

UCSF

UC San Francisco Previously Published Works

Title

Sleep debt: the impact of weekday sleep deprivation on cardiovascular health in older women.

Permalink

<https://escholarship.org/uc/item/9m708082>

Journal

Sleep, 42(10)

ISSN

0161-8105

Authors

Cabeza de Baca, Tomás
Chayama, Koharu Loulou
Redline, Susan
et al.

Publication Date

2019-10-09

DOI

10.1093/sleep/zsz149

Peer reviewed



ORIGINAL ARTICLE

Sleep debt: the impact of weekday sleep deprivation on cardiovascular health in older women

Tomás Cabeza de Baca^{1,*}, Koharu Loulou Chayama², Susan Redline^{3,4},
Natalie Slopen⁵, Fumika Matsushita⁶, Aric A. Prather⁷, David R. Williams^{8,9},
Julie E. Buring^{10,11}, Alan M. Zaslavsky¹² and Michelle A. Albert¹³

¹Department of Psychology, School of Mind, Brain, and Behavior, University of Arizona, Tucson, AZ, ²British Columbia Centre on Substance Use, Providence Health Care, Vancouver, British Columbia, Canada, ³Harvard Medical School, Brigham and Women's Hospital, Boston, MA, ⁴Beth Israel Deaconess Medical Center, Boston, MA, ⁵Department of Epidemiology and Biostatistics, University of Maryland College Park, School of Public Health, College Park, MD, ⁶Division of Cardiology, Department of Medicine, University of California, San Francisco, CA, ⁷Department of Psychiatry, University of California, San Francisco, CA, ⁸Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA, ⁹Department of African and African American Studies, Harvard University, Cambridge, MA, ¹⁰Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ¹¹Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, ¹²Department of Health Care Policy, Harvard Medical School, Boston, MA and ¹³Division of Cardiology, Department of Medicine, University of California, San Francisco, CA

*Corresponding author: Tomás Cabeza de Baca, Department of Psychology, School of Mind, Brain, and Behavior, University of Arizona, Tucson, AZ. Email: tdebaca@email.arizona.edu.

Abstract

Study Objectives: Short sleep duration is associated with increased cardiovascular disease (CVD) risk. However, it is uncertain whether sleep debt, a measure of sleep deficiency during the week compared to the weekend, confers increased cardiovascular risk. Because sleep disturbances increase with age particularly in women, we examined the relationship between sleep debt and ideal cardiovascular health (ICH) in older women.

Methods: Sleep debt is defined as the difference between self-reported total weekday and weekend sleep hours of at least 2 hours among women without apparent CVD and cancer participating in the Women's Health Stress Study follow-up cohort of female health professionals (N = 22 082). The ICH consisted of seven health factors and behaviors as defined by the American Heart Association Strategic 2020 goals including body mass index, smoking, physical activity, diet, blood pressure, total cholesterol, and glucose.

Results: Mean age was 72.1 ± 6.0 years. Compared to women with no sleep debt, women with sleep debt were more likely to be obese and have hypertension ($p_{adj} < .05$). Linear regression models adjusted for age and race/ethnicity revealed that sleep debt was significantly associated with poorer ICH ($B = -0.13$ [95% CI = -0.18 to -0.08]). The relationship was attenuated but remained significant after adjustment for education, income, depression/anxiety, cumulative stress, and snoring.

Conclusion: Sleep debt was associated with poorer ICH, despite taking into account socioeconomic status and psychosocial factors. These results suggest that weekly sleep duration variation, possibly leading to circadian misalignment, may be associated with cardiovascular risk in older women.

Key words: cardiovascular disease; sleep; sleep debt; ideal cardiovascular health; AHA 2020 goals

Statement of Significance

In the United States, a third of individuals report not sleeping an adequate amount. This is especially true of health professionals who often face shift changes at work. In addition to shift work, older women often report greater sleep disturbances when compared to men. Although much work exists suggesting that short and low-quality sleep is associated with a number of health ailments—most notably cardiometabolic syndrome—examination of whether sleep debt, a 2-hour sleep discrepancy during the week compared to the weekend, affects cardiovascular health, a composite variable created by the American Heart Association (AHA) to track population-level trends in cardiovascular disease is relatively unknown. This study seeks to examine whether sleep debt is associated with poorer cardiovascular health in older female health professionals. As such, because sleep characteristics are not typically included in the AHA's cardiovascular health guidelines, the present research could potentially help inform future research and cardiovascular care.

Submitted: 20 December, 2018; Revised: 10 May, 2019

© Sleep Research Society 2019. Published by Oxford University Press on behalf of the Sleep Research Society.
All rights reserved. For permissions, please e-mail journals.permissions@oup.com.

Introduction

Every day, one-third of individuals in the United States wake up drowsy from inadequate levels of sleep (e.g. <7 hours [1]). Health professionals such as nurses and physicians are particularly vulnerable to sleep deprivation due to fluctuating work schedules [2]. Although inadequate sleep can affect short-term outcomes such as work or cognitive performance [2–4] and increase cardiometabolic risk factors through effects on body mass, appetite, and energy expenditure [5–7], insufficient sleep can also contribute to more serious long-term outcomes including cardiovascular disease (CVD), which may ultimately lead to death [8–11]. Weight gain, diabetes, hypertension [12], and inflammation [13] are implicated pathways through which sleep disturbance might result in increased CVD risk.

