ORIGINAL RESEARCH

How Are Sleep Characteristics Related to Cardiovascular Health? Results From the Population-Based HypnoLaus study

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Background—Although sleep characteristics have been linked to cardiovascular disease and cardiovascular risk factors, the association between sleep characteristics measured by polysomnography and cardiovascular health (CVH) remains unknown.

Methods and Results—In a population-based sample (n=1826), sleep characteristics were assessed by both sleep questionnaires and polysomnography. Global, behavioral, and biological CVH were defined according to the American Heart Association. Multinomial logistic regressions were performed to estimate relative risk ratios and 95% CI. Strong dose-response associations were found between all oxygen saturation–related variables (oxygen desaturation index, mean oxygen saturation, and percentage of total sleep time spent under 90% oxygen saturation) and obstructive sleep apnea (severity categories and apnea/hypopnea index) and global, behavioral, and biological CVH. Mean oxygen saturation had the strongest positive association (relative risk ratios 1.31 [CI 1.22-1.41]; 1.78 [CI 1.55-2.04] for intermediate relative to ideal CVH), and oxygen desaturation index had the strongest negative association (relative risk ratios 0.71 [CI 0.65-0.78]; 0.45 [CI 0.34-0.58] for intermediate relative to ideal CVH) with global CVH, and these associations were also the most robust in sensitivity analyses. The impacts of sleep architecture and sleep fragmentation were less consistent.

Conclusions—Mean oxygen saturation, oxygen desaturation index, and apnea/hypopnea index were associated with CVH. Conversely, most variables related to sleep architecture and sleep fragmentation were not consistently related to CVH. Sleep-disordered breathing and the associated oxygen (de)saturation were associated with CVH more strongly than with sleep fragmentation. **(*J Am Heart Assoc*. 2019;8:e011372. DOI: 10.1161/JAHA.118.011372.)**

Key Words: cardiovascular disease prevention • cardiovascular health • mean oxygen saturation • oxidative stress • oxygen desaturation index • polysomnography • sleep

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Cardiovascular disease is the leading cause of mortality worldwide.[1] Although a sizable fraction of cardiovascular disease events could be prevented by simple measures,[2] preventive measures toward cardiovascular disease are still insufficiently implemented.[3] Recently, the American Heart Association has reemphasized the need for primordial prevention, ie, the prevention of cardiovascular risk factors, to promote cardiovascular health (CVH).[4] Indeed, several population-based cohort studies have demonstrated the importance of the CVH concept, as they found substantial risk reductions in cardiovascular disease incidence and mortality for subjects with ideal CVH compared with those with poor CVH.[5,6] The American Heart Association defined 4 behavioral (smoking status, body mass index [BMI], physical activity, diet) and 3 biological (fasting blood glucose, total cholesterol, blood pressure) cardiovascular risk factors to assess CVH.[4] Thus, behavioral CVH is modifiable by lifestyle changes, whereas a change in biological CVH usually requires pharmacological interventions.

Sleep-related disorders such as obstructive sleep apnea, excessive daytime sleepiness, and insufficient sleep are highly prevalent in the population[7-9] and have been associated with cardiovascular disease.[7] In a recent review several sleep characteristics including obstructive sleep apnea, excessive daytime sleepiness, and insufficient sleep were linked with cardiovascular risk factors such as obesity, sedentary lifestyle, poor diet, diabetes mellitus, and high blood pressure.[7] Although some sleep characteristics measured by polysomnography (PSG) have previously been associated with

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Clinical Perspective

What Is New?

- This study confirms that higher oxygen saturation is associated with better cardiovascular health.
- Respiratory disturbances during sleep and the associated oxygen (de)saturation are stronger determinants of cardiovascular health than sleep architecture or fragmentation.

What Are the Clinical Implications?

- Because respiratory disturbances during sleep are highly prevalent in the general population and have been found to be associated with worse cardiovascular health, clinicians should be educated to expedite diagnosis and treatment.
- Our results suggest that treatment of obstructive sleep apnea might improve cardiovascular health because the associated oxygen desaturation was consistently associated with cardiovascular health.

cardiovascular disease[10] and with some cardiovascular risk factors,[7,11,12] no study has ever assessed the effect of sleep characteristics measured by PSG on CVH.

Hence, we aimed to investigate the association between various sleep characteristics measured by questionnaire and by PSG and CVH. We hypothesized that subjects with optimal sleep characteristics were more likely to have ideal CVH compared with people with poor sleep characteristics or sleep disorders such as obstructive sleep apnea or excessive daytime sleepiness.

Methods

Due to the sensitivity of the data and the lack of consent for online posting, individual data cannot be made accessible. Only metadata will be made available in digital repositories. Metadata requests can also be performed via the study website (www.colaus-psycolaus.ch).

Population Sampling

HypnoLaus is a population-based sleep cohort study conducted in Lausanne, Switzerland. The HypnoLaus study was performed between September 1, 2009 and June 30, 2013, and participants were recruited among the CoLaus/PsyCoLaus study.[13] This observational prospective study was conducted to assess the prevalence and determinants of cardiovascular risk factors and cardiovascular disease and to identify new determinants of these risk factors. Participants of the CoLaus/PsyCoLaus were identified from a random sample of all adults aged 35 to 75 years living in the city of Lausanne, Switzerland (117 161 habitants), and the initial cohort included 6733 participants (52.5% women).[13]

For the HypnoLaus study, the first 3043 consecutive participants of the first follow-up of the CoLaus/PsyCoLaus study were invited to have a full PSG at home. Of these, 2168 (71%) accepted the invitation; 60 (3%) had technical problems and were invited to undergo a second PSG; 6 participants declined, and 54 participants agreed.[8] Therefore, 2162 complete PSG recordings were obtained in the HypnoLaus cohort and included in this study. The ethics committee of the University of Lausanne approved the CoLaus/HypnoLaus study. The study complies with the Declaration of Helsinki, and written informed consent was obtained from all participants.

Clinical Data Collection

Participants from the CoLaus/HypnoLaus study were invited to attend the outpatient clinic at the University Hospital of Lausanne (CHUV, Lausanne, Switzerland) in the morning after an overnight fast for questionnaire completion, clinical assessment, and blood sample collection. Body weight and height were measured using a calibrated scale and a vertical stadiometer, respectively (Seca, Hamburg, Germany). Systolic and diastolic blood pressure were evaluated in triplicate on the left arm at 5-minute intervals with the participant seated and resting for at least 10 minutes using a calibrated automated oscillometric sphygmomanometer (Omron HEM-907, Matsusaka, Japan).[14] Overnight fasting blood samples were taken from the antecubital vein of each participant. Glucose and total cholesterol were quantified by colorimetric assays as previously described.[13]

These assays were performed within 2 hours on fresh blood samples by the CHUV Clinical Laboratory (Lausanne, Switzerland).

Cardiovascular Health

Global CVH was based on and adapted from the 7 metrics defined by the American Heart Association[4]: 4 behavioral (smoking, BMI, diet, physical activity) and 3 biological (fasting blood glucose, total cholesterol, blood pressure). Global CVH was measured according to the number of metrics at ideal level and categorized into poor (0-2), intermediate (3-4), and ideal (5-7), irrespective of whether subjects had 1 missing CVH metric. Poor, intermediate, and ideal behavioral CVH were defined as having 0-1, 2, and 3-4 behavioral metrics at ideal level, respectively; for biological CVH, these levels were defined as 0-1, 2, and 3 biological metrics at ideal level. The definitions of the CVH metrics are described in Data S1, and the thresholds and categorization of the CVH metrics are summarized in Table S1.

