Do early life exposures explain associations in mid-adulthood between workplace factors and risk factors for cardiovascular disease?

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Accepted 10 November 2009

Background Workplace factors (night work, long working hours, psychosocial work stress) have been reported to be associated with increased risk of cardiovascular disease (CVD). We investigated whether (i) workplace factors are associated with CVD risk factors independently of each other, (ii) workplace factors interact, thereby modifying associations and (iii) associations are explained by early life exposures.

Methods A total of 7916 employed participants in the 1958 British birth cohort underwent a clinical assessment at age 45 years. Regression analysis was used to examine associations between workplace factors and CVD risk factor levels with adjustment for early life exposures.

Results Night work was associated with adverse levels of most CVD risk factors. Working ≥48 h/week was positively associated with body mass index (BMI) and waist circumference (WC). Low job control was positively associated with glycosylated haemoglobin (HbA1c) and inflammatory factors, and inversely associated with high-density lipoprotein (HDL)-cholesterol. Low demands were positively associated with systolic blood pressure (SBP), triglycerides and inflammatory factors and inversely associated with HDL-cholesterol. Several associations were weakened when workplace factors were adjusted for each other. Night workers in low-demand jobs had higher BMI [0.78 kg/m²; 95% confidence interval (CI) 0.35, 1.21], WC (1.49 cm; 0.45, 2.52) and SBP (1.38 mmHg; –0.04, 2.81). HDL was lower for low control plus night work (−0.04 mmol/l; −0.08, −0.01) or long hours (−0.12; −0.18, −0.69). Adjustment for early life exposures explained 30–50% of most associations, e.g. night work/low demands associations reduced by 50% for BMI and WC, and by 39% for SBP.

Conclusions Associations between workplace factors and CVD risk factors in mid-adulthood arise in part from social and health disadvantage originating earlier in life.

Keywords Cardiovascular disease, cohort studies, employment
**Introduction**

Work is a determinant of socio-economic inequalities in health, recognized by policy makers as an important point for intervention to improve health.1 The nature of work has changed over the past two decades, moving towards a 24-hour society with increasing demand for goods and services to be provided around the clock.2 Consequently, workplace exposures, such as psycho-social stress, shift-work and long working hours, have been reported to be associated with increased risk of cardiovascular disease (CVD). Night workers are estimated to have a 40% increased risk for coronary heart disease (CHD) and associations have been reported for a range of CVD risk factors.3–9 Associations with CVD have also been reported for longer hours of work,10 although most focus has been on the psychosocial aspects of work.11,12

There are several ways in which adverse workplace factors could increase the risk of CVD: direct metabolic consequences of circadian disruption for night workers, neuroendocrine effects of work stress and changes in health behaviours due to unfavourable or stressful work patterns.13,14 One study estimated that health behaviours accounted for 32% of the association between work stress and CHD.15 Others have argued that the observed health effects of work stress could be due to socio-economic confounding.16,17 Since individuals who experience an unfavourable social environment in early life are at greater risk of CVD independent of their circumstances in adulthood,18 associations for workplace factors could be due to circumstances earlier in life. Furthermore, developmental factors related to CVD risk are associated with poorer educational and occupational outcomes in adulthood.19–23 A recent examination of work stress and CHD found that father’s socio-economic position (SEP), household crowding, short stature and education explained 65% of the association.24

The aim of this study is to determine whether relationships between workplace factors and risk factors for CVD in mid-adulthood are explained by early life exposures. Because workplace factors are correlated,25 it is important to disentangle the effects of long work hours, work stress and the timing of hours worked. For instance, associations between long work hours and morbidity were not found when experienced in combination with high control over work hours.25 Therefore, this article addresses the following questions. (i) Are workplace factors associated, independently of each other, with CVD risk factors in mid-adult life? (ii) Do workplace factors interact so that combinations of factors carry additional risk for CVD? (iii) Are associations between workplace factors and CVD risk factors explained by early life exposures?

**Methods**

**Sample**

The 1958 British birth cohort consists of 18 558 individuals: 17 638 participants born in March 1958 in England, Scotland and Wales, and 920 immigrants (≤16 years) with the same birth dates enrolled in the Perinatal Mortality Survey. The cohort has been interviewed in childhood (ages 7, 11 and 16 years) and adulthood (23, 33, 42 and 45 years).26 At age 45 years, 11 971 cohort members who had not died or emigrated and were still in contact with the survey were invited to a clinical examination at their homes by a trained nurse; 9377 (78%) participants were seen between September 2002 and March 2004. Ethical approval for the clinical examination was given by the South East Multi-Centre Research Ethics Committee. Analyses presented here are based on 7916 cohort members who were in paid employment at age 45 years.

