Socioeconomic differences in cardiometabolic factors: social causation or health-related selection? Evidence from the Whitehall II Cohort Study, 1991-2004.

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

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ABSTRACT

In this study, the health-related selection hypothesis (health predicts social mobility) and the social causation hypothesis (socioeconomic status influences health) were tested in relation to cardiometabolic factors. We screened 8,312 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 two ways, (1) childhood health problems as predictors of adult occupational position, (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 $p<0.002$). 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 $p<0.008$). These findings suggest that health-related selection operates at younger ages and that social causation contributes to socioeconomic differences in cardiometabolic health in midlife.

Key words*:* Socioeconomic status, health selection, longitudinal, cardiometabolic, public health.

Abbreviations: ATPIII, Adult Treatment Panel III; BMI, body mass index; CHD, coronary heart disease; CI, Confidence Interval; CRP, C-reactive protein; CS, Clerical and Support staff; EO, Executive Officer; IL-6, interleukin-6; HEO, Higher Executive Officer; HDL, high density lipoprotein; LDL, low density lipoprotein SEO, Senior Executive Officer; SES, socioeconomic status; UG, Unified Grade.

A graded association between socioeconomic status (SES), diabetes and coronary heart disease (CHD) incidence, with higher cardiometabolic risk in socially disadvantaged groups, 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 these determine the ability to consume goods and services, for example, high quality food or health care, which in turn affect 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 relationship between SES and health is not necessarily unidirectional as health can function as a selective mechanism in relation to SES (20, 21). It has been suggested that childhood health is linked to educational achievements 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 relationship 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 relationship between health and change in SES (11, 21, 29). Longitudinal research designs are needed to capture such life-stage dependent relationships. Furthermore, research using objective indicators of health would strengthen the existing evidence as self-reported measures may be biased by socially-patterned reporting of health.

In this study from the Whitehall II cohort (2), we investigate 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 examine the extent to which childhood health predicts socioeconomic mobility and the extent to which adult cardiometabolic factors, such as obesity, high blood pressure, lipid levels, glycaemia and inflammation, predict future promotion at work. To study social causation, we assess whether adult SES predicts change in cardiometabolic factors over a 10-year period.

MATERIALS AND METHODS

Study population and design

The Whitehall II study sample recruitment (phase 1) took place between late 1985 and early 1988 among all staff from 20 London-based Civil Service departments. With a response rate of seventy-three percent, 6,895 men and 3,413 women were enrolled into the study (2, 30). Since phase 1 there have been several further data collection phases. Baseline data on cardiometabolic factors for the present study are drawn from phase 3 (1991-1993). Repeat measures at 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 at phases 1, 3 and 5. Informed consent was gained 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 (Registrar General's Classification based on occupation), requested at 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 a 6-level civil service employment grade as the measure of SES at phases 3, 5 and 7. For those who left the civil service after phase 3, we used the last known employment grade reported at phases 5 and 7. The six employment grade categories were: Unified Grade 1-6 (UG1-6; highest grade), Unified Grade 7 (UG7), Senior Executive Officer (SEO), Higher Executive Officer (HEO), Executive Officer (EO), Clerical and Support staff (CS; lowest grade). Upward social mobility (promotion) was defined as ending up in a higher employment grade at follow up compared to grade at baseline using 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 the *Box*, the 6-level employment grade measure was strongly correlated with income (Pearson $r = 0.90$, $p<0.0001$), 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 at phases 3, 5 and 7 using standard protocols is presented briefly as it has been described previously (31-34). We assessed waist circumference, weight, and calculated body mass index (BMI, weight in kg/ height in meters squared). We measured systolic blood pressure and diastolic blood pressure twice in the sitting position after 5 minutes of rest with the Hawksley random-0 sphygmomanometer (phases 3 and 5) and OMRON HEM 907 (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. Known diabetics did not participate in this part of the screening. High density lipoprotein (HDL)-cholesterol and triglycerides 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. C-reactive protein (CRP) and interleukin-6 (IL-6) were determined in serum; samples were stored at -80°C (these data were available only for phases 3 and 7). Plasma glucose was measured using an electrochemical glucose oxidase method and serum insulin by radioimmunoassay using a polyclonal antiserum. Metabolic syndrome was determined using National Cholesterol Education Program Adult Treatment Panel III (ATPIII) criteria based on waist circumference, HDL cholesterol, triglycerides, blood pressure and fasting plasma glucose (35).

Statistical analysis

We used SAS 9.1 and Stata 11.0 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 ran separate sets of analyses to assess evidence for health selection and social causation as explanations of the associations between SES and cardiometabolic factors.

***Test of the health-related selection hypothesis*:** To test health-related selection (childhood health predicting adult SES) we divided participants into six groups on the basis of employment grade at phase 3 and used linear and multinomial logistic regression analysis to summarize the associations of childhood hospitalization (yes/no) and birth weight (lbs) 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 to staying in the same employment grade throughout the 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 heath-related selection hypothesis in adulthood, the effect of cardiometabolic factors at phase 3 on promotion over 10 years (from phase 3 to phase 7) was modelled comparing those subsequently promoted; those demoted and those who stayed in the same grade, adjusted for age and sex. We added "non-response/death at 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, College Station, Texas, USA) (xtmixed and xtlogit procedures in Stata, College Station, Texas, USA) with robust estimation to take into account the fact that repeated measurements on the same participant are correlated. In these models, cardiometabolic factors at phase 3 were fitted as predictors of promotion between phases 3 and 5 and cardiometabolic factors at phase 5 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 phases 3 to 7) were examined using logistic regression analysis and analysis of variance as appropriate. To examine the extent to which employment grade at phase 3 predicted participation at follow-up, we performed a corresponding logistic regression analysis with non-response/death at 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, College Station, Texas, USA). In these models, employment grade at phase 3 was tested as a predictor of change in cardiometabolic factors between phases 3 and 5, and employment grade at phase 5 as a predictor of

change in these factors between phases 5 and 7.