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Polysomnography

The detailed PSG procedure has been described previously.[8] The following PSG measures were used in the analyses: total sleep time (time spent asleep in minutes from sleep onset to morning awakening, categorized as <6, 6 to 8, or >8 hours); stages 1 and 2 sleep, slow-wave sleep, and rapid-eye-movement (REM) sleep (measured as percentage of total sleep time); sleep efficiency (percentage of total time in bed spent asleep); arousal index (number of arousals measured by electroencephalogram per hour of total sleep time divided by 5); autonomic arousal index (number of autonomic arousals measured by pulse wave amplitude drops of at least 30% of baseline pulse wave amplitude per hour of total sleep time [Figure S1]; pulse wave amplitude drops were obtained from finger photoplethysmography and reflect peripheral vasoconstriction[15]); autonomic arousal duration (mean duration of autonomic arousals in seconds [Figure S1]); periodic limb movement index during sleep (number of periodic limb movements divided per hours of sleep); apnea/hypopnea index (AHI) (number of apneas/hypopneas per hour of sleep); severity of obstructive sleep apnea (no [AHI<5 per hour], mild [5≤AHI<15 events per hour of sleep], moderate [15≤AHI<30 events per hour of sleep], or severe [AHI≥30 events per hour of sleep]); oxygen desaturation index (number of ≥3% oxygen saturation drops per hour of sleep); mean oxygen saturation during sleep; and time spent under 90% oxygen saturation (percentage of total sleep time spent under a 90% oxygen saturation threshold).

Subjective Sleep Characteristics

Subjective sleep duration was self-reported and categorized as <6, 6 to 8, and >8 hours. Excessive daytime sleepiness was evaluated with the Epworth sleepiness scale[16] and was considered to be present with a sum score ≥11.

Exclusion Criteria

Participants were excluded from the analyses if they (1) had a previous history of cardiovascular disease, (2) lacked information for more than 1 CVH metric, (3) lacked information on sleep characteristics, or (4) lacked information for covariates.

Statistical Analyses

All statistical analyses were performed using STATA 15.1 (Stata-Corp, College Station, TX). To characterize the study population and to present the prevalence of sleep characteristics according to their CVH, continuous variables were summarized as mean±SD, and categorical variables as the number of subjects with column percentages. Pearson chi-squared (for categorical variables) or ANOVA (for continuous variables) was used to evaluate differences in sleep characteristics between global CVH categories. Because the proportional odds assumption for ordinal regressions was violated, we performed multinomial logistic regressions to assess the effect of sleep characteristics on global, behavioral, and biological CVH and to estimate relative risk ratios. We adjusted for age, sex, education, and living alone status and removed the covariates depression, use of sleeping pills, and alcohol consumption from the final analyses, as Akaike Information Criterion/Bayesian Information Criterion and likelihood ratio test indicated best model fit.

In order to check for the robustness of the results, we performed several sensitivity analyses. First, we operationalized CVH as a continuous variable with the number of metrics at ideal level (0-7) and the sum of metrics at poor, intermediate, or ideal level (score ranging from 0 to 14) (Table S1). Second, we reconstructed behavioral CVH without BMI and reran the analyses with and without adjustment for BMI. Third, we adjusted for depression and for sleeping pill and alcohol consumption (Data S1). Fourth, we performed multinomial regression including all sleep characteristics as explanatory variables for global CVH. Statistical significance was considered for a 2-sided test with $P<0.05$.

Results

Study Population and Characteristics

Of the initial 2162 subjects undergoing PSG, 336 (15.5%) were excluded due to previous self-reported history of cardiovascular disease (n=180), missing information for more than 1 CVH metric (n=104), or missing information on sleep characteristics (n=23) and covariates (n=1), resulting in a sample size of 1826 (84.5%, Figure 1). Excluded subjects were older, with lower educational levels, more often had depressive status, and consumed more sleeping pills and less alcohol than included ones (Table S2).

Table 1 summarizes the characteristics of the study sample according to the global CVH status. Almost half of the subjects had poor (46.2%) or intermediate (42.4%) global CVH, and only 11.5% of subjects had ideal global CVH. Subjects with poor global CVH were more frequently male, were older, had lower education, and were less frequently living alone than subjects with intermediate or ideal global CVH. Subjects with poor global CVH had shorter total sleep time, spent a higher percentage of total sleep time in stage 1 and 2, and lower percentages in slow-wave sleep and REM sleep than subjects with intermediate or ideal global CVH. They also had poorer sleep efficiency, higher arousal index, lower autonomic arousal index, longer autonomic arousal duration, and higher periodic limb movement index than subjects with intermediate or ideal global CVH. Further, subjects with poor global CVH had higher AHI, a higher oxygen

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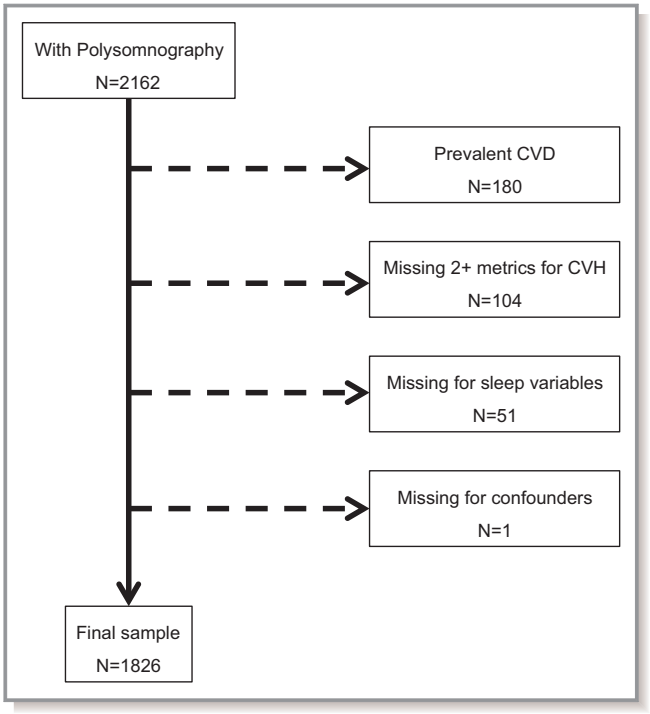

Figure 1. Flowchart of study population. CVD indicates cardiovascular disease; CVH, cardiovascular health.

desaturation index, lower mean oxygen saturation, and spent more time under 90% oxygen saturation than did subjects with intermediate and ideal global CVH. Subjects with poor global CVH were more likely to report short (<6 hours) and long (>8 hours) sleep duration than subjects with intermediate and ideal global CVH. No statistically significant differences for excessive daytime sleepiness were found between global CVH levels.

Sleep Architecture and CVH

Subjects with a higher percentage of stage 1 sleep were less likely, and those with a higher percentage of slow-wave sleep were more likely, to have intermediate global CVH versus poor CVH (Table 2). Similar associations were found for behavioral CVH but not for biological CVH (Table 3). Sleep efficiency was only associated with behavioral CVH. Subjects with a higher arousal index were less likely to have intermediate and ideal global CVH relative to poor CVH. Similar associations were found for behavioral and biological CVH. Autonomic arousal index was not significantly related to global CVH, but subjects with a higher autonomic arousal index were more likely to have intermediate and ideal behavioral CVH, and conversely less likely to have intermediate biological CVH, than those with poor CVH. Subjects with longer autonomic arousals were more likely to have intermediate global CVH than poor CVH. Finally, no associations were found between total sleep time, stage 2, REM, or periodic limb movement index and global, behavioral, or biological CVH.