**Risk factors for CVD**

Physical assessments at age 45 years, which included collection of non-fasted blood samples, were conducted by nurses using standardized protocols. Conventional (blood pressure, adiposity, blood lipids, blood glucose) and novel (inflammatory factors) markers of CVD risk were obtained. Blood pressure (BP) was measured three times using an Omron 705CP automated sphygmomanometer (Omron, Tokyo, Japan). Mean systolic BP (SBP) and diastolic BP (DBP) were calculated from an average of the measurements. Standing height was measured using a Leicester portable stadiometer and weight was measured to the nearest 0.1 kg using Tanita solar scales with participants lightly clothed and shoes removed. Body mass index (BMI) was calculated as kg/m². Waist circumference (WC) was measured mid-way between the costal margin and iliac crest. Blood glucose levels were measured by glycosylated haemoglobin (HbA1c) using ion-exchange high-performance liquid chromatography ( Tosoh A1c2.2 Glycohemoglobin Analyser, HLC-723GHB, Tosoh Corp., Tokyo, Japan). Triglycerides, total and high-density (HDL) cholesterol were measured by autoanalyzer. Fibrinogen was measured by the Claus assay in an MDA-180 automated coagulometer (Biomerieux, Basingstoke) and values ≥5.62 g/l (n = 9) were excluded.27 C-reactive protein (CRP) was measured on citrated plasma by high-sensitivity nephelometric analysis of latex particles coated with CRP monoclonal antibodies; values >10 mg/l (n = 154) were excluded.28

**Workplace factors**

Participants at age 45 years reported the total hours worked/week in their main job. Hours/week was categorized to identify part time (<35 h/week), full time...
Early life factors

Early life predictors of CVD (up to the minimum school leaving age of 16 years), were identified a priori from the literature, consisting of perinatal factors, socio-economic, environmental and parental factors. Physical growth and development, cognitive ability, adverse health behaviours and behavioural problems were also combined. At age 16 years, participants reported the number of cigarettes they smoked in the past week, and when they had last consumed alcohol.

Perinatal factors

Gestational age, birth weight, maternal age, smoking during pregnancy (number of cigarettes/day), maternal height and pre-pregnancy weight were recorded at birth. Birth weight was standardized for gestational age and sex. Pre-pregnancy BMI was calculated as described above. Pre-eclampsia was defined as albuminuria not attributable to urinary tract infection and DBP $>90$ mmHg. Duration of breastfeeding was reported when the child was 7 years old.

Socio-economic factors

Childhood SEP was based on the father’s occupation at birth (or at age 7 years if missing), using the Registrar General’s Social Classification (RGSC), categorized I or II, IIINM, IIIM, IV and V (including single mother households). Other indicators collected at birth, at age 7, 11 and 16 years were (i) number of persons/room and (ii) housing tenure (not collected at birth).

Parental factors

Education (age last attended school); divorce/separation by the time the child was 16 years of age; BMI (calculated from height/weight data collected when child was 11 years of age); smoking (number cigarettes/day when child was 16 years of age); physical neglect of child (dirty, scruffy, underfed appearance at 7 and 11 years of age); support of child (level of interest shown in education at 7, 11 and 16 years of age).

Physical factors

Height and weight were measured at age 7, 11 and 16 years; BMI was calculated as described above. Maturation was assessed as age at onset of menstruation for females and stage of axillary hair at age 16 years for males.

Cognitive ability

Cognitive ability was measured using age-appropriate math and reading tests at school at age 7, 11 and 16 years.

Behavioural maladjustment

Behavioural maladjustment was measured using the Bristol Social Adjustment Guide at age 7 and 11 years; the Rutter Scale at age 16 years, categorized as well adjusted, intermediate or poor.

Health behaviours

Frequency of television (TV) viewing and physical activity, collected at age 11 and 16 years, is described in detail elsewhere. In brief, cohort members reported how often they watched TV. Physical activity at age 11 years was assessed through five questions on the child’s use of parks, recreation grounds, indoor play centres and swimming pools and participation in sport, which were combined to give four categories (least to most active). At age 16 years, participants were asked how often they played indoor and outdoor games or sports, went dancing and swimming, which were also combined. At age 16 years, cohort members reported the number of cigarettes they smoked in the past week, and when they had last consumed alcohol (ranging from never to <1 week ago in seven categories).

Data analysis

Multiple linear regression was used to examine the associations between workplace factors and CVD risk factors. Triglycerides, CRP and HbA1c were log transformed as the distributions were positively skewed; geometric means and standard deviations are presented plus robust estimators were used for regression analyses of HbA1c. Regression coefficients from log transformed variables were multiplied by 100 and interpreted as percentage difference in mean levels.

The modelling strategy consisted of four steps: (i) examination of simple associations between workplace factors and CVD risk factors individually with assessment of gender interactions using the likelihood ratio (LR) test; (ii) estimation of the independent effects of workplace factors, i.e. adjusted for each other, on each CVD risk factor; (iii) testing of interactions between the workplace factors using the LR test; where interactions were found, stratum-specific estimates were calculated; and (iv) adjustment of associations between workplace factors and CVD risk factors for early life exposures.
As multiple early life indicators are available in the 1958 cohort, e.g. socio-economic and physical health measures collected at different ages, a subset from within each group of variables (perinatal, socio-economic, physical, cognitive, parental, maladjustment, health behaviours) was selected for inclusion in the models. Specific variables were selected from each group on an empirical basis using the change-in-estimate (CE) criterion. Variables were removed sequentially in a step-wise fashion where the association between exposure and CVD risk factor changed by $\geq 5\%$ with the removal of the early life variable from the model.\textsuperscript{62,63} To illustrate, for BMI at age 45 years, 12 variables (smoking in pregnancy, childhood social class, BMI at age 16 years, math and reading scores at age 11 years, problem behaviour at age 11 and 16 years, mother/father BMI, age mother/father last attended school, TV viewing at age 11 years) were identified using this criterion. Models were adjusted for each subset (i.e. perinatal, physical, etc.) separately and together.

