A Prospective Study of Change in Sleep Duration: Associations with Mortality in the Whitehall II Cohort

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Study Objectives: Although sleep curtailment has become widespread in industrialised societies, little work has examined the effects on mortality of change in sleep duration. We investigated associations of sleep duration and change in sleep duration with all-cause, cardiovascular, and non-cardiovascular mortality.

Design: Prospective cohort study. Data are from baseline (Phase 1, 1985-88) and Phase 3 (1991-93), with mortality follow-up of 17 and 12 years respectively.

Setting: The Whitehall II study of 10,308 white-collar British civil servants aged 35-55 at baseline.

Participants: 9,781 participants with complete data were included in the analyses at Phase 1, and 7,729 of the same participants were included in the analyses at Phase 3 and the analyses of change in sleep duration.

Interventions: None.

Measurements and Results U-shaped associations were observed between sleep (≤5, 6, 7, 8, ≥9 hours) at Phase 1 and Phase 3 and subsequent all-cause, cardiovascular, and non-cardiovascular mortality. A decrease in sleep duration among participants sleeping 6, 7, or 8 hours at baseline was associated with cardiovascular mortality, hazard ratio 2.4 (95% confidence intervals 1.4-4.1). However, an increase in sleep duration among those sleeping 7 or 8 hours at baseline was associated with non-cardiovascular mortality, hazard ratio 2.1 (1.4-3.1). Adjustment for the socio-demographic factors, existing morbidity, and health-related behaviours measured left these associations largely unchanged.

Conclusions This is the first study to show that both a decrease in sleep duration and an increase in sleep duration are associated with an increase in mortality via effects on cardiovascular death and non-cardiovascular death respectively.

Keywords: sleep duration, change in sleep duration, all-cause mortality, cardiovascular mortality, non-cardiovascular mortality, white collar.

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INTRODUCTION

A CONSIDERABLE NUMBER OF STUDIES HAS EXAMINED THE EFFECT OF SLEEP DURATION ON MORTALITY.[1-13] ABOUT HALF OF THESE STUDIES DEMONSTRATE a U-shaped association between sleep and all-cause mortality in both sexes.[1-3,5,7,12,13] However, other studies have not found such uniform effects,[6,8-11] or have found no association.[4] In addition to all-cause mortality, a number of these studies have examined associations between sleep duration and cause-specific mortality.[3,7-11,13] Most have examined mortality from cardiovascular diseases and either non-cardiovascular death or death from cancer or other causes. Findings for these causes of death are less consistent than for all-cause mortality. However, the two largest studies, one in each sex, demonstrate U-shaped associations between sleep and cardiovascular mortality in men and sleep and non-cardiovascular mortality in both sexes.[7,13]

Fewer hours sleep and greater levels of sleep disturbance have become widespread in industrialised societies.[14] This change, largely the result of sleep curtailment to create more time for leisure and shift work, has meant that reports of fatigue, tiredness and excessive daytime sleepiness are more common than a few decades ago.[15] Sleep represents the daily process of physiological restitution and recovery, and lack of sleep has far-reaching effects on endocrinology, immunology, and metabolism.[14] Despite this, hardly any research appears to have examined the effects of change in sleep duration on mortality. Sleep measures obtained on two occasions from a cohort of Scottish workers showed no associations between increased or decreased sleep and all-cause or cardiovascular mortality in either sex.[9]

In the present study we examine sleep duration and change in sleep duration as predictors of all-cause, cardiovascular, and non-cardiovascular mortality in longitudinal data from the Whitehall II study of British civil servants.

METHODS

The target population for the Whitehall II study was all London-based office staff aged 35 to 55 years working in 20 civil service departments in 1985. With a response rate of 73%, the final cohort consisted of 10,308 participants; 3,413 women and 6,895 men. Although mostly white-collar, participants covered a wide range of grades from messenger to Ministerial Permanent Secretaries.[16] Baseline screening (Phase 1), between late 1985 and ear-

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ly 1988, involved a clinical examination and a self-administered questionnaire. Data collection at Phase 3 (1992-3) also included a clinical examination (8,104 participants) and questionnaire (8,642 participants).

Measures

Sleep: Sleep duration was measured at Phase 1 using a single question "How many hours of sleep do you have on an average week night?" Response categories were 5 hours or less, 6, 7, 8, and 9 hours or more. At Phase 3, sleep duration was determined from the question "On an average weekday how many hours do you spend on the following activities; (a) Work, (b) Time with family, (c) Sleep?" Response categories were 1 to 12 hours. These categories were collapsed to form categories identical to those at Phase 1. Participants taking sleep medication were identified through a questionnaire item which requested participants to indicate, from a list including sleeping pills, those doctor-prescribed medicines they had taken during the last 14 days. These participants (147 at Phase 1 and 91 at Phase 3) were included in the category ≤5 hours sleep.

