



## Original Contribution

# Socioeconomic Differences in Cardiometabolic Factors: Social Causation or Health-related Selection? Evidence From the Whitehall II Cohort Study, 1991–2004

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In this study, the health-related selection hypothesis (that health predicts social mobility) and the social causation hypothesis (that socioeconomic status influences health) were tested in relation to cardiometabolic factors. The authors screened 8,312 United Kingdom men and women 3 times over 10 years between 1991 and 2004 for waist circumference, body mass index, systolic and diastolic blood pressure, fasting glucose, fasting insulin, serum lipids, C-reactive protein, and interleukin-6; identified participants with the metabolic syndrome; and measured childhood health retrospectively. Health-related selection was examined in 2 ways: 1) childhood health problems as predictors of adult occupational position and 2) adult cardiometabolic factors as predictors of subsequent promotion at work. Social causation was assessed using adult occupational position as a predictor of subsequent change in cardiometabolic factors. Hospitalization during childhood and lower birth weight were associated with lower occupational position (both  $P$ 's  $\leq 0.002$ ). Cardiometabolic factors in adulthood did not consistently predict promotion. In contrast, lower adult occupational position predicted adverse changes in several cardiometabolic factors (waist circumference, body mass index, fasting glucose, and fasting insulin) and an increased risk of new-onset metabolic syndrome (all  $P$ 's  $\leq 0.008$ ). These findings suggest that health-related selection operates at younger ages and that social causation contributes to socioeconomic differences in cardiometabolic health in midlife.

cardiovascular diseases; health status disparities; longitudinal studies; metabolic syndrome X; public health; social class

Abbreviations: CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; OR, odds ratio; SES, socioeconomic status.

A graded association of lower socioeconomic status (SES) with increased incidence of diabetes and coronary heart disease has been shown repeatedly (1–7). These associations are often interpreted to indicate that SES affects health, either directly or indirectly (the social causation hypothesis). Low SES is associated with low income, poor career prospects, and greater risk of unemployment. All of these factors determine the ability to consume goods and services—for example, high-quality food or health care—which in turn affects health (8, 9). Income differences, even if income is above the poverty line, may also lead to differential access to social

participation and social capital, which are related to health inequalities (10–13). Low SES is also associated with higher exposure to occupational health hazards, both physical and psychosocial, potentially contributing to health problems (14–18). Furthermore, differences in social values and behavioral preferences between SES groups may create variations in health (19).

The relation between SES and health is not necessarily unidirectional, since health can function as a selective mechanism in relation to SES (20, 21). It has been suggested that childhood health is linked to educational achievement and

labor market prospects and thus to adult SES, which might account for the socioeconomic differences in health in adulthood (the health selection hypothesis) (22–25). Particularly severe and limiting health problems during adulthood may increase the risk of an income shortfall and poor career prospects. Although the strength of these associations is likely to be dependent on the health problem in question and the local social policy context, it has been argued that persons with severe chronic illness tend to be poorer because their illness endangers their economic potential and resources (26).

Taken together, this evidence is consistent with the hypothesis that the relation between SES and health is reciprocal, bound in a reinforcing cycle where the direction of causality is difficult to determine (27, 28). It is possible, for example, that although both health selection and social causation operate over the life course, their relative importance varies from one developmental stage to another. Health problems early in life may have severe and long-term consequences, as they affect educational attainment and subsequent adult SES (22, 24, 25). In contrast, health problems that emerge in adulthood may play only a minor role in the overall relation between health and change in SES (11, 21, 29). Longitudinal research designs are needed to capture such life-stage-dependent relations. Furthermore, research using objective indicators of health would strengthen the existing evidence, since self-report measures may be biased by socially patterned reporting of health.

In this study from the Whitehall II cohort (2), we investigated health-related selection and social causation using repeated measurements of objectively assessed cardiometabolic factors in adulthood. To assess the selection process at different stages of the life course, we examined the extent to which childhood health predicted socioeconomic mobility and the extent to which adult cardiometabolic factors, such as obesity, high blood pressure, lipid levels, glycemia, and inflammation, predicted future promotion at work. To study social causation, we assessed whether adult SES predicted change in cardiometabolic factors over a 10-year period.

## MATERIALS AND METHODS

### Study population and design

Recruitment of the Whitehall II Study sample (phase 1) took place between late 1985 and early 1988 among all staff from 20 United Kingdom civil service departments based in London. With a response rate of 73%, 6,895 men and 3,413 women were enrolled in the study (2, 30). Since phase 1, there have been several further data collection phases. Baseline data on cardiometabolic factors for the present study were drawn from phase 3 (1991–1993). Repeat measurements taken in phase 5 (1997–1999) and phase 7 (2003–2004) provided the 5-year and 10-year follow-up data, respectively. Data on childhood SES and health were collected retrospectively in phases 1, 3, and 5. Informed consent was obtained from all participants. The University College London Medical School Committee on the Ethics of Human Research approved the protocol.

