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The contribution of sleep to social inequalities in cardiovascular disorders: a multi-cohort study

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Aims Sleep disturbances exhibit a strong social patterning, and inadequate sleep has been associated with adverse health outcomes, including cardiovascular disorders (CVD). However, the contribution of sleep to socioeconomic inequalities in CVD is unclear. This study pools data from eight European cohorts to investigate the role of sleep duration in the association between life-course socioeconomic status (SES) and CVD.

Methods and results We used cross-sectional data from eight European cohorts, totalling 111 205 participants. Life-course SES was assessed using father's and adult occupational position. Self-reported sleep duration was categorized into recommended (6–8.5 h/night), long (>8.5 h/night), and short (<6 h/night). We examined two cardiovascular outcomes: coronary heart disease (CHD) and stroke. Main analyses were conducted using pooled data and examined the association between life-course SES and CVD, and the contribution of sleep duration to this gradient using counterfactual mediation. Low father's occupational position was associated with an increased risk of CHD (men: OR = 1.19, 95% CI [1.04; 1.37]; women: OR = 1.25, 95% CI [1.02; 1.54]), with marginal decrease of the gradient after accounting for adult occupational position (men: OR = 1.17, 95% CI [1.02; 1.35]; women: OR = 1.22, 95% CI [0.99; 1.52]), and no mediating effect by short sleep duration. Low adult occupational position was associated with an increased risk of CHD in both men and women (men: OR = 1.48, 95% CI [1.14; 1.92]; women: OR = 1.53, 95% CI [1.04; 2.21]). Short sleep duration meaningfully contributed to the association between adult occupational position and CHD in men, with 13.4% mediation. Stroke did not exhibit a social patterning with any of the variables examined.

Conclusion This study suggests that inadequate sleep accounts to a meaningful proportion of the association between adult occupational position and CHD, at least in men. With sleep increasingly being considered an important cardiovascular risk factor in its own terms, our study additionally points to its potential role in social inequalities in cardiovascular disease.

Keywords Socioeconomic status • Life-course • Sleep duration • Mediation • Cardiovascular disorders

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1. Introduction

Individuals experiencing adverse socioeconomic circumstances across the life-course are disproportionately affected by cardiovascular disorders (CVD), including coronary heart disease (CHD) and stroke.[1,2] Social differences in CVD are partly explained by behavioural or psychosocial factors.[3,4] However, a significant part of the socioeconomic gradient in cardiovascular disease remains unexplained.[4]

Among the factors that may potentially link social disadvantage to CVD is inadequate sleep. First, individuals who experienced social adversity across the life-course report sleep-related problems more frequently than those with more advantaged experiences.[5–7] In particular, people working in shifts, living in deprived neighbourhoods, or who have experienced adversity in childhood show an increased prevalence of sleep-related disorders.[6,8–12]

Second, inadequate sleep has been associated with an increased risk of cardiovascular disease.[13–15] Chronic sleep deprivation disrupts the function of several physiological systems including the dysregulation of key endocrine and metabolic processes, which may lead to an aberrant activation of the autonomous nervous system, and the impairment of immunity and inflammatory processes, altogether leading to an increased cardiovascular risk.[13,16,17] Excessively long sleep has also been associated with adverse cardiovascular health outcomes, although reverse causation processes whereby individuals sleep longer cannot be excluded.[18–21] To date, however, no large population-based study has assessed the contribution of sleep to the social gradient in CVD.[8,22]

In this study, we examine the associations between indicators of socioeconomic status (SES) across the life-course and CVD, namely CHD and stroke, by using cross-sectional data from eight cohort studies from four European countries. Further, we assess to what extent the associations between life-course SES and CVD are explained by sleep duration by applying the counterfactual mediation model.

2. Methods

2.1 Study population

This study is part of the Lifepath project[23] and uses cross-sectional data from eight cohorts: the French Constances (study period 2012–2016; $N = 65\ 843$), E3N (2005–2006; $N = 51\ 841$) and GAZEL (2014; $N = 10\ 203$), the English Whitehall II (1997–1998; $N = 6359$) and ELSA (2012; $N = 5083$), the Swiss COLAUS (2009–2011; $N = 4147$) and SKIPOGH (2013–2016; $N = 979$), and the Portuguese EPIPORTO (2005–2009; $N = 2410$).[11,24–30] Although five cohorts included adults from the general population, E3N, GAZEL, and Whitehall II were occupational cohorts and included women working in the French national education sector, employees of the French national gas and electricity company and British civil servants, respectively. All participants underwent a clinical examination and filled a questionnaire collecting data on demographic characteristics, health, medication, education, work, lifestyle, and sleep characteristics.

2.1.1 Ethics statement

Each study was approved by relevant local or national ethics committees and all procedures performed in these studies were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All participants gave written informed consent. This study does not contain any studies with animals performed by any of the authors.

2.2 Measures

2.2.1 Life-course SES

We used father's occupational position and last known adult occupational position as measures of SES across the life-course. Father's occupational position is a common indicator of SES in early life, whereas adult occupational position is the most used SES indicator in adulthood.[31] Both variables capture multiple dimensions of SES, including education, social prestige, wealth, and retirement benefits, and have been widely used in former studies exploring socioeconomic differences in health.[32] Although father's occupational position was self-reported by study participants in all cohorts, adult occupational position was retrieved through work registries in GAZEL and Whitehall II studies, and self-reported in the six other cohorts (see Supplementary material online, *Table S15*). Both SES indicators were coded according to the nine categories of the European Socio-economic Classification system (ESeC), which is a standard system for classifying professions in social epidemiology, and further grouped in three main categories: 'High' (higher professionals/managers, lower professionals/managers, higher clerical), 'Middle' (small employers and self-employed, farmers, lower supervisors, and technicians), and 'Low' (lower clerical, sales workers, skilled/unskilled workers).[33]

2.2.2 Cardiovascular disorders

Two CVDs were considered as outcomes: CHD and stroke. CHD was defined as reporting ischemic artery disease, angina pectoris, or myocardial infarction, whereas stroke was defined as reporting an ischemic or haemorrhagic stroke. The history of CVD events was based on self-report in GAZEL, ELSA, COLAUS, SKIPOGH, and EPIPORTO studies, whereas an objective assessment of cardiovascular outcomes was available in Constances, E3N, and Whitehall II cohorts, as these studies included thorough cardiological examinations at interview or had access to participant's medical records (see Supplementary material online, *Table S15*).

