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Original Article

Sleep and future cardiovascular risk: prospective analysis from the English Longitudinal Study of Ageing

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ABSTRACT

Study objectives: Hypertension and inflammation may contribute to the increased risk of cardiovascular disease in individuals with suboptimal sleep, but large prospective studies are lacking. This study tested whether sleep duration and disturbance were predictive of incident hypertension and inflammation four years later.
Methods: Participants were men and women aged 50 years and older from the English Longitudinal Study of Ageing. Sleep was assessed by self-report, incident hypertension ($N = 3068$) was defined by clinical examination and C-reactive protein and fibrinogen ($N = 3768$) were measures of inflammation.
Results: Both men (odds ratio, OR:1.73, confidence interval, C.I. 1.08–2.76) and women (OR: 1.44, C.I. 1.00–2.07) reporting short sleep at baseline had increased odds of incident hypertension 4 years later, after adjustment for covariates. Age-stratified analyses revealed that short sleep was predictive of incident hypertension in men (OR: 2.27, C.I. 1.01–5.11) and women (OR: 2.10, C.I. 1.08–4.09) younger than 60 years but not in older people. Disturbed sleep also predicted incident hypertension in men (OR: 1.20, C.I. 1.02–1.41). In women, disturbed sleep was associated with elevated C-reactive protein ($B = 0.030$, C.I. 0.00–0.06) and fibrinogen ($B = 0.030$, C.I. 0.01–0.05) at follow-up controlling for baseline inflammation and other covariates. Sleep duration was unrelated to inflammatory markers in either sex.
Conclusions: This study of older men and women adds to growing evidence that aberrant sleep patterns may increase the risk of cardiovascular outcomes through its adverse impact on blood pressure and inflammation.

1. Introduction

Disturbed sleep is common in developed countries including the UK [1,2]. Insufficient (typically <5 or <6 h) and too long (typically >8, >9 or >10 h) sleep hours are prospectively associated with higher risk of all-cause and cardiovascular disease (CVD) and CVD mortality [3–5]. Suboptimal and disturbed sleep are also linked to major cardiovascular risk factors including adverse metabolic outcomes [6], hypertension [7], and obesity [8].

Experimental sleep studies have reported that acute sleep deprivation is associated with an increase in inflammatory markers such as C-reactive protein and interleukin-6 (IL-6) [9,10]. This has led to the hypothesis that low-grade inflammation, a well-established cardiovascular risk factor [11], may be one biological mechanism through which aberrant sleep patterns increase the risk of future cardiovascular outcomes. Indeed, using data from the English Longitudinal Study of Ageing (ELSA) we have reported that in men, but not in women, long (>8 h) and disturbed sleep were both associated with raised concentrations of C-reactive protein and fibrinogen (another marker of inflammation implicated in the development of CVD) [12]. These findings are in line with previous studies [13], although some authors have found these relationships only in women [14–17].

Sleep and inflammatory markers have been largely explored in cross-sectional studies and the findings of prospective investigations [13,15,17,18] are inconsistent. Our previous investigation [12] was cross-sectional and therefore shed no light on the temporal precedence between sleep measures and inflammatory markers. Although abnormal sleep patterns may lead to poor health, for instance, through low-grade inflammation or metabolic dysfunction, poor health is also likely to impair sleep [19,20]. Therefore, the first aim of our study was to test prospective associations between self-reported sleep and inflammatory markers. We hypothesised that both short and long as well as disturbed sleep would be associated with higher levels of C-reactive protein and fibrinogen at a 4-year follow-up.

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Experimental studies suggest that sleep curtailment leads to increases in blood pressure [21]. This is thought to be mediated by increased sympathetic nervous activity and catecholamine concentrations [21–23], among other processes. The prevalence of hypertension is higher in sleep-disordered populations, in particular in those diagnosed with insomnia and sleep apnoea [24,25]. However, in population-based samples the evidence relating sleep measures with hypertension is conflicting. For example, in the Whitehall II and the Western New York Health studies, short sleep was (cross-sectionally) associated with hypertension only in women [26,27]. Analysis of the first National Health and Nutrition Examination Survey (NHANES I) revealed that short sleep was prospectively linked to hypertension in respondents younger than 60 years of age, but not in their older counterparts [28]. These age-dependent associations between sleep hours and hypertension were subsequently corroborated by a study in South Korea [29]. Relatedly, short sleep duration was unrelated to hypertension in samples of older Dutch and Spanish men and women [30,31]. However, in contrast with the NHANES I [28] and Korean studies [29], sleep hours were not predictive of hypertension in middle-aged women from the Study of Women's Health Across the Nation (SWAN) [32], or in young (mean age 36 years) Spanish adults [33]. More recently, objective short sleep duration and lower sleep efficiency were prospectively associated with an increase in diastolic and systolic blood pressure, but not with incident hypertension in early middle-aged respondents from the Coronary Artery Risk Development in Young Adults (CARDIA) study [34].