### SES and health in childhood

Father's social class (United Kingdom Registrar General's Classification, based on occupation), requested in phase 1, was used as a measure of parental SES. Self-reports of birth weight (phase 3) and hospitalization in childhood (phase 5—"Did any of the following things happen during your childhood (that is, up until you were 16)? You spent 4 or more weeks in hospital"—response format: yes/no) were used as indicators of childhood health.

### SES and social mobility in adulthood

We used civil service employment grade, in 6 levels, as the measure of SES in phases 3, 5, and 7. For persons who left the civil service after phase 3, we used the last known employment grade reported in phases 5 and 7. The 6 employment grade categories were: unified grades 1–6 (highest grade), unified grade 7, senior executive officer, higher executive officer, executive officer, and clerical and support staff (lowest grade). Upward social mobility (promotion) was defined as being in a higher employment grade at follow-up than at baseline according to the 6-level classification. We examined the cross-sectional correlation of employment grade with other indicators of SES: income, Registrar General's social class, and educational level. As can be seen in Table 1, the 6-level employment grade measure was strongly correlated with income (Pearson's  $r = 0.90$ ,  $P < 0.0001$ ), strongly correlated with Registrar's General social class ( $r = 0.73$ ,  $P < 0.0001$ ), and moderately correlated with educational level ( $r = 0.43$ ,  $P < 0.0001$ ).

### Cardiometabolic factors in adulthood

The measurement of cardiometabolic factors in phases 3, 5, and 7 using standard protocols is presented briefly here, as it has been described previously (31–34). We assessed waist circumference and weight and calculated body mass index (weight (kg)/height (m)<sup>2</sup>). We measured systolic blood pressure and diastolic blood pressure twice in the sitting position after 5 minutes of rest with a Hawksley random-0 sphygmomanometer (Hawksley & Sons Ltd., Lansing, Sussex, United Kingdom) (phases 3 and 5) and an Omron HEM 907 digital blood pressure monitor (Omron Healthcare, Inc., Bannockburn, Illinois) (phase 7). The average of 2 readings was taken to be the measured systolic and diastolic blood pressures. Oral glucose tolerance tests, according to the World Health Organization protocol, were administered following a minimum 5-hour fast. Persons with known diabetes did not participate in this part of the screening. High density lipoprotein (HDL) cholesterol and triglyceride levels were measured within 72 hours in serum stored at 4°C using enzymatic colorimetric methods. We used the Friedewald formula to calculate low density lipoprotein (LDL) cholesterol concentration. Levels of C-reactive protein and interleukin-6 were determined in serum; samples were stored at –80°C (these data were available only for phases 3 and 7). Plasma glucose level was measured using an electrochemical glucose oxidase method, and serum insulin level was measured by radioimmunoassay using polyclonal antiserum. Metabolic

**Table 1.** Cross-Sectional Association of Whitehall II Employment Grade With Other Indicators of Socioeconomic Status, Whitehall II Study, 1991–2004

	Whitehall II Employment Grade												Pearson's <i>r</i>	<i>P</i> Value	
	Unified Grades 1–6 (High)		Unified Grade 7		Senior Executive Officer		Higher Executive Officer		Executive Officer		Clerical/Support Staff (Low)				
	No. of Participants	%	No. of Participants	%	No. of Participants	%	No. of Participants	%	No. of Participants	%	No. of Participants	%			
United Kingdom Registrar General social class <sup>a</sup>															
I (high)	899	63												0.73	<0.0001
II	529	37	1,744	100	1,169	100	1,397	99	944	81	5	0			
III <sub>n</sub>							8	1	224	19	1,095	79			
III <sub>m</sub>									1	0	236	17			
IV															
V (low)											61	4			
Years of education <sup>b</sup>															
>18	583	75	843	64	464	42	578	39	336	28	332	18	0.43	<0.0001	
17–18	113	15	288	22	344	31	480	33	334	28	323	18			
≤16	78	10	180	14	307	28	413	28	516	43	1,168	64			
Annual income <sup>c</sup>															
<£15,000			2	0	2	0	11	2	15	4	220	50	0.90	<0.0001	
£15,000–<£20,000	1	0	4	1	2	0	18	3	204	51	193	43			
£20,000–<£25,000	10	2	8	1	22	5	357	63	116	29	25	6			
£25,000–<£35,000	12	2	116	16	372	85	165	29	58	14	5	1			
£35,000–<£50,000	178	30	565	77	37	9	16	3	8	2	1	0			
≥£50,000	389	66	36	5	2	0	3	0	1	0					

<sup>a</sup> Data were drawn from phase 3 (1991–1993) of the Whitehall II Study.

