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Exploring the relationship between sleep characteristics and cardiovascular biomarkers among adults aged 46–85 years measured in the Doetinchem cohort study

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We examined the associations between sleep characteristics and cardiovascular biomarkers among middle-aged and older adults from the general population and explored interactions by age and sex. Cross-sectional data from wave 6 (2013–2017) of the Doetinchem Cohort Study were used, including 3,437 adults aged 46–85 years. Sleep characteristics were measured with the Medical Outcomes Study Sleep Scale (MOS-SS). Sleep duration was categorized into short/moderate/long; sleep quality was expressed on a scale between 0 and 100 with higher scores reflecting poorer sleep quality (sleep disturbance, shortness of breath or headache, sleep adequacy, somnolence, snoring). Multivariable linear regression analyses were performed to assess the association between sleep characteristics with cardiovascular biomarkers (Body Mass Index (BMI), mean arterial pressure, cholesterol ratio). Effect-modification by sex and age was examined. Associations were adjusted for age, sex, educational level, cigarette smoking, alcohol consumption, physical activity and the other biomarkers. Almost all unhealthy sleep characteristics were associated with higher BMI, e.g. somnolence (β = 0.023, 95%CI: 0.014–0.031) and short sleep duration (β = 0.723, 95%CI: 0.154–1.291). The association of snoring with BMI was stronger for women (β = 0.044, 95%CI: 0.035–0.053). A higher cholesterol ratio was associated with somnolence and snoring (in particular age group 65–85 years). For hypertension no associations were found with one exception: somnolence was associated with lower mean arterial pressure. Unhealthy sleep characteristics seem predominantly associated with a higher BMI. More research is needed into the mechanisms underlying the associations between sleep characteristics and cardiovascular biomarkers.

Keywords Sleep, Cardiovascular biomarkers, Population-based, Cohort study

One promising area for prevention of cardiovascular diseases (CVD) is sleep[1]. Sleep health, a multifaceted concept, involves the multidimensional pattern of the sleep-wake cycle. Key characteristics of good sleep health include adequate sleep duration, good sleep quality/high sleep efficiency, and sustained alertness during the day[2]. In particular sleep duration has been studied in relation to coronary heart disease, stroke, diabetes mellitus, hypertension and obesity[1,3,4]. Both short and long sleep durations have been associated with these adverse outcomes compared to regular sleep duration, illustrating a U-shaped dose-response relationship[1,3,4]. Sleep duration is a predictor for CVD incidence on top of the well established four health-related lifestyle factors (alcohol consumption, smoking, physical activity and diet)[5]. Besides sleep duration, other sleep characteristics have also been found to be associated with CVD outcomes. For instance, snoring has been linked to a higher prevalence of hypertension among adults in the general population[6]. In adults aged 50–75 years, snoring has been associated with an increased likelihood of dyslipidemia[7]. Furthermore, daytime napping, particularly

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when lasting for more than 30 min per day, has been linked to an increased risk of the metabolic syndrome[8]. A previous longitudinal study suggests that this association is bi-directional, in which the metabolic syndrome leads to daytime napping and vice versa[9]. In addition, subjective sleep quality, often assessed using measures like the Pittsburgh Sleep Quality Index (PSQI), which considers various aspects of sleep, including latency, duration, efficiency, disturbances, medication use, and daytime dysfunction, has been associated with an increased likelihood of coronary artery disease and hypertension based on previous meta-analyses[10,11].

Apart from epidemiological studies, there is also experimental evidence indicating that sleep deficiency can lead to abnormalities in physiological functions related to obesity risk. For instance, sleep deficiency can cause disturbances in hormone levels, such as leptin and ghrelin, which play a critical role in energy and appetite regulation. The imbalances in these hormones could result in increased appetite and, in the longer run, obesity[12]. Conversely, obesity can also impair sleep due to increased visceral neck fat, which may obstruct the airway, leading to more sleep disturbances[13]. These mechanisms suggest the existence of a bidirectional pathway between sleep and obesity.