2.2.3 Sleep duration

Our study focused on sleep duration as this measure has previously been related to both SES and CVD and was available in all eight cohorts.[13,34] Sleep duration was self-reported in all eight cohorts as the average number of hours of sleep per night and subsequently categorized into recommended or normal sleep (6–8.5 h/night), short sleep (<6 h/night), and long sleep (>8.5 h/night). These thresholds were chosen from clinical practice which found that short sleep (<6 h/night) was associated with an increased risk of CVD,[14,35] whereas long sleep (>8.5 h/night) was related with pre-existent conditions, such as depression.[19,36]

2.2.4 Other covariates

Potential confounders we considered included cohort, study period, health behaviours, and flexible working hours. Health behaviours were self-reported in all eight cohorts and included smoking, sedentary behaviour, and alcohol intake. Smoking status was categorized as current vs. former/never smoker, sedentary behaviour was categorized as sedentary vs. non-sedentary based on the amount, frequency, and type of physical activity, whereas alcohol intake was categorized as hazardous intake (more than three daily alcohol units for men, more than two daily alcohol units for women) vs. non-hazardous intake. Flexible working hours were based on the ESeC classification of professions and were categorized as flexible (higher professionals and managers, lower professionals and managers; higher clerical, services and sales workers) and non-

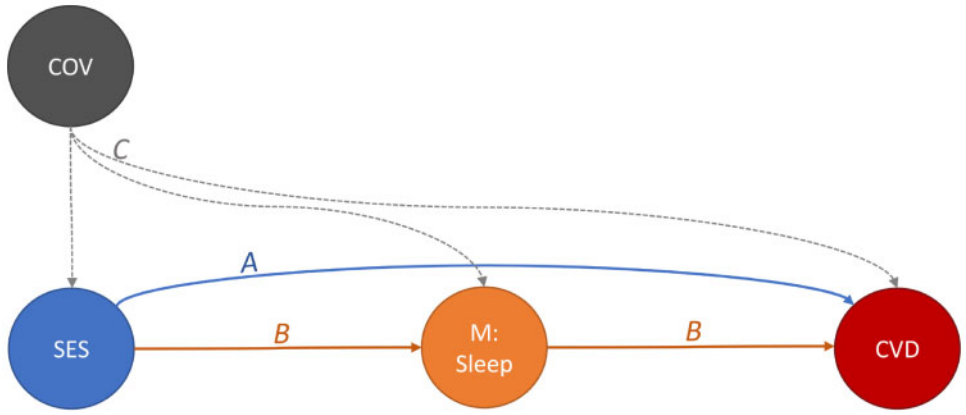

Figure 1 Directed acyclic graphs representing the counterfactual mediation model for the association between SES indicators and cardiovascular outcomes, mediated by sleep duration. (*A*) NDE, Natural direct effect: Effect of the predictor (SES) on the main outcome (CVD), through pathways which do not involve the mediator (sleep duration). (*B*) NIE: Natural indirect effect: Effect of the predictor (SES) on the main outcome (CVD), through pathways which involve the mediator (sleep duration). (*C*) Confounding effects by covariates. COV, covariates (age, cohort, study period, health behaviours, flexible working hours); SES, Adult/Father's occupational position; M, mediator—sleep duration; CVD, cardiovascular disorders; MTE, marginal total effect of the predictor (SES) on the main outcome (CVD): NDE + NIE (not represented). This figure was realized with MS Office-Excel.

flexible (small employers and self-employed; farmers; lower supervisors; technicians; lower clerical, services and sales workers, skilled and unskilled workers).

2.3 Statistical analyses

We tested the association between adult or father's occupational position (main exposure variables) and sleep duration (outcome), using a multinomial logistic regression model adjusted for age, cohort, study period, health behaviours, and flexible working hours. To account for the effect of adult occupational position in analyses using father's occupational position as the main exposure, we implemented an additional model that was further adjusted for adult occupational position.[37] We used the same set of covariates for the logistic model assessing the association between sleep duration (exposure) and CVD (outcome). We tested the associations between SES indicators and CVD and the mediating effect of each level of sleep duration by applying the counterfactual mediation method, using the same sets of covariates. The counterfactual mediation method is based on two regression models (Supplementary material online, *Annex S1*): a first model predicting the outcome (CHD, stroke) based on the main exposure variable (SES), the mediator (sleep duration), an interaction term between the main exposure and the mediator, and confounders, and a second regression model predicting the mediator based on the main exposure and confounders. The regression coefficients from the two models are subsequently used to compute counterfactual mediation estimates (*Figure 1*), namely the natural direct effects [NDE (odds ratio): effect of exposure on the outcome via pathways that do not involve the mediator], natural indirect effects [NIE (odds ratio): effect of exposure on the outcome operating through the mediator], marginal total effects [MTE (odds ratio)=NIE+NDE, total effect of the exposure on the outcome], and the proportion of the association between the exposure and the outcome which is mediated by the mediator (Proportion mediated-PM).[38] Confidence intervals for MTE, NDE, NIE, and PM parameters were computed through bootstrap procedure (random sample with replacement—10 000 simulations). The main statistical analyses were conducted using Stata v.14 (Stata Corp, TX). Statistical significances were set at *P*-value <0.05.

2.4 Individual cohort associations

To investigate for potential differences between individual cohorts, we repeated the associations between SES and sleep duration, sleep duration and CVD, and the counterfactual mediation models between SES, sleep duration and CVD, cohort by cohort. We also performed a meta-analysis of the eight individual cohorts to examine which studies contributed the most to the pooled data associations, and to explore the inter-study heterogeneity by computing the I^2 coefficient.

2.5 Additional sensitivity analyses

2.5.1 Cox regression models for time-to-event event longitudinal analyses

To examine whether the cross-sectional approach could have biased the main findings, we also conducted a series of longitudinal analyses using Cox regression models for the associations between SES at baseline and CVD occurrence, and between sleep duration at baseline and CVD occurrence, using time-to-event data from Whitehall II study through waves 1–8 (w1 1985–1988, w2 1989–1990, w3 1991–1993, w4 1995–1996, w5 1997–1999, w6 2001, w7 2003–2004, w8 2006).[27] We included 6805 individuals with complete data at waves 1–8, and tested the proportional hazard assumptions for Cox regression models by using log–log plots (not violated).

2.5.2 Multiple imputation for missing data for health behaviours

To test for bias that would result from missing values, we imputed missing data for health behaviours (confounding factors) using chained equations based on SES, CVD and major confounders (Stata procedure 'mi').[39]

2.5.3 Confounding by sleep quality indicators and other cardiometabolic disorders

We further explored potential confounding effects by four binary sleep quality indicators, namely 'Difficulty falling asleep', 'Difficulty waking up in the morning', 'Waking up during the night', and 'Waking up too early', by including them as co-variables in counterfactual mediation analyses between SES indicators, sleep duration, and CVD (Supplementary material online, *Annex S1*). We also explored the potential confounding/contribution to the main associations by further adjusting for two major cardiometabolic disorders, namely type 2 diabetes (T2D), and obesity (Supplementary material online, *Annex S2*).

2.5.4 Comparison of studies using objective assessment vs. self-reported data

To investigate whether the methodology of data acquisition could have affected our findings, we compared the gradients for the associations between SES and sleep duration, sleep duration and CVD, and the mediation by sleep duration to the SES gradient in CVD, between cohorts that either used an objective assessment of the data for the main endpoints (Constances, E3N, Whitehall II) cohorts that were based on self-report (GAZEL, ELSA, COLAUS, SKIPOGH, EPIPORTO).

2.5.5 Education as the main SES indicator

In addition to father's and adult occupational position, we also used education as the main exposure variable, in order to examine the association between education and sleep duration, and to assess the contribution of sleep duration to the educational gradient in CVD.

2.5.6 Extreme sleep duration thresholds

Finally, we repeated the associations between SES and sleep duration, sleep duration and CVD, and the contribution of sleep duration to the SES gradient in CVD using extreme sleep duration thresholds, namely 0–5 h for short sleep duration, and >10 h for long sleep duration.

3. Results

From the initial 188 238 participants from the eight cohorts, 37 682 were excluded due to missing information on health behaviours, 3691 for missing sleep duration, 17 328 for missing adult occupational position, and 18 332 participants for missing father's occupational position, leaving a total of 111 205 participants to be included in the study. Excluded participants were more frequently women (73% vs. 67%) and had a lower adult occupational position than those included in the study (20% vs. 26% in the high occupation group).