Multicollinearity was checked using the variance inflation factor. Where there were non-linear relationships for continuous covariates, quadratic terms were included in the models.

We checked whether factors associated with CVD risk factor measurement influenced the results, i.e. medication for diabetes, hypertension or high cholesterol, and influence of time of day, delay in the receipt of blood samples, month of nurse visit, recent food consumption, type of flooring, air temperature. Final models included adjustments for time of day (BP, triglycerides), and diabetes medication (HbA1c).

### Missing data

Sources of missing data were (i) attrition of the sample up to age 45 years and (ii) item non-response from missing data on CVD risk factors, work and early life exposures. Of 7916 participants in paid employment at age 45 years, data on CVD risk factors ranged from 99.8\% (BMI) to 82.8\% (fibrinogen) (Table 1). Complete data on workplace characteristics and CVD risk factors ranged from 82\% (BMI) to 68\% (fibrinogen). Inverse probability weighting was used to weight for non-response at age 45 years on the surviving cohort ($n=17313$). Weights were derived for 14352 cohort members using key predictors of attrition identified in childhood (Registrar General’s Social Class, cognition and behavioural difficulties) as described previously.\textsuperscript{64} Missing data on early life exposures gave rise to the largest source of item non-response. For example, 42\% had data on all 12 covariates in models for BMI; missing data on any one ranged from 3.6\% (maternal smoking) to 27\% (BMI at age 16 years) (Table S1, Supplementary data are available at IJE online). Compared with the complete sample for models of BMI ($n=2398$), the sample with incomplete data ($n=3300$) had slightly higher HbA1c levels and a less favourable profile on covariate variables (e.g. higher prevalence of maternal smoking) but did not differ with respect to other CVD risk factors (Table S1, Supplementary data are available at IJE online). We therefore used multiple imputation by chained equations (MICE) in STATA version 10.1 to impute missing covariate data according to current guidelines.\textsuperscript{65} Non-normally distributed variables were log transformed for imputation. A total of 10 imputed datasets were created using 20 cycles per imputation. Imputation models included all variables in the substantive models plus variables predictive of covariate values such as measures of BMI and cognitive ability measured at other time points. The distributions of variables were similar for observed and imputed values, with slightly higher prevalence of factors related to missing data for imputed values (Table S2, Supplementary data are available at IJE online).

### Results

Table 1 describes the distribution of workplace exposures and CVD risk factors. About 20\% participants worked $>$48 h/week and 30\% worked at night. Approximately 40\% reported either low job control or low demands.

There was overlap between workplace factors (Table 2): for example, night work and $>$48 h/week were positively correlated ($r=0.36$), that is 37\% of night workers worked $>$48 h/week and 48\% of those working $>$48 h/week also worked at night.

Mean levels in most CVD risk factors varied for at least one workplace factor, except for DBP and total cholesterol, which were not investigated further (Table 3). Despite gender differences in exposure to workplace factors and levels of CVD risk factors, there was no evidence that associations between work factors and CVD risk factors differed for men and women; therefore, results are presented for both sexes combined.

Night work was positively associated with CRP (7.62\%), triglycerides (4.32\%) and fibrinogen (0.04 g/l); associations did not attenuate following adjustment for other workplace factors (Table 4; note coefficients for fibrinogen are multiplied by 10). Low job demands was positively associated with CRP, fibrinogen and triglycerides (albeit weakly), and low control with HbA1c and fibrinogen; again adjustment for other work factors had little impact on effect sizes. Long working hours were positively associated with adiposity only: WC was 1 cm and BMI 0.31 kg/m$^2$ higher in those who worked $>$48 h/week compared with those who worked less, independent of other work factors. Night workers with low-demand jobs had increased BMI, WC and SBP (0.78 kg/m$^2$, 1.5 cm, 1.38 mmHg, respectively) compared with those who did not work at night and...
did not have low demands (interaction $P = 0.02, 0.05, 0.01$ for BMI, WC, SBP, respectively) (Table 4).

A three-way interaction between night work, $>48$ h/week and low control was found for HDL (interaction $P = 0.02$). Compared with those who did not work at night, $>48$ h/week or have low control, HDL was 0.04 and 0.12 mmol/l lower for those with low control in combination with either night work or long hours, respectively. HDL was also 0.05 mmol/l lower for night workers who did not work long hours or have low control.

Approximately 30–50% of the effect sizes for the associations between work factors and CVD risk factors were explained by early life exposures (Table 5). The positive association for low control was reduced by 40% for HbA1c and 54% for fibrinogen, with cognitive ability explaining the largest amount (24 and 40% HbA1c and fibrinogen, respectively; Table S3, Supplementary data are available at IJE online). Positive associations between night work and triglycerides, CRP and fibrinogen were reduced by approximately one-third, mainly due to health behaviours at