Despite growing awareness of the importance of sleep for prevention of CVD, previous studies have often focused solely on sleep duration[3,4,14], used different definitions for sleep quality[15–18], or did not differentiate between various aspects of sleep quality[10,11,19]. Moreover, associations between sleep characteristics and CVDs and related biomarkers may vary by age and sex[7,19–21], but most studies do not adequately explore these interactions. Therefore, the aim of this study is to examine the associations between different sleep characteristics and three cardiovascular biomarkers - Body Mass Index (BMI), mean arterial pressure, and cholesterol ratio - among middle-aged and older adults from the general population, and to explore potential interactions by age and sex. These specific biomarkers were chosen because they are important clinical targets in the prevention of CVDs[22–25].

Methods

Study design and participants

Data came from the Doetinchem Cohort Study, a long-running cohort study on health and health-related lifestyle among men and women aged 20–60 years, which started in 1987. At baseline 12,404 inhabitants of Doetinchem participated, which was 62% of an age-sex-stratified random sample. Following the initial wave, a random sample of two-thirds of the participants assessed at baseline was re-invited after five years, and every five years since then, with an average response rate of 78%[26]. The study's seventh wave was finalized in 2023. The study was conducted according to the principles of the World Medical Association Declaration of Helsinki and its amendments since 1964, and in accordance with the Medical Research Involving Human Subject Act (WMO), which was approved by the Medical Ethics Committee of the University Medical Center Utrecht, and all participants have given informed consent.

For this paper, we used data collected during the sixth wave of the Doetinchem Cohort Study, that was conducted from 2013 to 2017, of 3,437 adults aged between 46 and 85 years. We used self-reported data (demographics, sleep characteristics, health characteristics, lifestyle factors) and measured data (weight, height, blood pressure, and cholesterol levels).

Sleep characteristics

Sleep characteristics were assessed using the validated Medical Outcomes Study Sleep Scale (MOS-SS)[27,28], without the item on time falling asleep. Six sleep domains were distinguished. The sleep domain 'sleep disturbances' encompassed the items restless sleep, trouble falling asleep, and awakening during sleep time (see Table 1). 'Shortness of breath or headache' was based on one item on waking up with shortness of breath or a headache. 'Sleep inadequacy' consisted of not feeling rested upon waking up, and having had enough sleep. 'Somnolence' included items on feeling drowsy during the day, trouble staying awake, and daytime napping. 'Snoring' was based on a single item asking about snoring during sleep. For all MOS-SS items a six-point Likert scale ranging from 'all of the time' (= 0) to 'none of the time' (= 5) was used. Per domain numerical sum scores were calculated and then rescaled to a score between 0 and 100, with higher scores indicating more frequent occurrence of sleep problems (27,28). The domain 'sleep duration' was assessed by asking for the usual amount of hours of sleep during a 24-hour period with five response choices, representing 5 h or less, 6 h, 7 h, 8 h, and 9 h or more, which was categorized into: short sleep (≤ 6 h), moderate sleep (7–8 h), and long sleep (≥ 9 h).

Cardiovascular biomarkers

Blood pressure, both systolic and diastolic, was measured using a Durashock 65 from Welch and Allyn (DS65) at the left arm in seated position, ensuring that the participant had not talked for 2–3 min[26]. Mean arterial pressure was calculated using the formula: diastolic + 1/3(systolic-diastolic). Body weight was measured in light clothing without shoes, belts etc. using a weighting scale in kilograms (kg) with one decimal[26]. Body height was obtained with a measuring rod and the number was rounded to the nearest 0.5 centimeters (cm). BMI was calculated by dividing body weight (kg) by height (m) squared. BMI was categorized as normal weight (< 25 kg/m^2), overweight(≥ 25 kg/m^2) and obesity ≥ 30 kg/m^2.

Total- and HDL-cholesterol were measured in serum, from a sample of non-fasting venous blood, at the Lipid Reference Laboratory of Erasmus Medical Center in Rotterdam, using standardized enzymatic methods[26]. Cholesterol ratio was calculated by dividing the HDL-cholesterol by the total-cholesterol. A lower cholesterol ratio indicates better cardiovascular health[25].