Current literature has established that short sleep duration is associated with increased CVD risk. For instance, a dose–response risk of coronary heart disease events was found among short sleepers in a 10-year prospective follow-up of female nurses [14]. However, whether sleep debt, a measure of sleep deficiency during the week compared to the weekend, confers increased cardiovascular risk remains uncertain. Because sleep disturbances increase with age in women, we examine the relationship between sleep debt, defined as the difference between weekday and weekend sleep duration at least 2 hours, and ideal cardiovascular health (ICH), a composite index of seven health behaviors and factors, in a cohort of older female health professionals.

We hypothesize that women with sleep debt will be more likely to have greater dysregulation across cardiometabolic systems and decreased health-maintaining behaviors, operationalized as a poorer *ideal cardiovascular health* [15].

Method

Participants

This study used the follow-up cohort of the Women’s Health Study (WHS). The WHS cohort originally consisted of healthy middle-aged and older female health professionals from the United States ($N = 39\,876$), which began in 1993 as a randomized clinical trial examining the effect of aspirin and vitamin E on the prevention of CVD and cancer [16, 17]. Although the clinical trial ended in 2004, subsequent observational follow-up studies have been conducted every 6 months since 2005 and continue annually. All data collection procedures, measures, and subsequent follow-ups were approved by the institutional review board of Brigham and Woman’s Hospital, Boston, MA. The WHS stress follow-up study was approved by the institutional review boards of Brigham and Woman’s Hospital and the University of California at San Francisco.

This analyses use data from a subsample of WHS participants ($N = 25\,335$) who participated in an ancillary WHS study on psychosocial stress (2012–2013) and had no prior history of CVD [18]. All analyses included women ($N = 22\,082$) with no history of cancer and CVD and who had complete data on sleep debt and ICH. All women had complete information for ICH and 414 women had missing sleep debt information. Compared to women without missing sleep debt information, women missing sleep debt data were older ($r = .10$, $p < .0001$), were less educated (i.e. <BS degree; $r = -0.04$, $p < .0001$), and had lower

income (i.e. <\$50 000; $r = -0.04$, $p < .0001$). Additional analyses showed that women who had missing data across the covariates had the same characteristics as described previously. To account for these differences [19], we included these covariates in our present analyses.

Measures

Sleep debt.

Weekday and weekend sleep durations were self-reported via bedtime (e.g. “What time do you usually go to bed on weekdays or work days (weekends or days off)?”) and wake time (e.g. “What time do you usually wake up on weekdays or work days (weekends or days off)?”). Weekday sleep debt was calculated by first computing the mean sleep duration (in hours) separately for the weekend and the weekday. A difference score of the means (M) was then taken: ($\text{difference score} = M_{\text{weekend sleep}} - M_{\text{weekday sleep}}$). On the basis of the difference score, women who had at least 2 hours weekday sleep deficiency were classified as having weekday sleep debt; those who had less than 2 hours sleep deficiency were classified as having no weekday sleep debt.

Ideal cardiovascular health.

All measures used in ICH were obtained through participant self-report at stress study baseline (2011–2012), except for diet data collected in 2004. Previous analyses of the WHS have found high degree of concordance between self-reported measures of health behavior status and physician-ascertained reports [20–23]. Self-reported physical activity has been collected by the WHS since baseline and continues to be collected in follow-up assessments every 2–3 years. The WHS physical activity measures are based on instruments developed by the College Alumni Health Study, which have established instrument reliability and validity [24, 25]. A 131-item valid and reliable food frequency measure was administered to participants [26]. Five food components from the questionnaire were dichotomized and used to create the diet factor, including (1) consumption of fruits and vegetables (>75th percentile), (2) fish (>75th percentile), (3) fiber-rich-whole grains (>75th percentile), (4) sodium intake (<25th percentile), and (5) sugar-sweetened beverages (<25th percentile). The five food components were summed.

ICH was a composited sum score of seven modifiable lifestyle and physiological factors of CVD risk designed by the American Heart Association 2020 Impact goals [15] that include: (1) current smoking status (ideal = never; intermediate = past; poor = current), (2) body mass index (poor = ≥ 30 kg/m²; intermediate = 25–29.9 kg/m²; ideal = <25 kg/m²), (3) physical activity (ideal = moderate physical activity ≥ 150 minutes per week; intermediate = 1–150 minutes per week, poor = <1 minute per week), (4) diet (ideal = 4–5 components; intermediate = 2–3 components; poor = 0–1 components), (5) blood pressure (ideal = <120/<80 mm Hg; intermediate = systolic blood pressure [SBP] 120–139 or diastolic blood pressure [DBP] 80–89 mm Hg; poor = SBP >140 or DBP >90 mm Hg), (6) total cholesterol (ideal = <200 mg/dl; intermediate = 200–239 mg/dl; poor = ≥ 240 mg/dl), and (7) type II diabetes status (classified into two categories (yes/no) used instead of blood glucose level).

