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Social Mobility and Inflammatory and Metabolic Markers at Older Ages: The English Longitudinal Study of Ageing

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2. Abstract

Background

Because our knowledge of the associations between socioeconomic position (SEP) over the life course and inflammatory and metabolic markers, which are excellent predictors of cardiovascular disease, remains limited, we examined the association between social mobility over the life course and these markers at older ages.

Methods

Our study used cross-sectionally collected data from 6,142 participants aged 50 years and older from the English Longitudinal Study of Ageing. We estimated linear and logistic models of the associations between social mobility, using information on childhood and adult SEP, and C-reactive protein (CRP), fibrinogen, glycated haemoglobin (HbA1c), and high-density lipoprotein cholesterol (HDL). Our models were gradually adjusted for age, sex, chronic diseases, obesity, physical activity, alcohol consumption, smoking status, and depressive symptoms.

Results

Participants who experienced upward social mobility had higher CRP, fibrinogen, and HbA1c levels compared with those who had stable high SEP over the life course, but lower compared with those who experienced downward social mobility or had stable low SEP. They also had lower HDL levels compared with those who had stable high SEP or downwardly mobile. Adjustment for covariates partially explained the associations between social mobility and CRP and HDL, and fully explained those between social mobility and fibrinogen and HbA1c.

Conclusions

Social mobility is associated with inflammatory and metabolic markers at older ages with some of the observed associations persisting after accounting for covariates. Upward social mobility appears to partially reverse the damaging effect of childhood social disadvantage on inflammatory profiles in older ages.

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3. Main text

INTRODUCTION

A large body of evidence suggests that socioeconomic position (SEP) is an important determinant of cardiovascular and metabolic health.[1, 2] Lower childhood and adult SEP are associated with a higher risk of type 2 diabetes and cardiovascular disease (CVD), partly through chronic inflammation, which is associated with chronic stress.[3] People who experience social deprivation are thought to be subject to environmental, psychological, and behavioural stressors, which eventually wear and tear the neuroendocrine, nervous, and immunological systems, a process that is known as allostasis and is associated with an increased risk of chronic disease.[4, 5]

Systematic changes in SEP across the lifespan, which are best described by the term social mobility, are also associated with subsequent risk of chronic disease. People in upward social mobility, i.e., having higher SEP in later stages of the life course compared to earlier stages have decreased risk of various detrimental effects on health, such as psychiatric disorders,[6, 7] insulin resistance,[8] type 2 diabetes,[3, 9] cardiovascular mortality,[10] and all-cause mortality[11] compared with those in downward social mobility.

Although downward social mobility is associated with an increased risk of various chronic diseases,[9, 11, 12] its link with subclinical form of disease, which is very important in terms of disease prevention, remains underinvestigated. Inflammatory and metabolic markers, such as C-reactive protein (CRP), fibrinogen, glycated haemoglobin (HbA1c), and high-density lipoprotein (HDL) cholesterol are implicated in pathogenic processes [13] and widely used as predictors of cardiovascular and metabolic health.[14] Their association with social mobility, however, remains poorly understood. To our knowledge, scarce evidence suggests that downward social mobility is associated with increased levels of inflammatory markers, such as CRP and fibrinogen,[3, 15] and decreased levels of metabolic markers, such as HDL,[8] while the association with HbA1c has yet to be explored.

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Our study aims to examine the associations between changes in SEP over the life course and inflammatory and metabolic markers in older adults and add to the current knowledge of how social mobility might be associated with pathological processes and subclinical form of disease, with a particular interest in the role of later-life SEP and upward social mobility in reversing the harmful effects of social disadvantage in childhood on later-life inflammatory and metabolic profiles of older adults.

METHODS

Data source and study populations

The English Longitudinal Study of Ageing (ELSA) is a prospective observational study of community-dwelling people aged 50 years or older. It began in 2002-03 (wave 1) with a core sample of 11,391 participants who had earlier participated in Health Survey for England (HSE) 1998, 1999, and 2001 and were selected by using a multistage stratified random probability design. After the baseline, follow-up interviews and health examinations, including blood sample collections, took place at regular 2- and 4-year intervals, respectively. The National Research and Ethics Committee has approved ELSA, while informed consent has been obtained from all participants. More information on ELSA can be found at http://www.elsa-project.ac.uk/.

Our study uses data from ELSA wave 2 (2004-05). ELSA wave 2 had two components: the first follow-up interview and the first (baseline) health examination survey. Out of the 11,391 participants, 8,780 took part in the follow-up interview of which 7,666 participated in the health examination. Among those who participated in the health examination, 6,652 were eligible for blood sample collection (i.e., did not have a history of fits or convulsion, bleeding or clotting disorders, and never been prescribed anticoagulants) and consented to give blood sample. Our analytic sample comprised 6,142 participants (more details on the exclusion criteria are presented in Figure 1). To gain a better understanding of the non-response and its potential implications for our findings, we conducted an analysis of non-response, which is presented in supplementary material (Table S1).

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Measurements

Assessment of social mobility

Childhood SEP was measured using father's or main carer's occupation when participants were 14 years old. Participants whose fathers worked in managerial, professional, administrative, trade-related, and services-related occupations or were business owners were assigned to the high childhood SEP category, whereas low childhood SEP was assigned for those whose fathers had manual or casual occupations or those whose fathers were unemployed, sick, or disabled. Participants whose fathers were in the armed forces or retired when they were 14 years old (n=222), and those whose information about paternal occupation was missing (n=32) were excluded from analyses as their childhood SEP could not be classified.