3.1 Sample characteristics

We report the characteristics of the study population in *Table 1*. In the majority of the cohorts, low and middle father's occupational positions were the most prevalent, whereas the distribution of adult occupational position varied among studies and countries, with high and middle adult SES groups being generally more prevalent in English cohorts, and low and middle adult SES groups being more common in Southern European cohorts. The prevalence of short sleep ranged between 3% and 14% (6% for pooled data) and was higher in ELSA (14%) and lower in E3N and EPIPORTO (3% and 5%, respectively), while the prevalence of long sleep ranged between 9% and 27%, and was lower in Whitehall II, SKIPOGH, and COLAUS (2–5%), and higher in EPIPORTO (27%). The distribution of detrimental health behaviours varied substantially across the cohorts, and prevalence estimates ranged between 7% and 26% for current smoking, between 8% and 42% for hazardous alcohol intake, and between 6% and 81% for sedentary behaviour. The prevalence of CHD ranged between 1% and 13%, with highest prevalence estimates being observed in Whitehall II and ELSA (13%), while the prevalence of stroke ranged between 1% and 5%, with highest prevalence being in ELSA.

3.2 Association between life-course SES indicators and sleep duration

We show the association between life-course SES indicators and sleep duration using pooled data in *Table 2*. We found a U-shaped association between father's occupational position and sleep duration, with low SES being more strongly associated with short sleep (*A.* odds ratio (OR)=1.18, 95% CI [1.07; 1.31], women: OR = 1.31, 95% CI [1.20; 1.44]), than long sleep (*A.* OR = 1.01, 95% CI [0.92; 1.11], women: OR = 1.07, 95% CI [1.01; 1.14]). The association between father's occupational position and sleep duration persisted after accounting for adult SES. Larger effect size and stronger associations were observed for the association between adult occupational position and sleep duration, with stronger associations in men than in women. As for father's occupational position, however, we found stronger associations for short sleep (men: OR = 2.22, 95% CI [1.85; 2.66], women: OR = 2.12, 95% CI [1.82; 2.47]), than for long sleep (men: OR = 1.88, 95% CI [1.59; 2.23], women: OR = 1.14, 95% CI [1.03; 1.27]).

3.3 Association between sleep duration and CVD

The association between sleep duration and CVD is presented in *Table 3*. Short sleep was associated with an increased risk of CHD in both sexes (CHD-men: OR = 1.65, 95% CI [1.41; 1.92]; women: OR = 1.59, 95% CI [1.28; 1.97]), whereas it was associated with an increased risk of stroke in women but not in men (Stroke-men: OR = 1.16, 95% CI [0.84; 1.60]; women: OR = 1.31, 95% CI [1.03; 1.66]). We also observed a higher risk of stroke in participants with long sleep (men: OR = 1.51, 95% CI [1.17; 1.95]; women: OR = 1.24, 95% CI [1.06; 1.49]), while long sleep was also associated with an increased risk of CHD in women (OR = 1.24, 95% CI [1.03; 1.43]).

3.4 Association between life-course SES indicators and CVD, and the contribution of sleep duration

In *Figure 2*, we present the counterfactual mediation models for the associations between SES indicators and CVD, mediated by short sleep duration. We observed an inverse association between father's occupational position and CHD in both men and women (*A.* men: marginal total effect (MTE—OR scale)=1.19 95% CI [1.04; 1.37], women: MTE (OR) = 1.25 95% CI [1.02; 1.55]). Upon accounting for the effect of adult occupational position, the gradient between father's occupational position and CHD was marginally decreased (*B.* men: MTE (OR)=1.17 95% CI [1.02; 1.35], women: MTE (OR) = 1.22 95% CI [0.99; 1.51]). Sleep did not mediate the association between father's occupational position and stroke. We found a strong inverse association between adult occupational position and CHD risk in both sexes (*C.* men: MTE (OR)=1.45 95% CI [1.13; 1.86], women: MTE (OR) = 1.52 95% CI [1.07; 2.11]), with 13.4% mediation of this association by short sleep duration in men. We also evaluated the contribution of *long* sleep duration to the life-course socioeconomic

Table 1 General characteristics of included participants by cohort

	Constances N = 50 463	GAZEL N = 8760	E3N N = 39 258	Whitehall II N = 4356	ELSA N = 3838	COLAUS N = 2228	SKIPOGH N = 854	EPIPORTO N = 1448	Pooled data N = 111 205
% Women	26 437 (52)	2059 (24)	39 258 (100)	1239 (28)	2144 (56)	1149 (52)	432 (51)	864 (60)	73 582 (66)
Age (mean ± SD, years)	48.4 (±13)	68.9 (±3.4)	64 (±6.3)	55.7 (±6)	72 (±8.7)	53 (±8)	50.3 (±16.2)	52 (±13.3)	56.8 (±13.1)
Father's occupational position (*N*, %)									
High	10 933 (22)	3251 (37)	6303 (16)	426 (10)	396 (10)	718 (32)	215 (25)	195 (13)	22 437 (20)
Middle	20 504 (41)	1930 (22)	16 805 (43)	1335 (31)	1476 (38)	848 (38)	406 (48)	306 (21)	43 610 (39)
Low	19 026 (38)	3579 (41)	16 150 (41)	2595 (60)	1966 (51)	662 (30)	233 (27)	947 (65)	45 158 (41)
Adult occupational position (*N*, %)									
High	17 041 (34)	2527 (29)	5041 (13)	2412 (55)	1118 (29)	352 (16)	187 (22)	310 (21)	28 988 (26)
Middle	16 402 (33)	4649 (53)	28 411 (72)	1350 (31)	1679 (44)	818 (37)	293 (34)	313 (22)	53 915 (48)
Low	17 020 (34)	1584 (18)	5806 (15)	594 (14)	1041 (27)	1058 (47)	374 (44)	825 (57)	28 302 (25)
Flexible working hours (*N*, %)	17 041 (34)	2527 (29)	5041 (13)	3762 (86)	1118 (29)	352 (16)	185 (22)	310 (21)	30 336 (27)
Sleep duration (mean ± SD, h/n)	7.2 (±1.2)	7.3 (±1.1)	7.6 (±1.1)	6.7 (±1)	6.9 (±1.3)	6.9 (±1)	6.9 (±1.1)	7.8 (±1.5)	7.3 (±1.2)
Sleep duration (*N*, %)									
Normal sleep (6–8.5 h/n)	40 382 (80)	6676 (76)	31 532 (80)	3960 (91)	2962 (77)	1953 (88)	728 (85)	996 (69)	89 189 (80)
Long sleep (>8.5 h/n)	5934 (12)	1376 (16)	6670 (17)	66 (2)	325 (8)	80 (4)	42 (5)	385 (27)	14 878 (13)
Short sleep (<6 h/n)	4147 (8)	708 (8)	1056 (3)	330 (8)	551 (14)	195 (9)	84 (10)	67 (5)	7138 (6)
Health-related behaviours (*N*, %)									
Current smoking	9696 (19)	635 (7)	2639 (7)	452 (10)	354 (9)	496 (22)	224 (26)	327 (23)	14 823 (13)
Hazardous alcohol consumption[a]	5847 (12)	2468 (28)	16 601 (42)	1731 (40)	1057 (28)	401 (18)	72 (8)	475 (33)	28 652 (26)
Sedentary behaviour	11 689 (23)	2884 (33)	7874 (20)	259 (6)	1280 (33)	611 (27)	337 (39)	1169 (81)	26 103 (23)
Diabetes (*N*, %)	1683 (3)	1155 (13)	[b]	204 (5)	303 (12)	176 (8)	46 (5)	165 (11)	3732 (5)
Obesity (*N*, %)	5676 (11)	1177 (14)	2660 (7)	596 (18)	945 (29)	297 (13)	123 (14)	312 (22)	11 786 (11)
Cardiovascular disorders									
CHD (*N*, %)	660 (1)	518 (6)	460 (1)	574 (13)	445 (13)	93 (4)	21 (2)	92 (6)	2863 (3)
Stroke (*N*, %)	400 (1)	99 (1)	878 (2)	18 (0)	190 (5)	24 (1)	10 (1)	36 (2)	1655 (2)

CHD, coronary heart disease; h/n, hours per night.
[a]Hazardous alcohol consumption was defined as having more than three alcoholic drinks per day for men and more than two alcoholic drinks per day in women.
[b]This outcome was not assessed in the E3N cohort.

gradient in CVD, but found no meaningful mediation (see Supplementary material online, *Table S1*).