For the examination of changes in sleep duration between Phases 1 and 3 and mortality, participants were divided into 3 categories. We decided not to look at change in sleep duration for the few (68 participants, 2 deaths) who slept ≥9 hours at Phase 1. For the remaining 4 sleep-duration categories at Phase 1 we grouped the participants into those sleeping less, the same, or more hours at Phase 3. The 3 estimates for reduced sleep duration for the categories 6, 7, and 8 hours were pooled to form the category "decrease from 6, 7, or 8 hours." For increased sleep durations we hypothesised that an increase from 5 or 6 hours at Phase 1 would have a beneficial effect on mortality, whereas increases from 7 or 8 hours would have a detrimental effect. We therefore created 2 categories; "increase from 5 or 6 hours" at Phase 1, and "increase from 7 or 8 hours" at Phase 1. In each of the three sleep categories, we compared those sleeping less hours or more hours with the reference group, which in each case was comprised of participants who slept the same number of hours at Phase 3 as at Phase 1. For example, for the category "increase from 5 or 6 hours" the reference group was participants who slept either 5 or 6 hours at both phases.

Mortality: Mortality follow-up was available through the National Health Services Central Registry until 30th September 2004; a mean of 17.1 years from Phase 1 and a mean of 11.8 years from Phase 3. Registration of death within 5 days is a legal requirement in the U.K., so participants not registered can be assumed to be alive. Exceptions to this are the very small minority who emigrate or become unregistered with the National Health Service for other reasons. Dates of embarkation and deregistration are received from the National Health Services Central Registry and mortality follow-up is censored at these dates. Death certificates were coded using the 9th and 10th revisions of the International Classification of Disease (ICD) and categorised as cardiovascular disease ICD-9 codes 390-459 and ICD-10 codes I00-I99 and non-cardiovascular disease, all remaining codes.

Covariates and Risk Factors: (i) *Sociodemographic factors*: Age, employment grade, and marital status were derived from the Phase 1 and Phase 3 questionnaires. (ii) *Existing morbidity*: Psychiatric morbidity was assessed using a modified GHQ score derived from the 30-item General Health Questionnaire (GHQ) with the sleep specific questions removed; higher GHQ scores indicate greater morbidity. Self-rated health over the past 12 months was categorised as average, poor, or very poor versus good or very good. The presence or absence of 5 conditions; diabetes, diagnosed heart trouble, ECG abnormalities, hypertension, and/or respiratory illness were scored separately as 0/1. To describe the overall association of these conditions with sleep duration they were collapsed to form a composite physical illness indicator, again scored 0/1 depending on whether the participant had none, or had one or more of the 5 conditions. However, in all the remaining analyses the presence or absence of each condition was entered as a separate variable. Prevalent CHD was determined by self-report and confirmed in clinical records. (iii) *Cardiovascular risk factors*: The following risk factors were measured at the Phase 1 and 3 screening examinations, Body Mass Index (BMI) as weight in kilograms (kg)/height in metres $(m)^2$, systolic and diastolic blood pressure in millimetres of mercury (mm Hg), and total cholesterol concentration in millimoles/litre (mmol/L). (iv) *Health-related behaviors*: Participants were categorised as never smoker, ex-smoker, pipe and/or cigar only, or current cigarette smoker (manufactured or hand-rolled cigarettes). Adjustment for smoking included the number of cigarettes smoked per day. High alcohol consumption was defined as ≥14 units/week for women and ≥22 units/week for men. Leisure time physical activity was categorised by energy utilisation. The little exercise category comprised those who did <1 hour of moderate or vigorous activity per week. Further details of these methods have been published previously.[16] It should be noted that categorical covariates, such as self-rated health and smoking, were treated as dichotomous variables solely for the descriptive statistics of risk factors versus sleep duration. In the analyses of associations with mortality all the categories for these covariates were included in full.

Ethical Approval

Ethical approval for the Whitehall II study was obtained from the University College London Medical School committee on the ethics of human research.