For each of the ICH score components, participants were assigned a score of 0 if they did not meet the criteria for ideal or intermediate health, a score of 0.5 if they met the criteria

for intermediate, and a score of 1 for ideal health status (see [Supplementary Table S1](#) for a summary of each of the ICH variables). These scores derived from the seven metrics were summed to give a total continuous ICH score ranging between 0 and 7. Higher scores on the composited measure denoted better ICH. In addition to a continuous score, ICH was categorized into three categories: (1) poor (<4 ICH factors; 8.8% of participants fell in this category); (2) intermediate (between 3.5 and 5.5 ICH factors; 82.7% of participants fell in this category); and (3) ideal (between 6 and 7 ICH factors; 8.5% of participants fell in this category).

Covariates.

This study used self-reported demographic and clinical variables including age, race/ethnicity, highest education level attained, annual household income, depression/anxiety symptoms, cumulative stress, and snoring frequency. Depression/anxiety symptoms were measured by the five-item mental health subscale of the 36-Item Short Form Survey [27]. Cumulative psychosocial stress (cumulative stress) consisted of a composite of eight domains of acute (traumatic life events and negative life events) and chronic stress (work stress, work–family spillover, relationship stress, financial stress, neighborhood stress, perceived and discrimination). The measure and its components were previously described [18]. Snoring was measured by self-report (“How often have you snored”) and was reported as a four-point scale (never, rarely [1–2 nights/wk], sometimes [3–5 nights/wk], almost always [6–7 nights/wk]). All covariates were collected in 2012–2013. In addition, short and long sleep were included as covariates. Short sleep was defined as less than 6 hours/average nightly sleep and long sleep was defined as more than 9 hours/average nightly sleep.

Statistical analysis

Sample demographics and characteristics are reported as means or percentages, disaggregated by sleep debt status. All characteristics were examined for statistical differences using either analysis of variance or chi-squared tests. Multinomial logistic regression was used to examine the association between sleep debt and ICH categories (poor, intermediate, and ideal). First, the crude/unadjusted relationship between sleep debt and ICH was computed. Model 1 adjusted for age and race/ethnicity. Model 2 additionally controlled for socioeconomic status (income and education). Model 3 included Model 2, plus adjustment for depression/anxiety. Model 4 included Model 3 variables, plus adjustment for cumulative stress. Model 5 included snoring, separately, along with the previous covariates found in Model 4. Model 6 included Model 4 covariates and long sleep. Model 7 included Model 4 covariates along with short sleep. Finally, our fully adjusted Model 8 included all previous covariates, snoring, and short and long sleep. Linear regression analysis was additionally used to assess the continuous association between sleep debt and ICH. The model covariates and steps are identical to the multinomial logistic analyses.

A stratified analysis was performed to examine the effect of age on sleep debt and ICH. Additional analyses assessed for interactions between sleep debt and sleep duration (i.e. short sleep and long sleep) on ICH. Tolerance (<1) and variance inflation ratio (>10) diagnostics denoted that both short sleep and long sleep were not collinear with sleep debt.

All analyses were performed on SAS 9.4. Probability values for all analyses were two-tailed ($p < .05$).

Results

Baseline characteristics and bivariate associations

Table 1 presents the baseline characteristics of the participants. Women classified as having sleep debt were significantly younger, more likely to be divorced or single, and more likely to have an income at least \$50 000. Women with sleep debt were more likely to have a history of hypertension and diabetes and to be obese (body mass index ≥ 30 kg/m²). Regarding health behaviors, women with sleep debt were less physically active and less likely to report consuming alcohol (1+ alcoholic drink/day).

Sleep duration.

In the sample, 2.3% of women were classified as having short sleep (<6 hours) and 14.7% of women were classified as having long sleep (>9 hours). Of women categorized as having sleep debt, only 7.4% were classified as short sleepers. Likewise, only 11.5% of women were classified as having both sleep debt and long sleep.

Sleep debt and ideal cardiovascular health

Multinomial logistic regression.

ICH was categorized into three categories (**Table 2**): poor cardiovascular health, intermediate cardiovascular health, and ideal cardiovascular health (reference group). Unadjusted analyses indicated that sleep debt was significantly associated with an increased likelihood of poor cardiovascular health (odds ratio = 1.57 [95% CI = 1.21 to 2.04]). Intermediate cardiovascular was not statistically significant in the unadjusted model (odds ratio = 1.22, 95% CI = 0.99 to 1.51). After controlling for age, race/ethnicity, income, and education (Model 2), there was a statistically significant likelihood of being classified as having both poor (odds ratio = 1.61, 95% CI = 1.23 to 2.10) and intermediate cardiovascular health (odds ratio = 1.28 [95% CI = 1.04 to 1.59]) among participants categorized as having sleep debt compared to those without sleep debt. Fully adjusted models that additionally controlled for depression/anxiety, cumulative stress, snoring, long and short sleep maintained statistical significance for higher odds of poor cardiovascular health (Model 8; odds ratio = 1.39 [95% CI = 1.06 to 1.82]).