Adult SEP was measured using data from the last main job of participants, which then was dichotomized into low and high occupational class according to the National Statistics Socioeconomic Classification (NS-SEC) scheme. Participants in managerial, professional, or intermediate occupations were assigned to high adult SEP, while those who worked in routine, manual, or semi-manual occupations were assigned to low adult SEP. The small numbers of participants who had never worked (n=86) or were of unknown occupation (n=2) were excluded from analyses because they could be classified in any of the existing categories. We then combine dichotomous childhood SEP and adult SEP to derive a social mobility variable with the following four categories: stable high SEP (high childhood and adult SEP), downward social mobility (high childhood SEP, but low adult SEP), upward social mobility (low childhood SEP, but high adult SEP), and stable low SEP (low childhood and adult SEP).

Inflammatory and metabolic markers

CRP, fibrinogen, HbA1c, and HDL were measured from blood samples collected by nurses at participants' homes during the ELSA wave 2 health examination survey. More information on the measurement of these markers can be obtained from the HSE 2004 technical report (http://www.hscic.gov.uk/catalogue/PUB01170/hea-surv-ethn-min-eng-2004-rep-v2.pdf) as both

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ELSA and HSE used the same protocols and infrastructure to analyse the blood samples . We log-transformed these four markers as they were positively skewed. To provide more clinically meaningful information, HbA1c and HDL levels were in addition categorised into binary variables based on clinical cut-off. For HbA1c, the levels of ≤5.6% were grouped as normal, while those between 5.7-6.4% were grouped as prediabetes as per American Diabetes Association recommendation. Because the study of diabetes was outside the scope of this work, we excluded participants whose HbA1c ≥6.5%, which is a criterion for the clinical diagnosis of type 2 diabetes.[16] Regarding HDL, we dichotomised it by assigning men with HDL levels <1 mmol/l (40 mg/dl) and women with HDL levels <1.3 mmol/l (50 mg/dl) in the sub-optimal HDL group.[17]

Covariates

Based on previous evidence, we used age, age squared, sex, and baseline (that is ELSA wave 2) cardiovascular (i.e., hypertension, angina, heart attack, congestive heart failure, heart murmur, abnormal heart rhythm, and stroke) and non-cardiovascular diseases (i.e., chronic lung disease, asthma, arthritis, osteoporosis, cancer excluding minor skin cancers, Parkinson's disease, emotional/nervous/psychiatric problems, Alzheimer's disease, and dementia or other serious memory impairment) as potential confounders of the examined association,[15, 18] and elevated depressive symptoms (≥ 4 symptoms on the eight-item Center for Epidemiologic Studies Depression Scale: CES-D),[18] smoking (current smoker, ex-smoker, and never a smoker),[19] physical activity (physical inactivity, low-, moderate-, and vigorous-intensity physical activity at least once a week),[20, 21] and frequency of alcohol consumption (daily or almost daily, 1-2 times a week, 1-2 times a month, never or almost never) [22] as potential mediators of it.[15, 23] We also adjusted our models for the following anthropometric measures: body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR), which had also been measured during the wave 2 health examination.[24] and categorised using established cut-points.[25, 26] We include in the analysis different anthropometric measures, as each one of them may confer uniquely to CVD risk and be differential associated with social mobility.[26] To avoid unnecessary exclusions because of missing values in the following

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covariates: BMI, WC, WHR, alcohol consumption, and depressive symptoms, we applied the missing-indicator technique and added a category for missing values in all these variables.

Statistical analysis

We analysed the sample characteristics according to social mobility categories and estimated multivariable linear and logistic regression models of the association between social mobility and the four markers. We adjusted our models for age, age squared, and sex, then for prevalent CVD and non-CVD, and finally, for health behaviours, including obesity, alcohol consumption, smoking, physical activity, and elevated depressive symptoms. We reported the pooled sample as we did not find any significant sex interaction. The analyses were conducted using STATA version 12 (StataCorp LP, TX, USA).

RESULTS

Table 1 presents the characteristics of the sample. Compared with participants with stable high SEP or upwardly mobile, those in stable low SEP and downward social mobility were more likely to be older, obese, physically inactive, smokers, and depressed. They also had more comorbidities and consumed alcohol less frequently. Table 2 shows the overall distribution of inflammatory and metabolic markers. CRP, fibrinogen, and HbA1c levels were the highest (worse) among those in stable low SEP. Participants who were downwardly mobile had the second highest levels of the markers and were followed by those who were in upward social mobility trajectory. Those in stable high SEP had the lowest (best) levels in all these biomarkers. HDL levels were the highest (best) among people with stable high SEP and the lowest (worst) among those with stable low group. Proportion of prediabetes was the highest among those experiencing downward social mobility, but was the lowest among those in stable high SEP. In contrast, proportion of having sub-optimal HDL levels was the highest among those with stable high group but was the lowest among those with stable low group.