Obstructive Sleep Apnea Severity and CVH

Subjects with higher AHI were less likely to have intermediate and ideal global, behavioural, and biological CVH than those with poor CVH (Tables 2 and 3). The associations were strongest with global CVH, followed by biological and behavioral CVH. Subjects with more severe obstructive sleep apnea were less likely to have intermediate and even less likely to have ideal global CVH than subjects with no obstructive sleep apnea (Figure 2).

Oxygen Saturation–Related Variables and CVH

Subjects with higher oxygen desaturation index and higher time spent under 90% oxygen saturation were less likely to have intermediate and ideal global CVH versus poor CVH (Table 2). These associations were also significant for behavioral and biological CVH, except for time spent under 90% oxygen saturation and biological CVH (Table 3). The associations were strongest with global CVH, followed by biological and behavioral CVH. Moreover, subjects with higher oxygen saturation were more likely to have better global, behavioral, and biological CVH.

Subjective Sleep Characteristics and CVH

Subjects reporting short sleep duration were more likely to have poor global CVH and less likely to have intermediate and ideal CVH when compared with subjects reporting ideal sleep duration (6-8 hours) (Table 2). Subjects reporting long sleep duration were also less likely to have ideal global CVH compared with those reporting ideal sleep duration. Similar results were found for behavioral but not for biological CVH (Table 3). No relationship between excessive daytime sleepiness and CVH was found.

Sensitivity Analyses

In the first sensitivity analysis, sleep characteristics that were significantly associated with CVH in the main analyses retained their associations with global CVH scores (0-7 or 0-14) (Table S3). Additionally, autonomic arousal index and periodic limb movement index were significantly associated with global CVH (0-14). The standardized β coefficients revealed strongest effects for mean oxygen saturation followed by oxygen desaturation index and AHI.

In the sensitivity analysis using behavioral CVH without BMI, only the association between oxygen desaturation index and intermediate/ideal behavioral CVH (without adjustment for BMI) remained significant, and both mean oxygen saturation and time spent under 90% oxygen saturation retained their association with ideal behavioral CVH (with and without adjustment for BMI). Additionally, both subjective and PSG-assessed short sleep duration were associated with a lower relative risk of having ideal behavioral CVH (Table S4).

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Table 1. Characteristics of the Subjects According to Cardiovascular Health Levels, HypnoLaus Study, Lausanne, 2009-2013

	Cardiovascular Health			
	Poor (N=842)	Intermediate (N=775)	Ideal (N=209)	*P* Value
General characteristics				
Men	524 (62.2)	289 (37.3)	67 (32.1)	<0.001
Age, y	59.3 (10.0)	55.2 (9.7)	50.5 (8.1)	<0.001
Education				
High	142 (16.9)	206 (26.6)	68 (32.5)	<0.001
Middle	222 (26.4)	232 (29.9)	59 (28.2)	
Low	478 (56.8)	337 (43.5)	82 (39.2)	
Living alone status	299 (35.5)	352 (45.4)	95 (45.5)	<0.001
Alcohol consumption				
Never/rare	128 (17.2)	164 (25.1)	45 (26.8)	<0.001
1 to 2 drinks per day	595 (80.1)	483 (74.0)	122 (72.6)	
3+ drinks per day	20 (2.7)	6 (0.9)	1 (0.6)	
Sleeping pills	121 (14.4)	108 (13.9)	32 (15.3)	0.877
Depression	121 (15.4)	95 (13.1)	26 (13.1)	0.395
PSG sleep characteristics				
Total sleep time				
<6 h	241 (28.6)	176 (22.7)	31 (14.8)	0.001
6 to 8 h	503 (59.7)	494 (63.7)	149 (71.3)	
>8 h	98 (11.6)	105 (13.6)	29 (13.9)	
Stage 1 (% of TST)	13.1±7.6	10.7±6.2	9.8±4.2	<0.001
Stage 2 (% of TST)	46.7±10.3	45.5±9.8	45.0±8.0	0.005
Slow-wave sleep (% of TST)	18.7±8.5	21.1±8.0	21.8±7.8	<0.001
Rapid eye movement (% of TST)	21.5±6.1	22.7±5.5	23.3±5.7	<0.001
Sleep efficiency (%)	83.8±10.5	86.3±10.0	88.1±8.5	<0.001
Arousal index	23.5±11.9	19.0±9.0	16.6±7.3	<0.001
Autonomic arousal index	63.0 (23.6)	66.1 (23.1)	71.7 (23.1)	<0.001
Autonomic arousal duration	14.6 (3.3)	13.8 (2.8)	13.6 (2.7)	<0.001
Periodic limb movement index	16.2±25.1	10.5±19.1	7.8±14.2	<0.001
Apnea/hypopnea index	20.2±18.5	10.9±11.6	6.7±7.9	<0.001
Obstructive sleep apnea severity				
No (AHI<5/h)	135 (16.0)	282 (36.4)	127 (60.8)	<0.001
Mild (5≤AHI<15/h)	289 (34.3)	311 (40.1)	56 (26.8)	
Moderate (15≤AHI<30/h)	232 (27.6)	128 (16.5)	20 (9.6)	
Severe (AHI≥30/h)	186 (22.1)	54 (7.0)	6 (2.9)	
Oxygen desaturation index	1.5±1.8	0.6±1.0	0.3±0.6	<0.001
Mean oxygen saturation	93.5±1.8	94.6±1.6	95.4±1.2	<0.001
SpO_2<90	6.1 (14.6)	2.0 (8.7)	0.4 (2.2)	<0.001

Continued

In the sensitivity analysis adjusting for depression, sleeping pills, and alcohol consumption, the sleep characteristics that were significantly associated with CVH in the main analyses retained their significance—except that the association between stage 1, slow-wave sleep and subjective sleep duration was no longer associated with global CVH (Table S5).

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Table 1. Continued

	Cardiovascular Health			
	Poor (N=842)	Intermediate (N=775)	Ideal (N=209)	*P* Value
Subjective sleep characteristics				
Subjective sleep duration*				
<6 h	89 (10.7)	58 (7.6)	12 (5.7)	0.002
6 to 8 h	666 (79.9)	645 (84.0)	190 (90.9)	
>8 h	79 (9.5)	65 (8.5)	7 (3.4)	
Excessive daytime sleepiness†	106 (13.2)	106 (14.2)	26 (12.9)	0.817

N (%) or mean (SD). *P* values from Pearson chi squared or ANOVA when appropriate. AHI indicates apnea/hypopnea index; PSG, polysomnography; SpO_2<90, percentage of total sleep time spent under a 90% oxygen saturation threshold; TST; total sleep time.
*N=1811; †N=1750.

Conversely, the periodic limb movement index was significantly associated with intermediate CVH.

When all sleep characteristics were included as explanatory variables for CVH, mean oxygen saturation was significantly associated with intermediate and ideal CVH. The associations between oxygen desaturation index and ideal CVH as well as autonomic arousal duration and intermediate CVH remained significant. The periodic limb movement index was additionally associated with intermediate CVH (Table S5).

Finally, when sex-stratified analyses were performed and included age squared as a covariate, the results remained stable (results not shown).