Multiple regression.

Table 3 presents the unstandardized parameter estimates (B) and 95% confidence intervals from linear regression models for the relationship between sleep debt and ICH, modeled as a continuous variable. The presence of sleep debt was significantly associated with lower ICH in the crude model (Model 0; B = -0.12 [95% CI = -0.17 to -0.07]). Adjustment for age and race/ethnicity did not significantly change this relationship (Model 1; B = -0.13 [95% CI = -0.18 to -0.08]). Our fully adjusted model that controlled for age, race/ethnicity, education, income, depression/anxiety, cumulative stress, snoring, and short and long sleep modestly attenuated the magnitude of the association, which remained statistically significant (Model 8; B = -0.08 [95% CI = -0.13 to -0.03]), suggesting that the observed association between the

Table 1. Baseline characteristics of women by sleep debt, Women's Health Study Sample, N = 22 082

	Total sample	Sleep debt		P
		No	Yes	
Age, M (SD)	(N = 22 082) 72.1 (6.0)	(n = 20 317) 72.2 (6.0)	(n = 1412) 69.2 (4.5)	<.0001
Marital status, %				<.0001
Single	5.3	5.1	6.9	
Currently married	77.0	77.7	72.5	
Divorced or separated	13.1	12.7	17.3	
Widowed	4.5	4.6	3.3	
Education, %				.30
<BS degree	51.8	51.5	50.9	
≥BS degree	46.6	46.8	48.0	
Missing education	1.7	1.7	1.2	
Household income, %				.01
<\$50 000	48.0	37.9	36.0	
≥\$50 000	56.3	56.6	60.1	
Missing income	5.5	5.6	4.0	
History of hypertension, %	69.8	69.4	72.1	.04
History of diabetes mellitus, %	10.0	9.6	13.7	<.0001
Hypercholesterolemia, %	73.5	73.5	73.5	.39
Body mass index, % (kg/m ²)				<.0001
Normal/underweight (BMI <25)	42.7	43.2	36.2	
Overweight (BMI 25–29.9)	34.1	34.2	33.2	
Obese (BMI ≥30)	23.3	22.6	30.6	
METS, M (SD) (hrs/wk)	17.7 (16.7)	17.9 (16.7)	16.0 (16.5)	<.0001
Physical activity, %				.0009
Rarely/never	35.3	35.0	38.6	
<1	20.1	20.0	22.0	
1–3	32.7	33.0	29.3	
>3	11.8	12.0	10.2	
Alcohol use, %				.001
Rarely/never	85.1	84.8	88.0	
1+ Alcoholic drink/day	14.9	15.2	12.0	
Smoking status, %				.15
Never	50.1	50.0	51.2	
Past	45.1	45.3	43.2	
Current	4.8	4.7	5.6	

Table 2. The association between sleep debt and categorized ideal cardiovascular health

	Ideal cardiovascular health		
	Poor	Intermediate	Ideal
	OR	OR	OR
Model 0	1.57 (1.21 to 2.04)	1.22 (0.99 to 1.51)	1.0
Model 1	1.66 (1.27 to 2.16)	1.29 (1.05 to 1.60)	1.0
Model 2	1.61 (1.23 to 2.10)	1.28 (1.04 to 1.59)	1.0
Model 3	1.57 (1.20 to 2.05)	1.27 (1.03 to 1.57)	1.0
Model 4	1.44 (1.10 to 1.89)	1.22 (0.99 to 1.51)	1.0
Model 5	1.39 (1.06 to 1.83)	1.21 (0.97 to 1.50)	1.0
Model 6	1.46 (1.11 to 1.91)	1.22 (0.99, 1.52)	1.0
Model 7	1.41 (1.08 to 1.85)	1.24 (1.00 to 1.54)	1.0
Model 8	1.39 (1.06 to 1.82)	1.23 (0.99 to 1.52)	1.0

Model 0: Unadjusted.

Model 1: Age + race/ethnicity.

Model 2: Model 1 + education + income.

Model 3: Model 2 + depression/anxiety.

Model 4: Model 3 + cumulative stress.

Model 5: Model 4 + snoring.

Model 6: Model 4 + long sleep.

Model 7: Model 4 + short sleep.

Model 8: Model 4 + snoring + long sleep + short sleep.

Bolded odds ratios (OR) denote a significant ($p < .05$) association.

Table 3. Relationship between sleep debt and ideal cardiovascular health, N = 22 082

	B	P
Model 0	-0.12 (-0.17 to -0.07)	<.0001
Model 1	-0.13 (-0.18 to -0.08)	<.0001
Model 2	-0.12 (-0.17 to -0.07)	<.0001
Model 3	-0.11 (-0.16 to -0.07)	<.0001
Model 4	-0.09 (-0.14 to -0.04)	.0003
Model 5	-0.08 (-0.13 to -0.03)	.001
Model 6	-0.09 (-0.14 to -0.04)	.0002
Model 7	-0.09 (-0.14 to -0.04)	.001
Model 8	-0.08 (-0.13 to -0.03)	.002

Model 0: Unadjusted.