3.5 Individual cohort associations

We further examined the associations between SES and sleep duration, sleep duration and CVD, and the mediating effect of short sleep duration to the association between SES and CVD on each cohort separately (see Supplementary material online, *Tables S2–S8*). Overall, we found that low adult occupational position was associated with an increased risk of short and long sleep duration in the majority of cohorts (Constances, E3N, Whitehall II, ELSA, COLAUS, SKIPOGH, EPIPORTO), with generally stronger OR for short sleep than long sleep, whereas there were fewer associations between father's occupational position and sleep duration, with stronger associations in the model unadjusted for adult occupational position. We also found associations between short sleep duration and an increased risk of CHD, with significant associations being observed in Constances, GAZEL, E3N, and Whitehall II cohorts, whereas there were fewer associations between sleep duration and stroke, in both unadjusted and adjusted models for adult occupational position. Furthermore, in most of the studies, results from mediation analyses were uninformative and yielded non-significant estimates for the mediation by short sleep duration due to low statistical power, the few exceptions being the inverse associations between father's occupational position and CHD in Constances and Whitehall II studies (see Supplementary material online, *Tables S6 and S7*), and a strong inverse association between adult occupational position and CHD in Whitehall II (see Supplementary material online, *Table S8*). Finally, we performed a meta-analysis using adult occupational position, sleep duration, and CHD, in order to examine which cohorts contributed the most to the pooled data associations (weights), and to examine the degree of heterogeneity across the cohorts (see Supplementary material online, *Figure S1*). We found a high inter-study heterogeneity for the SES-sleep duration gradient, while there were more consistent gradients for the associations between sleep duration and CHD, the adult occupational gradient in CHD (MTE), and the mediating effect by sleep duration (NIE) across the cohorts. The observed heterogeneity for the SES-sleep duration gradient may be explained by the different gradients found in GAZEL, SKIPOGH, and EPIPORTO studies when compared to the other cohorts. A possible explanation for these differences may be the lack of statistical power, as well as a weaker socioeconomic patterning of sleep duration in these studies.

3.6 Additional sensitivity analyses

3.6.1 Cox regression models for time-to-event event longitudinal analyses

As there is currently no methodology allowing to apply counterfactual mediation modelling to time-to-event longitudinal analysis, main analyses

Table 2 Association between SES indicators and sleep duration based on pooled cohort data

		OR (95% CI)	*P*-value	*N*
Men				
(*A*) Father's occupational position (unadj. adult occ.) (High: 7.15 h; Mid: 7.13 h; Low: 7.07 h)[a]	Short sleep (0–6 h)	1.18 [1.07; 1.31]	0.002	37 623
	Normal sleep (6–8.5 h) (ref. outcome)	1.00		
	Long sleep (>8.5 h)	1.01 [0.92; 1.11]	0.805	
(*B*) Father's occupational position (adj. adult occ.) (High: 7.15 h; Mid: 7.13 h; Low: 7.07 h)[a]	Short sleep (0–6 h)	1.12 [1.01; 1.24]	0.036	37 623
	Normal sleep (6–8.5 h) (ref. outcome)	1.00		
	Long sleep (>8.5 h)	0.97 [0.89; 1.07]	0.560	
(*C*) Adult occupational position (High: 7.11 h; Mid: 7.12 h; Low: 7.09 h)[a]	Short sleep (0–6 h)	2.22 [1.85; 2.66]	<0.001	37 623
	Normal sleep (6–8.5 h) (ref. outcome)	1.00		
	Long sleep (>8.5 h)	1.88 [1.59; 2.23]	<0.001	
Women				
(*A*) Father's occupational position (unadj. adult occ.) (High: 7.37 h; Mid: 7.41 h; Low: 7.37 h)[a]	Short sleep (0–6 h)	1.31 [1.20; 1.44]	<0.001	73 582
	Normal sleep (6–8.5 h) (ref. outcome)	1.00		
	Long sleep (>8.5 h)	1.07 [1.01; 1.14]	0.014	
(*B*) Father's occupational position (adj. adult occ.) (High: 7.37 h; Mid: 7.41 h; Low: 7.37 h)[a]	Short sleep (0–6 h)	1.24 [1.13; 1.36]	<0.001	73 582
	Normal sleep (6–8.5 h) (ref. outcome)	1.00		
	Long sleep (>8.5 h)	1.07 [1.01; 1.13]	0.028	
(*C*) Adult occupational position (High: 7.33 h; Mid: 7.46 h; Low: 7.27 h)[a]	Short sleep (0–6 h)	2.12 [1.82; 2.47]	<0.001	73 582
	Normal sleep (6–8.5 h) (ref. outcome)	1.00		
	Long sleep (>8.5 h)	1.14 [1.03; 1.27]	0.014	

CI, confidence interval; OR, odds ratio.
A. Multinomial logistic regression for the association between father's occupational position (predictor-Lowest vs. Highest) and three category sleep duration (outcome-Short: <6 h/night; Normal: ≥6–8.5/night; Long: ≥8.5 h/night), adjusted for age, cohort, study period, flexible working hours, and health behaviours.
B. Multinomial logistic regression for the association between father's occupational position (predictor-Lowest vs. Highest) and three category sleep duration (outcome-Short: <6 h/night; Normal: ≥6–8.5/night; Long: ≥8.5 h/night), adjusted for age, adult occupational position, cohort, study period, flexible working hours, and health behaviours.
C. Multinomial logistic regression for the association between adult occupational position (predictor-Lowest vs. Highest) and three category sleep duration (outcome-Short: <6 h/night; Normal: ≥6–8.5/night; Long: ≥8.5 h/night), adjusted for age, cohort, study period, flexible working hours, and health behaviours.
[a]Average sleep duration per SES categories.

presented in this study were performed cross-sectionally. To assess whether this may have biased our findings for the main associations examined, the one between adult SES and CVD and the one between sleep duration and CVD, we repeated the analysis using a longitudinal design in a cohort where repeated data were available (Whitehall II). Using time-to-event analyses fitted through Cox regression models, we observed that low occupational position and short sleep (baseline, wave 1) were systematically associated with a higher risk of CHD events through waves 1–8 when compared to higher adult occupational position, and normal or long sleep duration. There were no clear gradients in women and for stroke, likely due to lack of statistical power and insufficient number of events (see Supplementary material online, *Tables S9 and S10 and Figures S2 and S3*).