Study Sample and Statistical Analysis

Of the 10,308 participants at baseline, 8,354 (81%), responded at Phase 3. Of the 1954 (19%) who responded at Phase 1 but did not respond at Phase 3, 97 (5%) were nonresponders because they had died before follow-up. The remaining 95% were nonresponders for other reasons (incomplete response, refusal, could not locate, etc.). Removal of participants with missing data left 9,781 women and men in the analyses at Phase 1, and 7,729 in the analyses at Phase 3 and in the analyses of change in sleep duration. Age-standardized mortality rates per 1000 person years were calculated for the 566 deaths from Phase 1 and the 292 deaths from Phase 3 to the 30th September 2004.

Cox proportional hazards models with follow-up period as the time scale were used to determine the hazard ratio (and 95% confidence interval), using 7 hours of sleep as the reference category. As results were virtually identical in women and men, pooled estimates are presented. Differences in proportions were tested for significance using the Mantel-Haenszel test. For continuous

Table 1—Mortality by Number of Hours Sleep at Phase 1 and Phase 3

Hours of sleep	≤5 hours	6 hours	7 hours	8 hours	≥9 hours
	Phase 1 (No. participants=9,781, Total deaths=566)				
Number of participants (deaths: all causes)	587 (56)	2642 (160)	4884 (256)	1579 (87)	89 (7)
Hazard ratio (95% CI) - Age adjusted	1.61 (1.20–2.15)	1.11 (0.91–1.35)	reference	1.08 (0.85–1.38)	1.77 (0.84–3.76)
- Fully adjusted #	1.24 (0.92–1.67)	1.00 (0.82–1.22)	reference	1.07 (0.84–1.36)	1.54 (0.72–3.28)
Number of participants (CVD deaths)	585 (19)	2642 (47)	4881 (69)	1579 (31)	89 (2)
Hazard ratio (95% CI) - Age adjusted	2.11 (1.26-3.52)	1.22 (0.84–1.76)	reference	1.47 (0.96–2.25)	2.18 (0.53 –8.92)
- Fully adjusted #	1.17 (0.68–2.00)	1.01 (0.69–1.48)	reference	1.39 (0.91–2.14)	1.53 (0.37–6.32)
Number of participants (non-CVD deaths)	585 (35)	2642 (113)	4881 (184)	1579 (56)	89 (5)
Hazard ratio (95% CI) - Age adjusted	1.38 (0.96–1.99)	1.09 (0.86–1.37)	reference	0.95 (0.71–1.29)	1.66 (0.68–4.05)
- Fully adjusted #	1.18 (0.81–1.71)	1.02 (0.80–1.29)	reference	0.96 (0.71–1.30)	1.61 (0.66–3.94)
	Phase 3 (No. participants=7,729, Total deaths=292)				
Number of participants (deaths: all causes)	420 (29)	1626 (61)	3501 (112)	1950 (74)	232 (16)
Hazard ratio (95% CI) - Age adjusted	2.07 (1.38–3.13)	1.21 (0.89–1.66)	reference	1.13 (0.85–1.52)	2.00 (1.18–3.38)
- Fully adjusted #	1.78 (1.17–2.71)	1.13 (0.83–1.55)	reference	1.11 (0.82–1.48)	1.95 (1.15–3.31)
Number of participants (CVD deaths)	419 (13)	1626 (22)	3499 (34)	1949 (14)	232 (6)
Hazard ratio (95% CI) - Age adjusted	3.12 (1.64–5.94)	1.48 (0.86–2.53)	reference	0.69 (0.37–1.28)	2.31 (0.97–5.51)
- Fully adjusted #	2.25 (1.15–4.38)	1.22 (0.70–2.10)	reference	0.64 (0.34–1.20)	2.23 (0.93–5.38)
Number of participants (non-CVD deaths)	419 (15)	1625 (38)	3499 (76)	1949 (59)	232 (10)
Hazard ratio (95% CI) - Age adjusted	1.57 (0.90–2.74)	1.10 (0.75–1.63)	reference	1.35 (0.95–1.89)	1.88 (0.97–3.64)
- Fully adjusted #	1.43 (0.81–2.52)	1.07 (0.72–1.58)	reference	1.34 (0.96–1.89)	1.88 (0.97–3.66)

Fully adjusted hazard ratios are adjusted for:- age, sex, marital status, employment grade, smoking status, physical activity, alcohol consumption, self-rated health, body mass index, systolic blood pressure, cholesterol, physical illness, modified GHQ score, prevalent CHD

variables least squares means were calculated for the age-adjusted means. Tests of differences across sleep duration categories were calculated using analysis of covariance. All analyses were conducted using the SAS statistical program (SAS Institute, Cary, NC, USA).

