

Association between Sleep Disturbances and Cardiovascular Diseases: Results from NHANES

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Abstract

Objectives: The relationship between sleep disturbances and cardiovascular disease (CVD) is not well established. This study assesses the association between sleep disturbances and CVD, and the effect of sleep duration on the relationship between sleep disturbances and CVD among adults in the United States (US). **Design:** Cross-sectional analysis. **Setting:** NHANES (National Health and Nutrition Examination Survey). **Participants:** A total of 5660 adults were included from the 2015-2016 cycle of the NHANES survey. **Measurements:** The main outcome was the presence of any CVD and included self-reported angina, congestive heart failure, coronary heart disease, hypertension and myocardial infarction. Associations between sleep disturbances and sleep duration with CVD were analyzed using logistic regression. Stratified models by sleep duration were used to assess effect modification. **Results:** We included 5660 participants (52.2% males), 32.7% of the participants reported having a disturbed sleep and 38% reported a CVD. Compared to those who did not report any sleep disturbances, those with sleep disturbance had 85% higher odds of CVD (OR 1.85, 95% CI 1.43 - 2.39). Similarly, there were 40% higher odds of CVD (OR 1.40, 95% CI 1.01 - 1.95) among those with shorter sleep duration compared with those that slept for 6 to 9 hours. However, there was no evidence of effect modification by sleep duration. **Conclusions:** Our findings show that sleep disturbance is associated with higher odds of CVD. Clinicians and other healthcare providers need to consider the consequence of sleep disturbances and implement strategies in the treatment of patients with or at high risk of CVD.

Keywords

Sleep Disturbance, Cardiovascular Disease, Sleep Duration, NHANES

1. Introduction

Sleep is a crucial function of health, coordinated by the brain; consisting of interplays between rapid eye movement and non-rapid eye movement sleep (NREM) [1]. For decades, sleep has been regarded as an essential lifestyle behavior that can impact cardiovascular disease (CVD) and mortality [2]. The American Academy of Sleep Medicine (AASM) and the Center for Disease Control and Prevention (CDC) recommend adults (18 - 64 years) should have at least 7 or more hours of sleep per night on a regular basis to optimize health [3] [4]. Over 10% of the United States (US) adults suffer from sleep disturbances with insomnia, sleep apnea and restless legs syndrome cited as the most common causes [5]. Symptoms are relatively more common among women, and increase with age [6]. Sleep disorders have been associated with a reduced quality of life and a heavy financial loss in damages and lost productivity [6].

Cardiovascular diseases (CVDs) are a leading cause of death in the US and globally [7]. Moreover, there is growing evidence that sleep disorders may adversely impact cardiovascular health [8]. In 2016, the American Heart Association closely examined evidence relating to sleep disorders and CVD and asked health organizations to come up with sleep recommendations regarding a number of sleep disorders [9]. Several epidemiological studies have reported an increased risk of CVDs or death in individuals with long sleep duration [10] [11], whereas other studies found contradictory results [12] [13] [14]. There is growing evidence of adverse effects of obstructive sleep apnea (OSA) on neurocognition and the cardiovascular system, with 4.7% of coronary heart disease being attributed to sleep disturbances [15].

Owing to the adverse effects of sleep-related disturbances, sleep disturbance is rapidly becoming a Public Health problem. Although several studies have examined the relationship between sleep duration and cardiovascular outcomes [16] [17] [18], there is little information from population-based studies showing association between the presence of sleep disturbance and all-cause cardiovascular events. To fill the knowledge gap, our study examined the association between self-reported sleep disturbances, as well as sleep duration and CVD. We also assessed the effect of sleep duration on the association between sleep disturbances and CVD. The National Health and Nutritional Examination Survey (NHANES) includes demographic, dietary, health related, and socioeconomic questions, making it a great data system for a population-based assessment on the association between sleep disturbances and CVD.