Multiple multivariate imputation for missing values: To retain all participants, multiple imputed values were generated for the missing data from the variables used in the analysis, by means of PROC MI (SAS 9.1.3 SAS Institute, Cary, North Carolina, USA). Ten datasets were randomly selected, and analyses were conducted on each of these imputed datasets. The mean of these estimates was presented 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 a P-value of less than 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 non-respondents or had missing data on employment grade. At recruitment to the study (phase 1), those excluded from the current analyses were slightly older (44.8 years compared to 44.4 years, p=0.002), more likely to be women (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 1. Most of the participants were in the intermediate employment grade categories (grade levels SEO,HEO and EO, 45.0%) at phase 3 and in the high grade categories at phase 7 (grade levels UG1-UG7, 45.6%). 18.4% had been promoted during follow-up. Adverse changes were observed for most cardiometabolic factor levels during the follow-up, although the cholesterol profile improved. At baseline, 10.8% of participants and at follow-up 13.6% were classified as having the metabolic syndrome.

Health-related selection from childhood to adulthood

As shown in Table 2, poor childhood health (indicated by hospitalization in childhood and lower birth weight) predicted lower adult employment grade at phase 3, with no statistical evidence of sex differences (p for sex-interaction >0.37). These associations were attenuated after adjustment for parental SES [by 31% from -0.21 (95% CI: -0.03, -0.10) to -0.15, (95% CI -0.24, -0.05) for hospitalization, N=5,750 in both models; and by 47% from 0.05, (95% CI: 0.02, 0.08) to 0.03 (95% CI: 0.00, 0.05) for birth weight, N=4,701 in both models]. The proportion of participants 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 to the civil service was used as an outcome. (Online Annex *eTable1* and *eTable2*)

Participants from lower employment grades were more likely to have missing data for childhood variables than those from the highest employment grade (*eTable1* and *eTable2*). However, as can be seen from a comparison of Tables 2 and 3, 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 1.24, 95% CI: 1.09, 1.42), younger age (odds ratio per year 0.91, 95% CI: 0.90, 0.92) and higher employment grade (odds ratio 1.22, 95% CI 1.18, 1.27) were all associated with promotion. There was no firm evidence of an association between educational level at phase 1 and promotion (odds ratio for over 18 vs up to 16 years of education 1.17, 95% CI: 0.99, 1.38).

As expected, adverse cardiometabolic risk factor levels were related to higher levels of non-response and death (*eTable3*). As shown in Table 2, 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 2). The findings were similar after exclusion of participants who retired before the end of the follow-up (eTable4). Multilevel analyses of promotion over 5 year intervals appeared to show larger waist, lower diastolic blood pressure and lower LDL cholesterol to be associated with higher odds of promotion (eTable5). In the entire baseline cohort with missing data imputed, there were no associations between cardiometabolic factors and promotion over a 10-year interval (Table 3). For the association between BMI 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 are shown in the lower halves of Tables 2 and 3. Participants in higher employment grades had smaller increases in waist circumference, BMI, 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, *eTable6*). For BMI, 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 the online Annex (*eTable6* and *eTable7*). They indicate that the associations of employment grade with changes in BMI, 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 3) and in sub-cohorts composed of those with poor and good childhood health (*eTable 6* and *eTable7*). 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 (eTable8).

DISCUSSION

In this study of British civil servants, early health problems characterized by hospitalization during childhood and lower birth weight predicted lower socioeconomic status, assessed as civil service employment grade, in adulthood independent of parental socioeconomic status. However, after entering the civil service, we did not find strong evidence to suggest that a better cardiometabolic risk profile predicts promotion. In midlife lower socioeconomic status 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 the study provides evidence that health-related selection in childhood appears to influence socioeconomic status in adulthood, which in turn influences cardiometabolic profile in later life.

Strengths and weaknesses

Due to missing data, our analyses were based on between 4,542 and 8,312 men and women of the original population of 10,308. We found that lower SES, assessed using employment grade, was associated with higher non-response and death over the follow-up, 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 individuals with both poor childhood health and high employment grade compared to those with poor childhood health and low employment grade or for those with good health in childhood and low employment grade compared to those with good childhood health and high employment grade. Similarly, selective sample attrition of

those with high employment grade and adverse metabolic profiles or low employment grade and favorable profiles 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 multi-faceted concept and it could be argued that grade does not fully capture all 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 to examine the social causation hypothesis. However, education rather than income appears to be related 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 associated with education, probably provides a conservative test of the social causation hypothesis.

The validity of our measures of childhood health may be questioned as they were collected retrospectively, i.e., the participants were asked to recall their birth weight and hospitalizations of more than four weeks several decades after the events. However, previous studies suggest moderate to good accuracy for self-reported birth weight (39). The accuracy of self-reported birth weight has been shown to be high among those within the normal range for birth weight, as is the case for most of the participants in our study and a relatively high correlation (r=0.83-0.87) between self reported 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 compared with recorded birth weight (39).