RESULTS

Table 1 shows age-adjusted hazard ratios for all-cause, cardiovascular and non-cardiovascular mortality across each of the 5 categories of sleep at Phase 1 and Phase 3, using 7 hours sleep as the reference category. For each outcome, a U-shaped association is observed at both Phases, which is slightly stronger at Phase 3 than at baseline. At Phases 1 and 3 the proportion of participants who report short sleep (≤5 hours) is very similar, 6.0 and 5.4% respectively. However, the distribution of participants across the sleep categories changes between Phases 1 and 3. A greater proportion report more than 7 hours sleep at Phase 3, 28.2% compared with 17.1% at Phase 1, and the proportion that reports long sleep (≥9 hours) increases from 0.9% to 3.0%.

The distribution of sociodemographic factors, existing morbidity and health-related behaviours across the 5 categories of sleep at Phase 1 and Phase 3 are presented in Tables 2A and 2B respectively. An inverse association between age and sleep duration (older age - shorter sleep) was observed at Phase 1, but by Phase 3, in common with all the associations with employment grade, the association was U-shaped. Further inverse associations with sleep were observed for cigarette smoking (women only); GHQ score (Phase 1 only); and physical illness and prevalent CHD (men only, Phase 1 only). There was a uniformly positive association between sleep duration and marital status in women, such that marriage was associated with increased likelihood of longer sleep duration. In men, being married was more likely to be associated with 7 to 8 hours of sleep. The association between BMI and sleep was complex. A higher BMI was associated with short and long sleep in women at Phase 1, but only with short sleep in men. By Phase 3 there was no association in women, but a U-shaped association had emerged in men. All the remaining covariates conformed to the classic U-shape already observed for mortality, with the exception of high alcohol (women, Phase 1; both sexes, Phase 3), systolic blood pressure (Phase 1 only), diastolic blood pressure (women only), and cholesterol, which were unrelated to sleep.

Associations between sleep at baseline and subsequent mortality were attenuated after adjustment for the covariates and risk factors measured (Table 1). In every case, adjustment produced greater attenuation of the short sleep-mortality association than of the long sleep-mortality association. To check that associations were not due to ill-health induced sleep problems prior to death we repeated the analyses for deaths in the first five years of follow-up and excluding the first five years of follow-up. At both Phases analyses of these early and late follow-up periods produced U-shaped associations similar to those presented in Table 1 (data available on request).

Table 3 shows the distribution of all-cause mortality from Phase 3 by sleep duration at Phase 1 and Phase 3. The most con-

Table 2A—Characteristics[+] and Risk Factors by Number of Hours Sleep at Phase 1

		Hours of sleep					P-value for
		≤5 hours	6 hours	7 hours	8 hours	≥9 hours	heterogeneity
Number of subjects		587	2642	4884	1579	87	
Age, yr		46.4 (0.2)	44.9 (0.1)	44.1 (0.1)	44.0 (0.2)	43.4 (0.6)	<0.001
Sex (% female)		42.5	30.9	30.0	37.1	48.0	<0.001
Employment grade (% low grade)	- Women	52.7	44.8	45.4	52.4	70.4	<0.001
	- Men	20.3	10.5	7.0	9.9	19.2	<0.001
Marital status (% Married)	- Women	52.7	59.0	62.5	65.5	68.8	0.004
	- Men	71.2	80.1	82.6	80.4	63.0	<0.001
Current cigarette smoker (%)	- Women	26.0	25.3	23.5	18.0	15.4	0.009
	- Men	20.4	17.5	14.4	15.3	21.7	0.002
High alcohol (%)	- Women	7.0	9.7	11.3	8.4	9.9	0.32
	- Men	23.4	20.2	18.0	15.8	18.4	0.007
Little exercise (%)	- Women	29.4	27.2	26.4	30.4	57.7	<0.001
	- Men	19.9	12.0	9.4	9.8	34.9	<0.001
Modified GHQ score	- Women	6.6 (0.3)	4.2 (0.2)	3.3 (0.1)	2.6 (0.2)	2.7 (0.8)	<0.001
	- Men	5.5 (0.3)	3.4 (0.1)	2.8 (0.1)	2.8 (0.2)	1.9 (0.7)	<0.001
Self-rated health (% ≤ average)	- Women	51.5	39.7	32.0	31.6	41.4	<0.001
	- Men	36.4	23.6	20.3	21.3	36.7	<0.001
Physical Illness Indicator (% positive)	- Women	24.6	20.4	16.7	17.6	31.8	0.006
	- Men	27.8	19.8	19.2	16.6	12.3	0.001
Prevalent CHD (% positive)	- Women	6.8	5.9	4.0	3.2	5.6	0.02
	- Men	6.2	4.0	3.7	3.3	3.2	0.07
BMI (kg/m^{-2})	- Women	25.3 (0.2)	24.9 (0.1)	24.4 (0.1)	24.8 (0.1)	25.1 (0.5)	0.01
	- Men	25.1 (0.2)	24.9 (0.1)	24.4 (0.1)	24.4 (0.1)	24.5 (0.5)	<0.001
Systolic blood pressure (mmHg)	- Women	120.9 (1.0)	120.2 (0.5)	119.7 (0.4)	119.0 (0.6)	118.8 (2.1)	0.92
	- Men	125.8 (0.9)	125.0 (0.3)	124.2 (0.2)	125.2 (0.5)	125.0 (2.0)	0.09
Diastolic blood pressure (mmHg)	- Women	76.6 (0.7)	75.0 (0.3)	74.5 (0.3)	74.7 (0.4)	74.3 (1.6)	0.21
	- Men	79.0 (0.6)	78.2 (0.2)	77.5 (0.2)	78.1 (0.3)	79.8 (1.4)	0.01
Cholesterol (mmol/L)	- Women	5.97 (0.08)	5.88 (0.04)	5.86 (0.03)	5.89 (0.05)	6.02 (0.18)	0.65
	- Men	5.97 (0.07)	5.99 (0.03)	6.00 (0.02)	6.02 (0.04)	6.14 (0.16)	0.91