Taken together, the literature relating the relationship between sleep and hypertension is conflicting, which, at least in some studies, seems to be moderated by sex and age [7]. Given the high prevalence of both aberrant sleep patterns [2] and hypertension [35] in industrialised countries, further studies are warranted on this import health issue. In the present study, we hypothesised that both short sleep and disturbed sleep would be associated with incident hypertension four years later.

Gender differences in associations between sleep measures, inflammatory markers and hypertension have been reported in the literature [7,14,36]; so the analyses presented here were stratified by gender.

2. Methods

2.1. Participants and procedures

ELSA is a multi-disciplinary prospective cohort study representative of men and women aged 50 years and older living in England [37]. The study was established in 2002 and to date there have been six waves of data collection.

Analyses described here are based on waves 4 (2008–9) and 6 (2012–13) of ELSA. Wave 4 is the baseline since sleep measures were first introduced at that wave and then repeated four years later. Nurses visited participants' homes to measure blood pressure and collect medication information. Blood pressure recordings and medication records were used to define hypertension status at baseline; 8120 respondents had valid data of whom 3937 were normotensive (defined as diastolic blood pressure <90 mmHg and systolic blood pressure <140 mmHg, and not being on hypertensive medication). Blood pressure and medication were reassessed four years later in 6239 respondents. Blood samples were not collected from all participants as detailed below; so analyses of blood analytes are based on a smaller sample than those for blood pressure. C-reactive protein and/or fibrinogen were measured from 6087 participants at baseline and from 4752 participants four years later. In order to ensure comparability across blood analytes, we limited analysis to individuals with valid C-reactive protein and fibrinogen measures on both occasions, leaving an analytic sample of 3768.

Data collection consisted of a computer-assisted personal interview (CAPI) and a separate nurse visit few days later. Both assessments were conducted face to face in participants' home. Signed consent was obtained from all participants, and ethical approval was issued by the National Research Ethics Service.

2.2. Measures

2.2.1. Socio-demographic measures

Age at baseline was classified into four categories ('50–59', '60–69', '70–79' and '80+'). Socio-economic circumstances were estimated by total household wealth taking into account financial wealth (eg, savings), the value of any property (less mortgage), and the value of any business assets and physical wealth (eg, artwork) and net of debt. Wealth is the most reliable indicator of socio-economic position in ELSA, and was divided into quintiles for these analyses.

2.2.2. Sleep measures

Sleep data were collected during the CAPI. Sleep duration was assessed with an open-ended question asking respondents to indicate how many hours they slept on average during the week. For the purpose of analyses described here, sleep hours were categorised into '≤5 h' (short duration), '>5–6 h', '>6–7 h', '>7–8 h' (optimal sleep duration) and '>8 h' (long duration). The cut-offs for short, optimal and long sleep hours were based on the sleep literature [4,38].

Sleep problems were measured with three questions derived from the Jenkins Sleep Problems Scale [39], which refer to the most common complaints of insomnia such as difficulties with falling asleep, staying asleep and waking up in the morning feeling tired. Items were rated on a four-point Likert scale (anchored at 1 = 'not during the past month' to 4 = 'three of more times a week'), and scores were averaged (range 1–4) with higher scores indicating more sleep problems. The Cronbach's alpha at baseline in this sample was 0.60.

2.2.3. Cardiovascular health measures

Blood samples and blood pressure were obtained during the nurse visit. Blood samples were not taken from participants who had clotting disorders or who were taking anti-coagulant medication, and some blood samples failed to provide sufficient quantities for analysis from older patients. C-reactive protein was analysed using the N Latex C-reactive protein mono immunoassay on the Behring Nephelometer II analyser. Fibrinogen concentrations were quantified using a modification of the Clauss thrombin clotting method on the Organon Teknika MDA 180 analyser (Craig, Deverill, & Pickering, 2006). All blood samples were analysed in the Royal Victoria Infirmary laboratory in Newcastle upon Tyne, UK. For further details on blood analyses, see Craig et al. [40].

There were no exclusion criteria for providing blood pressure apart from pregnancy. Three (resting) blood pressure readings, separated by 1-min intervals, were taken by the nurse using the Omeron HEM-907 monitor. Participants were asked to abstain from eating, drinking alcohol, smoking or engaging in intensive exercise at least 30 min prior to having their blood pressure measured. In this study, blood pressure variables were computed by taking an average of three systolic and diastolic readings.

2.2.4. Other measures

The presence of chronic illness was assessed during the CAPI. Those who responded positively to this question were further requested to report whether their condition limited their activities. Answers were categorised into 'yes' for limiting long-standing illness and 'no' for its absence. Menopausal status was ascertained through information on whether a woman still had her period, and on surgical (eg, hysterectomy) or natural cessation of menses.