Thirteen percent of the participants reported long-term hospitalization before the age of 16. 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 was lower, varying from 4% to 10% (41). The validity of self reported use of health care, including hospitalization, have shown to be reasonably good with only small SES differences when the recall time is relatively short (up till 1 year)(42). Bergman and colleagues (43) found recall accuracy over a ten year period to be greater than 80 percent for most conditions leading to hospitalization, although the validity of self reported hospitalization was somewhat dependent on the specific health problems. In a systematic review, Bhandari and Wagner (44) concluded that as inpatient hospitalization tends to be rare it is highly memorable. Furthermore, it should be noted that for the oldest of our cohort members the period before age 16 spanned the years 1930 to 1946 when hospital stays were longer and periods of convalescence common. During those years a much larger share of inpatients were under 15 than now and the age distribution of inpatients has been 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 as 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 out of the labor force or those repeatedly entering or 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 over-estimates of the associations in the general population, which includes people not in employment.

Comparison with previous studies

We are not aware of any other study that has 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 suggests that the association between childhood health and adult SES is not accounted for by educational qualifications, childhood SES, mother's education and care-giving 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 (eg smoking and drinking) and mental health problems (49, 50). It has also been shown that mental disorders are more frequent among socioeconomically disadvantaged individuals (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 BMI 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 not only height but in men heft is also 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, in particular 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 from lower SES to a less favourable

cardiometabolic risk profile, rather than good cardiometabolic health 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 socioeconomic groups.

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BOX. Cross-sectional Association of Whitehall II Employment Grade with Other Indicators of Socioeconomic Status, the Whitehall II Study, 1991-2004.

	Whitehall II employment grade						
	UG1-UG6 (high)	UG7	SEO	HEO	EO	Clerical/support (low)	Pearson r
UK Registrar General social class*, n (%)							
I (high)	899 (63)						r = 0.73,
II	529 (37)	1744 (100)	1169 (100)	1397 (99)	944 (81)	5 (0)	*P<0.0001*
IIIn				8 (1)	224 (19)	1095 (79)	
IIIm					1 (0)	236 (17)	
IV							
V (low)						61 (4)	
Years of education†, n (row%)							
>18	583 (75)	843 (64)	464 (42)	578 (39)	336 (28)	332 (18)	r = 0.43,
17-18	113 (15)	288 (22)	344 (31)	480 (33)	334 (28)	323 (18)	*P<0.0001*
≤16	78 (10)	180 (14)	307 (28)	413 (28)	516 (43)	1168(64)	
Income‡, n (row%)							
<£15,000		2 (0)	2 (0)	11 (2)	15 (4)	220 (50)	r = 0.90,
£15,000 - <£20,000	1 (0)	4 (1)	2 (0)	18 (3)	204 (51)	193 (43)	*P<0.0001*
£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)		

*From phase 3. †From phase 1. ‡From phase 5

Table 1. Sample Characteristics at Study Baseline and at Follow-up, the Whitehall II Study, 1991-2004.

	Baseline (phase 3)		Follow up (phase 7)	
	Mean (SD)	**N (%)**	**Mean (SD)**	**N (%)**
Age (years)	49.6 (6.1)	8312	61.2 (6.0)	6586
Sex (%)				
Men		5733 (69.0)		4627 (70.3)
Women		2579 (31.0)		1959 (29.7)
Ethnicity (%)				
White		7642 (91.1)		6068 (92.3)
Non-white		741 (9.0)		510 (7.8)
Employment grade (%)				
UG1-UG6 (high)		1428 (17.2)		1655 (25.5)
UG7		1744 (21.0)		1299 (20.0)
SEO		1169 (14.0)		986 (15.2)
HEO		1405 (16.9)		1010 (15.6)
EO		1169 (14.1)		823 (12.7)
Clerical/support (low)		1397 (16.8)		709 (10.9)
Promotion (%)				
No				5291 (81.6)
Yes				1194 (18.4)
Waist circumference (cm)	85.8 (11.6)	7822	93.6 (12.3)	6151
BMI (kg/m^2)	25.3 (3.7)	7901	26.7 (4.4)	6146
Systolic blood pressure (mmHg)	120.6 (13.6)	7905	128.2 (16.8)	6168
Diastolic blood pressure (mmHg)	79.7 (9.4)	7904	74.4 (10.5)	6167
HDL-cholesterol (mmol/l)	1.43 (0.41)	7840	1.58 (0.45)	6073
LDL-cholesterol (mmol/l)	4.39 (1.04)	7714	3.50 (1.63)	6004
Fasting glucose (mmol/l)	5.24 (0.69)	7559	5.47 (1.32)	6063
Fasting insulin (pmol/l)	6.97 (6.07)	7074	10.08 (12.24)	5479
CRP (mg/l)	1.93 (4.35)	7475	2.59 (5.09)	5895
IL-6 (pg/ml)	1.94 (2.29)	7421	2.34 (2.13)	5451
Metabolic syndrome (%)				
Yes		836 (10.8)		823 (13.6)
No		6935 (89.2)		5250 (86.4)
Status at phase 7 (%)				
Employed in civil service				2010 (24.2)
Left civil service				1048 (12.6)
Retired				3424 (41.2)
Non-respondent				1411 (17.0)
Died				314 (3.8)
Unknown				105 (1.3)

Table 2. Test of the Health-related Selection Hypothesis (Health Predicts Social Mobility) and the Social Causation Hypothesis (Socioeconomic Status Influences Health), the Whitehall II Study, 1991-2004.