<sup>b</sup> Data were drawn from phase 1 (1985–1988) of the Whitehall II Study.

<sup>c</sup> Data were drawn from phase 5 (1997–1999) of the Whitehall II Study.

syndrome status was determined using National Cholesterol Education Program Adult Treatment Panel III criteria based on waist circumference, HDL cholesterol, triglycerides, blood pressure, and fasting plasma glucose (35).

### Statistical analysis

We used SAS 9.1 (SAS Institute Inc., Cary, North Carolina) and Stata 11.0 (StataCorp LP, College Station, Texas) statistical software for Windows for all analyses. There were no clear differences in our results between men and women, so the data were pooled and adjusted for sex. We conducted separate sets of analyses to assess evidence for health selection and social causation as explanations for the associations between SES and cardiometabolic factors.

**Test of the health-related selection hypothesis.** To test the hypothesis of childhood health-related selection (childhood health predicting adult SES), we divided participants into 6 groups on the basis of employment grade in phase 3 and used linear and multinomial logistic regression analysis to summarize the associations of childhood hospitalization (yes/no) and birth weight (pounds) with employment grade at baseline, adjusting for age, sex, and parental SES. Regression coefficients for employment grade, treated as a continuous outcome, were calculated using linear regression analysis. We also examined whether these childhood variables predicted promotion in adulthood compared with staying in the same employment grade throughout follow-up. To examine the extent to which missing childhood data were associated with adult employment grade, we performed a corresponding multinomial logistic regression analysis with the status of the missing data (yes/no) as the exposure and repeated the analysis after multiple multivariate imputation for missing values (a detailed description of the method is provided below).

To test the hypothesis of health-related selection in adulthood, we modeled the effect of cardiometabolic factors in phase 3 on promotion over 10 years (from phase 3 to phase 7), comparing those subsequently promoted, those demoted, and those who stayed in the same grade, adjusted for age and sex. We added "nonresponse/death in phase 7" (yes/no) as a further outcome category in order to examine selective sample retention. To examine the effect of sample attrition on the findings, we repeated the analysis after multiple multivariate imputation for missing values (see below). We additionally tested the selection hypothesis over 5-year intervals (i.e., from phase 3 to phase 5 and from phase 5 to phase 7) using multilevel longitudinal modeling (xtmixed and xtlogit procedures in Stata) with robust estimation to take into account the fact that repeated measurements on the same participant are correlated. In these models, cardiometabolic factors in phase 3 were fitted as predictors of promotion between phases 3 and 5 and cardiometabolic factors in phase 5 were fitted as predictors of promotion between phases 5 and 7. Levels of the cardiometabolic factors were allowed to change within subjects over time.

**Tests of the social causation hypothesis.** To test the social causation hypothesis, associations between baseline adult employment grade and changes in adult cardiometabolic factors over 10 years (from phase 3 to phase 7) were

examined using logistic regression analysis and analysis of variance as appropriate. To examine the extent to which employment grade in phase 3 predicted participation at follow-up, we performed a corresponding logistic regression analysis with nonresponse/death in phase 7 (yes/no) as the outcome. To test the robustness of our findings, we repeated the analyses in a subgroup excluding participants who had retired by phase 7. To test the causation hypothesis over 5-year intervals (i.e., from phase 3 to phase 5 and from phase 5 to phase 7), we used a multilevel modeling approach (xtmixed and xtlogit procedures in Stata). In these models, employment grade in phase 3 was tested as a predictor of change in cardiometabolic factors between phases 3 and 5, and employment grade in phase 5 was tested as a predictor of change in these factors between phases 5 and 7.

**Multiple multivariate imputation for missing values.** To retain all participants, we generated multiple imputed values for the missing data from the variables used in the analysis, by means of PROC MI (SAS 9.1.3). Ten data sets were randomly selected, and analyses were conducted on each of these imputed data sets. The mean of these estimates was calculated using SAS PROC MIANALYSE. This procedure takes account of the uncertainty in the imputation as well as uncertainty due to random variation (as in all multivariable analyses).