| Table 1 | Characteristics of 4132 male and 3784 female members of the 1958 cohort who were in paid employment at age 45 years |
|---|---|---|
| | Men | Women | Overall |
| Total hours worked/week | n (%) | n (%) | n (%) |
| <35 | 150 (3.6) | 1639 (43.3) | 1789 (22.6) |
| 35–40 | 1428 (34.6) | 1234 (32.6) | 2662 (33.6) |
| 41–48 | 878 (21.2) | 331 (8.7) | 1209 (15.3) |
| >48 | 1305 (31.6) | 323 (8.5) | 1628 (20.6) |
| Unknown | 371 (9.0) | 257 (6.8) | 628 (7.9) |
| Night/morning work, at age 42 years | | | |
| < 1/month | 2281 (55.2) | 2699 (71.3) | 4980 (62.9) |
| $\geq$ 1/month | 1584 (38.3) | 620 (16.4) | 2204 (27.8) |
| Unknown | 267 (6.5) | 465 (12.3) | 732 (9.2) |
| Job control | | | |
| Low | 1389 (33.6) | 1698 (44.9) | 3087 (39.0) |
| High | 2366 (57.3) | 1809 (47.8) | 4175 (52.7) |
| Unknown | 377 (9.1) | 277 (7.3) | 654 (8.3) |
| Job demands | | | |
| Low | 1546 (37.4) | 1496 (39.5) | 3042 (38.4) |
| High | 2187 (52.9) | 1986 (52.5) | 4173 (52.7) |
| Unknown | 399 (9.7) | 302 (8.0) | 701 (8.9) |
| Risk factors for CVD | n | Mean (SD) | n | Mean (SD) | Mean (SD) |
| BMI (kg/m$^2$) | 4128 | 27.83 (4.22) | 3775 | 26.89 (5.47) | 27.38 (4.88) |
| WC (cm) | 4113 | 98.36 (10.90) | 3754 | 92.15 (12.48) | 92.06 (13.42) |
| SBP (mmHg) | 4111 | 132.88 (14.81) | 3751 | 126.80 (15.34) | 126.80 (16.35) |
| DBP (mmHg) | 4111 | 82.04 (10.37) | 3751 | 78.91 (10.80) | 78.91 (10.80) |
| Triglycerides (mmol/l)$^a$ | 3503 | 2.09 (1.21) | 3144 | 1.35 (0.71) | 1.70 (1.02) |
| Total cholesterol (mmol/l) | 3516 | 6.07 (1.12) | 3150 | 5.69 (0.99) | 5.89 (1.08) |
| HDL-cholesterol (mmol/l) | 3504 | 1.44 (0.33) | 3148 | 1.70 (0.40) | 1.56 (0.39) |
| HbA1c (%)$^a$ | 3564 | 5.27 (0.61) | 3194 | 5.15 (0.29) | 5.21 (0.35) |
| CRP (mg/l)$^{ab}$ | 3394 | 0.92 (0.95) | 3018 | 0.94 (1.15) | 0.93 (1.03) |
| Fibrinogen (g/l)$^c$ | 3445 | 2.86 (0.55) | 3103 | 3.00 (0.61) | 2.93 (0.58) |

$^a$Geometric mean [standard deviation (SD)].
$^{ab}$CRP excludes values $>$ 10 mg/l, n = 154.
$^c$Fibrinogen excludes values $>$ 5 g/l, n = 9.
Table 3 Mean levels of CVD risk factors by workplace factors

|          | BMI (kg/m²) | WC (cm) | BP SBP (mmHg) | Triglycerides (mmol/l) | Cholesterol (mmol/l) | HDL (mmol/l) | HbA1c (%) | CRP (mg/l) | Fibrinogen (g/l) |
|----------|-------------|---------|---------------|------------------------|----------------------|--------------|------------|------------|------------------|
| Night work &> 48 h/week & Low control & High demands |
| <35      | 26.6        | 85.5    | 120.6         | 75.6                   | 1.35                 | 5.68         | 1.68       | 5.15       | 0.91             | 2.98             |
| 35–40    | 27.4        | 92.2    | 127.4         | 79.2                   | 1.75                 | 5.91         | 1.55       | 5.22       | 0.97             | 2.94             |
| 41–48    | 27.5        | 94.7    | 130.0         | 80.6                   | 1.85                 | 5.92         | 1.51       | 5.21       | 0.88             | 2.88             |
| >48      | 27.9        | 96.4    | 130.2         | 80.6                   | 1.92                 | 6.01         | 1.49       | 5.25       | 0.92             | 2.89             |
| Unknown  | 27.7        | 93.5    | 127.3         | 79.5                   | 1.76                 | 6.02         | 1.54       | 5.27       | 0.99             | 2.94             |
| P        | <0.001      | <0.001  | 0.537         | 0.299                  | 0.667                | 0.166        | 0.671      | 0.577      | 0.084            | 0.431            |
| Night work &< 1/month & >1/month & Unknown |
| Percentage | Night work | >48 h/week | Low control | High demands |
| Night work | –          | –         | –            | –                  |
| >48 h/week | 36.7       | 41.4      | 60.3         | 49.2               |
| Low control | 48.4       | –         | 23.7         | 74.5               |
| High demands | 30.0       | 12.5      | –            | –                  |
| Correlation (SE) | Night work | –         | –            | –                  |
| >48 h/week | –          | 0.36 (0.02) | –            | –                  |
| Low control | –          | –         | –            | –                  |
| High demands | –          | –         | –            | –                  |
| aEach column work factor given as percentage of row work factor, e.g. 36.7% of night workers worked >48 h/week. SE = standard error.