Exposure	Outcome	N	Estimate*	p-Value
Health-related selection (from childhood to adulthood) hypothesis			**Regression coefficient (95% CI)**	
Hospitalization in childhood (1=yes, 0=no)	Employment grade (1=low,... 6=high)	6547	-0.23 (-0.34 to -0.13)	<0.0001
Birth weight, per lb	Employment grade (1=low,... 6=high)	5294	0.05 (0.02 to 0.08)	0.002
Health-related selection (adulthood) hypothesis			**Odds ratio (95% CI)**	
Waist circumference, per 1 SD increase	10-year promotion (1=yes, 0=no)	6153	1.04 (0.96 to 1.12)	0.32
BMI, per 1 SD increase	10-year promotion (1=yes, 0=no)	6219	1.03 (0.97 to 1.10)	0.38
Systolic blood pressure, per 1 SD increase	10-year promotion (1=yes, 0=no)	6229	1.01 (0.94 to 1.08)	0.75
Diastolic blood pressure, per 1 SD increase	10-year promotion (1=yes, 0=no)	6228	0.99 (0.93 to 1.06)	0.80
HDL-cholesterol, per 1 SD increase	10-year promotion (1=yes, 0=no)	6175	0.96 (0.90 to 1.04)	0.31
LDL-cholesterol, per 1 SD increase	10-year promotion (1=yes, 0=no)	6076	1.08 (1.00 to 1.15)	0.04
Fasting glucose, per 1 SD increase	10-year promotion (1=yes, 0=no)	5967	0.96 (0.89 to 1.05)	0.37
Fasting insulin, per 1 SD increase	10-year promotion (1=yes, 0=no)	5567	1.02 (0.95 to 1.10)	0.63
LogCRP, per 1 SD increase	10-year promotion (1=yes, 0=no)	5881	1.06 (0.99 to 1.14)	0.08
LogIL-6, per 1 SD increase	10-year promotion (1=yes, 0=no)	5839	0.98 (0.91 to 1.05)	0.52
Metabolic syndrome (1=yes, 0=no)	10-year promotion (1=yes, 0=no)	6127	1.18 (0.95 to 1.47)	0.13
Social causation (adulthood) hypothesis	10-year change in		**Regression coefficient (95% CI)**	
Employment grade (1=low,... 6=high)	waist circumference, mm	5868	-0.16 (-0.28 to -0.04)	0.008
Employment grade (1=low,... 6=high)	BMI, kg/m2	5925	-0.06 (-0.10 to -0.03)	0.0003
Employment grade (1=low,... 6=high)	systolic blood pressure, mm Hg	5953	0.02 (-0.23 to 0.28)	0.86
Employment grade (1=low,... 6=high)	diastolic blood pressure, mm Hg	5951	0.26 (0.09 to 0.43)	0.003
Employment grade (1=low,... 6=high)	HDL-cholesterol, mmol/L	5824	0.015 (0.010 to 0.020)	<0.0001
Employment grade (1=low,... 6=high)	LDL-cholesterol, mmol/L	5691	0.022 (0.006 to 0.039)	0.007
Employment grade (1=low,... 6=high)	fasting glucose, mmol/L	5632	-0.05 (-0.07 to -0.03)	<0.0001
Employment grade (1=low,... 6=high)	fasting insulin, pmol/L	4822	-0.43 (-0.61 to -0.24)	<0.0001
Employment grade (1=low,... 6=high)	logCRP, mg/L	5421	-0.00 (-0.02 to 0.02)	0.90
Employment grade (1=low,... 6=high)	logIL-6, pg/ml	4979	0.000 (-0.011 to 0.012)	0.93
			Odds ratio (95% CI)	
Employment grade (1=low,... 6=high)	Metabolic syndrome at follow-up (1=yes, 0=no)	5208	0.88 (0.83 to 0.94)	<0.0001

*All models are adjusted for age and sex. Test of the association between employment grade and metabolic syndrome at follow-up was based on a subgroup with no metabolic syndrome at baseline

Table 3. Test of Health-related Selection and Social Causation Hypotheses After Multiple Multivariate Imputation for Missing Values*, the Whitehall II Study, 1991-2004.