**Correction for multiple testing.** In all analyses, statistical tests were 2-sided, and  $P < 0.05$  was considered statistically significant. Bonferroni-corrected  $P$  values were calculated, in addition to uncorrected  $P$  values, to reduce the risk of type 1 errors arising from multiple testing.

## RESULTS

Of the 10,308 participants, 8,312 participated in the phase 3 screening. Of the 1,996 participants excluded, 125 had died between phase 1 and phase 3 and 1,871 were nonrespondents or had missing data on employment grade. At recruitment into the study (phase 1), persons excluded from the current analyses were slightly older (44.8 years vs. 44.4 years;  $P = 0.002$ ), more likely to be female (41.8% vs. 31.0%;  $P < 0.0001$ ), and less likely to be from the highest employment grade (21.8% vs. 31.2%;  $P < 0.0001$ ).

Baseline characteristics of the study participants are shown in Table 2. Most of the participants were in the intermediate employment grade categories (senior executive officer, higher executive officer, and executive officer: 45.0%) in phase 3 and in the high grade categories (unified grades 1–7: 45.6%) in phase 7. A total of 18.4% had been promoted during follow-up. Adverse changes were observed for levels of most cardiometabolic factors during follow-up, although the cholesterol profile improved. At baseline, 10.8% of participants were classified as having the metabolic syndrome, and at follow-up, 13.6% were so classified.

### Health-related selection from childhood to adulthood

As shown in Table 3, poor childhood health (indicated by hospitalization in childhood and lower birth weight) predicted lower adult employment grade in phase 3, with no statistical

**Table 2.** Characteristics of Participants at Baseline and Follow-up, Whitehall II Study, 1991–2004

	Baseline (Phase 3, 1991–1993)			Follow-up (Phase 7, 2003–2004)		
	Mean (SD)	No. of Participants	%	Mean (SD)	No. of Participants	%
Age, years	49.6 (6.1)	8,312		61.2 (6.0)	6,586	
Sex						
Male		5,733	69.0		4,627	70.3
Female		2,579	31.0		1,959	29.7
Race/ethnicity						
White		7,542	91.1		6,068	92.3
Nonwhite		741	8.9		510	7.8
Employment grade						
Unified grades 1–6 (high)		1,428	17.2		1,655	25.5
Unified grade 7		1,744	21.0		1,299	20.0
Senior executive officer		1,169	14.0		986	15.2
Higher executive officer		1,405	16.9		1,010	15.6
Executive officer		1,169	14.1		823	12.7
Clerical/support staff (low)		1,397	16.8		709	10.9
Promotion during follow-up						
No					5,291	81.6
Yes					1,194	18.4
Waist circumference, cm	85.8 (11.6)	7,822		93.6 (12.3)	6,151	
Body mass index <sup>a</sup>	25.3 (3.7)	7,901		26.7 (4.4)	6,146	
Systolic blood pressure, mm Hg	120.6 (13.6)	7,905		128.2 (16.8)	6,168	
Diastolic blood pressure, mm Hg	79.7 (9.4)	7,904		74.4 (10.5)	6,167	
High density lipoprotein cholesterol, mmol/L	1.43 (0.41)	7,840		1.58 (0.45)	6,073	
Low density lipoprotein cholesterol, mmol/L	4.39 (1.04)	7,714		3.50 (1.63)	6,004	
Fasting glucose, mmol/L	5.24 (0.69)	7,559		5.47 (1.32)	6,063	
Fasting insulin, pmol/L	6.97 (6.07)	7,074		10.08 (12.24)	5,479	
C-reactive protein, mg/L	1.93 (4.35)	7,475		2.59 (5.09)	5,895	
Interleukin-6, pg/mL	1.94 (2.29)	7,421		2.34 (2.13)	5,451	
Metabolic syndrome <sup>b</sup>						
Yes		836	10.8		823	13.6
No		6,935	89.2		5,250	86.4
Status in phase 7						
Employed in civil service					2,010	24.2
Left civil service					1,048	12.6
Retired					3,424	41.2
Nonrespondent					1,411	17.0
Died					314	3.8
Unknown					105	1.3

Abbreviation: SD, standard deviation.

<sup>a</sup> Weight (kg)/height (m)<sup>2</sup>.