Discussion

To our knowledge, this is the first population-based study investigating the association between objective PSG-derived and subjective sleep characteristics and CVH. We found that all variables related to respiratory disturbances—especially those associated with oxygen (de)saturation—were strongly associated with global, behavioral, and biological CVH.

Sleep-Disordered Breathing and Oxygen (De) saturation

We found strong dose-response relationships between sleep-disordered breathing and associated oxygen saturation variables with CVH. Subjects with more severe obstructive sleep apnea (and higher AHI) were less likely to have high levels of global, behavioral, and biological CVH. Interestingly, the association between AHI and CVH became nonsignificant after adjustment for variables related to oxygen saturation. Obstructive sleep apnea is associated with increased sympathetic activity[17] and is characterized by intermittent hypoxia. Hypoxemia has been linked to endothelial dysfunction,[18] arterial stiffness,[19] and oxidative stress,[7,20,21] which are possible underlying mechanisms by which obstructive sleep apnea affects the cardio- and cerebrovascular systems. Our findings that mean oxygen saturation, oxygen desaturation index, and time spent under 90% oxygen saturation were gradually and consistently associated with global, behavioral, and biological CVH are in line with previous studies linking these oxygen saturation–related variables with glucose intolerance, hypertension, increased cholesterol, and obesity.[12,22,23] Moreover, sensitivity analyses revealed that mean oxygen saturation and oxygen desaturation index had the strongest and most robust effects on CVH. Hence, mean oxygen saturation and oxygen desaturation index probably explained the association between other sleep characteristics (stage 1, slow-wave sleep, arousal index, and AHI) and CVH.

Sleep Architecture

Although stage 1 and slow-wave sleep were associated with global and behavioral CVH, these associations were not robust in regard to sensitivity analyses. Because obese people suffer more often from obstructive sleep apnea and consequently have more awakenings during the night, they shift more frequently from slow-wave sleep and REM to light sleep (ie, stages 1 and 2). This suggests that obstructive sleep apnea may be responsible for these results.

Arousal index measured by electroencephalogram was consistently and inversely related to global, biological, and behavioral CVH. The increased sympathetic activity resulting from arousals (and also from hypoxia) can lead to vasoconstriction and has been linked to hypertension, diabetes mellitus, and dyslipidemia[17]—all of which are components of CVH.

Pulse-wave amplitude drops associated with autonomic arousals probably reflect vessel contractility[15]. Previous studies reported inverse associations between pulse-wave amplitude drops index and CV risk in patients with sleep-disordered breathing[24] and in those with obstructive sleep apnea treated with CPAP.[25] Our finding that an autonomic arousal index was positively related to biological CVH and that

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Table 2. Multivariable Analysis of the Associations Between Sleep Characteristics and Global Cardiovascular Health for Each Variable Separately, Adjusted for Age, Sex, Education, and Marital Status; HypnoLaus study, Lausanne, 2009-2013 (N=1826)

	Cardiovascular Health (Poor=Ref.)			
	Intermediate		Ideal	
	RRR (95% CI)	*P* Value	RRR (95% CI)	*P* Value
PSG sleep characteristics				
Total sleep time				
6 to 8 h (Ref.)	1		1	
<6 h	1.05 (0.82-1.35)	0.701	0.74 (0.48-1.16)	0.189
>8 h	0.96 (0.69-1.32)	0.790	0.83 (0.51-1.34)	0.442
Stage 1 (% of TST)	0.98 (0.96-1.00)	0.026	0.97 (0.94-1.00)	0.068
Stage 2 (% of TST)	1.00 (0.99-1.01)	0.477	1.00 (0.98-1.02)	0.924
Slow-wave sleep (% of TST)	1.02 (1.00-1.03)	0.021	1.02 (1.00-1.04)	0.129
Rapid eye movement (% of TST)	1.00 (0.99-1.02)	0.599	1.00 (0.97-1.03)	0.871
Sleep efficiency	1.00 (0.99-1.01)	0.908	1.00 (0.98-1.02)	0.834
Arousal index†	0.91 (0.86-0.96)	<0.001	0.82 (0.74-0.91)	<0.001
Autonomic arousal index†	1.00 (0.97-1.02)	0.764	1.02 (0.98-1.06)	0.296
Autonomic arousal duration	0.96 (0.92-0.99)	0.017	0.98 (0.92-1.05)	0.633
Periodic limb movement index	1.00 (0.99-1.00)	0.127	1.00 (0.99-1.01)	0.510
Apnea/hypopnea index‡	0.75 (0.69-0.82)	<0.001	0.55 (0.44-0.68)	<0.001
Oxygen desaturation index‡	0.71 (0.65-0.78)	<0.001	0.45 (0.34-0.58)	<0.001
Mean oxygen saturation (SpO_2)	1.31 (1.22-1.41)	<0.001	1.78 (1.55-2.04)	<0.001
SpO_2<90	0.97 (0.96-0.98)	<0.001	0.85 (0.77-0.94)	0.001
Subjective sleep characteristics				
Sleep duration§				
6 to 8 h (ref.)	1		1	
<6 h	0.68 (0.47-0.99)	0.044	0.48 (0.25-0.94)	0.031
>8 h	0.94 (0.65-1.38)	0.767	0.39 (0.17-0.90)	0.028
Excessive daytime sleepiness‖	0.97 (0.71-1.33)	0.868	0.71 (0.44-1.17)	0.181

PSG indicates polysomnography; Ref., reference value; RRR, relative risk ratio; SpO_2<90, percentage of total sleep time spent under a 90% oxygen saturation threshold; TST, total sleep time. N's for poor: N=842, intermediate: N=775, ideal: N=209.
†Divided by 5. ‡Divided by 10. §N=1811. ‖N=1750.

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autonomic arousal duration was inversely related to global CVH suggests that frequent and quickly reversible vasoconstrictions are related to increased CVH levels. However, the association between autonomic arousal index and behavioral CVH was unstable, and this hypothesis still needs to be further investigated by prospective studies. Surprisingly, autonomic arousal duration was not negatively associated with ideal CVH. A possible hypothesis is residual confounding because favorable health behaviors tend to cluster in subjects with ideal CVH[26]. These unmeasured health behaviors could affect autonomic arousal duration.

Although periodic limb movement index was not associated with global, behavioral, and biological CVH, the periodic limb movement index had significant effects on global CVH, when additional variables (depression, sleeping pills, alcohol consumption, and other sleep characteristics) were included in the model suggesting interactions with these additional variables. Our unstable findings regarding stage 1, slow-wave sleep, and arousal measures and the lack of a relationship between total sleep time, stage 2, and REM and CVH are in line with a previous study that found no association between sleep architecture and cardiovascular risk factors.[11] Because most variables related to sleep architecture were not consistently related to CVH, we conclude that sleep structure and sleep fragmentation have minor effects on CVH.