Exposure	Outcome	Estimate†	p-Value
Health-related selection (from childhood to adulthood) hypothesis		**Regression coefficient (95% CI)**	
Hospitalization in childhood (1=yes, 0=no)	Employment grade (1=low,... 6=high)	-0.24 (-0.35 to -0.13)	<0.0001
Birth weight, per lb	Employment grade (1=low,... 6=high)	0.05 (0.03 to 0.07)	0.008
Health-related selection (adulthood) hypothesis		**Odds ratio (95% CI)**	
Waist circumference, per 1 SD increase	10-year promotion (1=yes, 0=no)	1.02 (0.95 to 1.11)	0.59
BMI, per 1 SD increase	10-year promotion (1=yes, 0=no)	1.03 (0.96 to 1.11)	0.43
Systolic blood pressure, per 1 SD increase	10-year promotion (1=yes, 0=no)	0.99 (0.92 to 1.06)	0.79
Diastolic blood pressure, per 1 SD increase	10-year promotion (1=yes, 0=no)	0.97 (0.91 to 1.04)	0.43
HDL-cholesterol, per 1 SD increase	10-year promotion (1=yes, 0=no)	0.98 (0.90 to 1.07)	0.59
LDL-cholesterol, per 1 SD increase	10-year promotion (1=yes, 0=no)	1.05 (0.99 to 1.13)	0.12
Fasting glucose, per 1 SD increase	10-year promotion (1=yes, 0=no)	0.99 (0.91 to 1.06)	0.78
Fasting insulin, per 1 SD increase	10-year promotion (1=yes, 0=no)	1.00 (0.92 to 1.07)	0.94
LogCRP, per 1 SD increase	10-year promotion (1=yes, 0=no)	1.04 (0.97 to 1.13)	0.21
LogIL-6, per 1 SD increase	10-year promotion (1=yes, 0=no)	0.96 (0.90 to 1.03)	0.22
Metabolic syndrome (1=yes, 0=no)	10-year promotion (1=yes, 0=no)	1.13 (0.94 to 1.31)	0.16
Social causation (adulthood) hypothesis	10-year change in	**Regression coefficient (95% CI)**	
Employment grade (1=low,... 6=high)	waist circumference, mm	-0.13 (-0.23 to -0.03)	0.009
Employment grade (1=low,... 6=high)	BMI, kg/m2	-0.06 (-0.08 to -0.03)	0.0002
Employment grade (1=low,... 6=high)	systolic blood pressure, mm Hg	-0.10 (-0.31 to 0.12)	0.38
Employment grade (1=low,... 6=high)	diastolic blood pressure, mm Hg	0.13 (-0.01 to 0.28)	0.07
Employment grade (1=low,... 6=high)	HDL-cholesterol, mmol/L	0.013 (0.009 to 0.017)	<0.0001
Employment grade (1=low,... 6=high)	LDL-cholesterol, mmol/L	0.020 (-0.001 to 0.042)	0.06
Employment grade (1=low,... 6=high)	fasting glucose, mmol/L	-0.06 (-0.07 to -0.04)	<0.0001
Employment grade (1=low,... 6=high)	fasting insulin, pmol/L	-0.40 (-0.55 to -0.24)	<0.0001
Employment grade (1=low,... 6=high)	logCRP, mg/L	0.00 (-0.01 to 0.02)	0.56
Employment grade (1=low,... 6=high)	logIL-6, pg/ml	0.004 (-0.004 to 0.013)	0.37
		Odds ratio (95% CI)	
Employment grade (1=low,... 6=high)	Metabolic syndrome at follow-up (1=yes, 0=no)	0.90 (0.85 to 0.94)	<0.0001

*N=8312 in each of the 10 imputed copies of the dataset.

†All models are adjusted for age and sex. The association of employment grade and metabolic syndrome at baseline is additionally adjusted for metabolic syndrome at baseline.

ONLINE APPENDIX: SUPPLEMENTAL MATERIAL

Elovainio et al. Socioeconomic Differences in Cardiometabolic Factors—Social Causation or Health-related Selection? Evidence from the Prospective Whitehall II Cohort Study, 1991-2004. *Am J Epidemiol* 2010.

eTable1. Selection hypothesis (from childhood to adulthood): Age- and sex-adjusted association of indicators of childhood health with adult baseline employment grade, the Whitehall II study, 1991-2004

Childhood predictor	N	Employment grade at baseline						Regression coefficient (95% CI)‡
		UG1-UG6	UG7	SEO	HEO	EO	Clerical/ support	
		Odds ratio (95% CI)						
Hospitalization (≥4 wks) during childhood	Yes=861 No=5686	1.00 (ref)	1.09 (0.86 to 1.39)	1.33 (1.02 to 1.72)	1.36 (1.06 to 1.74)	1.45 (1.11 to 1.89)	1.65 (1.25 to 2.17)	-0.23 (-0.34 to -0.13)
P-value								<0.0001#
Childhood data missing	Yes=3018 N0=5294	1.00 (ref)	1.04 (0.89 to 1.21)	1.11 (0.93 to 1.31)	1.24 (1.05 to 1.45)	1.65 (1.39 to 1.96)	2.14 (1.80 to 2.55)	-0.35 (-0.42 to -0.28)
P-value								<0.0001#
		Difference (95% CI)						
Birth weight (mean difference, lbs)†	5294	0.00 (ref)	-0.07 (-0.13 to -0.00)	-0.04 (-0.11 to 0.04)	-0.08 (-0.15 to -0.01)	-0.06 (-0.14 to 0.01)	-0.14 (-0.22 to -0.06)	0.05 (0.02 to 0.08)
P-value								0.002#

†Average birth weight is 7.65 lbs (95% CI 7.57 to 7.73) in high grade (UG1-UG6) employees (N=939).

‡Linear regression with employment grade as a continuous outcome (1=low,...6=high).

#Statistically significant after Bonferroni correction for multiple testing.

eTable2. Selection hypothesis (childhood to adulthood): Age at entry to the Civil Service and sex-adjusted association of indicators of childhood health with first employment grade

Childhood predictor	N	Employment grade						Regression coefficient (95% CI)‡
		UG1-UG6	UG7	SEO	HEO	EO	Clerical/ support	
		Odds ratio (95% CI)						
Hospitalization (≥4 wks) during childhood	Yes=875 No=5804	1.00 (ref)	1.21 (0.57 to 2.57)	0.91 (0.44 to 1.88)	1.14 (0.55 to 2.38)	1.10 (0.54 to 2.23)	1.48 (0.74 to 2.98)	-0.13 (-0.21 to -0.05) p<0.0008#
P-value								
Childhood data missing	Yes=4650 N0=5365	1.00 (ref)	0.87 (0.55 to 1.36)	1.10 (0.72 to 1.67)	1.29 (0.84 to 1.99)	1.20 (0.79 to 1.81)	1.88 (1.25 to 2.83)	-0.22 (0.18 to 0.27) p<0.0001#
P-value								
		Difference (95% CI)						
Birth weight (mean difference, lbs)†	5365	0.00 (ref)	-0.04 (-0.26 to 0.18)	-0.05 (-0.25 to 0.18)	-0.06 (-0.27 to 0.15)	-0.03 (-0.23 to 0.18)	-0.10 (-0.30 to 0.10)	0.02 (0.002 to 0.04) p=0.03
P-value								

†Average birth weight is 7.69 lbs (95% CI 7.29 to 8.10) in high grade (UG1-UG6) employees (N=939).