<sup>b</sup> Metabolic syndrome status was determined using National Cholesterol Education Program Adult Treatment Panel III criteria based on waist circumference, high density lipoprotein cholesterol, triglycerides, blood pressure, and fasting plasma glucose (35).

evidence of sex differences (for sex interaction,  $P > 0.37$ ). These associations were attenuated after adjustment for parental SES (by 29%, to  $-0.15$  (95% confidence interval (CI):  $-0.24, -0.05$ ), for hospitalization ( $n = 5,750$  in both models) and by 40%, to  $0.03$  (95% CI:  $0.00, 0.05$ ), for birth weight ( $n = 4,701$  in both models)). The proportion of par-

ticipants hospitalized and with lower birth weight increased in a step-by-step manner with each decrease in adult employment grade category. This association was also seen when employment grade at entry into the civil service was used as an outcome (see Web Table 1 and Web Table 2, which appear on the *Journal's* website (<http://aje.oxfordjournals.org/>)).

**Table 3.** Test of the Health-related Selection Hypothesis (That Health Predicts Social Mobility) and the Social Causation Hypothesis (That Socioeconomic Status Influences Health), Whitehall II Study, 1991–2004

Exposure	Outcome	No. of Participants	Estimate <sup>a</sup>			P Value
			Regression Coefficient	Odds Ratio	95% Confidence Interval	
Health-related selection (from childhood to adulthood) hypothesis						
Hospitalization in childhood (1 = yes, 0 = no)	Employment grade <sup>b</sup> (1 = low, 6 = high)	6,547	−0.23		−0.34, −0.13	<0.0001
Birth weight, per pound	Employment grade	5,294	0.05		0.02, 0.08	0.002
Health-related selection (adulthood) hypothesis						
Waist circumference, per 1-SD increase	10-year promotion (1 = yes, 0 = no)	6,153		1.04	0.96, 1.12	0.32
Body mass index <sup>c</sup> , per 1-SD increase	10-year promotion	6,219		1.03	0.97, 1.10	0.38
Systolic blood pressure, per 1-SD increase	10-year promotion	6,229		1.01	0.94, 1.08	0.75
Diastolic blood pressure, per 1-SD increase	10-year promotion	6,228		0.99	0.93, 1.06	0.80
HDL cholesterol, per 1-SD increase	10-year promotion	6,175		0.96	0.90, 1.04	0.31
LDL cholesterol, per 1-SD increase	10-year promotion	6,076		1.08	1.00, 1.15	0.04
Fasting glucose, per 1-SD increase	10-year promotion	5,967		0.96	0.89, 1.05	0.37
Fasting insulin, per 1-SD increase	10-year promotion	5,567		1.02	0.95, 1.10	0.63
Log C-reactive protein, per 1-SD increase	10-year promotion	5,881		1.06	0.99, 1.14	0.08
Log interleukin-6, per 1-SD increase	10-year promotion	5,839		0.98	0.91, 1.05	0.52
Metabolic syndrome (1 = yes, 0 = no)	10-year promotion	6,127		1.18	0.95, 1.47	0.13
Social causation (adulthood) hypothesis						
Employment grade	Waist circumference, cm	5,868	−0.16		−0.28, −0.04	0.008
Employment grade	Body mass index	5,925	−0.06		−0.10, −0.03	0.0003
Employment grade	Systolic blood pressure, mm Hg	5,953	0.02		−0.23, 0.28	0.86
Employment grade	Diastolic blood pressure, mm Hg	5,951	0.26		0.09, 0.43	0.003
Employment grade	HDL cholesterol, mmol/L	5,824	0.015		0.010, 0.020	<0.0001
Employment grade	LDL cholesterol, mmol/L	5,691	0.022		0.006, 0.039	0.007
Employment grade	Fasting glucose, mmol/L	5,632	−0.05		−0.07, −0.03	<0.0001
Employment grade	Fasting insulin, pmol/L	4,822	−0.43		−0.61, −0.24	<0.0001
Employment grade	Log C-reactive protein, mg/L	5,421	−0.00		−0.02, 0.02	0.90
Employment grade	Log interleukin-6, pg/mL	4,979	0.000		−0.011, 0.012	0.93
Employment grade	Metabolic syndrome at follow-up (1 = yes, 0 = no)	5,208		0.88	0.83, 0.94	<0.0001

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein; SD, standard deviation.

<sup>a</sup> In all models, results were adjusted for age and sex. The test of the association between employment grade and metabolic syndrome at follow-up was based on participants with no metabolic syndrome at baseline.

<sup>b</sup> Civil service employment grade, in 6 levels, was used as the measure of socioeconomic status.

<sup>c</sup> Weight (kg)/height (m)<sup>2</sup>.

Participants from lower employment grades were more likely to have missing data for childhood variables than those from the highest employment grade (Web Tables 1 and 2). However, as can be seen from a comparison of Tables 3 and 4, analyses based on the entire baseline cohort with imputation suggested that missing data had little effect on estimates of the associations between hospitalization or birth weight and baseline grade.