Table 3 Mean levels of CVD risk factors by workplace factors

|          | BMI (kg/m²) | WC (cm) | BP SBP (mmHg) | Triglycerides (mmol/l) | Cholesterol (mmol/l) | HDL (mmol/l) | HbA1c (%) | CRP (mg/l) | Fibrinogen (g/l) |
|----------|-------------|---------|---------------|------------------------|----------------------|--------------|------------|------------|------------------|
| Total hours worked/week |
| <35      | 26.6        | 85.5    | 120.6         | 75.6                   | 1.35                 | 5.68         | 1.68       | 5.15       | 0.91             | 2.98             |
| 35–40    | 27.4        | 92.2    | 127.4         | 79.2                   | 1.75                 | 5.91         | 1.55       | 5.22       | 0.97             | 2.94             |
| 41–48    | 27.5        | 94.7    | 130.0         | 80.6                   | 1.85                 | 5.92         | 1.51       | 5.21       | 0.88             | 2.88             |
| >48      | 27.9        | 96.4    | 130.2         | 80.6                   | 1.92                 | 6.01         | 1.49       | 5.25       | 0.92             | 2.89             |
| Unknown  | 27.7        | 93.5    | 127.3         | 79.5                   | 1.76                 | 6.02         | 1.54       | 5.27       | 0.99             | 2.94             |
| P        | <0.001      | <0.001  | 0.537         | 0.299                  | 0.667                | 0.166        | 0.671      | 0.577      | 0.084            | 0.431            |
| Night work &< 1/month & >1/month & Unknown |
| Job control | Low        | 27.3    | 91.1          | 126.2                  | 78.6                 | 1.65         | 5.83       | 1.57       | 5.22             | 0.95             | 2.96             |
| High     | 27.4        | 92.5    | 127.2         | 79.1                   | 1.72                 | 5.92         | 1.56       | 5.20       | 0.90             | 2.89             |
| Unknown  | 27.7        | 93.4    | 127.0         | 79.2                   | 1.73                 | 5.99         | 1.54       | 5.28       | 1.04             | 2.97             |
| P        | 0.820       | 0.561   | 0.147         | 0.393                  | 0.169                | 0.104        | 0.026      | 0.003      | 0.048            | <0.001           |
| Job demands |
| Low      | 27.4        | 91.9    | 127.0         | 79.0                   | 1.70                 | 5.85         | 1.55       | 5.22       | 0.96             | 2.96             |
| High     | 27.3        | 91.9    | 126.6         | 78.8                   | 1.69                 | 5.90         | 1.57       | 5.20       | 0.89             | 2.90             |
| Unknown  | 27.7        | 93.4    | 126.9         | 79.2                   | 1.74                 | 5.99         | 1.55       | 5.27       | 1.02             | 2.96             |
| P        | 0.199       | 0.396   | 0.016         | 0.176                  | 0.049                | 0.084        | 0.002      | 0.025      | 0.011            | 0.001            |
| Total n  | 7903        | 7867    | 7862          | 6647                   | 6666                 | 5652         | 6758       | 6412       | 6548             |                  |

aData are geometric means for triglycerides, HbA1c and CRP.

bSBP, DBP and triglycerides are adjusted for time of day.

cHbA1c is adjusted for type 1 and type 2 diabetes treatment. Robust estimation is used for regression of HbA1c.

dCRP excludes values $>10$ mg/l ($n = 154$) and fibrinogen excludes values $>5$ g/l ($n = 9$).

P-values are from linear regression of trend adjusted for sex across categories of workplace factors (excluding category ‘unknown’).
Table 4  Differences in mean levels of CVD risk factors (95% CI) for workplace factors, derived from weighted regression models