2. Methods

We queried the NHANES data and conducted a cross-sectional study of adults who participated in the 2015-2016 cycle. NHANES is a program of the National Center for Health Statistics (NCHS), a part of Centers for Disease Control and Prevention (CDC) in charge of producing national vital and health statistics. The goal of NHANES is to produce national estimates on a variety of health informa-

tion, by conducting interviews, medical examinations, and laboratory analysis on a sample of participants [19]. The survey is conducted among a nationally representative sample of non-institutionalized participants, approximately 5000 persons each year, distributed in the different counties nationwide. We included participants ≥ 21 years old who took part in NHANES 2015-2016 cycle and responded to our questions [19]. Loss of participants was due to missing CVD data ($n = 3856$), missing sleep disturbance data ($n = 301$) and missing sleep duration data ($n = 174$). The NHANES is a publicly available database, thus non-exempt human subject research.

2.1. Main Exposures and Outcome Variables

Our main exposure variable was having a sleep disturbance. Sleep disturbances were assessed by self-report based on the question “Have you ever told a doctor or other health professional that you have trouble sleeping?” with responses of “yes” or “no”. To evaluate sleep duration, participants were asked “How much sleep do you usually get at night on weekends or workdays?” Responses ranged from 1 - 12 hours of sleep. We analyzed this variable both as a continuous and a categorical variable. Based on prior research [20] [21], we classified sleep duration into 3 categories; ≤ 6 hours, >6 to <9 hours (reference), ≥ 9 hours.

Our primary outcome was CVD. Participants self-reported CVD events based on the question “Has a doctor or health professional ever told you that you had [a particular disease]?” We classified participants as having a CVD if they reported any of the following conditions: angina, congestive heart failure, coronary heart disease, hypertension and myocardial infarction. Those responding “no” to all the diseases were placed in the no CVD group.

2.2. Covariates of Interest

Our socio-demographic characteristics included age, sex (male or female), race/ethnicity (White, African American, and Other), and income ($< \$20,000$, $\geq \$20,000$). Health variables included body mass index (BMI), depression, stroke, and diabetes. BMI was obtained based on participants' weights and heights. It was calculated by dividing weight by height in meters squared. We analyzed BMI both as a continuous variable and a categorical variable grouped into 4 categories: underweight ($< 18.5 \text{ kg/m}^2$), normal ($18.6 - 24.9 \text{ kg/m}^2$), overweight ($25 - 29.9 \text{ kg/m}^2$), and obese ($\geq 30 \text{ kg/m}^2$). Depression was assessed by the question “how often have you been bothered by feeling down, depressed, or hopeless?” with responses of “not at all, several days, more than half the days and nearly every day”. Those who responded “more than half the days” or “nearly every day” were classified as having depression. The self-report of stroke and diabetes were based on the question “Have you ever been diagnosed of [medical condition]?”.

2.3. Statistical Analysis

We conducted a bivariate analysis to assess association between covariates and

outcome of interest using chi-square for categorical variables and T-test for continuous variables. Confounders were selected based on literature and statistical significance ($p < 0.05$). Covariates that were statistically significant were included in the final model.

To assess the association between sleep disturbances and CVD, we calculated both the adjusted and unadjusted differences between both variables. Those without sleep disturbances were considered our reference category. We constructed a multivariable logistic regression model with CVD as outcome variable adjusting for significant covariates. We assessed the association between sleep duration and CVD, using logistic regression models; unadjusted model and adjusted models were used. Respondents who reported >6 to <9 hours of sleep were considered the reference category. To construct our adjusted model, potential confounders such as age, income, race, BMI, diabetes, stroke were added. Using multivariate logistic regression (adjusting for covariates which include age, income, BMI, depression, diabetes, stroke) we assessed the effect of sleep duration on the association between sleep disturbances and CVD with sleep duration as our interaction variable. All models utilized survey procedures to account for the complex survey design, and all statistical analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

3. Results

Our study sample included a total of 5660 participants (**Figure 1**). The mean age of the sample was 50.4 years (standard deviation (SD) = 0.40) with a slightly higher proportion of females compared to males (52.2% vs 47.8%). We identified CVD in 2148 (38%) of participants, with hypertension being the most predominant condition (71.7%). The demographic and baseline characteristics of study