Sociodemographic, health and lifestyle characteristics

Sex was defined as sex at birth, man or woman, as registered in civil registers. Age (in years) was dichotomized into middle-age (46–65 years) and older age (65–85 years). Marital status was described as unmarried, married,

	n	%	Missing
Demographics (%)			
Sex (women)	1827	53.2	0
Age (older than 65 years)	1539	44.8	0
Marital status (married)	2696	78.6	6
Level of education			
- Low	1464	43.4	
- Intermediate	1032	30.6	
- High	872	25.9	69
Lifestyle characteristics (%)			
Smoking	412	12.1	35
High alcohol consumption (≥ 1 glass per day)	1088	32.2	61
Physical activity (≥ 4 h per week)	1995	58.1	
Health characteristics (%)			
Chronic conditions			
- Heart attack	155	4.5	8
- Stroke	83	2.5	116
- Type 2 diabetes	249	7.3	3
- Cancer - ≥ 1	414 779	12.1 22.7	6 3
Overweight (25-<30 kg/m^2)	1550	45.2	10
Obesity (≥ 30 kg/m^2)	656	19.1	10
Hypertension (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or antihypertensive medication)	1692	49.3	7
Dyslipidemia (TC ≥ 6.5 mmol/L and/or cholesterol- lowering medication)	1324	38.5	0
Cardiovascular biomarkers (mean (SD))			
BMI (kg/m^2)	3427	26.8 (4.2)	10
Mean arterial pressure (mmHg)	3430	95.6 (10.4)	7
Cholesterol ratio	3426	4.04 (1.4)	11

Table 1. Descriptives of the study population, adults (N = 3437) aged of 46–85 years, Doetinchem cohort study. Abbreviations: BMI, Body Mass Index; SBP, systolic blood pressure, DBP, diastolic blood pressure, TC, total cholesterol, SD, standard deviation.

widower or divorced, and dichotomized into married or not married. Educational level was assessed as the highest level of education achieved, as reported in the fourth wave or third wave of the Doetinchem Cohort Study. Level of education was classified as low (primary, secondary or vocational school), intermediate (intermediate vocational or higher secondary) or high (higher vocational or university).

Hypertension was defined as a systolic blood pressure of 140 mmHg or higher, and/or a diastolic blood pressure of 90 mmHg or higher, and/or the use of antihypertensive medication. Dyslipidemia was defined as a total cholesterol of 6.5 mmol/L or higher, and/or use of cholesterol lowering medication. For chronic conditions, self-report of at least one of the following conditions was used: coronary heart disease, stroke, diabetes mellitus, high blood pressure or cancer. Physical activity was assessed based on self-reported time spent on sports, cycling and other physical activities of at least moderate intensity (> 4 METS) during leisure time. Spending 150 min or more per week on these activities was defined as being physically active[29]. Alcohol consumption was assessed based on the number of standard consumptions of alcohol per week, which was dichotomized into low (no alcohol consumption or < 1 glass per day) and high alcohol consumption (≥ 1 glass per day)[30]. Cigarette smoking was defined as never, former, or current, and dichotomized into (current) smokers and non-smokers.

Statistical analyses

Descriptive statistics were used to describe the study population using percentages for discrete variables, and mean and standard deviation (SD) for continuous variables. The association between sleep characteristics and cardiovascular biomarkers was examined by multivariable linear regression models as associations could be described by a linear equation. The small number respondents with missing values were excluded for those models including those variables. Separate models (n = 18) were built for each combination of a sleep characteristic (sleep disturbances, shortness of breath or headache, sleep inadequacy, somnolence, snoring and sleep duration) and a biomarkers, with the sleep characteristic as independent variable and the cardiovascular biomarkers (BMI, mean arterial pressure and cholesterol ratio) as dependent variable. For each combination of sleep characteristic and cardiovascular risk factor, three types of multivariate models were analyzed. The first model including age and sex gives the crude association between each sleep characteristic and cardiovascular biomarker. The second model included all presumed confounders, which were, in addition to age and sex (if no effect modifiers), educational level, alcohol consumption, smoking of cigarettes and physical activity. The third model included all presumed confounders and the other two cardiovascular biomarkers. Interaction by age and

sex was tested in the third, fully adjusted model by including interaction-terms with age (middle age (46–64 years) versus older age (65–85 years)), respectively sex (men versus women). In case of a statistically significant interaction ($p < 0.05$), these models were presented stratified by sex and/or age. A significance level of $p < 0.05$ was used to determine statistical significance for all associations. The data were analyzed with the Statistical Analysis Software (SAS) version 9.4.