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Table 1. Baseline characteristics of sample

Characteristics	Social Mobility					P-value[a]
	Stable High	Low to high	High to low	Stable low	Total	
	2,579 (42.0)	953 (15.5)	1,419 (23.1)	1,191 (19.4)	6,142 (100)	
Age, years mean (SD)	65.15 (9.29)	65.54 (9.15)	66.20 (9.12)	66.41 (9.04)	65.70 (9.19)	<0.001
Sex						
Men	1,206 (46.8)	457 (48.0)	607 (42.8)	539 (45.3)	2,809 (45.7)	0.044
Women	1,373 (53.2)	496 (52.0)	812 (57.2)	652 (54.7)	3,333 (54.3)	
Body mass index (kg/m^2)						
< 25	779 (30.2)	215 (22.6)	356 (25.1)	260 (21.8)	1,660 (26.2)	<0.001
25–29.9	1,106 (42.9)	437 (45.9)	584 (41.2)	453 (38.0)	2,580 (42.0)	
≥ 30	598 (23.2)	257 (27.0)	403 (28.4)	416 (34.9)	1,674 (27.3)	
Missing	96 (3.7)	44 (4.6)	76 (5.4)	62 (5.2)	278 (4.5)	
Waist circumference						
Normal	656 (25.4)	176 (18.5)	288 (20.3)	215 (18.0)	1,335 (21.7)	<0.001
High	723 (28.0)	246 (25.8)	356 (25.1)	271 (22.8)	1,596 (26.0)	
Very high	1,148 (44.5)	513 (53.8)	733 (51.7)	671 (56.3)	3,065 (49.9)	
Missing	52 (2.0)	18 (1.9)	42 (3.0)	34 (2.8)	146 (2.4)	
Waist-to-hip ratio						
Normal	1,075 (41.7)	306 (32.1)	523 (36.9)	377 (31.6)	2,281 (37.1)	<0.001
Increased	1,446 (56.1)	624 (65.5)	851 (60.0)	777 (65.2)	3,698 (60.2)	
Missing	58 (2.2)	23 (2.4)	45 (3.2)	37 (3.1)	163 (2.7)	
Physical activity (per week)						
No	135 (5.2)	65 (6.8)	88 (6.2)	90 (7.6)	378 (6.2)	<0.001
Mild	291 (11.3)	122 (12.8)	233 (16.4)	228 (19.1)	874 (14.2)	
Moderate	1,259 (48.8)	478 (50.2)	712 (50.2)	597 (50.1)	3,046 (49.6)	
Vigorous	894 (34.7)	288 (30.2)	386 (27.2)	276 (23.2)	1,844 (30.0)	
Alcohol consumption (times)						
Never	283 (11.0)	141 (14.8)	267 (18.8)	273 (22.9)	964 (15.7)	<0.001
1-2/ month	411 (15.9)	207 (21.7)	267 (18.8)	219 (18.4)	1,104 (18.0)	
1-2/ week	939 (36.4)	352 (36.9)	499 (35.2)	397 (33.3)	2,187 (35.6)	
Daily	762 (29.6)	183 (19.2)	252 (17.8)	162 (13.6)	1,359 (22.1)	
Missing	184 (7.1)	70 (7.4)	134 (9.4)	140 (11.8)	528 (8.6)	

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Characteristics	Social Mobility					
	Stable High 2,579 (42.0)	Low to high 953 (15.5)	High to low 1,419 (23.1)	Stable low 1,191 (19.4)	Total 6,142 (100)	P-value[a]
Smoking status						
Never	1,018 (39.5)	362 (38.0)	476 (33.5)	367 (30.8)	2,223 (36.2)	<0.001
Ex-smoker	1,297 (50.3)	474 (49.7)	702 (49.5)	573 (48.1)	3,046 (49.6)	
Current	264 (10.2)	117 (12.3)	241 (17.0)	251 (21.1)	873 (14.2)	
Depressive symptom	285 (11.0)	124 (13.0)	231 (16.3)	198 (16.6)	838 (13.6)	<0.001
Missing	18 (0.7)	8 (0.8)	16 (1.1)	13 (1.1)	55 (0.9)	
Prevalent CVD	667 (25.9)	255 (26.8)	362 (25.5)	359 (30.1)	1,643 (26.8)	0.027
Prevalent non-CVD	1,385 (53.7)	543 (57.0)	837 (59.0)	740 (62.1)	3,505 (57.1)	<0.001

n (%) unless specified elsewhere. [a] One-way ANOVA and chi-square for continuous and categorical variables, respectively, and p-value did not take into account the effect of missing group. Abbreviations: SD, standard deviation; CVD, cardiovascular disease; non-CVD, non-cardiovascular disease.

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Table 2. The distribution of studied markers across groups of social mobility

Studied markers	Social Mobility					
	Stable High	Low to high	High to low	Stable low	Total	P-value[a]
	2,579 (42.0)	953 (15.5)	1,419 (23.1)	1,191 (19.4)	6,142 (100)	
CRP (mg/litre)						
Mean (SD)	2.04 (1.72)	2.26 (1.83)	2.44 (1.84)	2.60 (1.88)	2.27 (1.81)	<0.001
Median (IQR)	1.50	1.60	1.90	2.10	1.70	
	(0.70 – 2.80)	(0.80 – 3.25)	(1.00 – 3.50)	(1.10 – 3.80)	(0.90 – 3.20)	
Missing[b]	463 (18.0)	184 (19.3)	333 (23.5)	291 (24.4)	1,271 (20.7)	
Fibrinogen (g/litre)						
Mean (SD)	3.13 (0.68)	3.23 (0.78)	3.27 (0.70)	3.32 (0.76)	3.22 (0.72)	<0.001
Median (IQR)	3.10	3.10	3.20	3.20	3.10	
	(2.70 – 3.50)	(2.70 – 3.60)	(2.80 – 3.70)	(2.80 – 3.70)	(2.70 – 3.60)	
Missing	291 (11.3)	96 (10.1)	186 (13.1)	146 (12.3)	719 (11.7)	
HbA1c (%)						
Mean (SD)	5.42 (0.34)	5.44 (0.36)	5.46 (0.33)	5.47 (0.35)	5.44 (0.34)	<0.001
Median (IQR)	5.40	5.40	5.50	5.50	5.40	
	(5.20 – 5.60)	(5.20 – 5.70)	(5.20 – 5.70)	(5.20 – 5.70)	(5.20 – 5.70)	
≤ 5.6 %	1,613 (62.5)	585 (61.4)	811 (57.2)	666 (55.9)	3,675 (59.8)	0.017
5.7–6.4 %	486 (18.8)	201 (21.1)	313 (22.1)	245 (20.6)	1,245 (20.3)	
Missing[c]	480 (18.6)	167 (17.5)	295 (20.8)	280 (23.5)	1,222 (19.9)	
HDL cholesterol (mmol/litre)						
Mean (SD)	1.57 (0.40)	1.49 (0.38)	1.51 (0.38)	1.46 (0.37)	1.52 (0.39)	<0.001
Median (IQR)	1.50	1.40	1.50	1.40	1.50	
	(1.30 – 1.80)	(1.20 – 1.70)	(1.20 – 1.70)	(1.20 – 1.70)	(1.20 – 1.80)	
Optimal levels	192 (7.4)	107 (11.2)	142 (10.0)	143 (12.0)	584 (9.5)	<0.001
Sub-optimal levels	2,113 (81.9)	754 (79.1)	1,099 (77.4)	904 (75.9)	4,870 (79.3)	
Missing	274 (10.6)	92 (9.6)	178 (12.5)	144 (12.1)	688 (11.2)	