‡Linear regression with employment grade as a continuous outcome (1=low,...6=high).

#Statistically significant after Bonferroni correction for multiple testing.

eTable3. Selection hypothesis (adulthood): Age- and sex-adjusted association of adult cardiometabolic factors at baseline with subsequent promotion and non-response or death over the 10-year follow-up, the Whitehall II study, 1991-2004.

Baseline risk factor (per 1 SD increase or per category)	No. of stable/promoted/non-responders*	Odds ratio (95% confidence interval) for		
		promotion during 10-year follow up*	P-value†	non-response/death*
Waist circumference	5015/1138/1669	1.04 (0.96 to 1.12)	0.32	1.10 (1.04 to 1.17)
BMI	5075/1144/1682	1.03 (0.97 to 1.10)	0.38	1.08 (1.02 to 1.14)
Systolic blood pressure	5078/1151/1676	1.01 (0.94 to 1.08)	0.75	1.12 (1.06 to 1.19)
Diastolic blood pressure	5077/1151/1676	0.99 (0.93 to 1.06)	0.80	1.11 (1.05 to 1.18)
HDL-cholesterol	5039/1136/1665	0.96 (0.90 to 1.04)	0.31	0.90 (0.85 to 0.96)
LDL-cholesterol	4960/1116/1638	1.08 (1.00 to 1.15)	0.04	1.11 (1.05 to 1.18)
Fasting glucose	4858/1109/1592	0.96 (0.89 to 1.05)	0.37	1.10 (1.04 to 1.16)
Fasting insulin	4542/1025/1507	1.02 (0.95 to 1.10)	0.63	1.11 (1.05 to 1.17)
LogCRP	4817/1064/1594	1.06 (0.99 to 1.14)	0.08	1.12 (1.06 to 1.19)
LogIL-6	4784/1055/1582	0.98 (0.91 to 1.05)	0.52	1.18 (1.11 to 1.25)
Metabolic syndrome (yes vs no)	4997/1130/1644	1.18 (0.95 to 1.47)	0.13	1.26 (1.06 to 1.50)

*Comparison with stable or demoted (combined) employment grade. For each risk factor, the total number of participants across the categories stable/promoted/non-response equals the number of participants at phase 3 screening (see table 1). Based on last known employment grade at the end at the 10 year follow up (including retired participants at phase 7).

†None of the p-values were statistically significant after Bonferroni correction for multiple testing.

eTable4. Selection hypothesis (adulthood): Age- and sex-adjusted association of adult cardiometabolic factors with subsequent promotion and drop out due to missing data, retirement or non-working at follow-up.

Risk factor (per 1 SD increase)	No. of stable/promoted/missing*	Odds ratio (95% confidence interval)	
		Promotion during follow up*	Missing*
Waist circumference	1312/624/5886	0.99 (0.89 to 1.10)	1.04 (0.96 to 1.12)
BMI	1326/626/5949	1.00 (0.91 to 1.10)	1.01 (0.95 to 1.08)
Systolic blood pressure	1327/628/5950	0.92 (0.83 to 1.03)	1.03 (0.96 to 1.11)
Diastolic blood pressure	1327/628/5950	0.96 (0.87 to 1.07)	1.11 (1.04 to 1.19)
HDL-cholesterol	1317/622/5901	0.98 (0.88 to 1.09)	1.01 (0.94 to 1.09)
LDL-cholesterol	1293/610/5810	1.12 (1.01 to 1.24)	1.07 (1.00 to 1.15)
Fasting glucose	1276/606/5677	0.93 (0.81 to 1.05)	1.04 (0.96 to 1.12)
Fasting insulin	1188/559/5327	1.06 (0.94 to 1.18)	1.08 (0.99 to 1.17)
LogCRP	1257/583/5635	1.12 (1.01 to 1.23)	1.06 (0.99 to 1.14)
LogIL-6	1248/577/5596	0.99 (0.90 to 1.10)	1.09 (1.02 to 1.17)
Metabolic syndrome (yes vs no)	1308/618/5845	1.12 (0.80 to 1.58)	1.08 (0.85 to 1.36)

*Comparison with stable or demoted (combined) employment grade. Missing refers to missing data at follow-up or not working due to retirement or other reasons at follow-up. For each risk factor, total number in categories of stable/promoted/missing equals to the number of participants in Phase 3 screening (in Table 1). None of the association with promotion were statistically significant after corrections for multiple testing.

Statistical analysis for 5-year change in employment grade and change in cardiometabolic factors

For the analyses of the prospective data, which are structured such that 5-yearly measurements (observations) are nested within individuals, we used multilevel linear and logistic regression analysis to model the association of cardiometabolic factors with subsequent change in employment grade across phases, that is cardiometabolic factors at phase 3 predicting promotion between phases 3 and 5 and those at phase 5 predicting promotion between phases 5 and 7 (eTable7). The levels of cardiometabolic factors were allowed to change within subjects over time, i.e., these variables were modelled as time variant, and the analysis used all available measurements from every subject at all phases. Repeated measurements within individuals constitute a cluster and the calculation of standard errors takes into account the non-independence of the measurements; that is, the same individual contributes more than one observation in the dataset and these observations are of course related. We used a similar approach to examine the association of employment grade with subsequent change in cardiometabolic factors (ie grade at phase 3 predicting change in cardiometabolic factors between phases 3 and 5, and grade at phase 5 predicting changes in these factors between phases 5 and 7 (eTable8). We used Stata 11.0 statistical software for Windows, procedures 'xtmixed' and 'xtlogit' for these analyses.