Height and weight were assessed by the nurse and were used to calculate body mass index (BMI, kg/m^2). Data on smoking were collected by asking respondents whether they have ever smoked, and those who responded positively were further asked to state if they still smoked. Responses were classified into 'no' for never/past smokers and 'yes' for current smokers. Physical activity was indexed by asking whether respondents participated in mild, moderate and vigorous physical activity. The possible answers were 'hardly ever or never', 'one to three times a month', 'once a week' and 'more than once a week'. In the analyses described here, physical activity was categorised into 'moderate or vigorous physical activity at least once a week' and 'moderate or vigorous physical activity less than once a week'.

Depressive symptoms were assessed with an eight-item version of the Centre for Epidemiologic Studies Depression scale (CES-D) originally modified for the Health and Retirement Study in the US [41]. In this study, the item concerning sleep was removed from the CES-D as to avoid the issue of shared variance with the measure of sleep problems. The seven-item scale was answered with 'yes' or 'no' responses. Scores were totalled (range 0–7) and greater scores were reflective of higher depressive symptoms. Using a validated cut-off point of 3 [41], a binary variable was computed to reflect absence or presence of elevated depressive symptoms. The internal consistency of the scale at baseline was 0.91.

2.3. Statistical approach

C-reactive protein was positively skewed, thus logarithmic transformation was performed to normalise the distribution. The remaining biological data followed a normal distribution.

In line with previous investigations based on ELSA [42], participants who did not provide blood analytes at both waves did not differ from those who had these data in terms of sex ($P = 0.479$), but they were slightly older (67.6 vs. 64.5, $P < 0.001$) and more likely to be in the lowest wealth quintile (18.2% vs. 14.1%, $P < 0.001$). They were also more likely to be current smokers (13.9% vs. 12.4%, $P = 0.042$), to have higher BMI (28.6 vs. 27.9, $P < 0.001$), elevated depressive symptoms (12.3% vs. 8.6%, $P < 0.001$), and a limiting long-standing illness (39.0% vs. 28.6%, $P < 0.001$), as well as to engage in moderate or vigorous physical activity less than once a week (42.3% vs. 29.4%, $P < 0.001$).

Linear regression analysis was performed to test whether sleep problems at baseline were prospectively associated with C-reactive protein and fibrinogen, and we used analysis of covariance to determine if sleep duration was prospectively associated with levels of biomarkers. Separate models were run for each biomarker, and were adjusted for age, wealth, BMI, smoking, physical activity, limiting long-standing illness, depressive symptoms, since these are related to sleep measures [43–45], and baseline levels of C-reactive protein or fibrinogen, as appropriate. Results are presented as unstandardised regression coefficients (B), 95% confidence intervals (C.I.) and *P*-values for linear regressions and *F*-statistics with *P*-values for analysis of covariance. Logistic regression analyses were used to test whether sleep problems and duration at baseline were predictive of hypertension four years later. These analyses were conducted only among those respondents who were normotensive at baseline, and were adjusted for covariates relevant to sleep experience, as detailed above. Results are presented as odds ratio (OR) and 95% C.I.

All analyses were performed using SPSS version 21.

3. Results

Baseline characteristic of study participants stratified by gender are shown in Table 1. Since the analyses relating sleep measures with blood analytes were performed on a smaller sample than those testing sleep and blood pressure, we report descriptive statistics for both samples. Across the samples, the differences in characteristics of men and women were comparable on most variables. Women reported greater sleep disturbance than men, and were more likely to sleep very short hours. Women were also more likely to report greater depressive symptoms and were physically less active than men. Men had lower levels of inflammatory markers but slightly higher diastolic and systolic blood pressure than women.

3.1. Baseline sleep measures and covariates

In the subsample who had blood analytes at both waves of data collection ($N = 3768$), sleep duration was associated with sex, age and wealth, with women, older and less wealthy respondents being more likely to report short sleep hours (see Supplementary Table S1). Smokers, respondents with elevated depressive symptoms, limiting long-standing illness, and higher BMI were also more likely to be categorised as short sleepers. Moderate and vigorous physical activity at least once per week was less prevalent among short sleepers as well.

Sleep problems were higher among female respondents, those with greater BMI, elevated depressive symptoms, limiting long-standing illness, and participants who were less likely to exercise moderately or vigorously at least once a week, as well as in current smokers. Sleep problems were also negatively associated with wealth ($P < 0.001$) but were unrelated to age (see Supplementary Table S1).

3.2. Sleep changes over time

In both sexes, sleep problems at baseline were moderately correlated with sleep problems at follow-up ($r = 0.6$, $P < 0.001$). The association between sleep duration categories over time was also highly significant ($P < 0.001$), with approximately half of participants remaining in the same sleep category 4 years later. This trend was observed in gender-stratified analysis as well (data not shown).

3.3. Sleep duration and cardiovascular risk factors

We found that of the 3068 normotensive participants at wave 4, who provided blood pressure and blood pressure medication data at wave 6, 566 (37.0%) men and 667 (38.6%) women had developed hypertension 4 years later. In comparison with the >7–8 h reference category, men sleeping ≤5 h were more likely to have hypertension at follow-up (see Table 2). Women reporting short sleep hours at baseline also had an increased risk of hypertension four years later.