n (%) unless specified elsewhere. HDL cholesterol: optimal levels ≥1.0 mmol/l (men) or ≥1.3 mmol/l (women); sub-optimal levels <1.0 mmol/l (men) or <1.3 mmol/l (women). [a] One-way ANOVA and chi-square for continuous and categorical variables, respectively, and p-value did not take into account the effect of missing group. [b]Also included participants who were excluded from analyses due to having CRP > 8 mg/l. [c]Also included participants who were excluded from analyses due to being diagnosed with type 2 diabetes or having HbA1c ≥ 6.5%. Abbreviations: SD, standard deviation; IQR, interquartile range; CRP; C-reactive protein; HbA1c, haemoglobin A, glycosylated; HDL, high-density lipoprotein.

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Table 3 presents the linear regression models. We found that CRP levels were the highest among participants in stable low SEP (1.348 mg/litre, 95%CI 1.259-1.45), followed by those who experienced downward social mobility (1.247 mg/litre, 95%CI 1.169-1.331), and then those who experienced upward social mobility (1.135 mg/litre, 95%CI 1.054-1.221), compared with people in stable high SEP. We also found a similar pattern of the association between social mobility and fibrinogen. Participants in upward social mobility did not differ significantly in terms of their HbA1c levels from those in stable high SEP, whereas those in downward trajectory or those in stable low SEP had significantly higher levels of HbA1c. The association between social mobility and HDL followed a slightly different pattern showing that participants experiencing downward social mobility had slightly higher HDL levels than those experiencing upward social mobility. The statistical controlling for health behaviours, obesity, and elevated depressive symptoms, fully explained the associations with fibrinogen and HbA1c, but only partially those with CRP and HDL. Interestingly, after adjusting for all covariates, CRP levels of those in upward social mobility were not significantly different from those in stable high SEP, while the CRP levels of participants in downward drift or stable low SEP remained significantly higher.

Table 4 shows the results from logistic models. We found that the risk of prediabetes among participants in upward SEP did not significantly differ from the risk of participants in stable SEP (OR 1.14, 95%CI 0.9-1.38). However, those downwardly mobile showed an increased risk of prediabetes by 25%, compared with those in stable high SEP independent of age, sex, and chronic conditions. The risk of having sub-optimal HDL levels among those in upward, downward, or stable low SEP were significantly higher than that among those in stable high SEP regardless of age, sex, and chronic conditions. Nevertheless, the strength of these associations was attenuated after accounting for health behaviours.

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Table 3. Linear regression for the associations between markers and social mobility

Social mobility	n	β (95%CI)			
		Model 1	Model 2	Model 3	Model 4
CRP (mg/litre)					
Stable High	2,116	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Low-High	769	**1.135 (1.054, 1.221)**	**1.127 (1.049, 1.213)**	**1.122 (1.043, 1.206)**	1.025 (0.959, 1.097)
High-Low	1,086	**1.247 (1.119, 1.331)**	**1.228 (1.150, 1.310)**	**1.224 (1.148, 1.305)**	**1.121 (1.055, 1.190)**
Stable Low	900	**1.348 (1.259, 1.348)**	**1.323 (1.235, 1.323)**	**1.310 (1.223, 1.402)**	**1.125 (1.054, 1.201)**
Fibrinogen (g/litre)					
Stable High	2,288	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Low-High	857	**1.028 (1.011, 1.046)**	**1.026 (1.010, 1.044)**	**1.025 (1.009, 1.043)**	1.009 (0.992, 1.025)
High-Low	1,233	**1.045 (1.028, 1.060)**	**1.038 (1.022, 1.053)**	**1.037 (1.022, 1.052)**	1.013 (0.998, 1.027))
Stable Low	1,045	**1.058 (1.041, 1.075)**	**1.049 (1.034, 1.066)**	**1.047 (1.030, 1.063)**	1.011 (0.995, 1.026)
HbA1c (%)					
Stable High	2,099	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Low-High	786	1.004 (0.999, 1.010)	1.004 (0.999, 1.009)	1.004 (0.999, 1.009)	0.999 (0.994, 1.004)
High-Low	1,124	**1.009 (1.004, 1.013)**	**1.007 (1.003, 1.012)**	**1.007 (1.003, 1.012)**	1.003 (0.998, 1.007)
Stable Low	911	**1.009 (1.004, 1.014)**	**1.007 (1.002, 1.012)**	**1.007 (1.002, 1.012)**	1.000 (0.995, 1.004)
HDL (mmol/litre)					
Stable High	2,305	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Low-High	861	**0.951 (0.932, 0.969)**	**0.953 (0.936, 0.970)**	**0.954 (0.938, 0.971)**	0.984 (0.968, 1.000)
High-Low	1,241	**0.964 (0.947, 0.980)**	**0.956 (0.941, 0.971)**	**0.955 (0.940, 0.970)**	**0.984 (0.970, 0.999)**
Stable Low	1,047	**0.939 (0.922, 0.957)**	**0.938 (0.922, 0.954)**	**0.941 (0.926, 0.957)**	0.985 (0.969, 1.001)