eTable5. Health-related selection hypothesis (adulthood): Age- and sex-adjusted association of adult cardiometabolic factors at baseline with promotion over 5 years. Random-intercept multilevel analysis across 3 study phases, the Whitehall II study, 1991-2004

Baseline factor (per 1 SD increase or per category)	No. of participants/ no. of observations	Odds ratio (95% confidence interval) for promotion over 5 years*	P-value
Waist circumference	5757/7429	1.11 (1.04 to 1.19)	0.003†
BMI	5829/7682	1.06 (0.99 to 1.12)	0.07
Systolic blood pressure	5852/8000	0.92 (0.87 to 0.98)	0.01
Diastolic blood pressure	5851/7999	0.87 (0.82 to 0.93)	<0.0001†
HDL-cholesterol	5787/7620	1.07 (1.00 to 1.15)	0.06
LDL-cholesterol	5707/7496	0.86 (0.81 to 0.92)	<0.0001†
Fasting glucose	5671/7718	0.98 (0.93 to 1.04)	0.54
Fasting insulin	5436/7350	1.04 (1.01 to 1.08)	0.03
Metabolic syndrome (yes vs no)	5768/7758	0.86 (0.69 to 1.07)	0.17

*Comparison with stable or demoted (combined). The highest grade at baseline is excluded to reduce ceiling effect.
†Statistically significant after Bonferroni correction for multiple testing.

eTable6. Causation hypothesis (adulthood): Age- and sex-adjusted association of baseline employment grade with medication use, new-onset metabolic syndrome and missingness at follow-up, the Whitehall II study, 1991-2004.

Employment grade at baseline	**Outcome at follow-up**			
	Use of lipid lowering drugs†	Use of antihypertensive drugs†	New onset metabolic syndrome (yes *v* no)‡	Non-response/death at follow-up (yes *v* no)
Total cohort	(N=7316)	N=7316	N=5208	N= 8312
1 (High)	1.00 (ref)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
2	0.86 (0.57 to 1.29)	1.06 (0.84 to 1.34)	1.36 (0.98 to 1.90)	1.18 (1.02 to 1.36)
3	0.61 (0.36 to 1.02)	1.10 (0.85 to 1.43)	1.53 (1.07 to 2.18)	1.16 (0.98 to 1.36)
4	1.21 (0.80 to 1.82)	1.58 (1.25 to 2.00)	1.56 (1.10 to 2.21	1.41 (1.21 to 1.65)
5	1.26 (0.81 to 1.96)	1.57 (1.22 to 2.02)	1.84 (1.28 to 2.65)	1.60 (1.35 to 1.88)
6 (Low)	1.50 (0.95 to 2.35)	1.88 (1.46 to 2.43)	2.08 (1.43 to 3.03)	2.28 (1.93 to 2.70)
P-value for trend	*0.02*	*<0.0001**	*<0.0001**	*<0.0001**
Subcohort with poor childhood health#	N=1188	N=1188	N=821	N=1232
1 (High)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00
2	1.11 (0.28 to 4.23)	2.23 (1.17 to 4.24)	0.98 (0.40 to 2.42)	1.04 (0.69 to 1.57)
3	1.26 (0.31 to 5.16)	1.96 (0.98 to 3.91)	0.89 (0.32 to 2.34)	0.99 (0.63 to 1.55)
4	2.79 (0.82 to 9.46)	2.93 (1.53 to 5.61)	1.53 (0.63 to 3.70)	1.07 (0.70 to 1.65)
5	3.25 (0.93 to 11.42)	1.92 (0.95 to 3.89)	1.37 (0.53 to 3.49)	1.21 (0.77 to 1.90)
6 (Low)	4.21 (1.23 to 14.38)	2.15 (1.09 to 4.26)	1.19 (0.45 to 3.14)	1.50 (0.97 to 2.33)
p-value for trend	*0.002**	*0.11*	*0.40*	*0.05*
Subcohort with good childhood health	N=5739	N=5739	N=4150	N=6152
1 (High)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
2	0.85 (0.54 to 1.33)	0.92 (0.71 to 1.20)	1.42 (0.99 to 2.06)	1.19 (1.01 to 1.41)
3	0.63 (0.35 to 1.11)	1.03 (0.76 to 1.38)	1.66 (1.13 to 2.46)	1.10 (0.91 to 1.33)
4	1.13 (0.71 to 1.80)	1.43 (1.09 to 1.87)	1.48 (1.00 to 2.18)	1.38 (1.16 to 1.65)
5	1.24 (0.76 to 2.04)	1.59 (1.20 to 2.10)	1.79 (1.19 to 2.70)	1.45 (1.21 to 1.78)
6 (Low)	1.25 (0.73 to 2.14)	1.96 (1.46 to 2.62)	2.27 (1.49 to 3.47)	1.95 (1.60 to 2.38)
p-value for trend	*0.17*	*<0.0001**	*0.0003**	*<0.0001**

*Statistically significant after Bonferroni correction for multiple testing. †Self-reported at phase 7. ‡Among those free of metabolic syndrome at baseline. #Low birthweight (<2.5kg) and/or hospitalization in childhood.

eTable7. Causation hypothesis (adulthood): Age- and sex-adjusted association of baseline employment grade with subsequent change in cardiometabolic factors over the 10-year follow up, the Whitehall II study, 1991-2004.