Model 1: age + race/ethnicity.

Model 2: Model 1 + education + income.

Model 3: Model 2 + Depression/anxiety.

Model 4: Model 3 + Cumulative stress.

Model 5: Model 4 + Reported snoring.

Model 6: Model 4 + Long sleep.

Model 7: Model 4 + Short sleep.

Model 8: Model 4 + reported snoring + long sleep + short sleep.

No sleep debt is the referent; as such, a negative B denotes lower ideal cardiovascular health in the presence of sleep debt. Bolded B denote a significant ($p < .05$) association.

Table 4. Relationships between sleep debt and ideal cardiovascular health, stratified by age categories

	<75 years old		≥75 years old	
	B	P	B	P
	n = 16 013		n = 6013	
Model 1	-0.14 (-0.19 to -0.09)	<.0001	-0.05 (-0.19 to 0.10)	.52
Model 2	-0.13 (-0.18 to -0.08)	<.0001	-0.05 (-0.20 to 0.10)	.48
Model 3	-0.12 (-0.17 to 0.07)	<.0001	-0.06 (-0.20 to 0.09)	.46
Model 4	-0.10 (-0.15 to 0.04)	.0004	-0.03 (-0.18 to 0.12)	.58
Model 5	-0.09 (-0.14 to -0.03)	.001	-0.02 (-0.17 to 0.13)	.80
Model 6	-0.10 (-0.15 to -0.05)	.0002	-0.02 (-0.17 to 0.12)	.74
Model 7	-0.09 (-0.14 to -0.04)	.0009	-0.02 (-0.17 to 0.12)	.72
Model 8	-0.08 (-0.14 to -0.03)	.002	-0.01 (-0.16 to 0.14)	.89

Model 0: Unadjusted.

Model 1: age + race/ethnicity.

Model 2: Model 1 + education + income.

Model 3: Model 2 + depression/anxiety.

Model 4: Model 3 + cumulative stress.

Model 5: Model 4 + reported snoring.

Model 6: Model 4 + long sleep.

Model 7: Model 4 + short sleep.

Model 8: Model 4 + reported snoring + long sleep + short sleep.

No sleep debt is the referent; as such, a negative B denotes lower ideal cardiovascular health in the presence of sleep debt. Bolded B denote a significant ($p < .05$) association.

presence of sleep debt and poorer ICH is in part related to these aforementioned variables.

Age stratification.

As sleep disturbances are more common with older age [28], we stratified participants by age (<75 years old; ≥75 years old; Table 4). The presence of sleep debt was significantly associated with poorer ICH in women less than 75 years old only. Among women more than 75 years old, there was no significant association of sleep debt with ICH.

Discussion

In this cross-sectional study of older female health professionals, we found that sleep debt, defined as the difference between weekday and weekend sleep deprivation of at least 2 hours, was associated with poorer ICH in women. Associations were most evident for women less than 75 years old. The association between sleep debt and diminished ICH persisted after adjustment for important demographic, behavioral, psychosocial confounders, and sleep factors, including snoring, and short and long sleep. Although the adverse effects of insufficient sleep on cardiometabolic health are increasingly recognized, it is often presumed that individuals can “catch up” on sleep on weekends. Our findings add to the literature by finding that weekday-to-weekend variation in sleep is associated with adverse CV health risk profile, an association that persists even after adjusting for multiple potential confounders. These findings may be due to the chronic physiological stressors of weekday short sleep, which are not compensated for by sleeping in on weekends, or by the adverse effects of variability in sleep duration and timing, which may contribute to circadian misalignment and cardiometabolic dysfunction. In addition, individuals with sleep debt may decrease in investment in somatic effort through disengagement in health-maintaining behaviors and resulting in poorer cardiovascular health. The results further suggest that concerted dysregulation across various cardiometabolic systems is exacerbated through reduction in salubrious behaviors, potentially leading to more serious CVD risk.

Our findings add to previous research by demonstrating that reduction of sleep during the weekday compared to the weekend of at least 2 hours is associated with poorer CVD health. Indeed, studies have shown that both long and short sleep increases CVD risk [14, 29] and all-cause mortality [30]. However, only limited prior research examined the role of sleep debt on CVD risk. For instance, women classified as having sleep debt were more likely to have greater prevalence of cardiometabolic disorder when compared to women not classified as having sleep debt [31]. Sleep disturbances can affect multiple organ systems, and post-menopausal older women may be more vulnerable than younger women due to their higher prevalence of sleep problems [32, 33]. As such, given the clinical priorities to understand the impact of sleep disturbance on older women’s cardiovascular health and the lack of empirical investigation in older women, our work adds an important contribution to the existing literature.