### Health-related selection during adulthood

To test potential health-related selection in adulthood, we analyzed whether cardiometabolic factors at baseline predicted promotion during follow-up. Of the demographic variables, male sex (odds ratio (OR) = 1.24, 95% CI: 1.09, 1.42), younger age (per year, OR = 0.91, 95% CI: 0.90, 0.92), and higher employment grade (per grade level, OR = 1.22, 95%

**Table 4.** Test of the Health-related Selection and Social Causation Hypotheses After Multiple Multivariate Imputation for Missing Values ( $n = 8,312^a$ ), Whitehall II Study, 1991–2004

Exposure	Outcome	Estimate <sup>b</sup>			P Value
		Regression Coefficient	Odds Ratio	95% Confidence Interval	
Health-related selection (from childhood to adulthood) hypothesis					
Hospitalization in childhood (1 = yes, 0 = no)	Employment grade <sup>c</sup> (1 = low, 6 = high)	−0.24		−0.35, −0.13	<0.0001
Birth weight, per pound	Employment grade	0.05		0.03, 0.07	0.008
Health-related selection (adulthood) hypothesis					
Waist circumference, per 1-SD increase	10-year promotion (1 = yes, 0 = no)		1.02	0.95, 1.11	0.59
Body mass index <sup>d</sup> , per 1-SD increase	10-year promotion		1.03	0.96, 1.11	0.43
Systolic blood pressure, per 1-SD increase	10-year promotion		0.99	0.92, 1.06	0.79
Diastolic blood pressure, per 1-SD increase	10-year promotion		0.97	0.91, 1.04	0.43
HDL cholesterol, per 1-SD increase	10-year promotion		0.98	0.90, 1.07	0.59
LDL cholesterol, per 1-SD increase	10-year promotion		1.05	0.99, 1.13	0.12
Fasting glucose, per 1-SD increase	10-year promotion		0.99	0.91, 1.06	0.78
Fasting insulin, per 1-SD increase	10-year promotion		1.00	0.92, 1.07	0.94
Log C-reactive protein, per 1-SD increase	10-year promotion		1.04	0.97, 1.13	0.21
Log interleukin-6, per 1-SD increase	10-year promotion		0.96	0.90, 1.03	0.22
Metabolic syndrome (1 = yes, 0 = no)	10-year promotion		1.13	0.94, 1.31	0.16
Social causation (adulthood) hypothesis					
	10-year change in:				
Employment grade	Waist circumference, cm	−0.13		−0.23, −0.03	0.009
Employment grade	Body mass index	−0.06		−0.08, −0.03	0.0002
Employment grade	Systolic blood pressure, mm Hg	−0.10		−0.31, 0.12	0.38
Employment grade	Diastolic blood pressure, mm Hg	0.13		−0.01, 0.28	0.07
Employment grade	HDL cholesterol, mmol/L	0.013		0.009, 0.017	<0.0001
Employment grade	LDL cholesterol, mmol/L	0.020		−0.001, 0.042	0.06
Employment grade	Fasting glucose, mmol/L	−0.06		−0.07, −0.04	<0.0001
Employment grade	Fasting insulin, pmol/L	−0.40		−0.55, −0.24	<0.0001
Employment grade	Log C-reactive protein, mg/L	0.00		−0.01, 0.02	0.56
Employment grade	Log interleukin-6, pg/mL	0.004		−0.004, 0.013	0.37
Employment grade	Metabolic syndrome at follow-up (1 = yes, 0 = no)		0.90	0.85, 0.94	<0.0001

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein; SD, standard deviation.

<sup>a</sup>  $n = 8,312$  in each of the 10 imputed copies of the data set.

<sup>b</sup> In all models, results were adjusted for age and sex. The test of the association between employment grade and metabolic syndrome at follow-up was based on participants with no metabolic syndrome at baseline.

<sup>c</sup> Civil service employment grade, in 6 levels, was used as the measure of socioeconomic status.

<sup>d</sup> Weight (kg)/height (m)<sup>2</sup>.

CI: 1.18, 1.27) were all associated with promotion. There was no firm evidence of an association between educational level in phase 1 and promotion (for >18 years of education vs. ≤16 years, OR = 1.17, 95% CI: 0.99, 1.38).

