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ORIGINAL RESEARCH

Association of Sleep Duration, Napping, and Sleep Patterns With Risk of Cardiovascular Diseases: A Nationwide Twin Study

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BACKGROUND: Although sleep disorders have been linked to cardiovascular diseases (CVDs), the association between sleep characteristics and CVDs remains inconclusive. We aimed to examine the association of nighttime sleep duration, daytime napping, and sleep patterns with CVDs and explore whether genetic and early-life environmental factors account for this association.

METHODS AND RESULTS: In the Swedish Twin Registry, 12 268 CVD-free twin individuals (mean age=70.3 years) at baseline were followed up to 18 years to detect incident CVDs. Sleep duration, napping, and sleep patterns (assessed by sleep duration, chronotype, insomnia, snoring, and daytime sleepiness) were self-reported at baseline. CVDs were ascertained through the Swedish National Patient Registry and the Cause of Death Register. Data were analyzed using a Cox model. In the multiadjusted Cox model, compared with 7 to 9 hours/night, the hazard ratios (HRs) of CVDs were 1.14 (95% CI, 1.01–1.28) for <7 hours/night and 1.10 (95% CI, 1.00–1.21) for ≥10 hours/night, respectively. Compared with no napping, napping 1 to 30 minutes (HR, 1.11 [95% CI, 1.03–1.18]) and >30 minutes (HR, 1.23 [95% CI, 1.14–1.33]) were related to CVDs. Furthermore, a poor sleep pattern was associated with CVDs (HR, 1.22 [95% CI, 1.05–1.41]). The co-twin matched control analyses showed similar results as the unmatched analyses, and there was no significant interaction between sleep characteristics and zygosity (*P* values >0.05).

CONCLUSIONS: Short or long sleep (<7 or ≥10 hours/night), napping, and poor sleep patterns are associated with an increased CVD risk. Genetic and early-life environmental factors may not account for the sleep–CVD association.

Key Words: cardiovascular diseases ■ cohort study ■ sleep ■ twin study

Sleep, a behavior that we typically perform every day, is vitally important to our health.[1] Sleep problems, including inappropriate or low-quality sleep, are a growing and underappreciated determinant of health. Poor sleep can, independent of primary sleep disorders, contribute to several molecular, immune, and neural changes that play a role in disease development.[2]

Previous studies have shown that sleep duration and quality may influence the development of cardiovascular diseases (CVDs).[3] Although insufficient sleep has been consistently reported to increase the risk of CVDs in several meta-analyses,[4–6] the association of excessive sleep and CVDs requires further investigation.[7,8] In addition, whether daytime napping is beneficial or

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CLINICAL PERSPECTIVE

What Is New?

- Short or long (<7 or ≥10 hours/night) nighttime sleep and daytime napping may increase the risk of cardiovascular diseases.
- Poor sleep patterns (comprising inappropriate sleep duration, evening chronotype, frequent insomnia, heavy snoring, or frequent daytime sleepiness) also serve as a risk factor for cardiovascular diseases.

What Are the Clinical Implications?

- Proper sleep duration (7 to 9 hours/night) is beneficial to prevent the development of cardiovascular diseases, but daytime napping may have adverse cardiovascular health effects.
- Sleep health should be evaluated in combination with multiple sleep characteristics (including sleep duration, chronotype, insomnia, snoring, and daytime sleepiness), and a healthy sleep pattern is conducive to reducing the risk of cardiovascular diseases.

Nonstandard Abbreviations and Acronyms

NPR	National Patient Registry
SALT	Screening Across the Lifespan Twin
STR	Swedish Twin Registry

detrimental to cardiovascular health has been debated,[9–11] and the joint effects of nighttime sleep and daytime napping on CVDs have not been well studied.[12] Moreover, as nighttime sleep and daytime napping only reflect parts of sleep behavior, a multidimensional sleep assessment including sleep duration, chronotype,[13] insomnia,[14] snoring,[15] and daytime sleepiness[16] has been introduced to evaluate the overall sleep pattern[17] and its impact on CVDs. However, studies undertaking this comprehensive approach to assess the impact of sleep on CVDs have been limited.[17,18]

Accumulating evidence showed that genetic and early-life environmental factors (such as natural environment, fetal environment, childhood socioeconomic status, etc) might influence sleep habits[8,19,20] and cardiovascular health.[21,22] However, it is unclear whether these factors could contribute to the association between sleep and CVDs. Twins who are raised together typically share their early-life environment and genetic background; therefore, a twin study design is useful to explore whether these unmeasurable factors could play a role in the sleep–CVDs association.[23,24]

In the current study, we aimed to (1) examine the association of nighttime sleep duration and daytime napping with CVDs, (2) assess the overall impact of sleep on CVDs using a comprehensive sleep pattern indicator, and (3) explore whether genetic and early-life environmental factors explain the observed associations using a long-term cohort study of nationwide Swedish twins.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

The study population was drawn from the nationwide STR (Swedish Twin Registry), which began in the 1960s. During 1998 to 2002, all living twins born in 1958 or earlier were recruited to participate in the SALT (Screening Across the Lifespan Twin) study conducted by computer-assisted telephone interview.[23] Of all participants, 14 388 twin individuals participated in the sleep survey in SALT. Of them, we excluded 120 individuals with missing information on nighttime sleep duration and/or daytime napping and 2000 individuals who had prevalent major CVDs (including coronary heart disease [CHD] and stroke) at baseline. Finally, 12 268 individuals remained and were followed up until December 31, 2016 (Figure 1).

Data Collection

Information on age, sex, education, marital status (married/cohabiting, single including divorced and living alone), zygosity status (monozygotic, dizygotic, undetermined zygosity), height, weight, smoking status (never, former/current), alcohol consumption (no/mild drinking, heavy drinking), and physical activity was collected in the SALT study. Education (<8 versus ≥8 years) was defined using the years of formal schooling. Body mass index, calculated as weight (kilograms) divided by height (meter squared), was categorized into the following 4 groups: underweight (<20 kg/m^2), healthy (20–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30 kg/m^2). The level of physical activity was dichotomized as low (including almost never and much less than average) and regular (including less than average, average, more than average, much more than average, and maximum) based on the annual exercise pattern.[25]

Information on the medical history of type 2 diabetes, hypertension, depression, and CVDs were ascertained from the Swedish NPR (National Patient Registry), which covers all inpatient diagnoses in Sweden from