Employment grade at baseline	Outcome (10-year change)									
	Waist circumference (cm)	BMI (kg/m^2)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	HDL-cholesterol (mmol/l)	LDL-cholesterol (mmol/l)	Fasting glucose (mmol/l)	Fasting insulin (pmol/l)	LogCRP (mg/l)	LogIL-6 (pg/ml)
Total cohort	N=5868	N=5925	N=5953	N=5951	N=5824	N=5691	N=5632	N=4822	N=5421	N=4979
1 (High)	8.24	1.38	8.2	-4.0	0.18	-0.75	0.08	2.31	0.44	0.19
2	8.30	1.42	9.0	-3,9	0.15	-0.74	0.10	2.83	0.41	0.21
3	8.68	1.53	8.7	-4.0	0.15	-0.76	0.19	2.89	0.41	0.17
4	8.50	1.46	8.2	-4.7	0.16	-0.78	0.23	2.97	0.43	0.20
5	8.98	1.65	8.4	-5.3	0.11	-0.83	0.25	3.68	0.42	0.17
6 (Low)	9.04	1.73	8.5	-4.9	0.09	-0.86	0.35	5.11	0.45	0.21
P-value for trend	*0.008*	*0.0003**	*0.86*	*0.003**	*<0.0001**	*0.007*	*<0.0001**	*<0.0001**	*0.90*	*0.93*
Subcohort with poor childhood health †	N=945	N=948	N=955	N=954	N=937	N=907	N=910	N=780	N=869	N=805
1 (High)	9.41	1.62	9.0	-3.4	0.20	-0.79	0.09	2.23	0.33	0.24
2	8.54	1.53	9.1	-4.4	0.18	-0.74	0.08	2.50	0.40	0.21
3	8.95	1.57	7.2	-4.2	0.17	-0.71	0.17	2.35	0.45	0.12
4	8.94	1.51	8.4	-5.1	0.19	-0.90	0.27	2.42	0.30	0.17
5	9.01	1.70	8.4	-4.9	0.17	-0.92	0.14	2.34	0.49	0.19
6 (Low)	8.73	1.50	6.7	-4.3	0.08	-0.97	0.43	4.65	0.50	0.23
p-value for trend	*0.78*	*0.94*	*0.27*	*0.35*	*0.005*	*0.03*	*0.01*	*0.02*	*0.30*	*0.72*
Subcohort with good childhood health	N=4647	N=4698	N=4718	N=4717	N=4618	N=4522	N=4466	N=3824	N=4300	N=3956
1 (High)	8.13	1.35	8.2	-4.1	0.18	-0.73	0.09	2.47	0.47	0.18
2	8.27	1.39	8.8	-3.9	0.15	-0.74	0.10	2.92	0.43	0.21
3	8.61	1.51	9.1	-4.0	0.15	-0.77	0.20	3.01	0.40	0.17
4	8.45	1.46	8.3	-4.5	0.15	-0.75	0.19	2.75	0.46	0.20
5	9.05	1.62	8.3	-5.5	0.10	-0,80	0.25	3.15	0.43	0.17
6 (Low)	9.17	1.82	8.6	-5.0	0.09	-0.83	0.32	5.55	0.45	0.22
p-value for trend	*0.003**	*<0.0001**	*0.95*	*0.008*	*<0.0001**	*0.06*	*<0.0001**	*0.0003**	*0.81*	*0.85*

*Statistically significant after Bonferroni correction for multiple testing. † Among those free of metabolic syndrome at baseline. #Low birthweight (<2.5kg) and/or hospitalization in childhood.

eTable8. Causation hypothesis (adulthood): Age- and sex-adjusted association of baseline employment grade with change in cardiometabolic factors over 5 years. Random-intercept multilevel analysis across 3 study phases, the Whitehall II study, 1991-2004.

	Outcome* (5-year change)								
Employment grade at baseline	**Waist circumference (cm)**	**BMI (kg/m^2)**	**Systolic blood pressure (mmHg)**	**Diastolic blood pressure (mmHg)**	**HDL-cholesterol (mmol/l)**	**LDL-cholesterol (mmol/l)**	**Fasting glucose (mmol/l)**	**Fasting insulin (pmol/l)**	**New onset metabolic syndrome (yes/no)†**
Total cohort: Number of observations /participants	6768/4716	7700/5420	8859/6229	8858/6228	7698/5455	7512/5344	8530/6025	7962/5747	7457/5325
1 (High)	0.00 (ref)	0.00 (ref)	0.00 (ref)	0.00 (ref)	0.00 (ref)	0.00 (ref)	0.00 (ref)	0.00 (ref)	1.00 (ref)
2	-0.04	0.06	0.66	0.36	-0.00	0.04	0.01	0.66	0.90
3	0.01	0.06	0.12	0.23	-0.01	0.04	0.04	0.41	1.41
4	-0.03	0.02	-0.12	-0.34	-0.02	0.02	0.08	0.39	1.23
5	0.07	0.07	0.06	-0.47	-0.02	-0.04	0.10	0.35	1.13
6 (Low)	-0.06	0.07	-0.37	-0.37	-0.03	-0.05	0.17	1.74	2.61
P-value for trend	*0.99*	*0.40*	*0.23*	*0.03*	*0.001‡*	*0.04*	*<0.0001‡*	*0.012*	*<0.0001‡*

*Mean difference (95% confidence interval) compared to the highest employment grade (odds ratio for new-onset metabolic syndrome).
†Among those free of metabolic syndrome at baseline.
‡Statistically significant after Bonferroni correction for multiple testing.