Results

The population consisted of 3,437 participants, of whom ca. 45% were older than 65 years and 53% were women (Table 1). Almost half of the population had overweight (45.1%), and one-fifth (19.1%) was obese. The prevalence of hypertension was 49% and of dyslipidemia 36%. Table 2 shows the distribution of the response categories and mean score for each sleep domain of the MOS-SS on a scale from 0 to 100. Most frequent sleep problems were snoring (37.4, SD 23.1), followed by sleep inadequacy (mean score 34.9, SD 24.1) and sleep disturbances (mean score 31.3, SD 18.8). Shortness of breath or headache had the lowest mean score (10.7, SD 16.8). A sleep duration of 7–8 h was found among 70.8% of respondents, 6 h or less among 22.9% and 9 or more hours a day by 6.3%.

Table 3 presents the associations of sleep characteristics with the cardiovascular biomarkers. Sex was a significant effect modifier in the association between snoring and BMI ($p < 0.001$) and age was an effect modifier in the association between snoring and cholesterol ratio ($p = 0.004$) in the fully adjusted model. Therefore these associations were presented stratified by respectively sex and age. After adjustment for potential confounders and the other biomarkers (model 3), BMI was positively associated with shortness of breath or headache after waking up (β = 0.013, 95%CI:0.004;0.021), sleep inadequacy (β = 0.006, 95%CI:0.00;0.012), somnolence (β = 0.023, 95%CI:0.014;0.031), snoring (β = 0.021, 95%CI:0.014;0.027 for men and β = 0.044, 95%CI:0.035;0.053 for women) and both short (β = 0.465, 95%CI:0.138;0.792) and long (β = 0.723, 95%CI:0.154;1.291) sleep duration. No association was observed for sleep disturbances.

After adjustment for potential confounders (model 2), the only sleep characteristic that was statistically significantly associated with mean arterial pressure was snoring (β = 0.025, 95%CI:0.010;0.039), which became statistically non-significant after adjustment for BMI and HDL/total cholesterol ratio. In the fully adjusted model, somnolence was statistically significant, but negatively, associated with mean arterial pressure (β=−0.024, 95%CI:−0.044;−0.003).

A higher cholesterol ratio was associated with somnolence (β = 0.003 95%CI:0.00;0.006 (model 3), and snoring, with the latter only statistically significant for those of older age (65–85 years (β = 0.004, 95%CI:0.001;0.006) in the full model.

Discussion

The aim of this study was to investigate the relationship between sleep characteristics and cardiovascular biomarkers in middle-aged and older adults, while also exploring potential interactions by age and sex. Unhealthy sleep characteristics seem to be highly intertwined with higher BMI. Snoring and somnolence were also associated with higher cholesterol ratio, while somnolence was associated with a lower mean arterial

Sleep characteristics (by domain and per item)	Response categories (%)						Mean* (SD)
	None of the time	Little of the time	Some of the time	Good bit of the time	Most of the time	All of the time	
Sleep Disturbances							31.3 (18.8)
Restless sleep	15.8	30.0	36.2	12.1	4.2	1.7	
Trouble falling asleep	23.7	30.0	32.0	7.7	4.1	2.5	
Awaken during sleep time	15.9	31.9	35.3	11.9	3.7	1.4	
Shortness of breath or headache	64.3	21.0	12.4	1.5	0.5	0.3	10.7 (16.8)
Sleep inadequacy							34.9 (24.1)
Not feeling rested after waking up	14.2	46.6	15.9	16.2	5.2	1.9	
Not getting the among of sleep needed	14.4	49.1	15.9	13.2	6.0	1.4	
Somnolence							25.9 (16.7)
Drowsy feeling during the day	18.7	39.0	34.9	5.8	1.2	0.3	
Trouble staying awake during the day	34.1	38.0	23.1	3.8	0.7	0.3	
Daytime napping	27.6	21.2	30.2	11.6	5.9	3.2	
Snoring	15.3	21.7	38.5	13.2	7.9	3.5	37.4 (23.1)
Sleep duration	≤ 6 h (%)		7–8 h (%)		≥ 9 h (%)		
	22.9		70.8		6.3		

Table 2. Distribution of response categories and mean score per domain of the MOS-SS among adults aged 46–85 years ($N = 3437$). Abbreviations: MOS-SS, Medical Outcomes Study Sleep Scale, SD, standard deviation. A higher mean score indicates more problems. * Per domain numerical sumscores were calculated and then rescaled to a score between 0 and 100, with higher scores indicating more frequent occurrence of sleep problems.