Model 1: Unadjusted model., Model 2: Models adjusted for age and sex., Model 3: Model 2 + adjusted for chronic diseases., Model 4: Model 3 + adjusted for health behaviours, including depressive symptom.

β values, including those in reference group derived from anti-log transformation of original values. Embolden values represented those that were statistically significant ($p<0.05$).

Abbreviations: CI, confidence interval; CRP, C-reactive protein; HbA1c, haemoglobin A, glycosylated; HDL, high-density lipoprotein cholesterol.

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Table 4. Logistic regression for the associations between social mobility, HbA1c, and HDL.

Social mobility	n	Odds Ratio (95% CI)			
		Model 1	Model 2	Model 3	Model 4
HbA1c[a]					
Stable high	2,099	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Low to high	786	1.14 (0.94, 1.38)	1.13 (0.93, 1.37)	1.12 (0.93, 1.36)	0.96 (0.79, 1.17)
High to low	1,124	**1.28 (1.08, 1.51)**	**1.25 (1.06, 1.47)**	**1.25 (1.06, 1.47)**	1.07 (0.90, 1.27)
Stable low	911	**1.22 (1.02, 1.46)**	1.17 (0.98, 1.40)	1.16 (0.97, 1.39)	0.89 (0.73, 1.07)
HDL[b]					
Stable high	2,305	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Low to high	861	**1.56 (1.22, 2.00)**	**1.59 (1.23, 2.04)**	**1.59 (1.22, 2.04)**	1.26 (0.97, 1.64)
High to low	1,241	**1.43 (1.14, 1.78)**	**1.37 (1.09, 1.72)**	**1.37 (1.09, 1.72)**	1.05 (0.83, 1.35)
Stable low	1,047	**1.75 (1.39, 2.17)**	**1.72 (1.35, 2.17)**	**1.64 (1.30, 2.08)**	1.09 (0.85, 1.41)

Model 1: Unadjusted model., Model 2: Models adjusted for age and sex., Model 3: Model 2 + adjusted for chronic diseases., Model 4: Model 3 + adjusted for health behaviours.

[a] Odds of participants who have prediabetes (i.e., HbA1c 5.7-6.4%), compared to those who have normal HbA1c levels (i.e., HbA1c ≤ 5.6%).

[b] Odds of participants who have sub-optimal HDL levels i.e., HDL < 1.0 mmol/l (men) or < 1.3 mmol/l (women), compared to those who have optimal HDL levels i.e., HDL ≥ 1.0 mmol/l (men) or ≥ 1.3 mmol/l (women).

Abbreviations: CI, confidence interval; HbA1c, haemoglobin A, glycosylated; HDL, high-density lipoprotein cholesterol.

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DISCUSSION

Our findings suggest that there are associations between social mobility and inflammatory (i.e., CRP and fibrinogen) and metabolic markers (i.e., HbA1c and HDL) with the association between social mobility and CRP persisting after adjustment for covariates. Participants in stable high SEP or upward social mobility had more favourable inflammatory and metabolic profiles characterised by lower levels of CRP, fibrinogen, and HbA1c, compared with those in stable low SEP or downward social mobility. However, they had lower HDL levels, compared with those who had stable high SEP or experienced downward social mobility. The results from both linear and logistic regression models are consistent. Adjustments for health behaviours, obesity, and elevated depressive symptoms fully explained the associations between social mobility and fibrinogen and HbA1c, but partially explained the association with CRP and HDL.

Methodological considerations

Our study is among the first to investigate the associations between social mobility and inflammatory and metabolic markers, and provide insight into the dynamic association between SEP and subclinical disease markers over the life course. An obvious strength of our study is the use of a large national community-dwelling sample and rich observational data from ELSA, which is a well-established survey. The first made our findings more applicable and generalizable to older adults, and the latter allows for a fuller exploration of the role of potential confounders and mediators.

Our study also had several limitations, which need to be considered when interpreting our findings. First, childhood SEP has been measured retrospectively and thus might be susceptible to recall bias. Nevertheless, this measure of childhood SEP appears to have good predictive validity as it has been successfully used to predict the incidence of disease[18] and mortality.[27] Second, it is uncertain whether the results can be generalized to younger generations, especially given changes to the structure of the labour market in the last fifty years. Our supplementary analysis found significant differences between respondents and non-respondents on a number of characteristics. To an extent our study has been affected by attrition and non-response bias and our analytic sample might not fully

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represent the original ELSA sample making our findings a rather conservative account of the true associations between social mobility and inflammatory and metabolic biomarkers Third, we could not account for important mediating factors, such as diet and medication usage, particularly HMG-CoA reductase inhibitors (statins).[25] Our social mobility variable did not encapsulate information on early adult SEP i.e. education and thus is an imperfect indicator of social mobility. It also did not capture SEP at a household- or a state-level, which were also reported to be associated with inflammatory markers.[28, 29] In addition, due to the lack of appropriately prospective data, we could not establish the temporality of events and draw causal conclusions about the role of covariates such as unhealthy behaviours in the observed association. With regard to the missing-indicator technique used in dealing with missing covariates, the benefit outweighs the impact on distorting the results as only small proportion of data (<10%) was missing.

