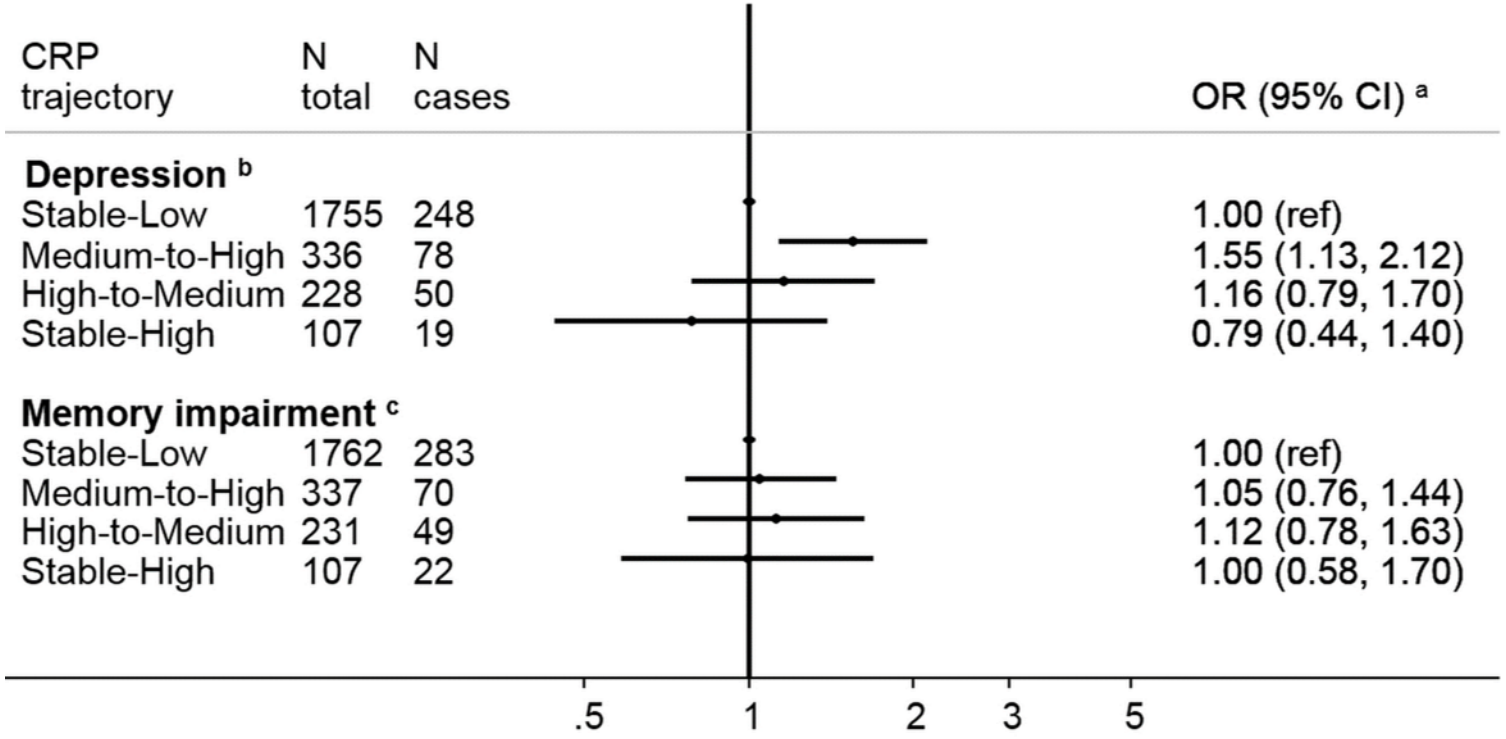


Results: Association with CVD risk factors

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



Results: Association with mental health



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

- Lassale C, *et al.* J Gerontol A Biol Sci Med Sci. 2018

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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