Implications

Sleep disorders are highly prevalent in the population[7-9] and have adverse effects on cardiovascular disease.[7,10]

Table 3. Multivariable Analysis of the Associations Between Sleep Characteristics and Behavioral and Biological Cardiovascular Health for Each Variable Separately, Adjusted for Age, Sex, Education, and Marital Status; HypnoLaus Study, Lausanne, 2009-2013

	Behavioral Cardiovascular Health (Poor=Ref.)				Biological Cardiovascular Health (Poor=Ref.)			
	Intermediate		Ideal		Intermediate		Ideal	
	RRR	*P* Value	RRR	*P* Value	RRR	*P* Value	RRR	*P* Value
PSG sleep characteristics								
Total sleep time								
6 to 8 h (Ref.)	1		1		1		1	
<6 h	0.89 (0.69-1.13)	0.338	0.73 (0.51-1.03)	0.069	0.95 (0.70-1.28)	0.725	1.47 (0.89-2.43)	0.137
>8 h	0.78 (0.57-1.08)	0.134	0.76 (0.50-1.14)	0.187	1.15 (0.82-1.61)	0.426	1.13 (0.64-2.01)	0.671
Stage 1 (% of TST)	0.98 (0.97-1.00)	0.046	0.96 (0.94-0.98)	0.002	1.00 (0.98-1.02)	0.854	0.98 (0.94-1.02)	0.312
Stage 2 (% of TST)	1.00 (0.99-1.01)	0.941	1.01 (0.99-1.02)	0.286	0.99 (0.98-1.00)	0.220	0.99 (0.97-1.02)	0.640
Slow-wave sleep (% of TST)	1.01 (1.00-1.03)	0.029	1.01 (1.00-1.03)	0.097	1.01 (0.99-1.02)	0.294	1.01 (0.99-1.04)	0.327
Rapid eye movement (% of TST)	0.99 (0.98-1.01)	0.580	0.99 (0.97-1.02)	0.562	1.01 (0.99-1.03)	0.458	1.01 (0.97-1.05)	0.752
Sleep efficiency	0.99 (0.98-1.00)	0.049	1.00 (0.99-1.02)	0.660	1.01 (1.00-1.03)	0.082	0.98 (0.96-1.00)	0.119
Arousal index†	0.94 (0.90-0.99)	0.025	0.88 (0.82-0.95)	0.001	0.91 (0.85-0.97)	0.005	0.82 (0.71-0.94)	0.004
Autonomic arousal index†	1.03 (1.01-1.06)	0.010	1.04 (1.00-1.07)	0.026	0.97 (0.95-1.00)	0.044	1.03 (0.98-1.08)	0.298
Autonomic arousal duration	0.97 (0.94-1.00)	0.069	0.98 (0.94-1.03)	0.458	0.98 (0.93-1.02)	0.254	0.96 (0.88-1.05)	0.353
Periodic limb movement index	1.00 (0.99-1.00)	0.223	1.00 (0.99-1.00)	0.429	1.00 (0.99-1.00)	0.398	0.99 (0.98-1.01)	0.405
Apnea/hypopnea index‡	0.84 (0.78-0.91)	<0.001	0.66 (0.57-0.76)	<0.001	0.80 (0.71-0.89)	<0.001	0.57 (0.41-0.79)	0.001
Oxygen desaturation index‡	0.82 (0.76-0.89)	<0.001	0.59 (0.50-0.69)	<0.001	0.76 (0.67-0.86)	<0.001	0.52 (0.37-0.75)	<0.001
Mean oxygen saturation (SpO_2)	1.19 (1.11-1.27)	<0.001	1.71 (1.53-1.91)	<0.001	1.18 (1.09-1.28)	<0.001	1.37 (1.17-1.61)	<0.001
SpO_2<90	0.99 (0.98-1.00)	0.012	0.88 (0.83-0.93)	<0.001	0.98 (0.97-1.00)	0.052	0.91 (0.82-1.01)	0.080
Subjective sleep characteristics								
Sleep duration§								
6 to 8 h (Ref.)	1		1		1		1	
<6 h	0.60 (0.41-0.87)	0.007	0.66 (0.40-1.08)	0.095	0.69 (0.44-1.06)	0.090	0.73 (0.34-1.54)	0.408
>8 h	0.93 (0.65-1.34)	0.697	0.45 (0.24-0.83)	0.010	0.79 (0.50-1.25)	0.313	0.39 (0.13-1.11)	0.078
Excessive daytime sleepiness‖	0.76 (0.56-1.04)	0.084	0.77 (0.51-1.16)	0.210	1.03 (0.74-1.45)	0.849	1.07 (0.62-1.84)	0.802

PSG indicates polysomnography; Ref., reference value; RRR, relative risk ratio; SpO_2<90, percentage of total sleep time spent under a 90% oxygen saturation threshold; TST, total sleep time. For behavioral CVH: Poor (N=758), intermediate (N=751), Ideal (N=317). For biological CVH: Poor (N=1251), Intermediate (N=454), Ideal (N=121).
†Divided by 5. ‡Divided by 10. §N=1811. ‖N=1750.

Hence, both clinicians and the public in general should be educated about sleep disorders to expedite diagnosis and treatment.[27] Treatment of obstructive sleep apnea might be a mean to improve CVH, as variables associated with oxygen saturation were consistently associated with global, behavioural, and biological CVH. This is of great public health relevance, since the modifications of the highly prevalent cardiovascular risk factors forming biological CVH otherwise require pharmacological intervention. However, the effect of obstructive sleep apnea treatment on cardiovascular disease has not been established[21] and prospective randomized studies should fill this gap in our clinical knowledge.

Limitations

We acknowledge several limitations. First, because HypnoLaus is a monocentric study focusing on middle-aged and

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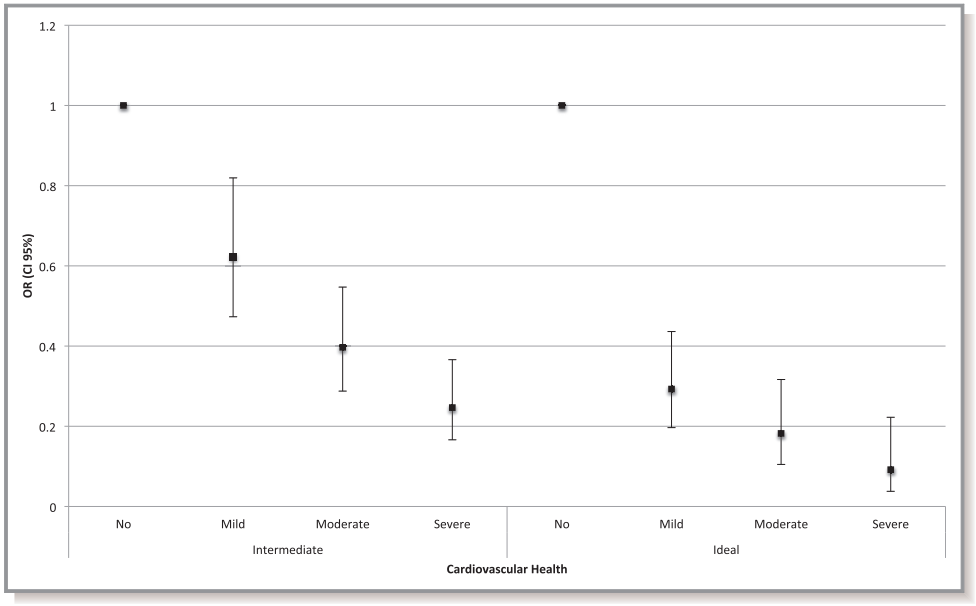

Figure 2. Association of obstructive sleep apnea severity with global cardiovascular health, HypnoLaus study, Lausanne, 2009-2013 (N=1826). RRR indicates relative risk ratio.