BMI (kg/m2)	Model 1[b] (β[c] (95% CI))[d]	Model 2[e] (β (95% CI))[d]	Model 3[f] (β (95% CI))[d]
Sleep disturbances	−0.001 (−0.008; 0.007)	−0.003 (−0.010; 0.005)	−0.002 (−0.010; 0.005)
Shortness of breath or headache	**0.016 (0.008; 0.025)**	**0.014 (0.005; 0.023)**	**0.013 (0.004; 0.021)**
Sleep inadequacy	**0.008 (0.002; 0.014)**	0.006 (−0.000; 0.012)	**0.006 (0.000; 0.012)**
Somnolence	**0.027 (0.019; 0.036)**	**0.025 (0.016; 0.034)**	**0.023 (0.014; 0.031)**
Snoring[g]			
Men	**0.026 (0.019; 0.033)**	**0.025 (0.018 (0.032)**	**0.021 (0.014; 0.027)**
Women	**0.048 (0.039; 0.057)**	**0.049 (0.040; 0.058)**	**0.044 (0.035; 0.053)**
Sleep duration[i]			
Long sleep duration	**0.658 (0.317; 0.999)**	**0.521 (0.177; 0.865)**	**0.465 (0.138; 0.792)**
Short sleep duration	**0.859 (0.262; 1.455)**	**0.680 (0.083; 1.277)**	**0.723 (0.154; 1.291)**
Mean Arterial Pressure (mmHg)			
Sleep disturbances	−0.010 (−0.029; 0.009)	−0.012 (−0.031; 0.008)	−0.011 (−0.030; 0.008)
Shortness of breath or headache	0.012 (−0.009; 0.033)	0.011 (−0.011; 0.032)	0.003 (−0.018; 0.023)
Sleep inadequacy	−0.006 (−0.020; 0.009)	−0.005 (−0.020; 0.010)	−0.009 (−0.023; 0.006)
Somnolence	−0.006 (−0.027; 0.015)	−0.007 (−0.028; 0.014)	**−0.024 (−0.044; −0.003)**
Snoring	**0.025 (0.011; 0.039)**	**0.025 (0.010; 0.039)**	0.000 (−0.014; 0.015)
Sleep duration[i]			
Long sleep duration	0.074 (−0.751; 0.899)	0.040 (−0.805; 0.884)	−0.215 (−1.033; 0.603)
Short sleep duration	−0.333 (−1.772; 1.107)	−0.406 (−1.871; 1.060)	−0.924 (−2.347; 0.498)
Cholesterol ratio			
Sleep disturbances	0.001 (−0.001; 0.003)	0.001 (−0.002; 0.003)	0.001 (−0.001; 0.004)
Shortness of breath or headache	0.002 (−0.001; 0.005)	0.000 (−0.003; 0.003)	−0.001 (−0.003; 0.002)
Sleep inadequacy	0.001 (−0.001; 0.003)	0.000 (−0.002; 0.002)	0.000 (−0.002; 0.002)
Somnolence	**0.005 (0.003; 0.008)**	**0.004 (0.002; 0.007)**	**0.003 (0.000; 0.006)**
Snoring[h]			
46–64 years	**0.005 (0.002; 0.008)**	**0.005 (0.002; 0.007)**	0.002 (−0.001; 0.005)
65–85 years	**0.006 (0.004; 0.009)**	**0.006 (0.003; 0.008)**	**0.004 (0.001; 0.006)**
Sleep duration[i]			
Long sleep duration	0.063 (−0.043; 0.170)	0.034 (−0.074; 0.142)	0.003 (−0.102; 0.109)
Short sleep duration	0.056 (−0.131; 0.242)	0.018 (−0.169; 0.206)	−0.009 (−0.193; 0.174)