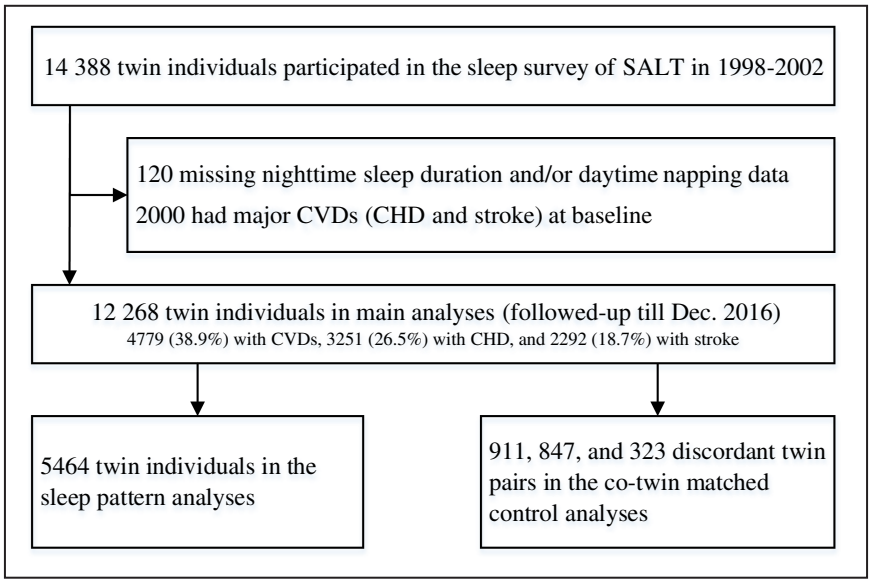

Figure 1. Flowchart of the study population.
CHD indicates coronary heart disease; CVDs, cardiovascular disease; and SALT, Screening Across the Lifespan Twin.

the 1960s and outpatient care (specialist clinic) since 2001.[26] Disease diagnoses were identified based on the *International Classification of Diseases* (*ICD*). The *International Classification of Diseases, Seventh Revision* (*ICD-7*) was used until 1968, the *International Classification of Diseases, Eighth Revision* (*ICD-8*) from 1969 to 1986, the *International Classification of Diseases, Ninth Revision* (*ICD-9*) from 1987 to 1996, and the *International Classification of Diseases, Tenth Revision* (*ICD-10*) since 1997.

All participants provided informed consent, and the study was approved by the Regional Ethics Board at Karolinska Institutet, Stockholm, Sweden, and the Institutional Review Board at the University of Southern California.

Assessment of Sleep Characteristics

Sleep was assessed at baseline based on the Karolinska Sleep Questionnaire, including nighttime sleep duration, daytime napping, chronotype, insomnia, snoring, and daytime sleepiness (Table S1).[27] Nighttime sleep duration was divided into 4 groups: <7, 7 to 9 (ie, ≥7 to <9), 9 to 10 (ie, ≥9 to <10), or ≥10 hours/night.[1,28] Daytime napping was categorized into no napping (0 minutes), 1 to 30 minutes, or >30 minutes/day. Total daily sleep duration was calculated as the sum of nighttime sleep duration and daytime napping duration.

A subsample of SALT participants (n=5464; 44.5%) had complete sleep information. Among these participants, we calculated composite sleep scores, which integrated 5 sleep characteristics (total daily sleep duration, chronotype, insomnia, snoring, and daytime sleepiness) to assess sleep patterns.[17] Low-risk sleep characteristics were defined as follows: total daily sleep duration of 7 to 9 hours, morning person (definitely/to some degree a morning person), never/seldom insomnia symptoms, never heavy snoring, or never/seldom daytime sleepiness. For each sleep characteristic, a score of 1 was assigned if defined as low risk, otherwise a score of 0. Thus, the sum of the aforementioned 5 sleep characteristic scores ranged from 0 to 5. We further categorized the sleep patterns as "healthy" (≥4 scores), "intermediate" (2–3 scores), and "poor" (≤1 score).[17]

Assessment of CVDs

The primary outcomes of this study were major CVDs (including CHD and stroke) according to the previous studies.[17] Diagnoses of CVDs were derived from the NPR and the Swedish Cause of Death Register (recording death dates and underlying and contributing death causes since 1952). CVDs were ascertained according to *ICD-7* through *ICD-10* codes: *ICD-7* codes 420 for CHD and codes 330–332 for stroke, *ICD-8*/*ICD-9* codes 410–414 for CHD and codes 430–434 for stroke, and *ICD-10* codes I20-I25 for CHD and codes I60-I66 for stroke. The date of CVD onset was recorded according to the earliest documented date of the CVD diagnosis in the NPR or the Swedish Cause of Death Register.

Statistical Analysis

Baseline characteristics of the study participants by nighttime sleep duration were compared using χ^2 tests

for categorical variables and ANOVA for continuous variables.

The hazard ratios (HRs) and 95% CIs for the associations between sleep characteristics and CVDs were estimated using Cox proportional hazard models in unmatched analysis among all individuals. Follow-up time was calculated from the baseline date until the date of incident CVDs, date of death, or the censoring date (December 31, 2016), whichever occurred first. The analyses were clustered on twin pairs to compute a robust variance that could control for twin dependency within pairs.[27] The proportional hazard assumption was assessed using the Schoenfeld residuals method, and no violation was observed. In the basic Cox model, we adjusted for age, sex, and education. In the multiadjusted Cox model, we additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes, hypertension, and depression.

We also used restricted cubic splines with 4 knots at the 5th, 35th, 65th, and 95th percentiles[29] to visualize the association of nighttime sleep duration with CVDs. In addition, to assess the joint effects of nighttime sleep duration and daytime napping on the risk of CVDs, we created dummy variables of 12 categories according to the cross-tabulation of nighttime sleep duration (<7, 7–9, 9–10, or ≥10 hours/night) and daytime napping (0, 1–30, or >30 minutes). Multiplicative interaction between nighttime sleep duration and daytime napping was examined by adding an interaction term to the model.[30]

Stratified Cox models by twin pairs were used in the co-twin matched control analyses to explore the role of familial background (ie, genetic and early-life environmental factors) in the association between sleep characteristics and CVDs. Twin pairs discordant both for sleep characteristics and for CVDs status (or CVDs onset dates) were included in these analyses. Finally, 911, 847, and 323 twin pairs were included in the co-twin matched control analyses regarding nighttime sleep duration, daytime napping, and sleep patterns, respectively (Figure 1). If the associations observed in the unmatched analyses among all twin individuals were attenuated in the co-twin matched control analyses, this suggests that genetic and early-life environmental factors might contribute to this association. In addition, the multiplicative interaction term between sleep characteristics and zygosity was included in the Cox model to further examine whether genetic background might account for the sleep–CVD associations.[21,24,31]

Missing values on education (n=52), marital status (n=3), body mass index (n=518), smoking status (n=25), alcohol consumption (n=60), and physical activity (n=4168) were imputed using "multivariate imputation by chained equations" under the missing at random assumption.[32]

In the sensitivity analysis, we performed the following analyses: (1) assessing the associations between sleep characteristics and different CVDs subtypes, including CHD, angina pectoris, myocardial infarction, stroke, hemorrhagic stroke, and ischemic stroke; (2) adjusting for daytime napping when analyzing the association of nighttime sleep duration with CVDs and vice versa; (3) adjusting for anxiety; (4) excluding participants who developed CVDs (n=571) in the first 2 years of follow-up; (5) excluding participants who developed atrial fibrillation (n=351) or heart failure (n=188) before baseline; (6) excluding participants with any missing values; and (7) using the Fine-Gray subdistribution hazard model to evaluate the association between sleep characteristics and CVDs in the presence of competing events (considering noncardiovascular death as a competitive risk factor).

Statistical analyses were performed using R software version 4.0.5 (R Foundation, Vienna, Austria). The R packages were used to impute the missing data (mice, version 3.13.0), to draw restricted cubic splines (rms, version 6.2–0), and to fit Cox proportional hazards models (survival, version 3.2–10). All *P* values were 2-sided, and $P<0.05$ was considered statistically significant.