elderly subjects, the external validity might be limited to similar aged populations. Second, we had to adapt the smoking and diet metrics as defined by the American Heart Association due to limited information (see Data S1 for more detail). However, such adaptions have previously been used and have yielded consistent results compared with the original American Heart Association CVH score.[28] Third, although PSG is the gold standard for sleep studies, the recording of a single night cannot account for night-to-night variability. In order to limit this so-called "first-night effect," PSG was performed at home, and 20 randomly selected participants underwent a second PSG at home to determine short-term variability. Only, the percentage of total sleep time spent in REM differed between the 2 nights (21.4±6.7% versus 24±5%, P=0.04). Finally, due to the cross-sectional design, causal inferences can only be drawn with caution, and future longitudinal studies are needed to confirm the observed effects. Further, longitudinal studies should also assess whether the associations between sleep characteristics and CVH are bidirectional because effects of cardiovascular risk factors such as diabetes mellitus, dyslipidemia, hypertension, or obesity on sleep have been established.[7,29]

In conclusion, higher oxygen saturation was associated with better CVH, whereas having a higher oxygen desaturation index and AHI were associated with worse CVH. Our results suggest that respiratory disturbances during sleep and their associated oxygen (de)saturation are stronger determinants of CVH than sleep architecture or sleep fragmentation.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

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Data S1.

Cardiovascular health metrics in CoLaus/HypnoLaus

Smoking status was adapted from the American Heart Association criteria, as time since smoking cessation was not available. Ideal smoking status was assigned to subjects that never smoked.

Body mass index (BMI) was categorized according to AHA criteria, with ideal BMI corresponding to a value <25 kg/m^2.

Physical activity was assessed by the physical activity frequency questionnaire (PAFQ), which has been validated in the population of Geneva [1]. This self-reported questionnaire assesses the type and duration of 70 kinds of (non)professional activities and sports during the previous week. We summed up the duration of all walking items including slow cycling and considered fast/uphill walking as vigorous activity together with all other sports assessed in the questionnaire. We counted the frequency of sports (incl. fast/uphill walking) per week and categorized subjects as having ideal physical activity, when subjects reported to either walk more than one hour daily or practicing sports at least three times per week.

Dietary intake was assessed using a self-administered, semi-quantitative food frequency questionnaire (FFQ) [2], which has been validated in the Geneva population [2,3]. Briefly, this FFQ assesses the frequency of 97 different food items of the previous 4 weeks [4]. We adapted the diet measure from the AHA criteria [5] as sodium intake was not available in CoLaus. Hence, the diet metric was constructed from the intake of fruits and vegetables, fiber, fish and sugar-sweetened beverages. Subjects reporting to consume at least 787 g/day fruits and vegetables, at least 85g/day of fiber-rich whole grains, at least 198 g/week fish and less than 153 ml/day of sugar-sweetened beverages were considered as having an ideal diet.

Ideal ***total cholesterol*** and ideal ***fasting plasma glucose*** were defined as untreated values <5.18 mmol/L and <5.55 mmol/L, respectively. Ideal ***blood pressure*** was defined as untreated values <120 mm Hg and <80 mm Hg for systolic and diastolic blood pressure, respectively. All three biological measures correspond to the AHA criteria.

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Covariates

Education level was categorized as low (mandatory education or apprenticeship), intermediate (high school diploma) and high (university diploma). Depressive status was measured with the previously validated 20-item CES-D questionnaire, and subjects were considered as presenting a depressive status when having a sum score of at least 17 for men and 23 for women[6]. Alcohol consumption was categorized as never/less than daily, one or two glasses per day and three or more glasses per day. Consumption of prescribed and over the counter sleep medications was self-reported (yes/no).

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Table S1. CVH metrics as defined by AHA and as used in CoLaus/HypnoLaus.

Metric		Poor	Intermediate	Ideal
Smoking status				
AHA		Current smoker	Former smoker, <12 months	Never or quit >12 months
CoLaus		Current smoker	Former smoker	Never smoker
Body mass index				
AHA		≥30 kg/m^2	25–29.9 kg/m^2	<25 kg/m^2
CoLaus		≥30 kg/m^2	25–29.9 kg/m^2	<25 kg/m^2
Physical activity				
AHA		None	1–149 min/week moderate intensity **or** 1–74 min/week vigorous intensity **or** 1–149 min/week moderate + vigorous	≥150 min/week moderate intensity **or** ≥75 min/week vigorous intensity **or** ≥150 min/week moderate + vigorous
CoLaus		<1 h/ daily, <1 sports weekly	<1 h/day walking **and** 1-2 times sports weekly	≥1 h/day **or** thrice sports weekly
Healthy diet score				
AHA	fruits/veg. ≥ 4.5 cups/day fish ≥twice 3.5oz/week fiber-rich whole grains≥3 oz/day sodium <1500 mg/day sw. beverages ≤ 36 oz/week	0–1 ideal components	2–3 ideal components	4–5 ideal components
CoLaus	fruits/veg. ≥ 787.5 g/day fish ≥198 g/week fiber-rich whole grains ≥85 g/day sw. beverages ≤1064 ml/week	0–1 ideal components	2–3 ideal components	4 ideal components
Total cholesterol				
AHA		≥240 mg/dL	200–239 mg/dL **or** treated to goal	<200 mg/dL
CoLaus		≥6.22 mmol/L	5.18-6.21 mmol/L **or** <5.18 mmol/L on medications	<5.18 mmol/L free of medication
Blood pressure				
AHA		SBP ≥140 **or** DBP ≥90 mm Hg	SBP 120–139 **or** DBP 80–89 mm Hg **or** treated to goal	SBP <120 **and** DBP<80 mm Hg
CoLaus		SBP ≥140 **or** DBP ≥90 mm Hg	SBP 120–139 **or** DBP 80–89 mm Hg **or** <120/80 mm Hg on medication	SBP <120 **and** DBP<80 mm Hg free of medication
Fasting plasma glucose				
AHA		≥ 126 mg/dL	100–125 mg/dL **or** treated to goal	<100 mg/dL
CoLaus		≥ 6.99 mmol/L	5.55-6.98 mmol/L **or** <5.55 mmol/L on medication	< 5,55 mmol/L free of medication

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Table S2. Characteristics of the included and excluded subjects.

	Included (n=1826)	Excluded (n=336)	p-value
Male sex	880 (48.2)	176 (52.4)	0.158
Age (years)*	56.6 ± 10.1	63.8 ± 10.9	<0.001
Education level			<0.001
Low	897 (49.1)	210 (62.9)	
Middle	513 (28.1)	76 (22.8)	
High	416 (22.8)	48 (14.4)	
Living alone	756 (40.9)	139 (43.4)	0.387
Alcohol			0.027
Never/rare	337 (21.6)	70 (26.6)	
1-2 drinks/day	1200 (76.7)	184 (70.0)	
≥3 drinks/day	27 (1.7)	9 (3.4)	
Depression	242 (14.2)	42 (19.6)	0.035
Sleeping pills	261 (14.3)	78 (23.2)	<0.001

N (%) or * mean ± SD. P-values from Pearson chi2 or ANOVA when appropriate

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Table S3. Results of sensitivity analyses for multivariate linear regression: effect of sleep characteristics on cardiovascular health measured as continuous variable ranging from 0-7 and 0-14.