Comparison of our findings with other studies

In accordance with previous studies, [3, 15] we found that participants in stable low SEP group had the highest CRP levels, followed those in downward social mobility trajectory and those in the upward social mobility, while those with stable high SEP had the best (lowest) CRP levels. These findings are also consistent with those of an earlier study suggesting that the association between adulthood SEP is associated with CRP levels independent of childhood SEP.[23] Our fibrinogen findings concur with those by Ploubidis *et al*., who reported negative associations between both childhood and adult SEP and fibrinogen levels in older adults.[30] Nevertheless, previous evidence failed to find an association between social mobility and fibrinogen levels.[15]

Unlike Lawlor *et al*., who found that in comparison with participants in stable high SEP only those who experienced low SEP throughout their life had significantly increased risk of low HDL[8], we found that those in upward and downward social mobility also had an increased risk of suboptimal HDL levels. The discrepancy between our findings and theirs possibly can be attributed to sample differences; Lawlor *et al*. used a sample of women aged 60 to 79 years, whereas we used as a sample that comprised men and women aged 50 years or older.

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Implication of our findings

Our study highlights the importance of changes in SEP for metabolic and inflammatory markers. The implications of our findings are considerable. First, the association between social mobility and CRP indicates that adult SEP is important for chronic inflammation, independent of childhood SEP, and likely can partially mitigate the effect of experiences of social disadvantage in childhood on it. The lack of any difference in HbA1c levels between participants in stable high SEP and those in upward social mobility groups further strengthens our argument about the role of upward social mobility as a factor that ameliorates the effect of social disadvantage in childhood. However, the findings that people who started off better but later experienced downward social mobility have better HDL levels compared with those in an upward trajectory suggest the importance of childhood SEP for HDL, irrespective of adult SEP.

In accordance with previous evidence [18], our findings also suggest that social mobility is associated with the inflammatory and metabolic profiles of older people through unhealthy behaviours, obesity, and depression. Regarding physical activity role in the examined associations, evidence suggests that people in stable high SEP and those in upward social mobility were likely to increase their levels of physical activity and physical fitness when they became adults,[20]while increased physical activity was found to be associated with reduced levels of CRP[31] and blood sugar,[32] but increased HDL levels.[33] Downward social mobility has also been associated with poorer self-reported mental health in men[34] and depression independent of childhood or adult SEP,[6] while associations between elevated depressive symptoms and increased CRP levels have also been demonstrated.[35] Further, downward social trajectory is associated with obesity,[36] which in turn is associated with increased CRP[31] and blood sugar levels[32] but decreased HDL levels.[33] One study also suggested that the upward social trajectory could protect women but not men from having high-risk adiposity profiles.[37] Downward family income trajectory is also associated with increased tobacco and alcohol use in adolescence,[19] which are associated with increased CRP[31] and fibrinogen levels[38] but decreased HDL levels.[33] The risk of unfavourable alcohol drinking in men was also found to be increased in a group of downward social mobility.[22]

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The potential mechanisms that health behaviours might interplay with social mobility was described in more detail in supplementary material.

CONCLUSION

Social mobility is associated with inflammatory and metabolic markers in older adults with some associations persisting after full adjustment for covariates. Compared to participants in stable high SEP or upward social trajectory, those who were in stable low SEP or experienced downward social mobility were more likely to have elevated levels of CRP, fibrinogen, and HbA1c. Participants who experienced upward, downward, or stable low SEP tend to have lower HDL levels with no discernible patterns, compared with those who remained in high SEP throughout their lives. Health behaviours explain some of these associations. Upward social mobility seems to be associated with a partial reversal of the effect of social disadvantage in childhood on older adults' inflammatory profile.

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4. Key-points

What is already known on this subject?

- Childhood and adult socioeconomic position (SEP) are associated with inflammatory and metabolic markers, which are excellent predictors of cardiovascular disease, at older ages.

What this study adds?

- The systematic changes in SEP across the lifespan, which are best described by the term social mobility, are also associated with inflammatory and metabolic markers at older ages.
- Participants in stable high SEP or upward social mobility were more likely to have a healthier biomarker profiles i.e., lower CRP, fibrinogen, and HbA1c, compared with those in stable low SEP or downward social mobility trajectory.
- Health behaviours, obesity, and depressive symptoms provided a partial explanation of the associations between social mobility and these markers.
- Adult SEP is important for chronic inflammation, independent of childhood SEP, and likely can partially mitigate and reverse life time inflammation- and metabolism-related pathogenic processes that are associated with experiences of social disadvantage in childhood.

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6. Competing interest

None declared.

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7. Contributorship statement

All authors conceived the study aims and design. NN contributed to the literature review, data cleaning, data analysis, interpretation of the findings, and writing the initial manuscript under the supervision of PD. PD critically revised the initial manuscript, and all authors participated in further revisions. The final manuscript was read and approved by all authors before submission.