Recent data suggest that lifestyle factors including psychosocial stress and socioeconomic status [34, 35] can affect duration of sleep, such as reducing sleep times during the week compared to the weekend [36]. A main lifestyle activity implicated with weekday short sleep is work [36]. Previous data among health professionals show that shift work likely interrupts sleep cycles in a manner that is associated with worsened CVD risk regardless of socioeconomic or psychosocial status. Although female health professionals in the WHS cohort have varied occupations ranging from licensed practical nurses to physicians and education level, we did not find heterogeneity in the relationship by education or occupation, albeit most WHS participants are retired. It is possible that a proportion of women continued working, particularly in health professions that have variable time schedules (i.e. shift work). Unfortunately, the WHS does not currently have a measure of women’s current employment and this cannot be accounted for.

There are data that suggest that older adults may be more resilient to sleep loss than younger adults [37]. Although statistical tests for interaction were nonsignificant, our stratified analyses suggested that associations are stronger in the women younger than 75 years compared to older women. It is possible that there might have been even stronger effects in younger individuals. Weekend-weekday variability has not been well studied in older cohorts and our findings in women averaging 72 years may be because older individuals may be more susceptible to certain sleep-related stressors than other stressors. There is a need to carefully consider how different dimensions of sleep health [38–40] (sleep, debt, short/long sleep, inter-individual variability in sleep times) may affect different health outcomes (e.g. cardiometabolic outcomes vs. cognitive functioning) across populations of different ages and underlying characteristics.

Insufficient sleep likely affects CVD risk via behavioral and biological mechanisms across the life-course. Several pathophysiological pathways of insufficient sleep have been proposed to impact markers of cardiometabolic health [7]. Sleep deprivation may result in substantial dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. Because cortisol and other glucocorticoids are implicated in sleep-wake cycles, short sleep produces systemic HPA dysregulation, producing “vigilant” states that can further produce sleep dysfunction [41]. It has been similarly proposed that sleep deprivation results in upregulation of the sympathetic-adrenal-medullary (SAM) axis. For instance, greater SAM activation, as measured by heart rate, was found in individuals with short sleep (<6 hours) in comparison with individuals who received 7–8.9 hours of sleep [42]. Inflammation from evoked innate immune response has also been implicated as another pathophysiological measure. Greater activation of IL-6 and IL- β , markers of evoked immune response, was associated with higher levels of sleep debt [43]. Other work suggests that diminished sleep contributes to CVD risk through unhealthy eating behaviors [44–46], such as snacking, contributing to obesity-related cardiovascular complications from obesity [47, 48]. Mechanisms include altered appetite-regulatory hormones such as ghrelin and leptin [46, 49], and activation of hedonic stimulus processing in the brain [50].

Long sleep duration has also been associated with adverse cardiovascular outcomes. However, the mechanisms underlying these associations are not well understood. Long sleep may reflect the effects of chronic health conditions and depression on the restorative properties of sleep, excessive sleepiness, and/or adverse sleep behaviors, and thus, associations with long sleep may reflect unmeasured confounders. In addition, long times in bed may associate with more sedentary behaviors, which are risk factors for CVD. Finally, individuals with long sleep duration may have misaligned circadian sleep-wake rhythms, including social jetlag, which also associated with cardiometabolic disorders [51].

Increased variability in sleep duration or timing also may adversely affect cardiometabolic risk factors or function, independent of average sleep duration, through circadian misalignment, which has been shown experimentally to alter insulin sensitivity, increase glucose and free fatty acid levels through altered gene expression [52]. Sleep debt may identify individuals who have variable sleep duration and timing, as well as individuals who may be chronically sleep deprived during weekdays.

Limitations of this study include its cross-sectional nature. Nonetheless, our results are consistent with previous sleep

duration and deprivation research conducted longitudinally [29], via experimental animal models [53], human studies [52, 54], and using daily diary methodologies [49, 55]. As the cohort consists of predominately white female health professionals, similar work should be conducted in diverse populations, including racial/ethnic US minorities. This is especially important, given that shift work is predominately performed by racial/ethnic minorities [56]. In addition, a measure of sleep debt—the variability of sleep from weekdays to weekends—was a significant predictor of cardiovascular health, highlighting that variation of sleep is a marker of adverse health outcomes even in groups without substantive sleep deprivation.

In addition, sleep duration and snoring were obtained by self-report, which is more readily obtainable in a large cohort. As such, the measurement of sleep duration may reflect time in bed or otherwise be influenced by reporting biases due to under- or overestimation of actual sleep time. Although self-reported measures of sleep may be only moderately correlated with objective measures [57, 58], the use of self-reported data may nonetheless be relevant when developing public health messages as these reflect behaviors individuals may be able to self-monitor. We acknowledge that there is no standard operational definition of sleep debt in the literature (e.g. sleep debt was defined as the difference between preferred duration of sleep and reported weekday sleep duration [59]) and additional research is needed to identify the most appropriate operational definitions of sleep debt across populations. Also, the interpretation of sleep debt as defined in this article should recognize that this term may identify several types of sleep-related stressors, such as exposure to periods of insufficient sleep without adequate compensation or day-to-day variability in sleep duration or to circadian misalignment due to changing sleep-wake patterns that are not synchronized with the multiple metabolic processes regulated by the internal biological clock. Finally, we acknowledge that information on hypnotic and cardiovascular medication use was not consistently ascertained in this cohort, precluding our ability to evaluate whether these medications influenced our findings.