Table 3. The association of sleep characteristics with cardiovascular biomarkers in adults between the ages of 46–85 years old. The associations are presented in regression coefficients (β) and confidence intervals (95% CI). Abbreviations: BMI, Body Mass Index. CI, Confidence Interval. [a]Measured with Medical Outcomes Study Sleep Scale (MOS-SS) and based on a range from 0–100, with a higher score indicating a more frequent occurrence of the sleep problem. [b]adjusted for age and sex. [c]Unstandardized regression coefficients. [d]Results in bold numbers were significant at p-value ≤ 0.05. [e]Adjusted for age, sex, education level, smoking cigarettes, alcohol consumption and physical activity. [f]Adjusted for age, sex, education level, smoking cigarettes, alcohol consumption, physical activity and the included cardiovascular biomarkers. [g]Significant interaction between snoring and sex in the analyses with BMI (*p<0.001*) in model 3. [h]Significant interaction between snoring and age in the analyses with cholesterol ratio (*p=0.004*) in model 3. [i]Sleep duration per day. Reference category is regular sleep (7–8 h per day).

pressure after adjustment for the other biomarkers. Interactions with sex and age were largely absent with two exceptions: the association between snoring and BMI seem higher for women compared to men, and snoring was associated with higher cholesterol in particular among those aged 65–85 years.

The quite consistent associations of sleep characteristics with BMI are in line with previous studies. Several studies already showed an association between poor sleep quality and overweight/obesity in (younger) adults[14,16,31–34]. Also, both short and long sleep duration were found to be associated with higher BMI in earlier studies[3,4]. Moreover, daytime napping – being part of the definition of somnolence – was a significant predictor of all aspects of the metabolic syndrome, including BMI, in both middle-aged and older adults from a Chinese population[8,9]. Previous studies reported that frequent snoring is associated with hypertension and dyslipidemia and that these associations were partly driven by BMI[6,35]. Findings from our study and previous research suggest the possible influence of healthy sleep on BMI. However, the direction of the association might also be the other way round, with higher BMI influencing the occurrence of sleep problems, for instance uncomfortable sleeping positions due to overweight could lead to frequent awakening during sleep time[31,36].

Our study showed that of all sleep dimensions, only snoring was associated with higher mean arterial pressure. However, this association appeared to be mainly driven by BMI and the cholesterol ratio. The association of snoring with hypertension has often been found[6,35]. Also poor sleep quality has been reported to

be significantly associated with a greater likelihood of hypertension, although this association was not found in European populations[11]. In a rural Chinese population it was shown that among men long sleep duration was associated with higher odds of hypertension[37]. In addition, another study found that the association between sleep duration and higher blood pressure levels also occurred in adults younger than 60 years[38]. In particular it seems that the association between short sleep duration and hypertension decreases with increasing age[20]. In Brazilian adults it was found that 'having sleep disturbances' was associated with a lower prevalence of ideal blood pressure[39]. A study based on the UK biobank demonstrated that a sum score of healthy sleep characteristics was associated with a lower risk of hypertension[40]. However, there are also studies showing no relationship between sleep characteristics, measured by sensor-based measurements, and hypertension[41]. Whether or not sleep characteristics are relevant for blood pressure especially in European population is still unclear, and more research is needed.

For cholesterol a small association with somnolence and snoring (limited to older aged adults) was observed. In line with our findings, other studies found little to no association between sleep quality and sleep disturbances with cholesterol levels[42,43]. Also for cholesterol the associations with sleep characteristics is open for further research.

We found a limited role of interaction by age and sex. Previous studies observed weaker or no associations between sleep problems and cardiovascular biomarkers with increasing age[7,19,21], and this is in contrast with our findings for cholesterol and snoring. The relevance of the interaction with age lies in the possibility that changes in physiological and lifestyle factors that occur with aging might modify the relationship between sleep and cardiovascular risk. However Age interactions might also be due to selective attrition, when those with severe sleep problems or increased cardiovascular risk might have passed away or opted not to participate in the study, potentially attenuating the associations observed. Until now the role of age is not firmly established.