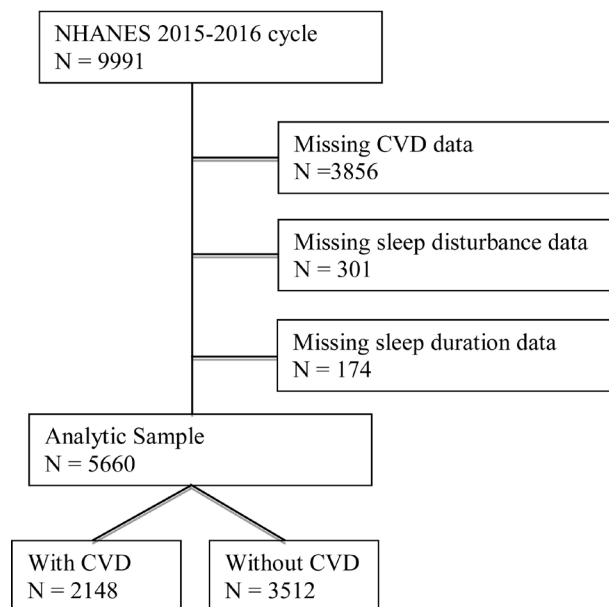


Figure 1. Flow diagram of study participants.

participants by CVD status are reported in **Table 1**. Compared to participants in the non-CVD group, those in the CVD group were more likely to be African Americans (25.8% vs. 18.2%), obese (52.9% vs. 32.4%) and to report a low income status (16.1% vs. 9.6%) ($p < 0.001$). Moreover, the CVD group were more likely to report having diabetes (26.8% vs. 5.9%), stroke (6.2% vs. 0.9%), and depression (25.0% vs. 21.8%) ($p < 0.001$). Overall, the mean duration of sleep in our study was 7.7 hours ($SD = 0.04$) with 25.8% of them reporting having trouble sleeping. Sleep disturbances were more prevalent in the participants with CVD (41.4% vs. 23.9%, $p < 0.001$). Majority of our population (61.1%) reported sleeping for >6 to <9 hours/day, 21.8% slept ≤ 6 hours/day while 17.8% slept ≥ 9 hours (data not shown).

Table 1. Demographics and baseline characteristics of participants.

	CVD (N = 2148)	No CVD (N = 3512)	P value
Age, mean \pm SD	58.3 \pm 0.4	42.5 \pm 0.3	<0.001
Sex, n (%)			
Male	1049 (48.4)	1658 (47.7)	0.6667
Female	1099 (51.6)	1854 (52.3)	
Race, n (%)			
African American	554 (25.8)	638 (18.2)	<0.001
White	731 (34.0)	1106 (31.5)	
Other	863 (40.1)	1768 (50.3)	
Income, n (%)			
<20,000 USD	512 (16.1)	497 (9.6)	<0.001
>20,000 USD	1481 (83.9)	2754 (90.4)	
BMI (kg/m²), mean \pm SD	31.6 \pm 0.2	28.3 \pm 0.1	
BMI, n (%)			
Underweight	14 (0.8)	61 (1.7)	
Normal	305 (14.3)	960 (29.3)	<0.001
Overweight	666 (32.0)	1209 (36.6)	
Obesity	1041 (52.9)	1096 (32.4)	
Hours of sleep, mean \pm SD	7.60 \pm 0.05	7.70 \pm 0.03	0.5258
Sleep categories, n (%)			
≤ 6 hours	378 (21.2)	524 (16.5)	0.007
>6 to <9 h	903 (62.7)	1624 (70.7)	
≥ 9 hours	312 (16.1)	391 (12.8)	
Sleep disturbances, n (%)	817 (41.4)	702 (23.9)	<0.001
CVD conditions, n (%)			
Angina	205 (7.1)		
Congestive heart failure	235 (8.3)		
Coronary heart disease	130 (4.6)		
Myocardial infarction	235 (8.3)		
Hypertension	2035 (71.7)		
Co-morbidities			
Diabetes, n (%)	690 (26.8)	266 (5.9)	<0.001
Stroke, n (%)	154 (6.2)	48 (0.9)	<0.001
Depression, n (%)	509 (25.0)	665 (21.8)	<0.001

Abbreviations: *CVD*, Cardiovascular disease; *BMI*, Body Mass Index; *SD*, Standard Deviation. P value estimated using chi-square for categorical variable and t-tests for continuous variables.