In conclusion, this study suggests that differences in weekday and weekend sleep duration of at least 2 hours are associated with decreased cardiovascular health in older female health professionals. The results support sleep hygiene recommendations that encourage consistent sleep schedules across the week. Future work should confirm the current findings in a prospective analysis, as they may inform policy or physician recommendations.

Supplementary material

Supplementary material is available at *SLEEP* online.

Funding

We are grateful to the Women’s Health Study (WHS) participants. The study was supported by grants HL080467, HL099355, HL043851, CA047988, and UM1-CA182913 from the National Heart, Lung, and Blood Institute and the National Cancer Institute. This study was funded by NIH R01 grant AG038492 (Dr MA Albert). S.R. was partially supported by NIH R35HL135818. A.P. was partially supported by NIH R01HL142051.

Disclosure

None.

References

- Liu Y, et al. Prevalence of healthy sleep duration among adults—United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2016;**65**(6):137–141.
- Eanes L. CE: the potential effects of sleep loss on a nurse's health. *Am J Nurs*. 2015;**115**(4):34–40; quiz 41.
- Pilcher JJ, et al. Effects of sleep deprivation on performance: a meta-analysis. *Sleep*. 1996;**19**(4):318–326.
- Muto V, et al. Local modulation of human brain responses by circadian rhythmicity and sleep debt. *Science*. 2016;**353**(6300):687–690.
- Bayon V, et al. Sleep debt and obesity. *Ann Med*. 2014;**46**(5):264–272.
- Horne J. REM sleep, energy balance and 'optimal foraging'. *Neurosci Biobehav Rev*. 2009;**33**(3):466–474.
- Javaheri S, et al. Insomnia and risk of cardiovascular disease. *Chest*. 2017;**152**(2):435–444.
- Rangaraj VR, et al. Association between sleep deficiency and cardiometabolic disease: implications for health disparities. *Sleep Med*. 2016;**18**:19–35.
- Tobaldini E, et al. Sleep, sleep deprivation, autonomic nervous system and cardiovascular diseases. *Neurosci Biobehav Rev*. 2017;**74**(Pt B):321–329.
- St-Onge MP, et al.; American Heart Association Obesity, Behavior Change, Diabetes, and Nutrition Committees of the Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; and Stroke Council. Sleep duration and quality: impact on lifestyle behaviors and cardiometabolic health: a scientific statement from the American Heart Association. *Circulation*. 2016;**134**(18):e367–e386.
- Wang D, et al. Sleep duration and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies. *Int J Cardiol*. 2016;**219**:231–239.
- Nagai M, et al. Sleep duration as a risk factor for cardiovascular disease- a review of the recent literature. *Curr Cardiol Rev*. 2010;**6**(1):54–61.
- Prather AA, et al. Gender differences in the prospective associations of self-reported sleep quality with biomarkers of systemic inflammation and coagulation: findings from the Heart and Soul Study. *J Psychiatr Res*. 2013;**47**(9):1228–1235.
- Ayas NT, et al. A prospective study of sleep duration and coronary heart disease in women. *Arch Intern Med*. 2003;**163**(2):205–209.
- Lloyd-Jones DM, et al.; American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;**121**(4):586–613.
- Ridker PM, et al. A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. *N Engl J Med*. 2005;**352**(13):1293–1304.
- Rexrode KM, et al. Baseline characteristics of participants in the Women's Health Study. *J Womens Health Gen Based Med*. 2000;**9**(1):19–27.
- Albert MA, et al. Cumulative psychological stress and cardiovascular disease risk in middle aged and older women: rationale, design, and baseline characteristics. *Am Heart J*. 2017;**192**:1–12.
- Schlomer GL, et al. Best practices for missing data management in counseling psychology. *J Couns Psychol*. 2010;**57**(1):1–10.
- Pradhan AD, et al. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA*. 2001;**286**(3):327–334.
- Song Y, et al. A prospective study of red meat consumption and type 2 diabetes in middle-aged and elderly women: the Women's Health Study. *Diabetes Care*. 2004;**27**(9):2108–2115.
- Rhodes ET, et al. Accuracy of administrative coding for type 2 diabetes in children, adolescents, and young adults. *Diabetes Care*. 2007;**30**(1):141–143.
- Liu S, et al. Vitamin E and risk of type 2 diabetes in the Women's Health Study randomized controlled trial. *Diabetes*. 2006;**55**(10):2856–2862.
- Lee I-M, Paffenbarger Jr RS. Design of present-day epidemiologic studies of physical activity and health. In: Lee I-M ed. *Epidemiologic Methods in Physical Activity Studies*. New York, NY: Oxford University Press; 2009:100–123.
- Wolf AM, et al. Reproducibility and validity of a self-administered physical activity questionnaire. *Int J Epidemiol*. 1994;**23**(5):991–999.
- Willett WC, et al. Reproducibility and validity of a semi-quantitative food frequency questionnaire. *Am J Epidemiol*. 1985;**122**(1):51–65.
- Ware JE Jr, et al. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary of results from the Medical Outcomes Study. *Med Care*. 1995;**33**(4 Suppl):AS264–AS279.
- Floyd JA, et al. Age-related changes in initiation and maintenance of sleep: a meta-analysis. *Res Nurs Health*. 2000;**23**(2):106–117.
- Cappuccio FP, et al. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. *Eur Heart J*. 2011;**32**(12):1484–1492.
- Cappuccio FP, et al. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep*. 2010;**33**(5):585–592.
- Gaston SA, et al. Multiple poor sleep characteristics and metabolic abnormalities consistent with metabolic syndrome among white, black, and Hispanic/Latina women: modification by menopausal status. *Diabetol Metab Syndr*. 2019;**11**:17.
- Dong C, et al. Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and hispanics: the northern Manhattan study. *Circulation*. 2012;**125**(24):2975–2984.
- Bots SH, et al. Sex differences in coronary heart disease and stroke mortality: a global assessment of the effect of ageing between 1980 and 2010. *BMJ Glob Health*. 2017;**2**(2):e000298.
- Bixler E. Sleep and society: an epidemiological perspective. *Sleep Med*. 2009;**10** (Suppl 1):S3–S6.
- Knutson KL. Sociodemographic and cultural determinants of sleep deficiency: implications for cardiometabolic disease risk. *Soc Sci Med*. 2013;**79**:7–15.
- Basner M, et al. American time use survey: sleep time and its relationship to waking activities. *Sleep*. 2007;**30**(9):1085–1095.
- Duffy JF, et al. Healthy older adults better tolerate sleep deprivation than young adults. *J Am Geriatr Soc*. 2009;**57**(7):1245–1251.