As expected, adverse cardiometabolic risk factor levels were related to higher levels of nonresponse and death (Web Table 3). As shown in Table 3, cardiometabolic factors in adulthood

did not predict promotion during the subsequent 10 years. The only exception was LDL cholesterol, which was associated with higher odds of promotion, but this finding did not survive correction for multiple testing ( $P = 0.44$ ) (Table 3). The findings were similar after exclusion of participants who retired before the end of follow-up (Web Table 4). Multilevel analyses of promotion over 5-year intervals appeared to show

larger waist circumference, lower diastolic blood pressure, and lower LDL cholesterol to be associated with higher odds of promotion (Web Table 5). In the entire baseline cohort with missing data imputed, there were no associations between cardiometabolic factors and promotion over a 10-year interval (Table 4). For the association between body mass index and promotion, but not for other cardiometabolic factors, there was evidence of sex differences ( $P$  for interaction = 0.008), with no association observed among women (OR = 0.93, 95% CI: -0.85, 1.02) and a weak direct association in men (OR = 1.13, 95% CI: 1.03, 1.23).

Thus, there was little consistent evidence that adults with better cardiometabolic health would be more likely to be promoted.

### Social causation in adulthood

The associations between adult employment grade and change in cardiometabolic factors during the 10-year follow-up period are shown in the lower halves of Tables 3 and 4. Participants in higher employment grades had smaller increases in waist circumference, body mass index, fasting glucose, and fasting insulin, more favorable changes in HDL cholesterol, and reduced risk of the metabolic syndrome. However, they also had a smaller reduction in diastolic blood pressure and LDL cholesterol (although higher employment grade was associated with reduced likelihood of being treated with lipid-lowering drugs and antihypertensive medication at follow-up (Web Table 6)). For body mass index, the effect was stronger in women (regression coefficient = -0.15, 95% CI: -0.22, -0.07) than in men (regression coefficient = 0.03, 95% CI: -0.07, 0.01) ( $P$  for interaction = 0.003).

Absolute changes in these factors by employment grade category are shown in Web Table 6 and Web Table 7. They indicate that the associations of employment grade with changes in body mass index, diastolic blood pressure, HDL cholesterol, fasting glucose, and fasting insulin and with lower risk of metabolic syndrome survived after adjustment for multiple testing. Except for diastolic blood pressure, these associations were also observed in the entire baseline cohort with missing data imputed (Table 4) and in subcohorts composed of persons with poor and good childhood health (Web Tables 6 and 7). In the 5-year follow-up, higher employment grade was associated with more favorable changes in HDL cholesterol and fasting glucose and with reduced risk of the metabolic syndrome (Web Table 8).

## DISCUSSION

In this study of British civil servants, early health problems, characterized by hospitalization during childhood and lower birth weight, predicted lower SES, assessed as civil service employment grade, in adulthood independently of parental SES. However, we did not find strong evidence that after participants entered the civil service, a better cardiometabolic risk profile predicted promotion. In midlife, lower SES was associated with adverse changes in adiposity and glucose metabolism over 10 years of follow-up and thus increased the risk of the metabolic syndrome. These associations appeared to be independent of early health problems.

Thus, this study provides evidence that health-related selection in childhood appears to influence SES in adulthood, which in turn influences cardiometabolic profile in later life.

### Strengths and weaknesses

Because of missing data, our analyses were based on 4,542–8,312 men and women from the original population of 10,308. We found that lower SES, assessed using employment grade, was associated with higher nonresponse and death over the follow-up period, consistent with its poorer risk factor status. In order to generate spurious support for health-related selection from childhood to adulthood, missingness should have been more common, either for persons with both poor childhood health and a high employment grade compared with those with poor childhood health and a low employment grade or for persons with good childhood health and a low employment grade compared with those with good childhood health and a high employment grade. Similarly, selective sample attrition of persons with a high employment grade and an adverse metabolic profile or a low employment grade and a favorable profile would lead to spurious support for social causation. We cannot see any reason why this would be the case. Furthermore, the main findings of this study were reproducible in the total cohort with missing values imputed using multivariate multiple imputation methods.

Longitudinal data from the Whitehall II Study have been used extensively to demonstrate and explain social gradients in adult health. As previously, we used employment grade as a marker of adult SES (2). SES is a multifaceted concept, and it could be argued that grade does not fully capture all of these dimensions. In this cohort, employment grade was more strongly associated with income (correlation 0.9) than with education (correlation 0.4). Previous research has shown income to be both a consequence of poor health (28, 36) and a predictor of cardiovascular disease (37), making employment grade an adequate SES indicator with which to examine the social causation hypothesis. However, education rather than income appears to be related to type 2 diabetes (38). Thus, in relation to diabetes-related metabolic factors, our use of employment grade as a measure of SES, given its moderate association with education, probably provided a conservative test of the social causation hypothesis.