Table 2 represents the crude and unadjusted odds ratios for the association between sleep disturbances and CVD. In the crude model, those with sleep disturbances had 2.25-fold higher odds of CVD (OR = 2.25, 95% CI 1.85 - 2.72) than those without sleep disturbances; however, after controlling for age, BMI, race, income status, diabetes, stroke, and depression, the association attenuated. After adjustment, those with sleep disturbances had 85% higher odds of reporting CVD than those without sleep disturbances (OR = 1.85 (1.43 - 2.39), $p < 0.001$).

Table 3 shows the crude and adjusted odds ratios for the association between sleep duration and cardiovascular diseases. Compared to participants with a normal sleep duration (>6 - <9 hours per night), those sleeping ≤ 6 hours and ≥ 9 hours per night had higher crude odds ratios for cardiovascular diseases of (OR = 1.45, 95% CI 1.13 - 1.85) and (OR = 1.42, 95% CI 1.14 - 1.78) respectively ($p < 0.001$). This relationship persisted after adjusting for age, BMI, race, income status, diabetes, stroke and depression; however, there was no evidence of an association between long sleep duration and CVD after adjustment (OR = 1.19 (0.90 - 1.60), $p = 0.28$).

Table 4 shows the crude and adjusted odd ratios for the effects of sleep duration on the association between sleep disturbances and CVD. There was no evidence of effect modification by sleep duration as shown by the overlapping confidence intervals even after adjusting for age, BMI, race, income status, diabetes, stroke and depression ($p = 0.15$).

4. Discussion

4.1. Main Findings of This Study

In this study, we found that sleep disturbances were associated with CVD in a large representative US sample. After adjusting for our confounders, those with sleep disturbances had 85% higher odds of reporting CVD than those without sleep disturbances. Compared to participants with a normal sleep duration (>6

Table 2. Association between sleep disturbances and cardiovascular diseases.

	Crude OR (95% CI)	Adj. OR [†] (95% CI)
YES	2.25 (1.85 - 2.72)	1.85 (1.43 - 2.39)
NO	Ref	Ref

Abbreviation: *Ref*, reference group. [†]Adjusted by age, BMI, race, income status, diabetes, stroke, depression.

Table 3. Association between sleep duration and cardiovascular diseases.

	Crude OR (95% CI)	Adjusted OR [†] (95% CI)
≤ 6 hours	1.45 (1.13 - 1.85)	1.40 (1.01 - 1.95)
>6 to <9 h	Ref.	Ref.
≥ 9 hours	1.42 (1.14 - 1.78)	1.19 (0.90 - 1.60)

Abbreviation: *Ref*, reference group. [†]Adjusted by age, BMI, race, income status, diabetes, stroke, depression.

Table 4. Effect of sleep duration on the association between sleep disturbances and cardiovascular diseases.

Sleep duration	Sleep disturbances	Crude OR (95% CI)	Adj. OR [†] (95% CI)
≤6 h	YES	1.90 (1.32 - 2.62)	1.64 (0.98 - 2.51)
>6 to <9 h		Ref	Ref
≥9 h		1.83 (1.21 - 2.74)	1.54 (0.55 - 2.8)
≤6 h	NO	1.16 (0.82 - 1.51)	1.21 (0.87 - 1.78)
>6 to <9 h		Ref	Ref
≥9 h		1.22 (0.87 - 1.70)	1.07 (0.72 - 1.58)

Abbreviation: *Ref*, reference group. [†]Adjusted by age, BMI, race, income status, diabetes, stroke, depression.

and <9 hours per night), those sleeping ≤6 hours and ≥9 hours per night had slightly higher crude odds ratios for cardiovascular diseases. This relationship persisted even after adjusting for age, BMI, race, income status, diabetes, stroke and depression; however, there was no evidence of an association between long sleep duration and CVD after adjustment. These findings suggest that short sleep durations are associated with cardiovascular diseases. The present study also found no evidence of effect modification by sleep duration as shown by the overlapping confidence intervals even after adjusting for our confounders.