|                      | Model Ia |                      | Model Ib |                      |
|----------------------|----------|----------------------|----------|----------------------|
| **HbA1c**<sup>cd</sup> (% change)  n = 4899 |          |                      |          |                      |
| > 48 h/week          | 0.12 (−0.49, 0.74) | 0.26 (−0.39, 0.91) |          |                      |
| Night work           | 0.44 (−0.07, 0.95) | 0.37 (−0.14, 0.88) |          |                      |
| Low control          | 0.73 (0.23, 1.22)** | 0.72 (0.21, 1.23)** |          |                      |
| Low demands          | 0.26 (−0.23, 0.75) | 0.19 (−0.31, 0.70) |          |                      |
| **Triglycerides**<sup>d,e</sup> (% change)  n = 4822 |          |                      |          |                      |
| > 48 h/week          | −0.20 (−4.14, 3.73) | −0.32 (−4.45, 3.80) |          |                      |
| Night work           | 4.32 (0.78, 7.86)*  | 4.40 (0.80, 8.01)*  |          |                      |
| Low control          | 0.86 (−2.26, 3.99) | 0.26 (−2.95, 3.47) |          |                      |
| Low demands          | 2.64 (−0.52, 5.81) | 2.63 (−0.63, 5.89) |          |                      |
| **CRP**<sup>d</sup> (% change)  n = 4654 |          |                      |          |                      |
| > 48 h/week          | 1.09 (−6.53, 8.72) | 2.16 (−5.81, 10.13) |          |                      |
| Night work           | 7.62 (0.71, 14.52)* | 7.24 (0.24, 14.24)* |          |                      |
| Low control          | 4.94 (−1.53, 11.41) | 3.93 (−2.67, 10.54) |          |                      |
| Low demands          | 6.92 (0.54, 13.31)* | 6.73 (0.17, 13.29)* |          |                      |
| **Fibrinogen** (g/l)  n = 4752* |          |                      |          |                      |
| > 48 h/week          | 0.06 (−0.35, 0.47) | 0.20 (−0.23, 0.63) |          |                      |
| Night work           | 0.41 (0.04, 0.79)*  | 0.37 (−0.01, 0.74) |          |                      |
| Low control          | 0.55 (0.21, 0.89)** | 0.50 (0.15, 0.85)** |          |                      |
| Low demands          | 0.48 (0.14, 0.82)** | 0.44 (0.09, 0.78)*  |          |                      |
| **BMI (kg/m<sup>2</sup>)**  n = 5698 |          |                      |          |                      |
| > 48 h/week          | 0.31 (0.01, 0.61)*  | 0.31 (−0.01, 0.62) |          |                      |
| Night work           | 0.39 (0.11, 0.67)** | – |          |                      |
| Low control          | −0.05 (−0.31, 0.21) | −0.06 (−0.33, 0.21) |          |                      |
| Low demands          | 0.17 (−0.09, 0.43) | – |          |                      |
| Nights plus high demands | – | 0.08 (−0.28, 0.44) |          |                      |
| No nights plus low demands | – | 0.03 (−0.28, 0.34) |          |                      |
| Nights plus low demands | – | 0.78 (0.35, 1.21)** |          |                      |
| **WC (cm)**  n = 5682 |          |                      |          |                      |
| > 48 h/week          | 0.98 (0.22, 1.73)** | 1.03 (0.24, 1.83)** |          |                      |
| Night work           | 0.71 (0.02, 1.39)*  | – |          |                      |
| Low control          | 0.00 (−0.63, 0.64) | 0.03 (−0.62, 0.68) |          |                      |
| Low demands          | 0.35 (−0.28, 0.98) | – |          |                      |
| Nights plus high demands | – | 0.01 (−0.89, 0.90) |          |                      |
| No nights plus low demands | – | 0.09 (−0.66, 0.85) |          |                      |
| Nights plus low demands | – | 1.49 (0.45, 2.52)** |          |                      |
| **SBP**<sup>c</sup> (mmHg)  n = 5044 |          |                      |          |                      |
| > 48 h/week          | −0.50 (−1.55, 0.54) | −0.11 (−1.19, 0.98) |          |                      |
| Night work           | −0.15 (−1.10, 0.79) | – |          |                      |
| Low control          | 0.81 (−0.06, 1.68) | 0.65 (−0.24, 1.53) |          |                      |
| Low demands          | 0.94 (0.08, 1.80)*  | – |          |                      |

(Continued)
Table 4 Continued

| Model Ia | Model IIb |
|----------|-----------|
| Nights plus high demands | – | –1.15 (–2.35, 0.04) |
| No nights plus low demands | – | 0.09 (–0.96, 1.13) |
| Nights plus low demands | – | 1.38 (–0.04, 2.81) |
| **HDL-cholesterol (mmol/l) n = 4826** | | |
| >48 h/week | 0.02 (–0.22, 0.26) | – |
| Night work | –0.27 (–0.49, –0.05)* | – |
| Low control | –0.18 (–0.39, 0.03) | – |
| Low demands | –0.31 (–0.52, –0.10)** | –0.31 (–0.52, –0.10)** |
| >48 h/week and low control | – | –1.24 (–1.80, –0.69)*** |
| Nights and low control | – | –0.41 (–0.77, –0.05)* |
| Night work (≤48 h/week, high control) | – | –0.46 (–0.82, –0.09)* |
| Other | – | –0.10 (–0.34, 0.14) |

Model numbers are determined by data on CVD risk factor, exposures and weights.
- Model I: separate associations between work factors and CVD risk factors, adjusted for sex.
- Model II: associations between work factors and CVD risk factors mutually adjusted for other workplace factors, and for sex, with stratified results for interactions between night work and job demands. Reference category for night/demands interaction is the combination of not working nights and having high job demands.
- HbA1c additionally adjusted for diagnosis of type 1 diabetes and medication for type 2 diabetes.
- Triglycerides, HbA1c and CRP are presented as percentage change by log transforming and multiplying by 100.
- Coefficients are small and have therefore been multiplied by 10.
- Categories from the stratified HDL models have been collapsed for presentation purposes (i.e. ‘other’ category includes >48 h/week only, low control only, >48 h/week and nights, all three for which no associations were observed).
- P ≤ 0.05; **P ≤ 0.01; ***P ≤ 0.001.

Most CVD risk factors were associated with at least one workplace factor. Night work was associated with most CVD risk factors examined, whereas long working hours was only associated with increased adiposity. Low job demands and control tended to modify the effects of night work and long hours.

Discussion

Most CVD risk factors were associated with at least one workplace factor. Night work was associated with most CVD risk factors examined, whereas long working hours was only associated with increased adiposity. Low job demands and control tended to modify the effects of night work and long hours. Associations observed between workplace factors and CVD risk factors were substantially reduced when early life exposures were taken into account. The main strength of this study is that it uses a large population-based cohort with advantages over occupational cohorts, i.e. results are generalizable to the whole working population and follow-up is not determined by employment status. Few population-based studies have published findings for exposures such as shift work despite collecting data, whereas others have less occupational diversity limiting their generalizability. The rich prospective measures of early life factors in the 1958 cohort allowed scrutiny of a broad range of exposures prior to entering the labour market. Early life factors were selected based on a priori knowledge of relationships with CVD risk, and an empirical method was used to identify key characteristics for each CVD risk factor. We examined several workplace factors, and interactions between them, and we based our definition of long working hours on current European policy. The cohort benefits from a range of biological risk factors for CVD measured in mid-adulthood, and particularly for night work, we were able to replicate findings across several measures.
### Table 5  Difference in mean levels of risk factors (95% CI) for workplace factors with adjustments for early life CVD risk factors