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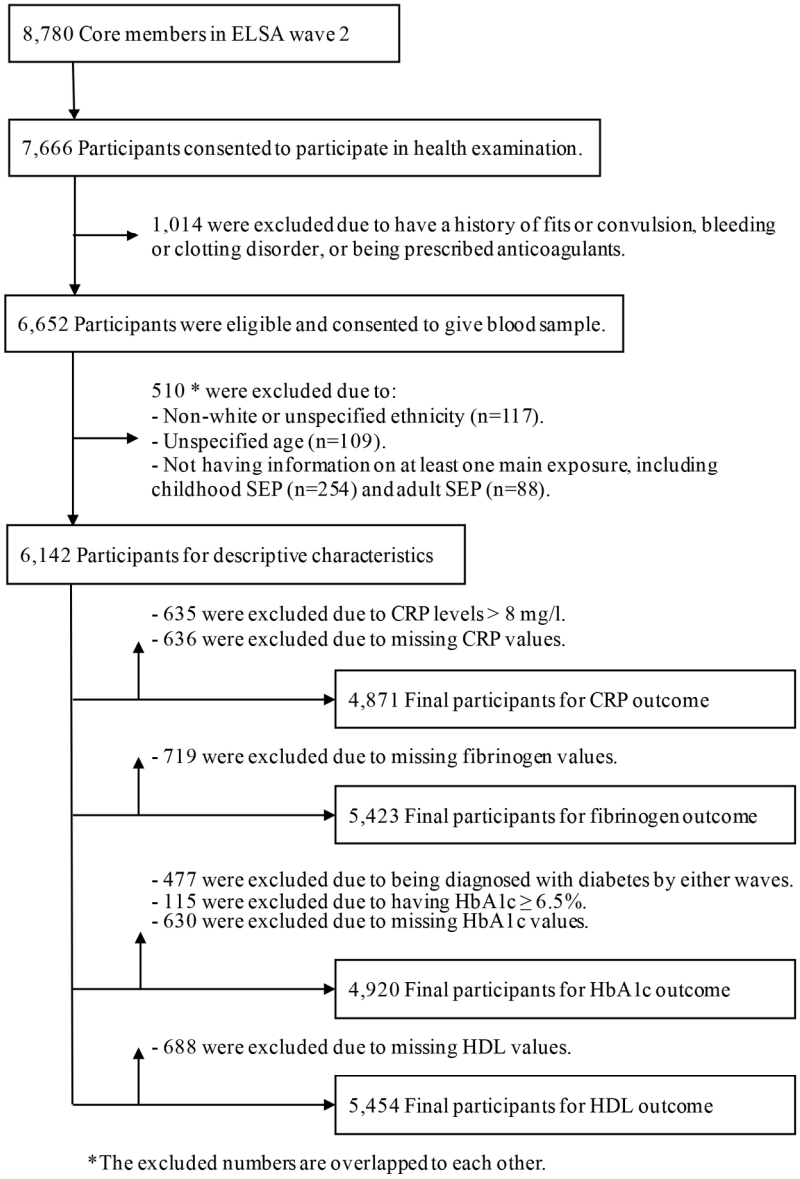

Figure 1. Sample selection process

145x207mm (300 x 300 DPI)

Social Mobility and Inflammatory and Metabolic Markers at Older Ages:

The English Longitudinal Study of Ageing

Supplementary material

SUPPLEMENTARY METHODS

Data source and studied population: non-response analysis

In a non-response analysis (Table S1), non-responders defined as those who had missing values on, at least, one outcome variable were more likely to be older, more obese, have lower SEP, current smokers, less physically active, more frequent alcohol drinkers, have elevated depressive symptoms, and have a higher prevalence of both cardiovascular and non-cardiovascular comorbidities than responders who had all outcome measurements (all p-value < 0.001). This non-responder profile was consistent with previous ELSA reports on attrition and non-response, in which the attrition in studies was related to older age, increased morbidity, elevated depressive symptoms, and lower SEP.[1-3] Moreover, responders were likely to have more favourable inflammatory and metabolic profiles characterised by lower levels of CRP, fibrinogen, and HbA1c, and higher levels of HDL, compared with those in non-responders.

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Table S1. Non-response analysis

Characteristics	Non-responders 4,060 (46.2)	Responders 4,720 (53.8)	Total 8,780 (100)	P-value[a]
Women	2,217 (54.6)	2,614 (55.4)	4,831 (55.0)	0.53
Age (year)				
Mean (SD)	67.82 (9.68)	65.42 (9.15)	66.52 (9.48)	< 0.001
Median (IQR)	67 (59-75)	64 (58-72)	65 (58-74)	< 0.001
BMI (kg/m^2)				
Mean (SD)	28.80 (5.40)	27.40 (4.48)	27.93 (4.89)	< 0.001
< 25 kg/m^2	641 (15.8)	1367 (29.0)	2008 (22.9)	< 0.001
25 – 30 kg/m^2	1087 (26.8)	2045 (43.3)	3132 (35.7)	
> 30 kg/m^2	972 (23.9)	1113 (23.6)	2085 (23.7)	
Missing	1360 (33.5)	195 (4.1)	1555 (17.7)	
Waist (cm)				
Mean (SD)	93.15 (25.82)	92.12 (18.30)	92.52 (21.51)	0.058
Normal waist	492 (12.1)	1148 (24.3)	1640 (18.7)	< 0.001
Increased risk	624 (15.4)	1313 (27.8)	1937 (22.1)	
Substantially increased	1677 (41.3)	2162 (45.8)	3839 (43.7)	
Missing	1267 (31.2)	97 (2.1)	1364 (15.5)	
Waist to hip ratio				
Mean (SD)	0.80 (0.45)	0.84 (0.29)	0.83 (0.36)	< 0.001
Normal	880 (21.7)	1,915 (40.6)	2,795 (31.8)	< 0.001
Increased risk	1,901 (46.8)	2,698 (57.2)	4,599 (52.4)	
Missing	1,279 (31.5)	107 (2.2)	1,386 (15.8)	