3.6.2 Multiple imputation for missing data for health behaviours

We performed further sensitivity analyses by imputing missing values for confounders using chained equations, and by investigating the potential confounding effects of four sleep quality indicators in the cohorts where this information was available. We observed that there were no important differences between the associations using the complete case data from those using imputed data (see Supplementary material online, *Tables S11 and S12* and *Tables 2* and *3*).

3.6.3 Confounding by sleep quality indicators

We also found that sleep quality indicators could act as potential confounders of the association between life-course SES, sleep duration, and CVD, as they were simultaneously associated with sleep duration and CVD in the counterfactual models (see Supplementary material online, *Tables S13 and S14*).

3.6.4 Comparison of studies using objective assessment vs. self-reported data

We further investigated whether the fact that several data were self-reported could have biased our results by comparing the associations between SES and sleep duration, sleep duration and CHD, the association between SES and CHD (MTE), and the mediation of this association by sleep duration between cohorts that used objective assessment of CHD and those with self-reported data (see Supplementary material online, *Tables S16–S18*). Results from cohorts that used objectively assessed data provided systematically stronger gradients than cohorts that were based on self-report, including meaningful mediation by short sleep duration (11.1%). However, we cannot conclude that these differences are exclusively attributed to the assessment method of CHD, as there were major regional differences between the two groups of cohorts.

3.6.5 Education as the main SES indicator

We also investigated to what extent education was associated with sleep duration, and whether the educational gradient in CVD outcomes was mediated by short sleep duration (see Supplementary material online, *Tables S19 and S20*). We observed that low education was associated with an increased risk of short sleep duration and a higher risk for CHD,

Table 3 Association between sleep duration and cardiovascular disorders based on pooled cohort data

	OR (95% CI)[a]	*P*-value	*N*
Men			
CHD			
Short sleep (0–6 h)	1.65 [1.41; 1.92]	<0.001	36 987
Normal sleep (6–8.5 h) (ref. predictor)	1.00		
Long sleep (>8.5 h)	1.02 [0.87; 1.19]	0.825	
Stroke			
Short sleep (0–6 h)	1.16 [0.84; 1.60]	0.381	36 759
Normal sleep (6–8.5 h) (ref. predictor)	1.00		
Long sleep (>8.5 h)	1.51 [1.17; 1.95]	0.001	
Women			
CHD			
Short sleep (0–6 h)	1.59 [1.28; 1.97]	<0.001	72 863
Normal sleep (6–8.5 h) (ref. predictor)	1.00		
Long sleep (>8.5 h)	1.24 [1.03; 1.49]	0.024	
Stroke			
Short sleep (0–6 h)	1.31 [1.03; 1.66]	0.028	72 819
Normal sleep (6–8.5 h) (ref. predictor)	1.00		
Long sleep (>8.5 h)	1.24 [1.06; 1.43]	0.005	

CHD, coronary heart disease; CI, confidence interval; OR, odds ratio.
[a]Logistic regression for the association between three category sleep duration (categorical predictor-Short: <6 h/night; Normal: ≥6–8.5/night; Long: ≥8.5 h/night) and cardiovascular disorders (outcome), adjusted for age, cohort, study period, flexible working hours, and health behaviours.

and that this association was significantly mediated by short sleep duration (9.2%). These associations and mediation were systematically weaker than those involving adult occupational position, and somewhat higher compared to associations using father's occupational position as main exposure.

3.6.6 Confounding/contribution by cardiometabolic disorders

Moreover, we also performed a series of additional analyses where associations between adult occupational position, sleep duration, and CHD were further adjusted for T2D and obesity (see Supplementary material online, *Tables S21–S23*). We observed that the associations between adult SES and short sleep, and between short sleep and CHD were attenuated upon adjustment for T2D and obesity, whereas the association between SES and CHD and the contribution of short sleep duration to this association were no longer significant.

3.6.7 Extreme sleep duration thresholds

Finally, we also examined the associations between adult SES, sleep duration, and CHD, using more extreme thresholds for sleep duration; 0–5 h for short sleep duration, and >10 h for long sleep duration (see Supplementary material online, *Tables S24–S26*). We generally found stronger gradients for the association between adult SES and extreme sleep duration, and for extreme sleep duration and CHD, in particular for the 0–5 h sleep duration category. These findings indicate that extreme sleep patterns are more prevalent among socially disadvantaged individuals, and that they have stronger effects on cardiovascular outcomes. Furthermore, we also observed that there was a somewhat weaker mediation by extreme short sleep duration (0–5 h) when compared to the former threshold (0–6 h), which was due to a weaker indirect effect (NIE).

4. Discussion

In this study, we found that both father's and adult occupational position were associated with abnormal sleep duration patterns, with stronger associations for adult than for early life SES, and for short sleep than for long sleep. Furthermore, abnormal sleep duration was associated with an increased risk of CVD, with stronger associations for short sleep than for long sleep. Finally, we observed that there were inverse associations between both life-course SES indicators and CHD, and that the association between adult occupational position and CHD was partly explained by short sleep duration, at least in men.

Our results on life-course socioeconomic gradient in short sleep duration tend to be in line with previous studies.[6,12,34] Former research has reported that adverse socioeconomic circumstances in childhood affect sleep health in adulthood through a latent effect, and that this association may be related to the fact that stressful childhood experiences lead to disrupted emotion regulation in adulthood, which in turn has a negative impact on adult sleep.[12,40] The adult occupational gradient in sleep duration may be related to the fact that individuals with lower grade occupations often have to combine several jobs, work in shifts, and live in noisy environments, thus experiencing greater levels of stress, altogether leading to sleep deprivation.[5,11,22] The stronger association between adult occupational position and short sleep duration when compared with father's occupational position and education may be related to the fact that adult occupational position directly acts on proximal exposures which affect sleep, such as poor housing, work stress, and recent psychosocial exposures, whereas father's occupational position and education likely act through more indirect effects that have occurred in early life.[7,40,41] Interestingly, we also observed that individuals with low father's and adult occupational position were more likely to have excessively long sleep duration, when compared to high SES individuals. However, while short sleep duration is more probably the consequence of adverse socioeconomic circumstances, later leading to adverse health outcomes, long sleep duration more probably results from pre-existing conditions, such as depression, that affect socially disadvantaged individuals more.[18–21,35]

Our study also confirms the relationship between short sleep duration and an increased risk of CHD and stroke.[13] Mechanistic studies suggest that chronic sleep deprivation may result in hypertension, elevated inflammation, and atherosclerosis through an aberrant activation of the sympathetic nervous system, as well as to an increased risk of T2D and obesity, altogether leading to cardiovascular events.[13,15,42] In a series of sensitivity analyses additionally adjusted for T2D and obesity, we observed that the association between adult SES and CHD, and the contribution of sleep duration were no longer significant, which may be attributed to potential confounding or even mediation, whereby T2D and obesity could constitute an additional intermediate step between chronic sleep deprivation, and the eventual occurrence of CHD or stroke. The potential role of inappropriate nutrition as an additional step in this chain of causation could not be investigated in our study and shall be the subject of additional research.