RESULTS

Characteristics of the Study Population

Of the 12 268 participants, 7036 (57.4%) were female participants, and the mean (SD) age at baseline was 70.3 (7.6) years. The mean (SD) nighttime sleep duration in the population was 8.5 (1.2) hours/night. Among all participants, 830 (6.8%), 6410 (52.2%), 3608 (29.4%), and 1420 (11.6%) had <7, 7 to 9, 9 to 10, and ≥10 hours of sleep/night at baseline, respectively. In total, 5082 (41.4%) had daytime napping, including 2897 (23.6%) with ≤30 minutes and 2185 (17.8%) with >30 minutes.

Compared with those with 7 to 9 hours of sleep/night, individuals with <7 hours of sleep/night were younger; more educated; more likely to be male sex, smokers, and heavy drinkers; and had a higher body mass index. Those with ≥10 hours of sleep/night were older, less educated, and more likely to be female sex and to have type 2 diabetes. In addition, participants with <7 or ≥10 hours of sleep/night were more likely to be single; have a low level of physical activity; and have depression, habitual daytime napping, and poor sleep patterns (Table 1). Baseline characteristics of the study population by sleep pattern are shown in Table S2.

Association Between Sleep Characteristics and CVDs

During a median follow-up of 12.9 years, 4779 participants developed CVDs, including 3251 CHD and 2292 stroke cases. Restricted cubic spline demonstrated a

Table 1. Baseline Characteristics of the Study Population by Sleep Duration (n=12 268)

Characteristics	Sleep duration, h/night				*P* value
	<7 (n=830)	7 to 9 (n=6410)	9 to 10 (n=3608)	≥10 (n=1420)	
Age, y	66.3±8.0	68.9±7.3	72.0±6.8	74.5±7.8	<0.001
Female sex	336 (40.5)	3419 (53.3)	2299 (63.7)	982 (69.2)	<0.001
Education*					
<8 y	421 (51.0)	3394 (53.1)	2068 (57.5)	848 (60.3)	<0.001
≥8 y	404 (49.0)	2994 (46.9)	1528 (42.5)	559 (39.7)	
Marital status*					
Married/cohabiting	493 (59.5)	4232 (66.0)	2320 (64.3)	788 (55.5)	<0.001
Single	336 (40.5)	2176 (34.0)	1288 (35.7)	632 (44.5)	
Zygosity					
Monozygotic	159 (19.2)	1319 (20.6)	776 (21.5)	330 (23.2)	0.006
Dizygotic	567 (68.3)	4425 (69.0)	2511 (69.6)	961 (67.7)	
Undetermined zygosity	104 (12.5)	666 (10.4)	321 (8.9)	129 (9.1)	
Body mass index, kg/m^2*	25.7±3.8	25.1±3.4	25.0±3.4	24.9±4.0	<0.001
<20 (underweight)	38 (4.7)	294 (4.7)	184 (5.4)	109 (8.5)	<0.001
20–24.9 (healthy weight)	321 (39.8)	3024 (48.5)	1663 (48.6)	586 (45.6)	
25–29.9 (overweight)	351 (43.5)	2408 (38.6)	1325 (38.7)	489 (38.1)	
≥30 (obese)	97 (12.0)	509 (8.2)	251 (7.3)	101 (7.9)	
Smoking status*					
Never	390 (47.1)	3658 (57.1)	2319 (64.4)	903 (63.9)	<0.001
Former/current smoking	438 (52.9)	2744 (42.9)	1281 (35.6)	510 (36.1)	
Alcohol consumption*					
No/mild drinking	754 (91.5)	6105 (95.6)	3467 (96.5)	1345 (95.8)	<0.001
Heavy drinking	70 (8.5)	284 (4.4)	124 (3.5)	59 (4.2)	
Physical activity*					
Regular	480 (73.8)	3734 (80.4)	1731 (80.2)	455 (70.2)	<0.001
Low	170 (26.2)	909 (19.6)	428 (19.8)	193 (29.8)	
Type 2 diabetes	55 (6.6)	430 (6.7)	280 (7.8)	149 (10.5)	<0.001
Hypertension	334 (40.2)	2616 (40.8)	1494 (41.4)	560 (39.4)	0.625
Depression	34 (4.1)	107 (1.7)	70 (1.9)	56 (3.9)	<0.001
Daytime napping, min					
0	476 (57.3)	3880 (60.5)	2075 (57.5)	755 (53.2)	<0.001
1–30	208 (25.1)	1551 (24.2)	852 (23.6)	286 (20.1)	
>30	146 (17.6)	979 (15.3)	681 (18.9)	379 (26.7)	
Sleep pattern†	442	3024	1454	544	
Healthy	99 (22.4)	1454 (48.1)	171 (11.8)	60 (11.0)	<0.001
Intermediate	287 (64.9)	1395 (46.1)	991 (68.2)	350 (64.3)	
Poor	56 (12.7)	175 (5.8)	292 (20.1)	134 (24.6)	

Data are presented as mean±SD, number, or number (proportion).

*Missing data: 52 for education, 3 for marital status, 518 for body mass index, 25 for smoking status, 60 for alcohol consumption, and 4168 for physical activity.

†Sleep patterns were analyzed in a subsample (n=5464).

U-shaped curve for the association between nighttime sleep duration and CVDs, with the indication that people with 7 to 9 hours of nighttime sleep had the lowest risk of CVDs (Figure 2). Therefore, 7 to 9 hours of sleep/night was used as the reference group in the analyses.

In multivariable-adjusted Cox models, compared with 7 to 9 hours of sleep/night, <7 (HR, 1.14 [95% CI, 1.01–1.28]) and ≥10 (HR, 1.10 [95% CI, 1.00–1.21]) hours of sleep/night were associated with an increased risk of CVDs. Compared with no napping, 1 to 30 minutes

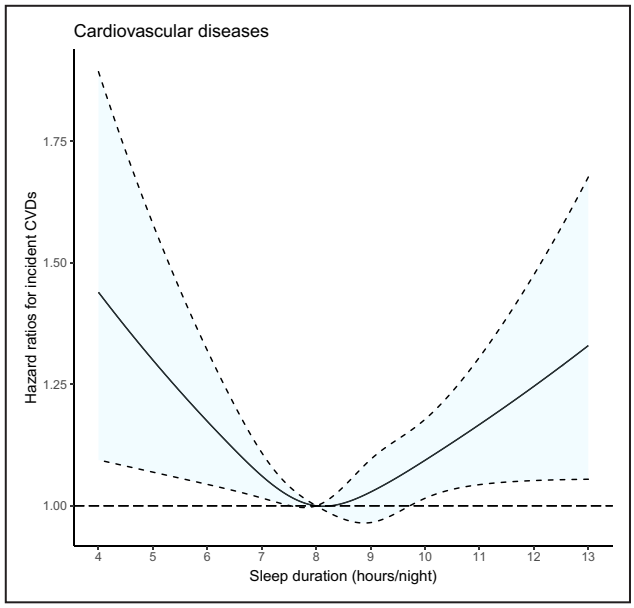

Figure 2. Restricted spline curve for the association of nighttime sleep duration with cardiovascular diseases (CVDs).
Adjusted for age, sex, education, marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes, hypertension, and depression. *P* values for nonlinear associations were <0.05.