Sleep duration was unrelated to C-reactive protein in men or women (see Table 2). Similarly, there was no prospective association between sleep hours and fibrinogen in either men or women.

3.4. Sleep problems and cardiovascular risk factors

Men reporting more disturbed sleep at baseline had an increased risk of incident hypertension at follow-up after covariates had been taken into account (see Table 3). No such association was found in women. Follow-up analysis confirmed that the interaction between sex and sleep problems on incident hypertension was significant ($P = 0.028$). By contrast, disturbed sleep was unrelated to C-reactive protein four years later in men, but did predict follow-up C-reactive protein concentrations in women. Similarly, women reporting more sleep disturbance at baseline had higher fibrinogen concentrations at follow-up, after adjustment for covariates, with no significant association in men. The interactions between sex and sleep problems were not significant for C-reactive protein or fibrinogen.

Table 1
Baseline characteristics of study participants.

Variable	Mean (SD) /frequency (%)					
	Participants included in the analyses of blood analytes			Participants included in the analyses of incident hypertension		
	Men ($N = 1678$)	Women ($N = 2090$)	P-value	Men ($N = 1723$)	Women ($N = 2214$)	P-value
Age			0.626			0.501
50–59 years	547 (32.6)	643 (30.8)		587 (34.1)	800 (36.1)	
60–69 years	681 (40.6)	857 (41.0)		652 (37.8)	826 (37.3)	
70–79 years	367 (21.9)	478 (22.9)		352 (20.4)	436 (19.7)	
80+ years	83(4.9)	112 (5.4)		132 (7.7)	152 (6.9)	
Wealth quintiles			0.112			<0.001
Poorest quintile	217 (12.9)	305 (14.6)		252 (14.6)	387 (17.5)	
2nd quintile	245 (14.6)	352 (16.8)		255 (14.8)	431 (19.5)	
3rd quintile	370 (22.1)	439 (21.0)		345 (20.0)	418 (18.9)	
4th quintile	372 (22.2)	456 (21.8)		380 (22.1)	461 (20.8)	
Richest quintile	441 (26.3)	499 (23.9)		451 (26.2)	466 (21.0)	
Smoking status			0.484			0.652
No	1470 (87.6)	1809 (86.6)		1430 (85.9)	1886 (85.2)	
Yes	200 (11.9)	264 (12.6)		234 (13.6)	311 (14.0)	
Moderate/vigorous physical activity			<0.001			<0.001
Less than once a week	433 (25.8)	676 (32.3)		515 (29.9)	837 (37.8)	
At least once a week	1245 (74.2)	1414 (67.7)		1208 (70.1)	1376 (62.1)	
Limiting long-standing Illness			0.029			0.221
No	1228 (73.2)	1461 (69.9)		1164 (67.6)	1454 (65.7)	
Yes	450 (26.8)	628 (30.0)		559 (32.4)	759 (34.3)	
Depressive symptoms			<0.001			<0.001
No	1582 (94.3)	1843 (88.2)		1587 (92.1)	1910 (86.3)	
Yes	88 (5.2)	234 (11.2)		120 (7.0)	285 (12.9)	
BMI	27.8 (3.8)	28.0 (5.2)	0.133	27.7 (3.9)	27.7 (5.3)	0.905
Sleep duration			<0.001			0.003
≤5 h	172 (10.3)	313 (15.0)		186 (10.8)	323 (14.6)	
>5–6 h	318 (19.0)	420 (20.1)		330 (19.2)	451 (20.4)	
>6–7 h	594 (35.4)	636 (30.4)		570 (33.1)	662 (29.9)	
>7–8 h	501 (29.9)	564 (27.0)		509 (29.5)	617 (27.9)	
>8 h	92 (5.5)	150 (7.2)		127 (7.4)	152 (6.9)	
Sleep disturbance	2.1 (0.8)	2.4 (0.9)	<0.001	2.1 (0.8)	2.4 (0.9)	<0.001
C-reactive protein (mg/L)[a]	3.0 (4.6)	3.5 (4.8)	0.001	3.0 (4.7)	3.3 (4.6)	0.056
Fibrinogen (g/L)	3.3 (0.5)	3.4 (0.5)	<0.001	3.3 (0.6)	3.4 (0.5)	<0.001
Diastolic BP (mmHg)	76.1 (10.3)	74.7 (10.0)	<0.001	71.3 (9.0)	70.9 (8.6)	0.157
Systolic BP (mmHg)	134.6(15.8)	132.1(17.7)	<0.001	124.7 (9.8)	122.4 (11.0)	<0.001

SD = standard deviation; BMI = body mass index; BP = blood pressure.
[a] Untransformed data.

Table 2
Prospective associations between sleep duration and cardiovascular risk factors in men and women.