	Cardiovascular health (0-7)		Cardiovascular health (0-14)	
	Beta	**p-value**	**Beta**	**p-value**
Total sleep time				
6-8h (ref.)	0		0	
<6h	-0.015	0.485	-0.021	0.352
>8h	-0.016	0.454	-0.014	0.537
Stage 1	**-0.069**	**0.002**	**-0.087**	**<0.001**
Stage 2	0.001	0.969	-0.009	0.667
Slow wave sleep	**0.049**	**0.024**	**0.059**	**0.008**
Rapid eye movement	0.005	0.807	0.028	0.212
Sleep efficiency	-0.015	0.513	-0.021	0.363
Arousal index§	**-0.104**	**<0.001**	**-0.124**	**<0.001**
Autonomic arousal index§	0.023	0.297	**0.063**	**0.006**
Autonomic arousal duration	**-0.043**	**0.048**	-0.014	0.523
Periodic limb movement index	-0.030	0.176	**-0.061**	**0.008**
Apnea/hypopnea index‖	**-0.184**	**<0.001**	**-0.218**	**<0.001**
Oxygen desaturation index‖	**-0.201**	**<0.001**	**-0.239**	**<0.001**
Mean oxygen saturation (SpO_2)	**0.241**	**<0.001**	**0.280**	**<0.001**
SpO_2<90*	**-0.111**	**<0.001**	**-0.139**	**<0.001**
Subj. sleep duration[1]				
6-8h (ref.)	0		0	
<6h	**-0.056**	**0.008**	**-0.046**	**0.034**
>8h	-0.041	0.055	**-0.054**	**0.013**
Excessive daytime sleepiness [2]	-0.011	0.621	-0.024	0.288

§ divided by 5; ‖ divided by 10; [1] N=1811 [2] N=1750

* Percentage of total sleep time spent under a 90% oxygen saturation threshold

Results are expressed as standardized regression coefficients

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Table S4. Results of sensitivity analyses for multinomial logistic regressions: Effects of sleep characteristics on behavioral CVH constructed without BMI 1) and no adjustment 2) with adjustment for BMI.

	Behavioral CVH without BMI (poor=ref)				**Behavioral CVH without BMI (poor=ref) – adjusted for BMI**			
	Intermediate		**Ideal**		**Intermediate**		**Ideal**	
	RRR	**p-value**	**RRR**	**p-value**	**RRR**	**p-value**	**RRR**	**p-value**
Total sleep time								
6-8h (ref.)	1		1		1		1	
<6h	0.97 (0.69 - 1.36)	0.853	**0.63 (0.43 - 0.91)**	**0.014**	0.96 (0.68 - 1.35)	0.818	0.62 (0.43 - 0.91)	0.013
>8h	0.69 (0.44 - 1.07)	0.094	0.72 (0.46 - 1.14)	0.162	0.71 (0.45 - 1.10)	0.121	0.75 (0.47 - 1.19)	0.222
Stage1	0.98 (0.96 – 1.00)	0.082	0.98 (0.96 – 1.00)	0.062	0.99 (0.97 - 1.01)	0.203	0.99 (0.96 - 1.01)	0.188
Stage2	1.00 (0.99 - 1.02)	0.812	1.01 (0.99 - 1.02)	0.487	1.00 (0.99 - 1.02)	0.805	1.01 (0.99 - 1.02)	0.466
Slow wave sleep	1.01 (0.99 - 1.03)	0.228	1.01 (0.99 - 1.03)	0.504	1.01 (0.99 - 1.03)	0.411	1.00 (0.98 - 1.02)	0.829
Rapid eye movement	1.00 (0.98 - 1.03)	0.954	1.00 (0.98 - 1.03)	0.831	1.00 (0.98 - 1.03)	0.976	1.00 (0.98 - 1.03)	0.882
Sleep efficiency	0.99 (0.98 - 1.01)	0.517	0.99 (0.98 - 1.01)	0.531	0.99 (0.98 - 1.01)	0.457	0.99 (0.98 - 1.01)	0.468
Arousal index[§]	0.98 (0.91 - 1.05)	0.490	0.98 (0.91 - 1.05)	0.500	1.00 (0.93 - 1.07)	0.999	1.01 (0.93 - 1.08)	0.859
Autonomic arousal index[§]	1.01 (0.97 - 1.04)	0.742	1.03 (1.00 - 1.07)	0.085	1.00 (0.97 - 1.04)	0.890	1.03 (0.99 - 1.06)	0.145
Autonomic arousal duration	0.98 (0.93 - 1.03)	0.388	1.01 (0.96 - 1.06)	0.843	0.99 (0.94 - 1.03)	0.575	1.01 (0.96 - 1.07)	0.596
Periodic limb movement index	1.00 (0.99 – 1.00)	0.360	1.00 (0.99 - 1.01)	0.907	1.00 (0.99 - 1.00)	0.539	1.00 (0.99 - 1.01)	0.632
Apnea/hypopnea index[‖]	0.92 (0.84 – 1.00)	0.060	0.91 (0.83 - 1.01)	0.063	0.96 (0.88 - 1.06)	0.447	0.98 (0.88 - 1.08)	0.678
Oxygen desaturation index[‖]	**0.89 (0.81 - 0.97)**	**0.011**	**0.90 (0.81 - 0.99)**	**0.036**	0.94 (0.85 - 1.03)	0.192	0.98 (0.88 - 1.09)	0.653
Mean oxygen saturation (SpO_2)	1.07 (0.98 - 1.16)	0.140	**1.20 (1.10 - 1.32)**	**<0.001**	1.01 (0.92 - 1.11)	0.774	**1.14 (1.03 - 1.26)**	**0.013**
SpO_2<90*	1.00 (0.99 - 1.01)	0.485	**0.98 (0.96 - 0.99)**	**0.001**	1.00 (0.99 - 1.01)	0.884	**0.98 (0.97 - 0.99)**	**0.009**
Subj. sleep duration[1]								
6-8h (ref.)	1		1		1		1	
<6h	0.72 (0.45 - 1.15)	0.174	**0.57 (0.34 - 0.96)**	**0.033**	0.75 (0.47 - 1.20)	0.229	0.60 (0.36 - 1.01)	0.053
>8h	0.87 (0.53 - 1.43)	0.582	0.71 (0.41 - 1.22)	0.213	0.90 (0.54 - 1.49)	0.677	0.74 (0.43 - 1.28)	0.285
Excessive daytime sleepiness [2]	1.05 (0.67 - 1.65)	0.831	0.87 (0.54 - 1.40)	0.560	1.07 (0.68 - 1.69)	0.764	0.89 (0.55 - 1.44)	0.637

[§] divided by 5; [‖] divided by 10; [1] N=1811 [2] N=1750

* Percentage of total sleep time spent under a 90% oxygen saturation threshold

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Table S5. Results of sensitivity analyses for multinomial logistic regressions: Effect of sleep characteristics on global CVH with adjustment for 1) depression, sleeping pills and alcohol (n=1469) and 2) all sleep characteristics (n=1741).