[+] Figures are means (standard errors) for continuous measures and percentages for categorical measures. All estimates (except for age) are adjusted for age.

sistent patterns in these data are the high mortality rates among participants who moved into the short sleep or long sleep categories by Phase 3, and the linear increase in mortality rate among those reporting the same number of hours sleep at both Phases; from 1.8 per 1000 person-years among participants who slept 8 hours to 4.3 for those who slept ≤5 hours. In addition there is an indication that mortality rates are lower among those who slept 5 or 6 hours at Phase 1, but who reported extended hours of sleep at Phase 3.

Table 4 presents hazard ratios (95% confidence intervals) for mortality by changes in sleep duration between Phases 1 and 3. In participants whose sleep increased from 5 or 6 hours at baseline there was a slight indication that mortality risk was lower than for participants who slept 5 or 6 hours at both time points. Conversely, there is good evidence that participants whose sleep decreased from 6, 7, or 8 hours per night were at higher risk of all-cause and cardiovascular mortality than those who retained the same sleep duration across the phases, hazard ratio for cardiovascular mortality 2.39 (1.41-4.05). Adjustment for the sociodemographic factors, existing morbidity and health-related behaviours measured at Phase 3 partially attenuated, but did not eliminate, this association. An increase in sleep from 7 or 8 hours at baseline is associated with an excess risk of all-cause and non-cardiovascular mortality, hazard ratio for non-cardiovascular mortality 2.09 (1.40-3.12). Evidence for these associations was strong and unaffected by adjustment for the covariates measured at Phase 3. Analyses re-run using a dataset that included the covariates measured at Phase 1, as well as at Phase 3, were very similar to those presented. Likewise, analyses re-run in a dataset that excluded participants on sleep medication were very similar to those presented (data available on request).

DISCUSSION

Although voluntary sleep curtailment and an increase in shiftwork have given rise to population-wide changes in sleeping patterns, hardly anything has been published on the effects of change in sleep duration on mortality. In this study we consistently demonstrate higher rates of all-cause mortality among participants who report short sleep (≤5 hours) or long sleep (≥9 hours) at follow-up, regardless of their sleep duration 5-6 years earlier. A decrease in sleep duration among those regularly sleeping 6, 7, or 8 hours at baseline was associated with a 110% excess risk of cardiovascular mortality. However, an increase in sleep duration among those regularly sleeping 7 or 8 hours at baseline was associated with a 110% excess risk of non-cardiovascular mortality. While there was some attenuation of the excess risk of cardiovascular mortality, the excess risk of non-cardiovascular mortality was unchanged after adjustment for the sociodemographic factors, existing morbidity and health-related behaviours measured.