	Percent/adjusted means (SD)	Adjusted odds ratio (95% C.I.)/ P-value for continuous data	Percent/adjusted means (SD)	Adjusted odds ratio (95% C.I.)/ P-value for continuous data
	Men		Women	
Incident hypertension				
≤5 h	50.9%	1.73 (1.08–2.76)	43.8%	1.44 (1.00–2.07)
>5–6 h	42.0%	1.16 (0.80–1.69)	39.1%	1.16 (0.84–1.60)
>6–7 h	41.3%	1.14 (0.83–1.56)	38.1%	1.11 (0.83–1.48)
>7–8 h	38.8%	Reference	36.0%	Reference
>8 h	39.5%	1.05 (0.62–1.79)	38.1%	1.11 (0.68–1.80)
C-reactive protein (mg/L)				
≤5 h	1.02 (0.67)	0.92	1.15 (0.79)	0.68
>5–6 h	1.06 (0.77)		1.11 (0.64)	
>6–7 h	1.05 (0.67)		1.09 (0.65)	
>7–8 h	1.04 (0.66)		1.11 (0.71)	
>8 h	0.99 (0.70)		1.12 (0.66)	
Plasma fibrinogen (g/L)				
≤5 h	2.97 (0.53)	0.70	3.05 (0.55)	0.45
>5–6 h	2.91 (0.53)		3.01 (0.49)	
>6–7 h	2.91 (0.54)		2.99 (0.49)	
>7–8 h	2.92 (0.53)		3.01 (0.51)	
>8 h	2.91 (0.51)		3.01 (0.50)	

All analyses are adjusted for age, wealth, BMI, smoking status, moderate or vigorous activity at least once per week, limiting long-standing illness, and depressive symptoms. Analyses of C-reactive protein are additionally adjusted for baseline C-reactive protein, while analyses relating fibrinogen are additionally adjusted for baseline fibrinogen.

Table 3
Prospective associations between sleep disturbance and cardiovascular risk factors in men and women.

	Adjusted odds ratio (95% C.I.)/unstandardised regression coefficient (95%C.I)[a]		Adjusted odds ratio (95% C.I.)/unstandardised regression coefficient (95%C.I)[a]	
	Men	*P*-value	Women	*P*-value
Incident hypertension	1.20 (1.02–1.41)		1.05 (0.92–1.19)	
C-reactive protein (mg/L)	−0.007 (−0.05–0.03)	0.73	0.030 (0.00–0.06)	0.048
Plasma fibrinogen (g/L)	−0.005 (−0.04–0.03)	0.73	0.030 (0.01–0.05)	0.01

[a] For incident hypertension, results are presented as OR and 95% C.I., and for C-reactive protein and fibrinogen, results are presented as *B* and 95% C.I., and P-values. All analyses are adjusted for age, wealth, BMI, smoking status, moderate or vigorous activity at least once per week, limiting long-standing illness and depressive symptoms. Analyses of C-reactive protein are additionally adjusted for baseline C-reactive protein, while analyses relating fibrinogen are additionally adjusted for baseline fibrinogen.

3.5. Sensitivity analyses

Since previous research has suggested that the association between sleep and incident hypertension varies between people older and younger than 60 years of age [28], we performed sensitivity analyses to check this possibility. For men younger than 60 years, short sleep was associated with higher odds of incident hypertension at follow-up (OR: 2.27, C.I. 1.01–5.11), independently of wealth, smoking, moderate/vigorous physical activity, BMI, limiting long-standing illness, and depressive symptoms. For men 60 years or older, short sleep duration was unrelated to incident hypertension (OR: 1.47, C.I. 0.83–2.60). Similarly, for women younger than 60 years short sleep was a significant predictor of incident hypertension 4 years later (OR: 2.10, C.I. 1.08–4.09), but no such association was found in women aged 60 years or older (OR: 1.27, C.I. 0.82–1.97). The corresponding analyses of sleep disturbance did not show any differences by age (data not shown).

4. Discussion

Our study found that in older men and women short sleep duration was predictive of incident hypertension at follow-up. Greater sleep problems were also associated with a higher risk of future hypertension in men. These associations were independent of sociodemographic factors, health behaviours, limiting long-standing illness and depressive symptoms. Our data further revealed that women with greater sleep disturbance had higher concentrations of C-reactive protein and fibrinogen four years later. Sleep duration was unrelated to inflammatory markers in our study. These findings lend partial support to our hypotheses about the importance of sleep for cardiovascular risk.

The association between sleep duration and blood pressure has been mainly explored in middle-aged individuals, and prospective studies in older populations are sparse, making comparisons with our results difficult. In line with our findings, Gangwisch et al. [28] reported that short sleep was prospectively associated with hypertension in the NHANES I, but only in respondents younger than 60 years. A more recent study in South Korea reported a similar pattern of findings [29]. In our sensitivity analyses, we also found that short sleep predicted incident hypertension only among men and women younger than 60 years of age. This corroborates data from two earlier investigations in elderly adults in which short sleep hours were not linked to future hypertension [30,31]. By contrast, in the Whitehall II study (mean age ~55 years) short sleep was related to hypertension only in cross-sectional and not longitudinal analyses [26]. We do not have an explanation for why our results are at odds with these data. In ELSA, blood pressure was measured by a nurse so the prevalence of hypertension was unlikely to be over- or underestimated, which can be an issue when relying on self-report. It has been suggested that the association between sleep hours and raised blood pressure may be stronger in younger people partly because of difference in lifestyles between those in employment and people who are retired, or due to the fact that people with chronic conditions such as hypertension are at a greater risk of premature mortality [22]. However, a meta-analytic review failed to find a significant effect of age on the sleep–blood pressure relationship [7].