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Characteristics	Non-responders	Responders	Total	P-value[a]
	4,060 (46.2)	4,720 (53.8)	8,780 (100)	
Social mobility				
Stable high	1,395 (36.8)	1,963 (43.8)	3,358 (40.6)	< 0.001
Low to high	536 (14.1)	714 (15.9)	1,250 (15.1)	
High to low	965 (25.5)	1,005 (22.4)	1,970 (23.8)	
Stable low	896 (23.6)	805 (17.9)	1,701 (22.5)	
Physical activity				
No on weekly basis	499 (12.6)	249 (5.3)	748 (8.6)	< 0.001
Mild	804 (20.3)	591 (12.5)	1,395 (16.0)	
Moderate	1,836 (46.3)	2,364 (50.1)	4,200 (48.4)	
Vigorous	828 (20.9)	1,514 (32.1)	2,342 (27.0)	
Alcohol consumption				
Daily/ almost daily	696 (17.1)	1,105 (23.4)	1,801 (20.5)	< 0.001
1-2 times/week	1,129 (27.8)	1,707 (36.2)	2,836 (32.3)	
1-2 times/month	633 (15.6)	801 (17.0)	1,434 (16.3)	
Never/ almost never	808 (19.9)	720 (15.2)	1,528 (17.4)	
Missing	794 (19.6)	387 (8.2)	1,181 (13.5)	
Smoking status				
Current smoker	724 (17.9)	605 (12.8)	1,329 (15.1)	< 0.001
Ex-smoker	1,956 (48.2)	2,307 (48.9)	4,263 (48.6)	
Never smoked	1,377 (33.9)	1,805 (38.3)	3,182 (36.3)	
CESD score ≥ 4				
Yes	758 (18.7)	582 (12.3)	1,340 (15.3)	< 0.001
No	3,126 (77.0)	4,093 (86.7)	7,219 (82.2)	
Missing	176 (4.3)	45 (1.0)	221 (2.5)	
Prevalent CVD	1,641 (40.4)	1,074 (22.8)	2,715 (30.9)	< 0.001

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Characteristics	Non-responders 4,060 (46.2)	Responders 4,720 (53.8)	Total 8,780 (100)	P-value[a]
Prevalent non-CVD	2,503 (61.6)	2,590 (54.9)	5,093 (58.0)	< 0.001
Outcome variables				
CRP (ln mg/liter), mean (SD)	0.62 (0.85)	0.46 (0.90)	0.48 (0.90)	< 0.001
Fibrinogen (ln g/liter), mean (SD)	1.28 (0.25)	1.11 (0.20)	1.15 (0.22)	< 0.001
HbA1c (ln %), mean (SD)	1.70 (0.07)	1.69 (0.06)	1.70 (0.06)	< 0.001
HDL (ln mmol/liter), mean (SD)	0.30 (0.25)	0.41 (0.24)	0.39 (0.25)	< 0.001

n (%) unless specified elsewhere.

[a]One-way ANOVA and chi-square for continuous and categorical variables, respectively, and p-value did not take into account the effect of missing group.

Abbreviations: SD, standard deviation; CESD, Center for Epidemiology Studies Depression Scale; CVD, cardiovascular disease; non-CVD, non-cardiovascular disease; HbA1c, haemoglobin A, glycosylated; HDL, high-density lipoprotein cholesterol.

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SUPPLEMENTARY DISCUSSION

Implication of our findings: how are health behaviours associated with social mobility?

To our knowledge, there are two main mechanisms that explain the association between social mobility and health behaviours. The social causation theory explains that social mobility influences health behaviours. For example, people who experience a downward social drift may encounter massive stress, which makes them engage in smoking and heavy alcohol drinking. In contrast, people who engage in heavy alcohol drinking may later confront a financial problem and mental illness, which result in a lower SEP, as they cannot study or work properly. This is known as the social (or health) selection theory.[4]

Although a combination of social causation and social selection processes may account for the association between SEP and health behaviours, the social causation theory is mostly endorsed,[4-13] and many studies simply define risky health behaviours as potential mediators for the association between life course SEP and clinical outcomes.[14, 15] A study by Burrow *et al.* showed that British men who upwardly mobile from manual background to the middle class were less likely to engage in risky health behaviours in terms of smoking and binge drinking, while those middle-class men who have remained within their class of origin have a greater odds of engaging in risky health behaviours. This would undermine a claim of the social selection process.[7] These findings are consistent with a study on alcohol use during adolescence, which shows that children on the downward drift in the family income trajectory, measured from 1 month of age through 15 years, were more likely to drink alcohol when they are 15 years.[6]

Social causation theory also explains the associations between social mobility and mental health and obesity. Heraclides *et al.* suggested that downward socially mobile women had a higher prevalence of overweight and obesity in adulthood than the socially stable of high SEP (52.0% vs. 36.1%). The results were still consistent, even after excluding participants, who had been obese as adolescents, to reduce the possibility of reverse causality.[5] Johnson *et al.* suggested that a low parental occupational status since offspring was born was significantly associated with an increased

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risk for depressive disorders in adolescent children, and these findings support the social causation theory because of an apparent time sequence.[4]

Due to the fact that our study used cross-sectional data, we cannot establish a clear temporal sequence and draw a causal conclusion about the exact role of unhealthy behaviours. Therefore, our explanation, on which social mobility and health behaviours interplay with each other, is based mainly on previous literature. Although existing evidence is likely to support that health behaviours are mediators (social causation theory), further studies, using a prospective design and a large community sample, are still required to address this issue. Nonetheless, we need to take health behaviours into consideration when we investigate the association, between social mobility and clinical outcomes, as what has been done successfully in previous studies.[14-16]

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