Table 2B—Characteristics[+] and Risk Factors by Number of Hours Sleep at Phase 3

		Hours of sleep					P-value for
		≤5 hours	6 hours	7 hours	8 hours	≥9 hours	heterogeneity
Number of subjects		420	1626	3501	1950	232	
Age, yr		50.4 (0.3)	49.4 (0.1)	49.4 (0.1)	49.8 (0.1)	50.3 (0.4)	<0.001
Sex (% female)		39.6	31.6	28.6	30.8	35.5	<0.001
Employment grade (% low grade)	- Women	37.4	42.3	35.8	35.2	40.2	0.10
	- Men	15.3	9.6	4.6	5.7	7.6	<0.001
Marital status (% Married)	- Women	52.2	57.6	64.8	69.3	70.5	<0.001
	- Men	70.2	78.7	84.3	85.2	81.7	<0.001
Current cigarette smoker (%)	- Women	23.2	19.8	15.8	12.3	12.1	<0.001
	- Men	19.9	15.6	10.8	10.5	12.8	<0.001
High alcohol (%)	- Women	10.8	7.2	10.3	10.4	6.9	0.23
	- Men	21.3	19.0	17.7	18.0	18.2	0.64
Little exercise (%)	- Women	36.2	32.6	31.2	36.6	44.9	0.03
	- Men	22.8	14.7	12.9	13.9	18.4	<0.001
Modified GHQ score	- Women	4.5 (0.4)	3.6 (0.2)	2.8 (0.1)	2.8 (0.2)	3.3 (0.5)	<0.001
	- Men	4.8 (0.3)	2.8 (0.1)	2.4 (0.1)	2.2 (0.1)	3.1 (0.4)	<0.001
Self-rated health (% ≤ average)	- Women	47.5	35.2	30.5	29.7	43.4	<0.001
	- Men	34.2	24.5	18.1	20.6	33.1	<0.001
Physical Illness Indicator (% positive)	- Women	21.9	22.9	20.7	22.7	33.9	0.04
	- Men	23.9	23.8	19.4	22.4	27.3	0.007
Prevalent CHD (% positive)	- Women	11.2	11.4	9.5	10.5	18.9	0.07
	- Men	10.6	8.8	7.0	7.4	8.2	0.17
BMI (kg/m^{-2})	- Women	25.7 (0.3)	25.8 (0.2)	25.5 (0.1)	25.6 (0.1)	26.4 (0.4)	0.43
	- Men	25.6 (0.3)	25.6 (0.1)	24.9 (0.1)	24.9 (0.1)	25.3 (0.3)	<0.001
Systolic blood pressure (mm Hg)	- Women	120.9 (1.1)	117.1 (0.6)	117.0 (0.4)	117.8 (0.5)	117.7 (1.5)	0.05
	- Men	124.4 (0.9)	122.1 (0.4)	121.6 (0.3)	122.3 (0.4)	123.0 (1.1)	0.03
Diastolic blood pressure (mm Hg)	- Women	78.2 (0.8)	76.3 (0.4)	76.5 (0.3)	76.9 (0.4)	77.1 (1.0)	0.25
	- Men	82.5 (0.6)	81.1 (0.3)	80.7 (0.2)	81.6 (0.2)	81.5 (0.7)	0.007
Cholesterol (mmol/L)	- Women	6.36 (0.09)	6.39 (0.05)	6.47 (0.04)	6.62 (0.05)	6.54 (0.12)	<0.001
	- Men	6.48 (0.08)	6.47 (0.03)	6.50 (0.02)	6.47 (0.03)	6.47 (0.09)	0.96

[+] Figures are means (standard errors) for continuous measures and percentages for categorical measures. All estimates (except for age) are adjusted for age.

U-shaped associations between sleep duration and mortality risk at baseline and follow-up replicated findings from a number of previous studies.

This study has the benefit of longitudinal data from a well-characterised cohort that enabled us to adjust for a number of well-known confounders of the sleep-mortality association. The main limitation is the single-item, self-reported measures of sleep duration, which were not identical at the two Phases and did not explicitly ask participants to differentiate time asleep from time in bed. However, it is not feasible to obtain more detailed and objective measures of sleep; sleep diaries, actigraphs, and polysomnography from large populations and small-scale investigations have shown high correlations between subjective estimates of sleep duration and diary, actigraphy, or polysomnography data.[13,17] Furthermore, assessments of sleep durations in the primary health care setting rely on self-reported data from patients. Loss to follow-up was 19% between Phases 1 and 3. While this is a potential source of bias, it is much below the 50% loss to follow-up in the only other published study of change in sleep duration.[9] A further limitation of an occupational cohort aged 35-55 at baseline and almost exclusively white-collar is that findings may not apply to wider populations.