While in our analysis of ELSA short sleep was prospectively linked to hypertension in both sexes but somewhat more strongly among men, in the Whitehall II and the Western New York Health studies [26,27] this relationship was only found in women. Sex differences in this context remain poorly understood, but it has been suggested that hormonal influences and psychosocial factors might be implicated, making the association between sleep measures and blood pressure stronger in women, especially those undergoing menopause [22]. For example, in the Western New York study described earlier, short sleep duration was significantly associated with hypertension only in pre-menopausal women [27]. In our data, 161 normotensive women at baseline were pre-menopausal, but only 16 of them reported short sleep (≤5 h); so we were unable to carry out meaningful analyses stratified by menopause status.

Our results also suggest that in older men disturbed sleep is prospectively linked to higher risk of hypertension. There is only a small body of evidence relating sleep quality with blood pressure, and our finding corroborates the extant data. For example, in the CARDIA study of early-middle aged adults, lower sleep maintenance, measured with actigraphy and defined as the proportion of the time spent asleep to the time spent in bed, was associated with greater increases in diastolic and systolic blood pressure at a 5-year follow-up [34]. In the SWAN study of middle-aged women, neither objective nor subjective sleep disturbance was prospectively associated with the development of hypertension [32].

Using data from this large, representative sample of community-dwelling older people, we found that in women disturbed sleep was predictive of higher C-reactive protein and fibrinogen concentrations four years later. Sleep disturbance remains under-explored in relation to low-grade inflammation in population-based studies. There have been a few investigations [14,16,46], including our previous analysis of ELSA [12], that reported associations between sleep problems and inflammatory markers, but these were based on cross-sectional data, making the direction of the sleep–inflammation relationship uncertain. In the Heart and Soul Study, disturbed sleep predicted raised levels of C-reactive protein and fibrinogen five years later in women and not in men, but since all participants had established coronary heart disease, this finding cannot be extrapolated to healthy community-dwelling adults [15].

In these data, sleep duration was not predictive of inflammatory markers at follow-up. This is in contrast with our cross-sectional analysis [12] where long sleep hours were more prevalent among men with elevated C-reactive protein levels. Short and/or long sleep duration have been linked to inflammatory markers in some [16,36], but not all [14,47,48] cross-sectional investigations in this field, and there has been only a handful of prospective studies relating sleep duration with inflammatory markers. An analysis of the Whitehall II study revealed that although decreasing sleep duration was related to higher C-reactive protein and interleukin-6 (IL-6) concentrations in crude statistical models, the association with

C-reactive protein did not survive adjustment for confounders [18]. Hale et al. [17] reported that in a sample of older females, long sleepers had higher fibrinogen levels, and that fibrinogen partly mediated the association between long sleep and coronary heart disease. On the other hand, higher levels of inflammatory marks, including C-reactive protein and fibrinogen, were predictive of longer but not shorter sleep duration approximately six years later in a sample of older Taiwanese men and women [13].

The analyses described here were based on a large and well-described cohort of older men and women living in England [37]. Another important strength of our study is its prospective design. During each wave of data collection, respondents are requested to provide a large number of economic, psychological, behavioural and health measures, which minimises the possibility that participants are aware of the researchers' interests in sleep and cardiovascular risk factors described here.

Our findings need to be interpreted in light of several limitations. Most important is that sleep parameters were assessed with self-report rather than with objective methods, and ratings of sleep can be affected by mood and psychosocial circumstances [49–51]. We addressed these issues by adjusting statistically for socio-economic circumstances, chronic illness and mood disturbances as indexed by the CES-D [41]. Individuals with obstructive sleep apnoea have higher rates of raised blood pressure than individuals with less disturbed/normal sleep [24,25]. Sleep disorders were not assessed in ELSA, but our analyses were adjusted for the presence of a limiting chronic illness, as well as for risk factors associated with sleep apnoea including age, BMI, and smoking [52]. Attrition is an issue in large prospective studies such as ELSA, and it is important to recognise that participants who provided blood differed from those who did not on a number of factors including wealth, depressive symptoms or chronic conditions; although we controlled our statistical models for a range of confounders, we cannot be certain that the same results would have emerged from people not included in the analyses.