The only interaction by sex was found for snoring and BMI, with a significantly stronger association in women. Some previous studies also found stronger associations in women between sleep characteristics and cardiovascular biomarkers, e.g. sleep duration and hypertension[20] and daytime sleepiness dyslipidemia[21]. Most other studies found no sex-specific associations between sleep characteristics and cardiovascular biomarkers[8,9,44], suggesting that there is currently no evidence for large differences between men and women with regard to the role of sleep characteristics in relation to cardiovascular biomarkers.

The strengths of this study are the large population based sample of men and women, covering a wide age range from 46 to 85 years, with a comprehensive collection of subjective and objective health-related data, including the validated and reliable MOS-SS scale to assess sleep, and measured cardiovascular biomarkers. Moreover, we studied the effect of the separate dimensions of the scale, considering that sleep characteristics may vary widely in health effects and prevalence, and should therefore not be studied in summary measures only[45].

This study had several limitations as well. As this study made use of data from the sixth wave of the Doetinchem Cohort Study, our sample only included participants who had not dropped out of the study, implying the risk of selection bias in our results. Those who participate in such long-running studies are more likely to be aware of their health and higher educated[46]. However, this could have led to an underestimation of the prevalence estimates of sleep and cardiovascular biomarkers, but it is unlikely that this would have led to bias in the examined associations between sleep characteristics and cardiovascular biomarkers[46]. A second limitation is that, ethnic heterogeneity in Doetinchem is relatively low, so the results might not be representative for other populations[47]. Thirdly, the sleep characteristics were measured with self-reported data, implying that the results of this study could be prone to recall bias. Such non-differential misclassification usually results in an underestimation of the associations found[48]. In contrast, differential misclassification could have occurred due to psychological factors and attitudes towards health. For example, participants who feel negatively and worry about their health might also be more likely to report sleeping problems in the questionnaire. This could potentially have led to an overestimation of the associations found in this study[49]. In order to validate the self-reported data, future studies could additionally make use of sensor-based measurements by which sleep patterns (total sleep, sleep onset latency, waking up after sleep onset and sleep efficiency) can be measured more objectively[50]. Also, we explored only a limited number of sleep characteristics. Specific sleep disorders, such as sleep apnea, are also risk indicators for cardiovascular health[7], but were not part of this study. Finally, because of the cross-sectional design of the study and the use of observational data, the causality between sleep quality indicators and cardiovascular biomarkers could not be determined. Also it is important to generate more understanding of the direction of the association between sleep and cardiovascular biomarkers and the mechanisms behind it. Although some statistically significant associations were found, the size of the effect seem to be relative small. With the increasing body of knowledge on sleep and (cardiovascular) health in the future we expect more insight in causality of the associations, the clinical significance and the possibilities of prevention. The current findings suggest that improving sleep quality (especially reducing daytime sleepiness and snoring) may have benefits on weight management and thus be relevant for obesity prevention. Future studies might also explore additional cardiovascular en metabolic biomarkers for sleep, such as inflammatory factors, insulin resistance and Advanced glycation end products (AGEs). This is a growing research field with besides the mentioned challenges many more issues, like the role of the menopause among women, role of chronotype and many more.

In conclusion, evaluating the associations of sleep characteristics with three cardiovascular biomarkers suggest that in particular sleep and BMI are intertwined and that most associations are not age- and sex-specific. Future studies should further explore the mechanisms underlying the associations between sleep characteristics and BMI in particular. This may be relevant for developing targeted interventions to improve cardiovascular outcomes and sleep quality.

Data availability

The data that support the findings of this study are available from National Institute for Public Health and the Environment but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the corresponding authors upon reasonable request and with permission of third party name National Institute for Public Health and the Environment by contacting the scientific committee of the Doetinchem Cohort Study by email: Doetinchemstudie@rivm.nl.

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Author contributions

HSJP and HW developed the idea for the analyses. All authors participated in writing the manuscript, and approved the final version. LWS participated in the data analyses. HSJP, WMMV participated in the data collection.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

The study was conducted according to the principles of the World Medical Association Declaration of Helsinki and its amendments since 1964, and in accordance with the Medical Research Involving Human Subject Act (WMO), which was approved by the Medical Ethics Committee of the University Medical Center Utrecht, and all participants have given informed consent.

Consent for publication

Not applicable.

Additional information

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