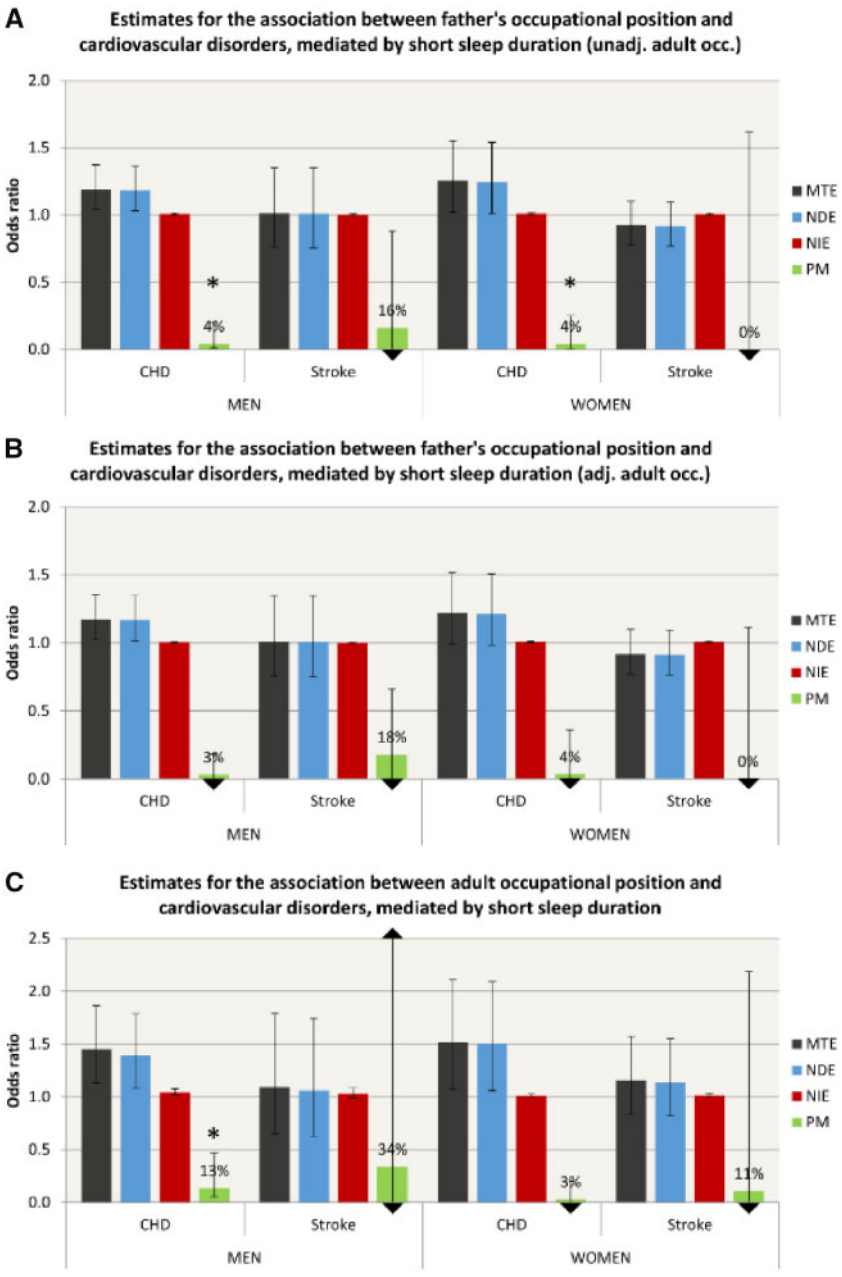

Figure 2 Counterfactual mediation estimates for the association between SES indicators and cardiovascular disorders, mediated by short sleep duration (<6 h/night), using pooled cohort data. (*A*) Association between father's occupational position and CVD, adjusted for age, cohort, study period, flexible working hours and health behaviours. (*B*) Association between father's occupational position and CVD, adjusted for age, adult occupational position, cohort, study period, flexible working hours and health behaviours. (*C*) Association between adult occupational position and CVD, adjusted for age, cohort, study period, flexible working hours and health behaviours. Sample size (*A*, *B*, *C*): Men: *N*=36 987 CHD, *N*=36 759 stroke; Women: *N*=72 863 CHD, *N*=72 819 stroke. CHD, coronary heart disease; MTE, marginal total effect (OR 95% CI); NDE: Natural direct effect (OR 95% CI); NIE, natural indirect effect (OR 95% CI); PM, proportion of the association between occupational position and cardiovascular disorders which is mediated by short sleep duration (*, significant mediation; lower ▼ and upper ▲ arrow indicate that CIs extend beyond the limits of the graph). This figure was realized with MSOffice-Excel.

We also found that long sleep duration is associated with an increased CVD risk, but to a lesser extent than short sleep, which is line with previous studies reporting that an excessively long sleep duration is also associated with adverse health outcomes, including CVD.[21] Nevertheless, the underlying mechanisms linking sleep duration and CVD are not the same for short and long sleep duration, and long sleep duration is often mentioned as a consequence of pre-existing illnesses rather than a cause.[18–21] Although there is no clear evidence that sleeping >8 h/night could lead to adverse health outcomes in healthy individuals, former research has often reported that major depressive disorder is a strong

predictor of excessive sleeping, suggesting that depression may confound the associations between long sleep and adverse health-related outcomes.[18]

Our study found that there was an inverse association between adult occupational position and CHD in both men and women, which is in line with previous research.[43] We also observed that short sleep duration significantly contributed to the adult occupational gradient in CHD in men, but not in women. The absence of mediation by short sleep duration in women may be related to the fact that there was a weaker adult occupational gradient in short sleep duration in women than in men. Overall, these gender-related differences may be explained by additional sociodemographic and socioeconomic factors, such as the fact that low SES women often have to combine the physical and psychosocial strain of manual, less paid jobs to that of numerous household responsibilities and stress, which eventually negatively affects their sleep and its health-restoring effects when compared to men.[11] Furthermore, we found an inverse association between father's occupational position and CHD, which was only marginally decreased upon accounting for adult occupational position. These findings indicate that father's occupational position likely affects CHD through latent mechanisms, whereby adverse socioeconomic circumstances in early life have left permanent biological imprints that translate into higher CHD risk in later life.[37,44] Finally, we also observed that there were no associations between both life-course SES indicators and stroke, which may be related to a differential socioeconomic patterning, and different pathophysiology and risk factors for these two CVDs.[45,46] Another explanation may be related to a lack of statistical power, as the occurrence of stroke was much lower than the occurrence of CHD events throughout the included cohorts.

4.1 Strengths and limitations

Our study has several strengths. First, to our knowledge this is the first study to investigate the contribution of sleep duration to the association between life-course SES and CVD. Second, we used data from eight cohorts conducted in four European countries, involving >111 000 participants. Our study also has some limitations to acknowledge. First, the demographic, epidemiological, and methodological differences between the eight cohorts represent a vast challenge in terms of data harmonization, and may result in important heterogeneity, particularly concerning the occurrence and assessment of cardiovascular outcomes. Although the difference in CHD prevalence between the Northern (Whitehall II, ELSA) and the Southern European cohorts (Constances, E3N, GAZEL, SKIPOGH, COLAUS) may be attributed to the well-established North–South gradient in CHD prevalence in Europe,[47] potential bias resulting from a differential reporting of cardiovascular outcomes cannot be excluded. In particular, the absence of objectively assessed health-related outcomes and the lack of access to medical records may result in important self-report and recall biases, eventually yielding differential SES-CVD and sleep duration-CVD gradients across included studies.[48,49] These types of systematic errors represent an important issue in epidemiological studies, especially given the fact that factors such as education and other SES variables were found to influence recall bias in retrospective cohorts.[48] Furthermore, another limitation related to procurement methodology is the systematic difference observed between self-reported and objectively measured sleep duration, which could not be accounted for in the present analyses.[50] Additional issues may be related to the statistical methodology applied in this study. In particular, cross-sectional analyses do not allow determining the causal direction of associations, which can be a particular issue for analyses involving sleep disturbances and health-related outcomes, as the relation between these two factors is not exclusively unidirectional. However, we managed to address this issue by performing a series of longitudinal analyses in Whitehall II study. Furthermore, apart from the contribution of sleep duration, we must acknowledge the role of other potential confounders or mediators of the socioeconomic gradient in CVD, including hypertension, hyperlipidaemia, life-related factors, working hours, psychosocial exposures, and environmental factors, whose contribution was not examined in this multi-cohort study. Finally, the lack of information on objectively measured sleep disorders (i.e. sleep-disordered breathing) as well as sleep quality indicators in the majority of cohorts may be another limiting factor in this study, as sleep apnoea and sleep quality have been found to be associated with CVD risk as well as sleep duration, and could potentially confound the causal pathways involving SES, sleep duration, and CVD.[51–53]