In conclusion, we found that in older men and women short sleep and disturbed sleep were associated with a higher risk of incident hypertension four years later, independently of covariates. Age-stratified analyses further revealed that short sleep was prospectively associated with incident hypertension only among men and women younger than 60 years. We also found that women with disturbed sleep were more likely to have elevated concentrations of C-reactive protein and fibrinogen at follow-up. This study adds to a growing body of evidence that aberrant sleep patterns may increase the risk of cardiovascular outcomes through its adverse impact on blood pressure and inflammation.

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Conflicts of interest

None.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2015.02.530.

Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.sleep.2015.02.530.

References

[1] Groeger JA, Zijlstra FRH, Dijk D. Sleep quantity, sleep difficulties and their perceived consequences in a representative sample of some 2000 British adults. J Sleep Res 2004;13(4):359–71.
[2] Institute of Medicine. Sleep disorders and sleep deprivation: an unmet public health problem. Washington, DC: The National Academies Press; 2006.
[3] Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. Sleep 2010;33(5):585–92.
[4] Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J 2011;32(12):1484–92.
[5] Gallicchio L, Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. J Sleep Res 2009;18(2):148–58.
[6] Schmid SM, Hallschmid M, Schultes B. The metabolic burden of sleep loss. Lancet Diabetes Endocrinol 2015;3(1):52–62.
[7] Guo X, Zheng L, Wang J, et al. Epidemiological evidence for the link between sleep duration and high blood pressure: a systematic review and meta-analysis. Sleep Med 2013;14(4):324–32.
[8] Patel SR, Hu FB. Short sleep duration and weight gain: a systematic review. Obesity (Silver Spring) 2008;16(3):643–53.
[9] Irwin MR, Wang MG, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. Arch Intern Med 2006;166(16):1756–62.
[10] van Leeuwen WMA, Lehto M, Karisola P, et al. Sleep restriction increases the risk of developing cardiovascular diseases by augmenting proinflammatory responses through IL-17 and CRP. PLoS ONE 2009;4(2):e4589.
[11] Libby P, Ridker PM, Hansson GK. Progress and challenges in translating the biology of atherosclerosis. Nature 2011;473(7347):317–25.
[12] Jackowska M, Kumari M, Steptoe A. Sleep and biomarkers in the English Longitudinal Study of Ageing: associations with C-reactive protein, fibrinogen, dehydroepiandrosterone sulfate and hemoglobin. Psychoneuroendocrinology 2013;38:1484–93.
[13] Dowd JB, Goldman N, Weinstein M. Sleep duration, sleep quality, and biomarkers of inflammation in a Taiwanese population. Ann Epidemiol 2011;21(11):799–806.
[14] Suarez EC. Self-reported symptoms of sleep disturbance and inflammation, coagulation, insulin resistance and psychosocial distress: evidence for gender disparity. Brain Behav Immun 2008;22(6):960–8.
[15] Prather AA, Epel ES, Cohen BE, Neylan TC, Whooley MA. Gender differences in the prospective associations of self-reported sleep quality with biomarkers of systemic inflammation and coagulation: findings from the Heart and Soul Study. J Psychiatr Res 2013;47(9):1228–35.
[16] Matthews KA, Zheng H, Kravitz HM, et al. Are inflammatory and coagulation biomarkers related to sleep characteristics in mid-life women?: study of Women's Health Across the Nation Sleep Study. Sleep 2010;33(12):1649–55.
[17] Hale L, Parente V, Dowd JB, et al. Fibrinogen may mediate the association between long sleep duration and coronary heart disease. J Sleep Res 2013;22(3):305–14.
[18] Ferrie JE, Kivimaki M, Akbaraly TN, et al. Associations between change in sleep duration and inflammation: findings on C-reactive protein and interleukin-6 in the Whitehall II study. Am J Epidemiol 2013;178(6):956–61.
[19] Zee PC, Turek FW. Sleep and health: everywhere and in both directions. Arch Intern Med 2006;166(16):1686–8.
[20] Gangwisch JE, Heymsfield SB, Boden-Albala B, et al. Sleep duration associated with mortality in elderly, but not middle-aged, adults in a large US sample. Sleep 2008;31(8):1087.
[21] Meerlo P, Sgoifo A, Suchecki D. Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stress systems and stress responsivity. Sleep Med Rev 2008;12(3):197–210.
[22] Dean E, Bloom A, Cirillo M, et al. Association between habitual sleep duration and blood pressure and clinical implications: a systematic review. Blood Press 2012;21(1):45–57.
[23] Chouchou F, Pichot V, Pepin JL, et al. Sympathetic overactivity due to sleep fragmentation is associated with elevated diurnal systolic blood pressure in healthy elderly subjects: the PROOF-SYNAPSE study. Eur Heart J 2013;34(28):2122–31.
[24] Vgontzas AN, Liao DP, Bixler EO, Chrousos GP, Vela-Bueno A. Insomnia with objective short sleep duration is associated with a high risk for hypertension. Sleep 2009;32(4):491–7.
[25] Calhoun DA, Harding SM. Sleep and hypertension. Chest 2010;138(2):434–43.
[26] Cappuccio FP, Stranges S, Kandala NB, et al. Gender-specific associations of short sleep duration with prevalent and incident hypertension – the Whitehall II study. Hypertension 2007;50(4):693–700.
[27] Stranges S, Dorn JM, Cappuccio FP, et al. A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women. J Hypertens 2010;28(5):896–902.
[28] Gangwisch JE, Heymsfield SB, Boden-Albala B, et al. Short sleep duration as a risk factor for hypertension: analyses of the First National Health and Nutrition Examination Survey. Hypertension 2006;47(5):833–9.
[29] Kim J, Jo I. Age-dependent association between sleep duration and hypertension in the adult Korean population. Am J Hypertens 2010;23(12):1286–91.
[30] van den Berg JF, Tulen JHM, Neven AK, et al. Sleep duration and hypertension are not associated in the elderly. Hypertension 2007;50:585–9.