The validity of our measures of childhood health may be questioned, since data were collected retrospectively; that is, the participants were asked to recall their birth weight and hospitalizations of more than 4 weeks several decades after the events. However, previous studies have suggested moderate-to-good accuracy for self-reported birth weight (39). The accuracy of self-reported birth weight has been shown to be high among persons within the normal range for birth weight, as was the case for most of the participants in our study, and a relatively high correlation ( $r = 0.83$ – $0.87$ ) between self-reported birth weight and register-based birth weight has been observed even among middle-aged and elderly participants (40). In addition, measurement imprecision may lead to weaker associations with self-reported birth weight in comparison with recorded birth weight (39).

Thirteen percent of the participants reported long-term hospitalization before the age of 16 years. This figure appears



high and should be interpreted with caution. In the prospective British 1946 birth cohort study, for example, the prevalence of an illness requiring hospitalization of 3 weeks or more under the age of 5 years was lower, varying from 4% to 10% (41). The validity of self-reported use of health-care services, including hospitalization, has been shown to be reasonably good, with only small SES differences when the recall time is relatively short (up to 1 year) (42). Bergman et al. (43) found recall accuracy over a 10-year period to be greater than 80% for most conditions leading to hospitalization, although the validity of self-reported hospitalization was somewhat dependent on the specific health problem. In a systematic review, Bhandari and Wagner (44) concluded that because inpatient hospitalization tends to be rare, it is highly memorable. Furthermore, it should be noted that for the oldest members of our cohort, the period before age 16 spanned the years 1930–1946, when hospital stays were longer and periods of convalescence were common. During those years, a much larger share of inpatients were under age 15 than at present, and the age distribution of inpatients changed dramatically from 1970 to 2006 (45).

By using a large number of cardiometabolic risk factors as indicators of ill health or factors contributing to ill health, we were able to avoid reliance on self-reported health measures, which may be subject to socially patterned reporting bias. We could have also used height as an objective measure of childhood health as in some of the previous studies (46). However, this indicator is problematic because height reflects early-life socioeconomic circumstances and genetic influences, in addition to health (47), and taller stature can contribute to upward mobility due to physical appearance as well as health.

Two-thirds of our cohort participants were male white-collar workers, potentially reducing the generalizability of our findings. Thus, it is not possible to draw inferences about the relative importance of either hypothesis for people who are not in the labor force or those repeatedly entering and leaving the labor force. Furthermore, occupational groups are, by their very nature, healthier than the general population, so the range of cardiometabolic factors and SES might be narrower. Besides, there is little downward social mobility in this cohort. Given these limitations, the associations reported here might be under- or overestimates of the associations in the general population, which includes people not in paid employment.

### Comparison with previous studies

We are not aware of any other study that has evaluated repeat data on SES alongside direct assessment of cardiometabolic factors over an extended follow-up period. A recent analysis of self-report data from Whitehall II suggested that the association between childhood health and adult SES is not accounted for by educational qualifications, childhood SES, mother's education, or caregiving or parents' illness (48). Our study supports previous studies that have found selection effects from early life, typically from adolescence to adulthood. Early life health selection has been shown for health behaviors (e.g., smoking and drinking) and mental health problems (49, 50). It has also been shown that mental

disorders are more frequent among socioeconomically disadvantaged persons (51). However, our findings do not support health-related selection as an important source of socioeconomic differences in adult cardiometabolic health. In men, but not in women, initial body mass index was associated with later promotion, and this may be related to gendered norms about masculinity and men's ideal body weight. There is some evidence to suggest that in men, not only height but also height is viewed positively (52).

A large body of evidence suggests greater morbidity and mortality and worse risk profiles among adults in lower SES groups compared with their counterparts in higher SES groups (2–5, 53–55). Our findings confirm these observations and additionally demonstrate that low adult SES tends to set a trajectory of adverse change in cardiometabolic factors, particularly adiposity, glucose metabolism, and new-onset metabolic syndrome.

### Meaning of the study and unanswered questions

Taken together, these findings suggest that multiple processes rather than a single underlying mechanism are likely to drive the socioeconomic differences in cardiometabolic health. We observed that health-related selection operated from childhood to adulthood. However, the direction of the causal association after entering work life seemed predominantly to be from lower SES to a less favorable cardiometabolic risk profile, rather than good cardiometabolic health's improving SES, modeled here as chances of promotion.

These findings have important implications for policy. The general recommendation would be to focus on the accumulation of risk factors and benefits throughout the life course. Such a strategy should ensure that children with health problems are not disadvantaged with respect to educational opportunities. Determined action is also required to remove material and psychosocial adversities likely to underlie the excess cardiometabolic risk in low-SES groups.

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