4.2 Conclusion

In summary, this large pan-European analysis suggests that short sleep duration is a potential mechanism underlying the association between adult occupational position and CHD. Additional longitudinal analyses shall be conducted to further investigate the causal relationship between SES, sleep duration, and CVD. Finally, the role of other sleep features, in particular sleep quality, shall further be investigated as potential confounders of the associations between SES, sleep duration, and CVD.

Supplementary material

Supplementary material is available at *Cardiovascular Research* online.

Authors' contributions

S.S., D.P., C.C., and M.C.H. designed the study. J.H.R., M.K.-I., P.Vi., M.K., M.G., F.R., A.D'E., M.B., P.Vo., H.B., S.F., M.G., M.Z., A.S., C.D., R.H., and S.S. actively contributed to data acquisition and harmonization. D.P., S.N., S.S., C.C., and M.C.H. analysed the data. D.P., S.S., C.C., M.C.H., J.H.R., C.D.M., M.K.-I., P.Vi., M.K., S.N., M.G., F.R., A.D'E., M.B., P.Vo., H.B., S.F., M.G., M.Z., A.S., C.D., and R.H. critically revised the article.

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References

1. Adler NE, Boyce WT, Chesney MA, Folkman S, Syme SL. Socioeconomic inequalities in health: no easy solution. *JAMA* 1993;**269**:3140–3145.
2. Smith GD, Hart C. Life-course socioeconomic and behavioral influences on cardiovascular disease mortality: the collaborative study. *Am J Public Health* 2002;**92**:1295–1298.
3. Matthews KA, Gallo LC, Taylor SE. Are psychosocial factors mediators of socioeconomic status and health connections? *Ann NY Acad Sci* 2010;**1186**:146–173.
4. Petrovic D, de Mestral C, Bochud M, Bartley M, Kivimäki M, Vineis P, Mackenbach J, Stringhini S. The contribution of health behaviors to socioeconomic inequalities in health: a systematic review. *Prev Med* 2018;**113**:15.
5. Anders MP, Breckenkamp J, Blettner M, Schlehofer B, Berg-Beckhoff G. Association between socioeconomic factors and sleep quality in an urban population-based sample in Germany. *Eur J Public Health* 2014;**24**:968–973.
6. Jarrin DC, McGrath JJ, Silverstein JE, Drake C. Objective and subjective socioeconomic gradients exist for sleep quality, sleep latency, sleep duration, weekend oversleep, and daytime sleepiness in adults. *Behav Sleep Med* 2013;**11**:144–158.
7. Stamatakis KA, Kaplan GA, Roberts RE. Short sleep duration across income, education, and race/ethnic groups: population prevalence and growing disparities during 34 years of follow-up. *Ann Epidemiol* 2007;**17**:948–955.
8. Van Cauter E, Spiegel K. Sleep as a mediator of the relationship between socioeconomic status and health: a hypothesis. *Ann NY Acad Sci* 1999;**896**:254–261.
9. Hill TD, Burdette AM, Hale L. Neighborhood disorder, sleep quality, and psychological distress: testing a model of structural amplification. *Health Place* 2009;**15**:1006–1013.
10. Grandner MA, Patel NP, Gehrman PR, Xie D, Sha D, Weaver T, Gooneratne N. Who gets the best sleep? Ethnic and socioeconomic factors related to sleep complaints. *Sleep Med* 2010;**11**:470–478.
11. Stringhini S, Haba-Rubio J, Marques-Vidal P, Waeber G, Preisig M, Guessous I, Bovet P, Vollenweider P, Tafti M, Heinzer R. Association of socioeconomic status with sleep disturbances in the Swiss population-based CoLaus study. *Sleep Med* 2015;**16**:469–476.
12. Tomfohr LM, Ancoli-Israel S, Dimsdale JE. Childhood socioeconomic status and race are associated with adult sleep. *Behav Sleep Med* 2010;**8**:219–230.
13. Mullington JM, Haack M, Toth M, Serrador JM, Meier-Ewert HK. Cardiovascular, inflammatory, and metabolic consequences of sleep deprivation. *Prog Cardiovasc Dis* 2009;**51**:294–302.
14. Ayas NT, White DP, Manson JE, Stampfer MJ, Speizer FE, Malhotra A, Hu FB. A prospective study of sleep duration and coronary heart disease in women. *Arch Intern Med* 2003;**163**:205–209.
15. Cappuccio FP, Miller MA. Sleep and Cardio-Metabolic Disease. *Curr Cardiol Rep* 2017;**19**:110.
16. Motivala SJ, Irwin MR. Sleep and immunity: cytokine pathways linking sleep and health outcomes. *Curr Dir Psychol Sci* 2007;**16**:21–25.
17. Born J, Muth S, Fehm H. The significance of sleep onset and slow wave sleep for nocturnal release of growth hormone (GH) and cortisol. *Psychoneuroendocrinology* 1988;**13**:233–243.
18. Patel SR, Malhotra A, Gottlieb DJ, White DP, Hu FB. Correlates of long sleep duration. *Sleep* 2006;**29**:881.
19. Knutson KL, Turek FW. The U-shaped association between sleep and health: the 2 peaks do not mean the same thing. *Sleep* 2006;**29**:878–879.
20. Stranges S, Dorn JM, Shipley MJ, Kandala N-B, Trevisan M, Miller MA, Donahue RP, Hovey KM, Ferrie JE, Marmot MG, Cappuccio FP. Correlates of short and long sleep duration: a cross-cultural comparison between the United Kingdom and the United States: the Whitehall II Study and the Western New York Health Study. *Am J Epidemiol* 2008;**168**:1353–1364.
21. Buxton OM, Marcelli E. Short and long sleep are positively associated with obesity, diabetes, hypertension, and cardiovascular disease among adults in the United States. *Soc Sci Med* 2010;**71**:1027–1036.
22. Sekine M, Chandola T, Martikainen P, McGeoghegan D, Marmot M, Kagamimori S. Explaining social inequalities in health by sleep: the Japanese civil servants study. *J Public Health* 2006;**28**:63–70.
23. Stringhini S, Carmeli C, Jokela M, Avendaño M, Muennig P, Guida F, Ricceri F, d'Errico A, Barros H, Bochud M, Chadeau-Hyam M, Clavel-Chapelon F, Costa G, Delpierre C, Fraga S, Goldberg M, Giles GG, Krogh V, Kelly-Irving M, Layte R, Lasserre AM, Marmot MG, Preisig M, Shipley MJ, Vollenweider P, Zins M, Kawachi I, Steptoe A, Mackenbach JP, Vineis P, Kivimäki M, Alenius H, Avendano M, Barros H, Bochud M, Carmeli C, Carra L, Castagné R, Chadeau-Hyam M, Clavel-Chapelon F, Costa G, Courtin E, Delpierre C, d'Errico A, Dugué P-A, Elliott P, Fraga S, Gares V, Giles G, Goldberg M, Greco D, Hodge A, Irving MK, Karisola P, Kivimäki M, Krogh V, Lang T, Layte R, Lepage B, Mackenbach J, Marmot M, McCrory C, Milne R, Muennig P, Nusselder W, Panico S, Petrovic D, Polidoro S, Preisig M, Raitakari O, Ribeiro AI, Ribeiro AI, Ricceri F, Robinson O, Valverde JR, Sacerdote C, Satolli R, Severi G, Shipley MJ, Stringhini S, Tumino R, Vineis P, Vollenweider P, Zins M. Socioeconomic status and the 25× 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1· 7 million men and women. *Lancet* 2017;**389**:1229–1237.