(HR, 1.11 [95% CI, 1.03–1.18]) and >30 minutes of napping (HR, 1.23 [95% CI, 1.14–1.33]) were significantly associated with CVDs. Furthermore, compared with the healthy sleep pattern, the poor sleep pattern was associated with an increased risk of CVDs (HR, 1.22 [95% CI, 1.05–1.41]; Figure 3 and Table S3).

Next, we explored the combined effect of nighttime sleep duration and daytime napping on the risk of CVDs. Compared with those with 7 to 9 hours of sleep/night and no napping, participants with both <7 hours of sleep/night and daytime napping of >30 minutes were at the highest risk of CVDs (HR, 1.47 [95% CI, 1.14–1.89]). Moreover, among those with adequate nighttime sleep (7 to 9 hours/night), daytime napping was also related to a higher risk of CVDs (Figure S1). Nevertheless, the overall multiplicative interaction between nighttime sleep duration and daytime napping was not significant (*P* values >0.05).

Association Between Sleep Characteristics and CVDs in Co-Twin Matched Control Analysis

In the co-twin matched control analysis, the association between nighttime sleep duration and CVDs became nonsignificant, but the direction of this association was similar to the initial unmatched analyses. Compared with no napping, daytime napping of 1 to 30 (HR, 1.22 [95% CI, 1.00–1.49]) or >30 (HR, 1.44 [95% CI, 1.13–1.85]) minutes was associated with a higher risk of CVDs. Furthermore, compared with the healthy sleep pattern, the poor sleep pattern (HR, 1.73 [95% CI, 1.10–2.74]) was related to CVDs (Table 2). In general, the associations between sleep characteristics and CVDs were similar in unmatched and co-twin matched control analyses. Moreover, there was no statistically significant interaction between sleep characteristics and zygosity on CVDs (all *P* values >0.05). Therefore, genetic and early-life environmental factors might not contribute to the sleep–CVDs association.

Supplementary Analysis

Similar results were obtained when we repeated the following analyses: (1) analyzing the association of sleep characteristics with CHD, angina pectoris, myocardial infarction, stroke, hemorrhagic stroke, and ischemic stroke separately (Table S4); (2) adjusting for nighttime sleep duration and daytime napping mutually (Table S5); (3) adjusting for anxiety (Table S6); (4) excluding participants who developed CVDs within the first 2 years of follow-up (Table S7); (5) excluding participants who developed atrial fibrillation or heart failure before baseline (Table S8); (6) excluding participants with any missing values (Table S9); and (7) performing competing risk analysis (Table S10).

DISCUSSION

In this large-scale prospective cohort study of nationwide Swedish twins, we found the following: (1) both short and long nighttime sleep (<7 or ≥10 hours/night) and daytime napping were associated with a moderately increased risk of CVDs, (2) poor sleep patterns comprising negative sleep characteristics (ie, insufficient/excessive sleep, evening chronotype, frequent insomnia, heavy snoring, frequent daytime sleepiness) was associated with CVDs, and (3) genetic and early-life environmental factors might not account for the sleep–CVD association.

In line with previous studies, we observed a U-shaped association between nighttime sleep duration and CVDs, indicating that both short and long nighttime sleep were detrimental to cardiovascular health.[4–6,33] However, the definitions of short (such as <5, <6, or <7 hours)[5] and long sleep (such as >8, >9, or >10 hours)[33] have been variable in previous studies. A Joint Consensus Statement has recommended that the optimal nighttime sleep duration for adults is 7 to 9 hours, and sleeping <7 hours/night is considered to be associated with adverse health outcomes.[28] In line with this definition, our study found that nighttime sleep of <7 hours was detrimental to cardiovascular health.[28] Similar to several previous studies, we observed that sleeping ≥10 hours/night was also related to a higher risk of CVDs.[33,34]

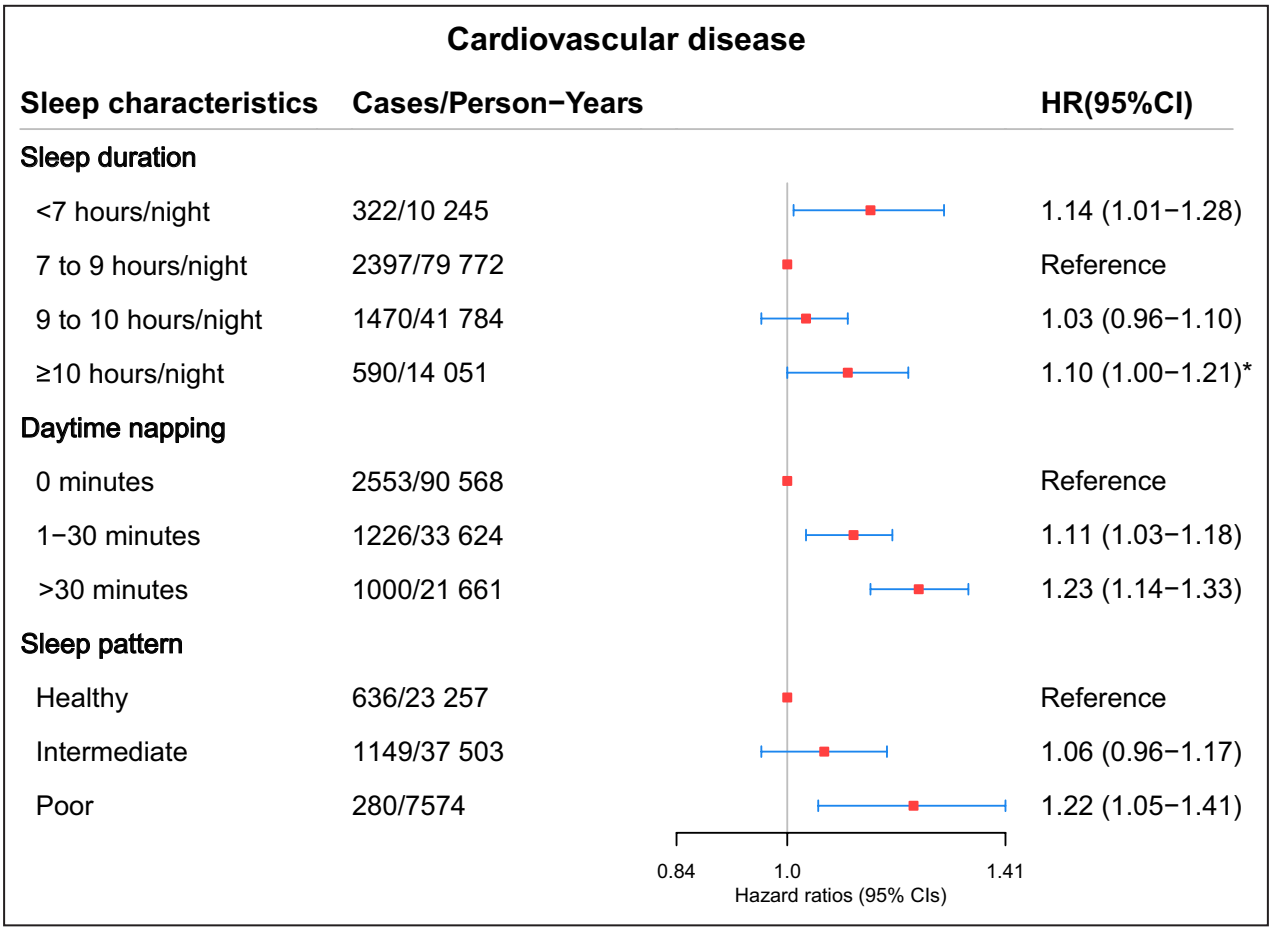

Figure 3. Sleep characteristics and risks of cardiovascular diseases.
Forest plot illustrating the estimated hazard ratios (HRs) and 95% CIs of cardiovascular diseases in relation to sleep characteristics. Adjusted for age, sex, education, marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes, hypertension, and depression. *P<0.05.