	Global CVH (poor=ref) †				Global CVH (poor=ref) ǂ			
	Intermediate		Ideal		Intermediate		Ideal	
	RRR	**p-value**	**RRR**	**p-value**	**RRR**	**p-value**	**RRR**	**p-value**
Total sleep time								
6-8h (ref.)	1		1		1		1	
<6h	1.00 (0.76 - 1.33)	0.992	0.70 (0.43 - 1.15)	0.160	1.04 (0.77 - 1.40)	0.810	0.73 (0.43 - 1.22)	0.226
>8h	1.04 (0.71 - 1.54)	0.828	0.98 (0.55 - 1.73)	0.945	1.06 (0.75 - 1.51)	0.727	1.12 (0.67 - 1.89)	0.664
Stage1	0.99 (0.97 - 1.01)	0.319	0.98 (0.94 - 1.01)	0.207	0.82 (0.18 - 3.83)	0.805	0.66 (0.09 - 4.79)	0.682
Stage2	0.99 (0.98 – 1.00)	0.178	1.00 (0.98 - 1.02)	0.956	0.83 (0.18 - 3.84)	0.808	0.66 (0.09 - 4.82)	0.686
Slow wave sleep	1.02 (1.00 - 1.03)	0.043	1.01 (0.99 - 1.04)	0.285	0.83 (0.18 - 3.86)	0.813	0.67 (0.09 - 4.84)	0.690
Rapid eye movement	1.01 (0.98 - 1.03)	0.589	1.00 (0.96 - 1.03)	0.924	0.82 (0.18 - 3.82)	0.804	0.65 (0.09 - 4.71)	0.669
Sleep efficiency	1.00 (0.98 - 1.01)	0.506	1.00 (0.97 - 1.02)	0.737	1.00 (0.98 - 1.01)	0.828	0.99 (0.97 - 1.02)	0.463
Arousal index[§]	**0.92 (0.87 - 0.98)**	**0.009**	**0.85 (0.76 - 0.95)**	**0.004**	1.04 (0.96 - 1.13)	0.348	0.92 (0.81 - 1.06)	0.260
Autonomic arousal index[§]	1.00 (0.98 - 1.03)	0.909	1.02 (0.97 - 1.06)	0.422	0.99 (0.96 - 1.01)	0.319	1.01 (0.97 - 1.05)	0.664
Autonomic arousal duration	**0.94 (0.91 - 0.98)**	**0.004**	0.99 (0.93 - 1.06)	0.851	**0.94 (0.91 - 0.98)**	**0.005**	0.95 (0.89 - 1.02)	0.188
Periodic limb movement index	**0.99 (0.99 – 1.00)**	**0.026**	1.00 (0.98 - 1.01)	0.457	**0.99 (0.99 – 1.00)**	**0.038**	1.00 (0.99 - 1.01)	0.874
Apnea/hypopnea index[‖]	**0.78 (0.71 - 0.86)**	**<0.001**	**0.61 (0.49 - 0.76)**	**<0.001**	0.87 (0.69 - 1.09)	0.225	1.02 (0.66 - 1.58)	0.930
Oxygen desaturation index[‖]	**0.74 (0.67 - 0.82)**	**<0.001**	**0.51 (0.39 - 0.67)**	**<0.001**	0.87 (0.68 - 1.11)	0.267	**0.58 (0.35 - 0.97)**	**0.037**
Mean oxygen saturation (SpO_2)	**1.35 (1.24 - 1.47)**	**<0.001**	**1.79 (1.54 - 2.09)**	**<0.001**	**1.27 (1.15 - 1.41)**	**<0.001**	**1.59 (1.35 - 1.87)**	**<0.001**
SpO_2<90*	**0.97 (0.95 - 0.98)**	**<0.001**	**0.84 (0.75 - 0.94)**	**0.004**	1.00 (0.99 - 1.02)	0.500	1.00 (0.94 - 1.06)	0.971
Subj. sleep duration[1]								
6-8h (ref.)	1		1		1		1	
<6h	0.66 (0.43 - 1.01)	0.056	0.53 (0.26 - 1.10)	0.089	0.74 (0.50 - 1.10)	0.140	0.57 (0.29 - 1.14)	0.113
>8h	0.97 (0.62 - 1.53)	0.905	0.40 (0.15 - 1.07)	0.068	1.03 (0.68 - 1.56)	0.893	0.42 (0.18 - 1.02)	0.054
Excessive daytime sleepiness [2]	1.06 (0.75 - 1.51)	0.726	0.68 (0.38 - 1.22)	0.197	1.06 (0.76 - 1.48)	0.714	0.83 (0.50 - 1.40)	0.490

[§]divided by 5; [‖] divided by 10; [1] 1) N=1461 [2] 1) N= 1428

† adjusting for depression, sleeping pills and alcohol; ǂ adjusting for all sleep characteristics; * Percentage of total sleep time spent under a 90% oxygen saturation threshold

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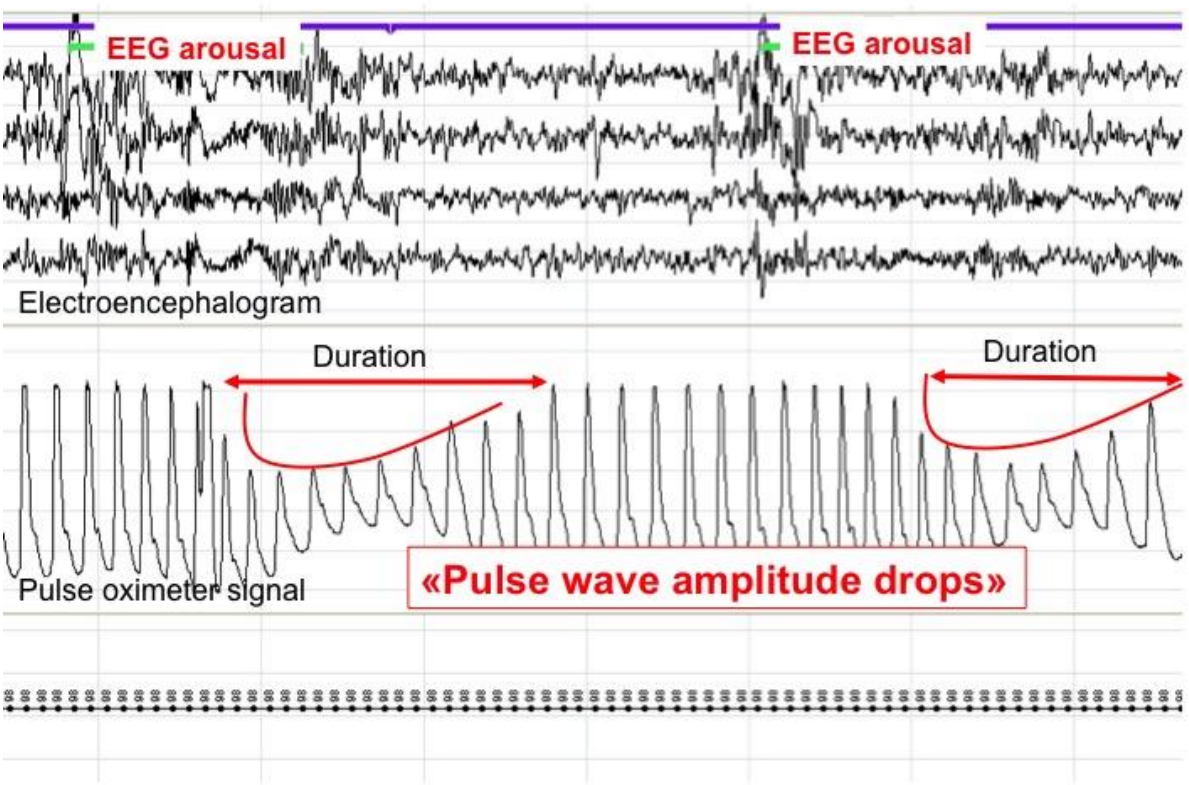
Figure S1. Measurement of pulse wave amplitude drops of at least >30% of baseline pulse wave amplitude.



EEG: Electroencephalography

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