24. Zins M, Bonenfant S, Carton M, Coeuret-Pellicer M, Guéguen A, Gourmelen J, Nachtigal M, Ozguler A, Quesnot A, Ribet C, Rodrigues G, Serrano A, Sitta R, Brigand A, Henny J, Goldberg M. The CONSTANCES cohort: an open epidemiological laboratory. *BMC Public Health* 2010;**10**:479.
25. Clavel-Chapelon F, Group E. Cohort profile: the French E3N cohort study. *Int J Epidemiol* 2015;**44**:801–809.
26. Goldberg M, Leclerc A, Zins M. Cohort profile update: the GAZEL cohort study. *Int J Epidemiol* 2015;**44**:77–77g.
27. Marmot M, Brunner E. Cohort profile: the Whitehall II study. *Int J Epidemiol* 2005;**34**: 251–256.
28. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English longitudinal study of ageing. *Int J Epidemiol* 2013;**42**:1640–1648.
29. Petrovic D, Pivin E, Ponte B, Dhayat N, Pruijm M, Ehret G, Ackermann D, Guessous I, Younes SE, Pechère-Bertschi A, Vogt B, Mohaupt M, Martin P-Y, Paccaud F, Burnier M, Bochud M, Stringhini S. Sociodemographic, behavioral and genetic determinants of allostatic load in a Swiss population-based study. *Psychoneuroendocrinology* 2016;**67**:76–85.
30. Fraga S, Marques-Vidal P, Vollenweider P, Waeber G, Guessous I, Paccaud F, Barros H, Stringhini S. Association of socioeconomic status with inflammatory markers: a two cohort comparison. *Prev Med* 2015;**71**:12–19.
31. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Smith GD. Indicators of socioeconomic position (part 1). *J Epidemiol Commun Health* 2006;**60**:7–12.
32. Stringhini S, Batty GD, Bovet P, Shipley MJ, Marmot MG, Kumari M, Tabak AG, Kivimäki M. Association of lifecourse socioeconomic status with chronic inflammation and type 2 diabetes risk: the Whitehall II prospective cohort study. *PLoS Med* 2013;**10**:e1001479.
33. d'Errico A, Ricceri F, Stringhini S, Carmeli C, Kivimaki M, Bartley M, McCrory C, Bochud M, Vollenweider P, Tumino R. Socioeconomic indicators in epidemiologic research: a practical example from the LIFEPATH study. *PLoS One* 2017;**12**:e0178071.
34. Ertel KA, Berkman LF, Buxton OM. Socioeconomic status, occupational characteristics, and sleep duration in African/Caribbean immigrants and US White health care workers. *Sleep* 2011;**34**:509.
35. Steptoe A, Peacey V, Wardle J. Sleep duration and health in young adults. *Arch Intern Med* 2006;**166**:1689–1692.
36. Patel SR, Ayas NT, Malhotra MR, White DP, Schernhammer ES, Speizer FE, Stampfer MJ, Hu FB. A prospective study of sleep duration and mortality risk in women. *Sleep* 2004;**27**:440–444.
37. Marmot M, Shipley M, Brunner E, Hemingway H. Relative contribution of early life and adult socioeconomic factors to adult morbidity in the Whitehall II study. *J Epidemiol Commun Health* 2001;**55**:301–307.
38. Valeri L, VanderWeele TJ. Mediation analysis allowing for exposure–mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. *Psychol Methods* 2013;**18**:137.
39. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? *Int J Methods Psychiatr Res* 2011;**20**: 40–49.
40. Gregory AM, Caspi A, Moffitt TE, Poulton R. Family conflict in childhood: a predictor of later insomnia. *Sleep* 2006;**29**:1063–1067.
41. Marmot M, Wilkinson R. *Social Determinants of Health*. Oxford: OUP; 2005.
42. Kato M, Phillips BG, Sigurdsson G, Narkiewicz K, Pesek CA, Somers VK. Effects of sleep deprivation on neural circulatory control. *Hypertension* 2000;**35**: 1173–1175.
43. Stringhini S, Dugravot A, Shipley M, Goldberg M, Zins M, Kivimäki M, Marmot M, Sabia S, Singh-Manoux A. Health behaviours, socioeconomic status, and mortality: further analyses of the British Whitehall II and the French GAZEL prospective cohorts. *PLoS Med* 2011;**8**:e1000419.
44. Kuh D, Ben-Shlomo Y, Lynch J, Hallqvist J, Power C. Life course epidemiology. *J Epidemiol Commun Health* 2003;**57**:778–783.
45. Salonen JT. Socioeconomic status and risk of cancer, cerebral stroke, and death due to coronary heart disease and any disease: a longitudinal study in eastern Finland. *J Epidemiol Commun Health* 1982;**36**:294–297.
46. Rogot E, Hrubec Z. Trends in mortality from coronary heart disease and stroke among US veterans; 1954–1979. *J Clin Epidemiol* 1989;**42**:245–256.
47. Müller-Nordhorn J, Binting S, Roll S, Willich SN. An update on regional variation in cardiovascular mortality within Europe. *Eur Heart J* 2008;**29**:1316–1326.
48. Coughlin SS. Recall bias in epidemiologic studies. *J Clin Epidemiol* 1990;**43**:87–91.
49. Kuper H, Marmot M. Job strain, job demands, decision latitude, and risk of coronary heart disease within the Whitehall II study. *J Epidemiol Commun Health* 2003;**57**: 147–153.
50. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? *Epidemiology* 2008;**19**:838–845.
51. Gami AS, Hodge DO, Herges RM, Olson EJ, Nykodym J, Kara T, Somers VK. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. *J Am Coll Cardiol* 2007;**49**:565–571.
52. Hoevenaar-Blom MP, Spijkerman AMW, Kromhout D, van den Berg JF, Verschuren W. Sleep Duration and Sleep Quality in Relation to 12-Year Cardiovascular Disease Incidence: the MORGEN Study. *Sleep* 2011;**34**:1487–1492.
53. Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. *Am J Respir Crit Care Med* 2002;**166**:159–165.

Translational perspective

This study, including data on 111 205 participants from eight cohorts in four European countries, suggests that inadequate sleep accounts for a meaningful proportion of the socioeconomic gradient in CHD, at least in men. With inadequate sleep increasingly being considered an important cardiovascular risk factor in its own terms, our study additionally points to its potential role in social inequalities in cardiovascular disease, and should encourage health professionals to consider these factors as major contributors to the pathophysiology of CHD.