Although daytime napping is perceived as a common behavior in older adults,[35] its long-term effect on cardiovascular health remains unclear. A meta-analysis showed that daytime napping of ≥60 minutes was associated with an increased risk of CVDs.[9] In contrast, a Swiss cohort study found that napping once or twice a week was protective against CVDs.[11] In the present study, compared with no napping, both napping 1 to 30 and >30 minutes were associated with an increased risk of CVDs.

The importance of taking into account daytime napping in understanding the association of nighttime sleep duration with cardiovascular risk has been addressed,[12,36] but few studies have been able to study the interplay between daytime napping and nighttime sleep on CVDs. One study found that daytime napping was associated with increased CVDs in those who slept >6 hours/night, but not in those who slept ≤6 hours/night.[34] Another study showed joint effects of sleeping ≥9 hours/night and midday napping >90 minutes on stroke.[10] In the current study, the highest risk of CVDs was shown in individuals with <7 hours of sleep/night and napping ≥30 minutes, and daytime napping was still related to a higher risk of CVDs, even in those with adequate nighttime sleep (7 to 9 hours/night). However, we did not detect a statistically significant interaction in our study.

In addition to nighttime sleep and daytime napping, chronotype, insomnia, snoring, and daytime sleepiness also contribute to the overall sleep pattern. Individuals with later chronotype were more prone to sleep complaints such as insufficient sleep and insomnia.[13] Previous studies found that short sleep with insomnia[30] or poor sleep quality[37] and snoring with daytime sleepiness[38] were associated with a higher risk of CVDs. Snoring could indicate sleep-disordered breathing, which might cause acute or long-term adverse effects on heart health.[39,40] Therefore, it is plausible that different sleep characteristics may influence each other and jointly affect cardiovascular health. By applying a comprehensive assessment of sleep incorporating these characteristics,[17] in line with 2 previous

Table 2. HRs and 95% CIs for the Association Between Sleep Characteristics and Cardiovascular Diseases Among Co-Twin Matched Pairs: Results From Stratified Cox Models

Sleep characteristics	No. of pairs	HR (95% CI)*	HR (95% CI)†
Sleep duration, h/night	911		
<7		1.11 (0.79–1.55)	1.03 (0.72–1.46)
7–9		Reference	Reference
9–10		1.02 (0.85–1.22)	1.01 (0.83–1.21)
≥10		1.10 (0.83–1.47)	1.09 (0.81–1.47)
Daytime napping, min	847		
0		Reference	Reference
1–30		1.28 (1.06–1.55)	1.22 (1.00–1.49)‡
>30		1.50 (1.19–1.90)	1.44 (1.13–1.85)
Sleep pattern	323		
Healthy		Reference	Reference
Intermediate		1.53 (1.14–2.05)	1.61 (1.17–2.23)
Poor		1.79 (1.17–2.74)	1.73 (1.10–2.74)

HR indicates hazard ratio.
*Adjusted for sex and education.
†Additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes, hypertension, and depression.
‡$P<0.05$.

studies,[17,18] we found that the poor sleep pattern was associated with a higher risk of CVDs.

Because genetic or early-life environmental factors can influence sleep habits and cardiovascular health,[8,19–22] it is important to consider these unmeasured factors when evaluating the sleep–CVD association. To our knowledge, this is the first twin study to explore the effects of genetic and early-life environmental factors on the association between sleep and CVDs. We found that genetic and early-life environmental factors may not account for such association. However, considering the smaller sample size of discordant twin pairs in this study, caution is warranted when drawing the conclusion from our findings.

The biological mechanisms underlying the association of multiple sleep characteristics with CVDs are complex and require further understanding. Evidence has suggested that insufficient and poor sleep can trigger insulin resistance,[41] decrease leptin secretion,[42] elevate inflammatory mediators,[43] increase sympathetic activity,[44] and disrupt circadian rhythms,[45,46] which in turn can accelerate the occurrence of cardiovascular risk factors such as diabetes, obesity, atherosclerosis, and hypertension. Prolonged sleep, however, may be a marker that requires medical, neurological, or psychiatric evaluations, especially for older adults.[35] These subclinical states manifested by long sleep may be the underlying cause of CVDs.[33] In addition, after daytime napping, the activation of the sympathetic nervous system can lead to a rapid rise in blood pressure and heart rate.[47,48] A prolonged nap can enter deep slow-wave sleep but often fail to complete the normal sleep cycle, thereby disrupting circadian rhythms.[9]

The strengths of our study include the large sample of nationwide twins, the long-term follow-up period, and the comprehensive assessment of sleep. The twin cohort provides us a unique opportunity to explore the role of genetic and early-life environmental factors in the sleep–CVD association. However, several limitations need to be acknowledged. First, all sleep characteristics were self-reported, which may lead to potential misclassification. However, the misclassification is likely to be nondifferential, thus leading to an underestimation of the observed associations. Although objective sleep measures, such as actigraphy or polysomnography, can provide more accurate sleep assessments, self-reported sleep measures may be used as an easy tool to target individuals at risk of health outcomes. Second, sleep was evaluated only at baseline; therefore, the potential fluctuation of sleep during follow-up was not taken into account. Third, although we included multiple potential confounders in our analyses, residual confounding (such as air pollution[49] and rural–urban environments,[50] etc) could not be taken into account in the analysis because such data were unavailable. Finally, the present study was conducted on twin individuals in Sweden where relatively the wintertime is longer and daytime is shorter than in other countries. Thus, caution is required when generalizing our findings to the general population in other countries.

CONCLUSIONS

In conclusion, our study provides evidence that insufficient (<7 hours/night) or excessive (≥10 hours/night) nighttime sleep, daytime napping, and a poor sleep pattern are associated with an increased risk of CVDs. Genetic and early-life environmental factors may not account for the observed associations. Our findings encourage the adoption of an appropriate night sleep duration (7–9 hours/night) and a healthy sleep pattern to prevent the development of CVDs.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S10
Figure S1

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Supplemental Material

Table S1. Sleep characteristic information questionnaire.

Sleep characteristics	Questionnaire	Response options
Nighttime sleep duration*	What time do you usually go to bed and get up?	Get up at [time] Go to bed at [time]
Daytime napping	Do you usually take a nap at least every second day? If yes, how long do you nap?	Yes [minutes] No
Chronotype	Try to determine to what degree you are a 'morning person' or a 'night person'.	Definitely a morning person To some degree a morning person To some degree a night person Definitely a night person
Insomnia	Have you experienced difficulty falling asleep or continuously waking up and difficulty falling asleep again?	Never Seldom Sometimes Usually Always
Snoring	Have you experienced heavy snoring?	Never Seldom Sometimes Usually Always
Daytime sleepiness	Have you experienced sleepiness during day time?	Never Seldom Sometimes Usually Always

* Nighttime sleep duration was defined as the time difference between "Go to bed" and "Get up".