4.2. Comparing Our Findings to the Literature

Our findings are similar to those who have evaluated the relationship between sleep disturbances and CVD. There's a paucity of literature regarding association between disturbed sleep and CVD. Few studies have found increasing evidence of association of sleep apnea and CVD [22]. Although we had a general sleep disturbance variable, these associations are similar to what we found in our study. Also, studies of insomnia have found a positive association with coronary heart disease [23]. Coronary heart disease was one of the conditions included in our overall CVD outcome. Likewise, there is growing evidence between the relationship between sleep disruption and subsequent increase in blood pressure [23].

Studies specifically evaluating sleep duration have found mixed results. Covassin *et al.* found a U-shaped relationship between self-reported sleep length and hypertension in a large (N = 71,455) national representative sample (National Health Interview Survey, NHIS) with both ends of the tail exhibiting larger age-standardized prevalence of hypertension (<6 hours/night: 32.4%; ≥10 hours/night: 32.5%) compared to the referent category (8 hours/night, 23.2%) [24]. Likewise, in a Japanese based study, they found that men who sleep <6 hours a day have a greater risk of developing cardiovascular events than those sleeping 7 to 7.9 hours [25]. A dysregulation in endocrine and metabolic functions have been speculated to account for the association between short sleep duration and CVD. A lack of sleep results in increased sympathetic activity, increased blood pressure, impaired glucose tolerance all of which augment the risk for atherosclerosis [26]. Sleep deprivation studies in rats have shown similar en-

doctrine and metabolic dysregulations [27].

However, in the pooled analysis of a systematic review and meta-analysis of prospective studies evaluating sleep duration on cardiovascular found that short sleep duration was not significantly associated with the greater risk of developing CVD [1.03 (0.93 - 1.15); $p = 0.52$] while the long duration of sleep was strongly associated with the CVD [1.41 (1.19 - 1.68); $p < 0.0001$] [16]. In our study, we found that compared to participants with a normal sleep duration (>6 and <9 hours per night), those with short sleep duration (≤ 6 hours) did have a significant 40% increased odds for CVD, whereas, there was no evidence of an association with CVD in those with long sleep duration (≥ 9 hours). The difference in these results is unclear. Future research is required to better understand the association between long sleep duration and CVD.

4.3. What This Study Adds

We found that sleep disturbances even when adjusted for age, BMI, race, income status, diabetes, stroke, and depression, was independently associated with cardiovascular diseases. This is the first study to investigate the effect modification with adjustment of known confounders. Our findings although includes observational study of one cycle, provides the basis needed to further explore the association between sleep disturbances and cardiovascular disease and how the trend has changed from then to now.

4.4. Limitations and Strengths

Our study has some strengths and limitations. NHANES is a nationally representative sample with a large sample size with both male and female included in our study. We modeled our outcome variable to include any cardiovascular disease. We adjusted for covariates in our study which include age, income, BMI, depression, diabetes, and stroke. Limitations of our study include secondary analysis of self-report may lead to misclassification of outcome and information bias. Our study is cross-sectional; causality and incidence rates cannot be determined. Also, the temporal relationship between sleep disturbance and cardiovascular diseases is questionable based on cross-sectional design. Residual confounding remains as we were unable to adjust for all factors potentially confounding the sleep disturbance and CVD relationship. To eliminate the possibility of information bias from self-report, future studies should employ a more objective approach to measure sleep quality, such as polysomnography and actigraphy, and objective medical data for covariates of interest. Future research should be conducted on obtaining medical records to confirm CVD diagnosis. Retrospective analysis may be conducted on association between trends of sleep duration and CVD.

5. Conclusion

We found that sleep disturbances are associated with higher odds of cardiovas-

cular diseases. Likewise, shorter sleep durations were associated with CVD. However, we did not find any evidence of interaction between sleep duration and sleep disturbance. This study shows that sleep duration and sleep disturbances could be important modifiable risk factors for CVD. Sleep disturbances and CVD events incur tremendous economic costs relating to the loss of quality of life. Clinicians and other health professionals need to heavily consider the bifacial consequence of sleep disturbances and implement strategies in the treatment of patients with or a high risk of cardiovascular diseases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

Financial/Nonfinancial Disclosures

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