| Risk Factor | Basic model | Adjusted | % |
|-------------|-------------|----------|---|
| **HbA1c (% change)**<sup>b</sup> | | | |
| Low control | 0.72 (0.21, 1.23) | 0.43 (–0.01, 0.95) | –40 |
| **Triglycerides (% change)**<sup>c</sup> | | | |
| Night work | 4.40 (0.80, 8.01) | 3.00 (–0.58, 6.59) | –32 |
| **CRP (% change)**<sup>d</sup> | | | |
| Night work | 7.24 (0.24, 14.24) | 4.15 (–2.68, 10.99) | –43 |
| Low demands | 6.73 (0.17, 13.29) | 2.69 (–3.82, 9.20) | –60 |
| **Fibrinogen (g/l)**<sup>e,j</sup> | | | |
| Night work | 0.37 (–0.01, 0.74) | 0.21 (–0.17, 0.58) | –43 |
| Low control | 0.50 (0.15, 0.85) | 0.23 (–0.12, 0.58) | –54 |
| Low demands | 0.44 (0.09, 0.78) | 0.25 (–0.10, 0.59) | –43 |
| **BMI (kg/m<sup>2</sup>)**<sup>f</sup> | | | |
| 44 h/week | 0.31 (–0.01, 0.62) | 0.26 (–0.01, 0.53) | –16 |
| Night work/low demands<sup>k</sup> | 0.78 (0.35, 1.21) | 0.38 (0.03, 0.74) | –51 |
| **WC (cm)**<sup>g</sup> | | | |
| 44 h/week | 1.03 (0.24, 1.83) | 0.71 (0.01, 1.41) | –31 |
| Night work/low demands<sup>k</sup> | 1.49 (0.45, 2.52) | 0.74 (–0.17, 1.65) | –50 |
| **SBP (mmHg)**<sup>h</sup> | | | |
| Night work/low demands<sup>k</sup> | 1.38 (–0.04, 2.81) | 0.84 (–0.60, 2.27) | –39 |
| **HDL-cholesterol (mmol/l)**<sup>i,j</sup> | | | |
| Low demands | –0.31 (–0.52, –0.10) | –0.20 (–0.41, 0.01) | –35 |
| >48 h/week and low control<sup>i</sup> | –1.24 (–1.80, –0.69) | –0.99 (–1.54, –0.44) | –20 |
| Nights and low control<sup>i</sup> | –0.41 (–0.77, –0.05) | –0.16 (–0.53, 0.21) | –61 |
| Night work (≤48 h/week, high control)<sup>i</sup> | –0.46 (–0.82, –0.09) | –0.46 (–0.82, –0.10) | 0 |

<sup>a</sup>Missing confounder data imputed and the sample is weighted for non-response at age 45 years.

<sup>b</sup>Adjusted for sex, housing tenure at age 7 years, math score at 11 years, reading score at 16 years, Bristol Social Adjustment Guide (BSAG) at 11 years, age mother last attended school, smoking at 16 years, alcohol at 16 years, diagnosis of type 1 diabetes, treatment for type 2 diabetes.

<sup>c</sup>Smoking in pregnancy, persons/room at age 7 years, BMI at 16 years, math score at 16 years, Rutter at 16 years, age father last attended school, smoking at 16 years, time of day.

<sup>d</sup>Smoking in pregnancy, father's social class (SC) at age 0 and 7 years, persons/room at 0, 7 and 16 years, tenure at 11 years, BMI at 16 years, height at 11 years, puberty, reading score at 11 and 16 years, math score at 16 years, Rutter at 16 years, age mother last attended school, age father last attended school, mother's BMI, smoking at 16 years.

<sup>e</sup>Smoking in pregnancy, father's SC at 0 and 7 years, housing tenure at age 7 years, persons/room at 7 years, BMI at 16 years, reading score at 11 and 16 years, math score at 16 years, BSAG at 11 years, Rutter at 16 years, age mother last attended school, mother's BMI, father's BMI, father's interest in education at 11 years.

<sup>f</sup>Smoking in pregnancy, father's SC at 0 and 7 years, housing tenure at age 7 years, persons/room at 7 years, BMI at 16 years, reading score at 11 years, math score at 11 years, BSAG at 11 years, Rutter at 16 years, age mother last attended school, mother's BMI, father's BMI, father's interest in education at 11 years, physical activity at 11 years, smoking at 16 years, alcohol consumption at 16 years.

<sup>g</sup>Smoking in pregnancy, father's SC at 0 and 7 years, housing tenure at age 7 years, persons/room at 7 years, BMI at 16 years, height at 7 years, pubertal development, reading score at 11 years, math score at 7 and 16 years, Rutter at 16 years, age mother last attended school, mother's BMI, father's BMI, smoking at 16 years, physical activity at 11 years.

<sup>h</sup>Smoking in pregnancy, father's SC at 0 and 7 years, housing tenure at age 7 years, persons/room at 7 years, BMI at 16 years, reading score at 7 years, math score at 7 and 16 years, Rutter at 16 years, age mother last attended school, mother's BMI, father's BMI, father's smoking habit at age 11 years, physical activity at 11 years, smoking at 16 years, alcohol consumption at 16 years.