[31] Lopez-Garcia E, Faubel R, Guallar-Castillon P, Leon-Munoz L, Banegas JR, Rodriguez-Artalejo F. Self-reported sleep duration and hypertension in older Spanish adults. J Am Geriatr Soc 2009;57(4):663–8.
[32] Matthews KA, Chang YF, Kravitz HM, et al. Sleep and risk for high blood pressure and hypertension in midlife women: the SWAN (Study of Women's Health Across the Nation) Sleep Study. Sleep Med 2014;15(2):203–8.
[33] Beunza JJ, Martinez-Gonzalez MA, Ebrahim S, et al. Sedentary behaviors and the risk of incident hypertension – the SUN cohort. Am J Hypertens 2007; 20(11):1156–62.
[34] Knutson KL, Van Cauter E, Rathouz PJ, et al. Association between sleep and blood pressure in midlife: the CARDIA Sleep Study. Arch Intern Med 2009;169(11): 1055–61.
[35] Gillespie C, Kuklina EV, Briss PA, Blair NA, Hong Y. Vital signs: prevalence, treatment, and control of hypertension-United States, 1999–2002 and 2005–2008 (Reprinted from MMWR, vol 60, pg 103–108, 2011). J Am Med Assoc 2011;305(15):1531–4.
[36] Miller MA, Kandala NB, Kivimaki M, et al. Gender differences in the cross-sectional relationships between sleep duration and markers of inflammation: whitehall II study. Sleep 2009;32(7):857–64.
[37] Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English Longitudinal Study of Ageing (ELSA). Int J Epidemiol 2013;42(6):1640–8.
[38] Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry 2002;59(2):131–6.
[39] Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. J Clin Epidemiol 1988;41(4):313–21.
[40] Craig R, Deverill C, Pickering K. Quality control of blood, saliva and urine analytes. In: Spronston K, Mindell J, editors. Health Survey for England 2004, methodology and documentation, vol. 2. London: The Information Centre; 2006. p. 34–41.
[41] Steffick DE. Documentation of affective functioning measures in the Health and Retirement Study. Ann Arbor, MI: HRS Health Working Group; 2000.
[42] Hamer M, Chida Y. Associations of very high C-reactive protein concentration with psychosocial and cardiovascular risk factors in an ageing population. Atherosclerosis 2009;206(2):599–603.
[43] Arber S, Bote M, Meadows R. Gender and socio-economic patterning of self-reported sleep problems in Britain. Soc Sci Med 2009;68(2):281–9.
[44] Stranges S, Dorn JM, Shipley MJ, et al. 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(12):1353–64.
[45] Benca RM, Peterson MJ. Insomnia and depression. Sleep Med 2008;9:S3–9.
[46] Liukkonen T, Rasanen P, Ruokonen A, et al. C-reactive protein levels and sleep disturbances: observations based on the northern Finland 1966 birth cohort study. Psychosom Med 2007;69(8):756–61.
[47] Miller MA, Kandala NB, Kumari M, Marmot MG, Cappuccio FP. Relationships between sleep duration and von Willebrand factor, factor VII, and fibrinogen Whitehall II Study. Arterioscler Thromb Vasc Biol 2010;30(10):2032–8.
[48] Taheri S, Austin D, Lin L, Nieto FJ, Young T, Mignot E. Correlates of serum C-reactive protein (CRP) – No association with sleep duration or sleep disordered breathing. Sleep 2007;30(8):991–6.
[49] van den Berg JF, Miedema HME, Tulen JHM, Hofman A, Neven AK, Tiemeier H. Sex differences in subjective and actigraphic sleep measures: a population-based study of elderly persons. Sleep 2009;32(10):1367–75.
[50] Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? Epidemiology 2008;19(6):838–45.
[51] Jackowska M, Dockray S, Hendrickx H, Steptoe A. Psychosocial factors and sleep efficiency: discrepancies between subjective and objective evaluations of sleep. Psychosom Med 2011;73(9):810–16.
[52] Kasai T, Floras JS, Bradley D. Sleep apnea and cardiovascular disease: a bidirectional relationship. Circulation 2012;126:1495–510.