Table S2. Baseline characteristics of the study population by sleep pattern (N =5464).

Characteristics	Sleep pattern			*P* value
	Healthy (n = 1784)	Intermediate (n = 3023)	Poor (n = 657)	
Age (years)	67.5±8.3	69.0±8.4	69.7±8.5	<0.001
Female	882 (49.4)	1721 (56.9)	387 (58.9)	<0.001
Education *				
<8 years	914 (51.3)	1619 (53.8)	375 (57.2)	0.029
≥8 years	867 (48.7)	1389 (46.2)	281 (42.8)	
Marital status				
Married/cohabiting	1257 (70.5)	2077 (68.8)	445 (67.7)	0.321
Single	527 (29.5)	944 (31.2)	212 (32.3)	
Zygosity				
Monozygotic	328 (18.4)	554 (18.3)	132 (20.1)	0.253
Dizygotic	1260 (70.6)	2176 (72.0)	471 (71.7)	
Undetermined zygosity	196 (11.0)	293 (9.7)	54 (8.2)	
Body mass index (kg/m^2) *	24.8±3.4	25.1±3.5	25.5±3.9	<0.001
<20 (Underweight)	84 (4.9)	160 (5.5)	22 (3.5)	0.001
20−24.9 (Normal weight)	898 (51.9)	1377 (47.1)	286 (45.0)	
25−29.9 (Overweight)	637 (36.8)	1147 (39.2)	265 (41.7)	
≥30 (Obese)	112 (6.5)	242 (8.3)	62 (9.8)	
Smoking status *				
Never	1049 (58.9)	1756 (58.2)	363 (55.3)	0.285
Former/current smoking	733 (41.1)	1260 (41.8)	293 (44.7)	
Alcohol consumption *				
No/mild drinking	1715 (96.3)	2854 (94.9)	614 (94.3)	0.031
Heavy drinking	65 (3.7)	154 (5.1)	37 (5.7)	
Physical activity *				
Regular	1017 (80.9)	1506 (77.1)	262 (67.7)	<0.001
Low	240 (19.1)	448 (22.9)	125 (32.3)	
Type 2 diabetes mellitus	90 (5.0)	217 (7.2)	55 (8.4)	0.003
Hypertension	664 (37.2)	1190 (39.4)	272 (41.4)	0.127
Depression	30 (1.7)	67 (2.2)	24 (3.7)	0.013

Data are presented as mean ± standard deviation or number (proportion, %).

* Missing data: 19 for education, 173 for body mass index, 10 for smoking status, 25 for alcohol consumption, and 1866 for physical activity.

Table S3. Hazard ratios (HRs) and 95% confidence intervals (CIs) of cardiovascular diseases in relation to sleep characteristics; results from Cox models.

Sleep characteristics	Cases/ Person-Years	**HR (95% CI)** [*]	**HR (95% CI)** [†]
Sleep duration (hours/night)			
<7	322/10 245	1.18 (1.05–1.32)	1.14 (1.01–1.28)
7 to 9	2397/79 772	Reference	Reference
9 to 10	1470/41 784	1.02 (0.96–1.09)	1.03 (0.96–1.10)
≥10	590/14 051	1.10 (1.00–1.21) [§]	1.10 (1.00–1.21) [§]
Daytime napping (minutes)			
0	2553/90 568	Reference	Reference
1–30	1226/33 624	1.14 (1.06–1.22)	1.11 (1.03–1.18)
>30	1000/21 661	1.30 (1.20–1.40)	1.23 (1.14–1.33)
Sleep pattern [‡]			
Healthy	636/23 257	Reference	Reference
Intermediate	1149/37 503	1.09 (0.99–1.20)	1.06 (0.96–1.17)
Poor	280/7574	1.27 (1.09–1.47)	1.22 (1.05–1.41)

[*] Adjusted for age, sex, and education.

[†] Additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, and depression.

[‡] Sleep patterns were analyzed in a subsample (n=5464).

[§] P <0.05.

Table S4. Hazard ratios (HRs) and 95% confidence intervals (CIs) of cardiovascular disease subtypes in relation to sleep characteristics; results from Cox models.

Sleep characteristics	Coronary heart diseases			Stroke		
	Cases/Person-Years	HR (95% CI) *	HR (95% CI) †	Cases/Person-Years	HR (95% CI) *	HR (95% CI) †
Sleep duration (hours/night)						
<7	228/10 767	1.21 (1.05–1.39)	1.17 (1.02–1.35)	152/11 399	1.17 (0.99–1.38)	1.13 (0.96–1.34)
7 to 9	1618/83 695	Reference	Reference	1166/87 373	Reference	Reference
9 to 10	1013/43 972	1.06 (0.98–1.15)	1.07 (0.98–1.16)	678/45 933	0.94 (0.86–1.04)	0.96 (0.87–1.05)
≥10	392/14 988	1.11 (0.99–1.24)	1.10 (0.98–1.23)	296/15 292	1.11 (0.97–1.27)	1.11 (0.97–1.27)
Daytime napping (minutes)						
0	1715/94 894	Reference	Reference	1228/98 312	Reference	Reference
1–30	857/35 432	1.17 (1.08–1.28)	1.13 (1.04–1.23)	572/37 329	1.09 (0.99–1.20)	1.07 (0.96–1.18)
>30	679/23 096	1.29 (1.18–1.42)	1.22 (1.12–1.34)	492/24 356	1.29 (1.15–1.43)	1.23 (1.11–1.37)
Sleep pattern ‡						
Healthy	432/24 206	Reference	Reference	318/24 981	Reference	Reference
Intermediate	787/39 478	1.09 (0.96–1.22)	1.06 (0.94–1.19)	555/41 080	1.00 (0.87–1.15)	0.98 (0.85–1.12)
Poor	196/7968	1.31 (1.10–1.56)	1.25 (1.05–1.49)	126/8492	1.05 (0.85–1.30)	1.01 (0.82–1.25)
	Angina pectoris			**Myocardial infarction**		
Sleep duration (hours/night)						
<7	116/11 147	1.14 (0.94-1.38)	1.14 (0.93-1.38)	136/11 476	1.26 (1.05-1.52)	1.22 (1.01-1.47)
7 to 9	826/86 619	Reference	Reference	926/88 311	Reference	Reference
9 to 10	484/45 496	1.06 (0.94-1.19)	1.06 (0.94-1.19)	584/46 643	1.05 (0.94-1.16)	1.05 (0.95-1.17)
≥10	155/15 579	0.95 (0.79-1.13)	0.96 (0.80-1.14)	234/15 704	1.15 (0.99-1.33)	1.13 (0.97-1.31)