The U-shaped associations between sleep and all-cause mortality at both Phases reflect those from other studies that have either looked at women and men separately and found similar results for both sexes,[1,2,5,12,13] or have looked at the sexes combined.[3,7] Other smaller studies have documented different effects in women and men.[6,8-11] Discrepancy between the findings from studies of sleep duration and mortality may partially be explained by differences in the level of control for pre-existing morbidity and other known predictors of morbidity and mortality, such as psychosocial and environmental exposures. Similarly in the present study, there may be residual confounding due to pre-existing morbidity, either undetected or poorly captured by our survey measures, and other covariates, such as employment grade. The association between low employment grade and mortality is consistently U-shaped. Although our mortality analyses are adjusted for grade, this may not completely account for all the social and economic factors likely to be patterned by employment grade. As for most health-related behaviors, poor sleep hygiene is likely to be more common in the lower grades. Similarly, low employment grade is associated with higher levels of a number of stressors such as work stress, low control at home, job insecurity, and financial insecurity and economic difficulties. Some of these stressors have been associated with poorer patterns of sleep and all have been associated with higher levels of morbidity.[18-22]

Studies that have examined associations between sleep and cardiovascular or non-cardiovascular mortality have provided mixed findings.[7,9,10,13] One study has observed an association between short sleep and cardiovascular mortality in women,[9] while other studies have observed associations between long sleep

Table 3—All-Cause Mortality from Phase 3 Onwards by Number of Hours of Sleep at Phases 1 and 3

Sleep at Phase 1	Sleep at Phase 3				
	≤ 5 hours	6 hours	7 hours	8 hours	≥ 9 hours
≤5 hours					
Number of subjects	145	144	90	40	10
No. of deaths	(9)	(6)	(2)	(1)	(1)
Mortality rate+	4.3	3.2	~	~	~
6 hours					
Number of subjects	186	872	807	214	24
No. of deaths	(14)	(35)	(32)	(10)	(3)
Mortality rate+	6.3	3.5	3.1	3.6	~
7 hours					
Number of subjects	75	563	2246	961	87
No. of deaths	(5)	(19)	(61)	(47)	(6)
Mortality rate+	5.7	3.1	2.3	4.0	4.8
8 hours					
Number of subjects	12	44	346	704	91
No. of deaths	(1)	(1)	(17)	(15)	(5)
Mortality rate+	~	~	4.8	1.8	4.9
≥9 hours					
Number of subjects	2	3	12	31	20
No. of deaths	(0)	(0)	(0)	(1)	(1)
Mortality rate+	~	~	~	~	~

+ Age standardised mortality rates per 1000 person years
~ Mortality rate not given where number of deaths is <5

and cardiovascular mortality in both sexes[7] or in men only.[10] A U-shaped association between sleep and cardiovascular mortality was observed in the Nurses Health study.[13] Those studies that have also examined non-cardiovascular mortality have observed a strong U-shaped association in women[13] and an association with long sleep in men.[10] Our findings add to this existing literature by demonstrating U-shaped associations between sleep duration and cardiovascular and non-cardiovascular mortality, which are stronger with sleep duration measured at second follow-up than sleep measured at baseline 5-6 years earlier.

The only study that appears to have examined change in sleep duration used data from a working cohort, the West of Scotland study. Sleep duration was measured at two time points 4-7 years apart. Similar to the findings for prolonged exposure to shorter sleep durations in the present study, the West of Scotland study found that women and men who reported <7 hours sleep at both time points were at increased risk of all-cause and cardiovascular mortality. However, no associations were observed between increased or decreased sleep and all-cause or cardiovascular mortality in either sex.[9] These findings are in contrast to those of our own study in which a decrease in sleep duration among those regularly sleeping 6, 7, or 8 hours was associated with an excess risk of all-cause mortality via effects on cardiovascular mortality and an increase in sleep duration among those regularly sleeping 7 or 8 hours was associated with an excess risk of all-cause mortality via effects on non-cardiovascular mortality.