<sup>i</sup>Adjusted for sex, housing tenure at age 7 years, math score at 11 years, reading score at 16 years, Bristol Social Adjustment Guide (BSAG) at 11 years, age mother last attended school, smoking at 16 years, alcohol at 16 years, diagnosis of type 1 diabetes, treatment for type 2 diabetes.

<sup>j</sup>Smoking in pregnancy, father's social class (SC) at age 0 and 7 years, persons/room at 0, 7 and 16 years, tenure at 11 years, BMI at 16 years, height at 11 years, puberty, reading score at 11 and 16 years, math score at 16 years, Rutter at 16 years, age mother last attended school, age father last attended school, mother's BMI, smoking at 16 years, physical activity at 11 years, smoking at 16 years, alcohol consumption at 16 years.

<sup>k</sup>Reference category is ‘no night work/high demands’.

<sup>l</sup>Reference category ‘not nights, >48h/week or low control’.

Percentage change calculated as $100 \times \frac{(\text{coeff}_{\text{adj}} - \text{coeff}_{\text{unadj}})}{\text{coeff}_{\text{unadj}}}$
The main limitation of this study was that, due to attrition, the sample with complete data was less than half of the original birth cohort, leading to under-representation of participants from disadvantaged backgrounds in terms of SEP, cognitive and behavioural problems. Because associations between work and health may be underestimated in a more advantaged population, analyses were weighted to allow for bias. We found no evidence that associations between workplace factors and CVD risk factors differed for men and women; however, the power of our study to detect gender differences may be limited by the small number of women who undertook night work or worked long hours. We used HbAlc as a marker of long-term glucose homeostasis and plasma glucose was not measured. Non-fasting blood was collected that has implications for triglyceride levels, which are lower after fasting. However, fasting and non-fasting triglyceride levels are positively correlated, and a recent meta-analysis found no significant variation in results for triglycerides by fasting status.

We hypothesized that associations between workplace factors and CVD risk factors may be modified by each other. Although it is known that night workers tend to work long hours, such interactions have rarely been studied in relation to adult health status. Although we found no interaction between night work and work hours, we found that night workers in low-demand jobs had adverse levels of several CVD risk factors whereas night workers in high-demand jobs did not. We also found that HDL-cholesterol levels were lower for individuals who not only worked >48 h/week or at night but also had low control over their work. Our findings are consistent with a previous study where BP and lipid levels were elevated only in night workers with effort–reward imbalance. These results suggest that circadian disruption of metabolic processes is not as important as previously hypothesized.

We found that working >48 h/week was associated with increased adiposity independent of night work and the psychosocial work environment consistent with other studies, but found no independent associations for long hours with other CVD risk factors. Evidence for an effect of long work hours on CVD risk is inconsistent mainly due to methodological differences between studies, including inconsistent definitions of long hours. Firmer support is needed to establish health effects of moderate and extensive overtime. We found no evidence of effects of job strain (low control and high demands) on CVD risk factors in this study but, as reported elsewhere, we found associations for low rather than high job demands.

Several mechanisms have been proposed that underlie associations between workplace factors and CVD risk such as mediating influences of health behaviours, and activation of neurobiological stress responses. Alternatively, associations may be due to confounding by socio-economic circumstances or increased CVD risk prior to entering a work role. In this study, we found that social, economic and physical risk factors for CVD measured before participants last attended school (at age <16 years) explained ~50% of the work/CVD associations in mid-adulthood, consistent with a previous study of low job control and risk of CHD. Very few associations had CIs that excluded the null after adjustment for early life circumstances, suggesting that there was no difference in levels of most CVD risk factors for those exposed to particular workplace factors compared with those who were not. This interpretation supports the hypothesis that relationships between workplace factors and CVD risk factors are confounded by early life characteristics that may select individuals into particular working environments. Our results could also be interpreted that the modestly sized point estimates persisting after adjustment for early life factors are real and may be further explained by mediating mechanisms, such as health behaviours. Future studies examining mediating effects need to adequately control for pre-existing CVD risk factors.

To conclude, associations between work factors such as night work and risk factors for CVD are at least partly due to social and health disadvantage originating earlier in life. These results taken with other studies of work and health show that particular groups of workers, such as night workers and, to a lesser extent, those working >48 h/week (i.e. above the current European Policy) are at increased risk of CVD, regardless of the underlying mechanism, and therefore represent sub-groups of the population for which healthy life-style policies could be directed.

Supplementary Data
Supplementary data are available at IJE online.

Funding
This work was undertaken at GOSH/UCL Institute of Child Health, which received a proportion of funding from the Department of Health’s National Institute of Health Research, Biomedical Research Centres funding scheme. The Centre for Paediatric Epidemiology and Biostatistics also benefits from funding support from the Medical Research Council in its capacity as the MRC Centre of Epidemiology for Child Health. This work was supported by the Economic Social Research Council (RES-163-27-1011 to C.T.) and the Medical Research Council (G000934).

Conflict of interest statement: None declared.
KEY MESSAGES

- All work place factors examined (night work, >48 h/week, psychosocial environment) were related to at least one CVD risk factor measured in mid-life.
- Most notably, night workers had adverse levels of several CVD risk factors in mid-life and for some CVD risk factors the associations only existed for night workers in low-demand jobs.
- Cross-sectional associations between workplace factors and CVD risk factors in mid-life were partly explained by early life exposures up to the age of 16 years.

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