Sleep characteristics	Angina pectoris			Myocardial infarction		
	Cases/Person-Years	HR (95% CI) *	HR (95% CI) †	Cases/Person-Years	HR (95% CI) *	HR (95% CI) †
Daytime napping (minutes)						
0	818/97 901	Reference	Reference	980/99 744	Reference	Reference
1–30	439/36 756	1.28 (1.14-1.44)	1.23 (1.10-1.39)	511/37 661	1.19 (1.06-1.32)	1.15 (1.03-1.28)
>30	324/24 183	1.37 (1.20-1.56)	1.30 (1.14-1.49)	389/24 728	1.23 (1.09-1.39)	1.16 (1.03-1.31)
Sleep pattern ‡						
Healthy	211/24 891	Reference	Reference	247/25 335	Reference	Reference
Intermediate	387/40 777	1.11 (0.94-1.31)	1.09 (0.92-1.29)	437/41 881	1.04 (0.89-1.21)	1.01 (0.86-1.18)
Poor	104/8287	1.44 (1.14-1.83)	1.39 (1.09-1.77)	121/8 482	1.38 (1.11-1.72)	1.30 (1.04-1.63)
	Hemorrhagic stroke			**Ischemic stroke**		
Sleep duration (hours/night)						
<7	45/11 961	1.59 (1.15-2.20)	1.53 (1.10-2.13)	109/11 543	1.06 (0.87-1.29)	1.04 (0.85-1.26)
7 to 9	240/91 790	Reference	Reference	909/88 147	Reference	Reference
9 to 10	114/48 467	0.82 (0.65-1.02)	0.83 (0.66-1.04)	542/46 374	0.97 (0.87-1.08)	0.98 (0.88-1.09)
≥10	54/16 317	1.11 (0.82-1.50)	1.10 (0.81-1.50)	228/15 475	1.11 (0.95-1.29)	1.11 (0.96-1.30)
Daytime napping (minutes)						
0	260/103 075	Reference	Reference	941/99 231	Reference	Reference
1–30	105/39 465	0.93 (0.73-1.17)	0.90 (0.72-1.14)	454/37 671	1.13 (1.01-1.27)	1.11 (0.99-1.24)
>30	88/25 995	1.12 (0.87-1.44)	1.08 (0.84-1.38)	393/24 637	1.35 (1.19-1.52)	1.29 (1.14-1.46)

Sleep characteristics	Hemorrhagic stroke			Ischemic stroke		
	Cases/Person-Years	HR (95% CI) [*]	HR (95% CI) [†]	Cases/Person-Years	HR (95% CI) [*]	HR (95% CI) [†]
Sleep pattern [‡]						
Healthy	66/26 089	Reference	Reference	247/25 214	Reference	Reference
Intermediate	99/43 337	0.88 (0.65-1.20)	0.86 (0.63-1.17)	444/41 480	1.03 (0.88-1.20)	1.01 (0.87-1.19)
Poor	25/8964	1.06 (0.67-1.67)	1.01 (0.64-1.61)	95/8557	1.03 (0.81-1.31)	0.99 (0.78-1.26)

[*] Adjusted for age, sex, and education.

[†] Additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, and depression.

[‡] Sleep patterns were analyzed in a subsample (n=5,464).

Table S5. Hazard ratios (HRs) and 95% confidence intervals (CIs) of cardiovascular disease in relation to nighttime sleep duration and daytime napping; results from Cox models.

Sleep characteristics	Cases/ Person-Years	**HR (95% CI)** *
Sleep duration (hours/night)		
<7	322/10 245	1.14 (1.01–1.28)
7 to 9	2397/79 772	Reference
9 to 10	1470/41 784	1.03 (0.96–1.10)
≥10	590/14 051	1.09 (0.99–1.20)
Daytime napping (minutes)		
0	2553/90 568	Reference
1–30	1226/33 624	1.11 (1.03–1.18)
>30	1000/21 661	1.23 (1.14–1.33)

* Adjusted for age, sex, education, marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, depression, nighttime sleep duration, and daytime napping, if applicable.

Table S6. Hazard ratios (HRs) and 95% confidence intervals (CIs) of cardiovascular diseases in relation to sleep characteristics by additionally adjusting for anxiety; results from Cox models.

Sleep characteristics	Cases/ Person-Years	**HR (95% CI)** [*]
Sleep duration (hours/night)		
<7	322/10 245	1.14 (1.01–1.28)
7 to 9	2397/79 772	Reference
9 to 10	1470/41 784	1.03 (0.96–1.10)
≥10	590/14 051	1.10 (1.00–1.21) [‡]
Daytime napping (minutes)		
0	2553/90 568	Reference
1–30	1226/33 624	1.11 (1.03–1.19)
>30	1000/21 661	1.23 (1.14–1.33)
Sleep pattern [†]		
Healthy	636/23 257	Reference
Intermediate	1149/37 503	1.06 (0.96–1.17)
Poor	280/7574	1.22 (1.05–1.41)

[*] Adjusted for age, sex, education, marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, depression, and anxiety.

[†] Sleep patterns were analyzed in a subsample (n=5464).

[‡] P <0.05.

Table S7. Hazard ratios (HRs) and 95% confidence intervals (CIs) of cardiovascular disease in relation to sleep characteristics by excluding participants with CVDs in the first two years of follow-up (N=11 697); results from Cox models.

Sleep characteristics	Cases/ Person-Years	**HR (95% CI)** [*]	**HR (95% CI)** [†]
Sleep duration (hours/night)			
<7	286/10 204	1.18 (1.04–1.34)	1.15 (1.01–1.30)
7 to 9	2135/79 498	Reference	Reference
9 to 10	1301/41 605	1.02 (0.95–1.10)	1.03 (0.96–1.11)
≥10	486/13 942	1.06 (0.96–1.18)	1.06 (0.96–1.17)
Daytime napping (minutes)			
0	2288/90 285	Reference	Reference
1–30	1090/33 488	1.14 (1.06–1.23)	1.11 (1.03–1.19)
>30	830/21 477	1.25 (1.15–1.35)	1.18 (1.09–1.29)
Sleep pattern [‡]			
Healthy sleep	570/23 189	Reference	Reference
Intermediate sleep	1026/37 367	1.09 (0.98–1.21)	1.07 (0.97–1.19)
Poor sleep	247/7537	1.27 (1.09–1.48)	1.23 (1.05–1.43)

[*] Adjusted for age, sex, and education.

[†] Additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, and depression.

[‡] Sleep patterns were analyzed in a subsample (n=5242).

Table S8. Hazard ratios (HRs) and 95% confidence intervals (CIs) of cardiovascular disease in relation to sleep characteristics by excluding participants with atrial fibrillation and heart failure before baseline (N=11 817); results from Cox models.

Sleep characteristics	Cases/ Person-Years	HR (95% CI) *	HR (95% CI) †
Sleep duration (hours/night)			
<7	307/10 089	1.16 (1.03-1.31)	1.13 (1.00-1.27)
7 to 9	2301/78 207	Reference	Reference
9 to 10	1402/40 787	1.03 (0.96-1.10)	1.03 (0.97-1.11)
≥10	535/13 415	1.08 (0.98-1.19)	1.08 (0.98-1.19)
Daytime napping (minutes)			
0	2446/88 980	Reference	Reference
1–30	1167/32 709	1.15 (1.07-1.23)	1.11 (1.03-1.19)
>30	932/20 810	1.30 (1.20-1.41)	1.23 (1.14-1.33)
Sleep pattern ‡			
Healthy sleep	616/22 886	Reference	Reference
Intermediate sleep	1104/36 831	1.09 (0.98-1.20)	1.06 (0.96-1.18)
Poor sleep	265/7433	1.25 (1.08-1.45)	1.20 (1.03-1.39)

* Adjusted for age, sex, and education.

† Additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, and depression.

‡ Sleep patterns were analyzed in a subsample (n=5302).

Table S9. Hazard ratios (HRs) and 95% confidence intervals (CIs) of cardiovascular disease in relation to sleep characteristics by excluding participants with any missing values (N=7865); results from Cox models.

Sleep characteristics	Cases/ Person-Years	HR (95% CI) *	HR (95% CI) †
Sleep duration (hours/night)			
<7	224/8392	1.23 (1.06-1.41)	1.14 (0.98-1.32)
7 to 9	1502/61 943	Reference	Reference
9 to 10	710/27 593	1.01 (0.92-1.10)	1.03 (0.94-1.13)
≥10	219/7720	1.15 (0.99-1.33)	1.07 (0.93-1.24)
Daytime napping (minutes)			
0	1540/69 354	Reference	Reference
1–30	676/23 415	1.16 (1.06-1.27)	1.12 (1.02-1.22)
>30	439/12 878	1.34 (1.20-1.49)	1.24 (1.11-1.38)
Sleep pattern ‡			
Healthy sleep	379/18 035	Reference	Reference
Intermediate sleep	598/27 108	1.09 (0.96-1.23)	1.07 (0.94-1.21)
Poor sleep	141/5061	1.35 (1.11-1.65)	1.27 (1.04-1.55)

* Adjusted for age, sex, and education.

† Additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, and depression.

‡ Sleep patterns were analyzed in a subsample (n=3521)

Table S10. Subdistribution hazard ratios (sHRs) and 95% confidence intervals (CIs) of cardiovascular diseases in relation to sleep characteristics; results from Fine-Gray competitive risk models.

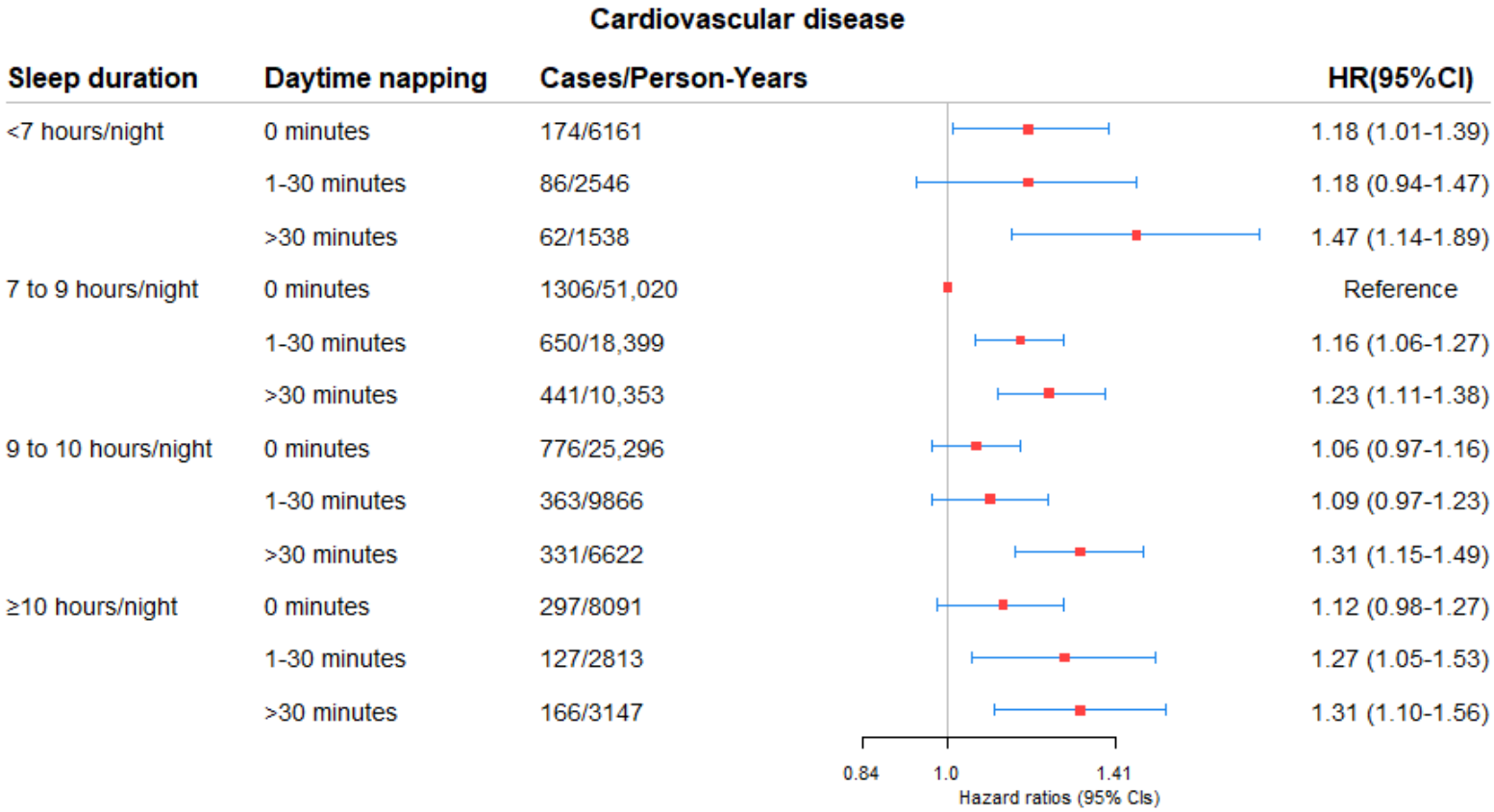
Sleep characteristics	Cases/ Person-Years	**sHR (95% CI)** [*]	**sHR (95% CI)** [†]
Sleep duration (hours/night)			
<7	322/10 245	1.12 (0.99-1.25)	1.09 (0.97-1.23)
7 to 9	2397/79 772	Reference	Reference
9 to 10	1470/41 784	1.04 (0.97-1.11)	1.04 (0.97-1.11)
≥10	590/14 051	0.99 (0.90-1.09)	1.01 (0.91-1.11)
Daytime napping (minutes)			
0	2553/90 568	Reference	Reference
1–30	1226/33 624	1.14 (1.07-1.23)	1.11 (1.04-1.19)
>30	1000/21 661	1.20 (1.11-1.30)	1.15 (1.07-1.25)
Sleep pattern [‡]			
Healthy	636/23 257	Reference	Reference
Intermediate	1149/37 503	1.07 (0.97-1.18)	1.04 (0.95-1.15)
Poor	280/7574	1.22 (1.05-1.41)	1.17 (1.01-1.35)

[*] Adjusted for age, sex, and education.

[†] Additionally adjusted for marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, and depression.

[‡] Sleep patterns were analyzed in a subsample (n=5464).

Figure S1. Hazard ratios (HRs) and 95% confidence intervals (CIs) of the joint effect of nighttime sleep duration and daytime napping on cardiovascular disease.



Adjusted for age, sex, education, marital status, body mass index, smoking status, alcohol consumption, physical activity, type 2 diabetes mellitus, hypertension, and depression.

P value for multiplicative interaction was 0.740.