Loss of sleep has some, limited, direct effects on mortality through certain sleep disorders and sleepiness due to inadequate sleep and sleeping difficulties.[23-25] Unfortunately, these difficulties, which increase with age, were not measured at Phases 1 and 3 of the Whitehall II study. Recent research has shown that loss of sleep may affect all-cause and cardiovascular mortality indirectly via effects on endocrinology, immunology and metabolism. Short sleep has been shown to be a risk factor for weight gain, insulin resistance and type 2 diabetes via deleterious effects on glucose metabolism and appetite regulation.[26,27] It has been suggested that the mechanism behind this association could be obstructive sleep apnoea or chronic low-grade inflammation, both linked to insomnia and risk of type 2 diabetes.[14,28] Short sleep is also accompanied by increased cortisol levels and abnormal growth hormone secretion,[14,29] and has been associated with hypertension and some cardiovascular diseases.[30,31] While associations between short sleep

Table 4—Mortality from Phase 3 Onwards by Change in the Number of Hours Sleep Between Phase 1 and Phase 3

Cause of death	Change in hours of sleep between Phase 1 and Phase 3			
	Increase from 5 or 6 hours[a]	Reference group (No change in hours)	Decrease from 6, 7, or 8 hours[b]	Increase from 7 or 8 hours[c]
All-causes				
Number of deaths	55		57	58
Hazard ratio (95% CI) - Age adjusted	0.88 (0.60–1.28)	1.0	1.72 (1.25–2.38)	1.84 (1.31–2.58)
Hazard ratio (95% CI) - Fully adjusted #	0.92 (0.63–1.35)	1.0	1.62 (1.17–2.25)	1.75 (1.24–2.47)
CVD				
Number of deaths	16		24	12
Hazard ratio (95% CI) - Age adjusted	0.74 (0.37–1.46)	1.0	2.39 (1.41–4.05)	1.29 (0.64–2.59)
Hazard ratio (95% CI) - Fully adjusted #	0.85 (0.42–1.70)	1.0	2.04 (1.20–3.49)	1.22 (0.60–2.48)
Non-CVD				
Number of deaths	38		33	45
Hazard ratio (95% CI) - Age adjusted	0.97 (0.61–1.54)	1.0	1.48 (0.98–2.23)	2.09 (1.40–3.12)
Hazard ratio (95% CI) - Fully adjusted #	0.98 (0.62–1.57)	1.0	1.44 (0.95–2.18)	2.06 (1.38–3.08)

Fully adjusted hazard ratios are adjusted for the following Phase 3 measures:- age, sex, marital status, employment grade, smoking status, physical activity, alcohol consumption, self-rated health, body mass index, systolic blood pressure, cholesterol, physical illness, modified GHQ score, prevalent CHD
[a] 5 or□
[b] □ 11 deaths)
[c] 7 or 8 hours sleep at Phase 1 and >7 or 8 hours, respectively, at Phase 3; reference is either 7 or 8 hours at both phases (76 deaths)

and all-cause and cardiovascular mortality in the present study were partially explained by the covariates and risk factors measured, which included body mass index and hypertension, these did not include apnoea, inflammatory markers, insulin resistance, cortisol, or growth hormone.

Although there is evidence that aging is associated with shorter sleep duration,[32] the proportion of participants who reported >7 hours sleep per night increased between baseline and follow-up. It is possible that older and nonworking participants spend more time in bed and reported this rather than time asleep. In contrast to the short sleep-mortality association it appears that no potential mechanisms by which long sleep could be associated with increased mortality have yet been investigated.[33] An examination of the correlates of long sleep in the Nurses Health II study demonstrated strong associations with depression and low socioeconomic status, in particular unemployment.[34] Although analyses in the present study were adjusted for GHQ score and employment grade, GHQ score is more a measure of well-being than depression and employment grade is an accurate measure of socioeconomic status only for those in employment. Another possible candidate is cancer-related fatigue. However, it will remain difficult to propose underlying mechanisms to explain our observed association between an increase in sleep and non-cardiovascular mortality until the study has sufficient power to examine the constituent causes of death that make up the non-cardiovascular category.

In terms of prevention, our findings indicate that consistently sleeping 7 or 8 hours per night is optimal for health. The indication that mortality rates are lower in participants who slept 5-6 hours or less at Phase 1 but who reported extended hours of sleep at Phase 3 imply that increasing sleep duration in short sleepers is likely to have health benefits. In contrast to this, the finding that an increased duration of sleep among those sleeping 7-8 hours is associated with higher levels of mortality implies that sleep restriction should at least be considered.[35]

In summary, our findings suggest that either a decrease in sleep duration from a regular 6, 7, or 8 hours or an increase from a regular 7 or 8 hours predict all-cause mortality. A decrease in sleep duration affects all-cause mortality via increases in cardiovascular deaths, while an increase in sleep duration affects overall mortality via an increase in non-cardiovascular deaths. Patients reporting a decrease in sleep should be regarded as higher risk populations for cardiovascular and all-cause mortality. Further work is required to determine which causes of death contribute most to the excess non-cardiovascular mortality observed among people whose sleep duration increases.

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