38. Tobaldini E, et al. Short sleep duration and cardiometabolic risk: from pathophysiology to clinical evidence. *Nat Rev Cardiol*. 2019;16(4):213–224.
39. Grandner MA, et al. Sleep disturbance is associated with cardiovascular and metabolic disorders. *J Sleep Res*. 2012;21(4):427–433.
40. Ashby T, Louis M. Circadian misalignment and cardiovascular risk. *Cardiovasc Innov Appl*. 2019;3:435–440.
41. van Dalsen JH, Markus CR. The influence of sleep on human hypothalamic–pituitary–adrenal (HPA) axis reactivity: a systematic review. *Sleep Med Rev*. 2018;39:187–194.
42. Castro-Diehl C, et al. Sleep duration and quality in relation to autonomic nervous system measures: the Multi-Ethnic Study of Atherosclerosis (MESA). *Sleep*. 2016;39(11):1927–1940.
43. Prather AA, et al. Normative variation in self-reported sleep quality and sleep debt is associated with stimulated pro-inflammatory cytokine production. *Biol Psychol*. 2009;82(1):12–17.
44. Chaput JP. Sleep patterns, diet quality and energy balance. *Physiol Behav*. 2014;134:86–91.
45. Chaput J-P, et al. The association between short sleep duration and weight gain is dependent on disinhibited eating behavior in adults. *Sleep Med*. 2011;12:S13.
46. Chaput JP, et al. Short sleep duration is associated with reduced leptin levels and increased adiposity: results from the Quebec Family Study. *Obesity*. 2007;15(1):253–261.
47. Li TY, et al. Obesity as compared with physical activity in predicting risk of coronary heart disease in women. *Circulation*. 2006;113(4):499–506.
48. Manson JE, et al. A prospective study of obesity and risk of coronary heart disease in women. *N Engl J Med*. 1990;322(13):882–889.
49. Taheri S, et al. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. *PLoS Med*. 2004;1(3):e62.
50. St-Onge MP, et al. Sleep restriction increases the neuronal response to unhealthy food in normal-weight individuals. *Int J Obes (Lond)*. 2014;38(3):411–416.
51. Morris CJ, et al. Circadian misalignment increases cardiovascular disease risk factors in humans. *Proc Natl Acad Sci U S A*. 2016;113(10):E1402–E1411.
52. Wefers J, et al. Circadian misalignment induces fatty acid metabolism gene profiles and compromises insulin sensitivity in human skeletal muscle. *Proc Natl Acad Sci USA*. 2018;115(30):7789–7794.
53. Andersen ML, et al. Effects of paradoxical sleep deprivation on blood parameters associated with cardiovascular risk in aged rats. *Exp Gerontol*. 2004;39(5):817–824.
54. Buxton OM, et al. Adverse metabolic consequences in humans of prolonged sleep restriction combined with circadian disruption. *Sci Transl Med*. 2012;4(129):129ra43.
55. Arora T, et al. The impact of sleep debt on excess adiposity and insulin sensitivity in patients with early type 2 diabetes mellitus. *J Clin Sleep Med*. 2016;12(5):673–680.
56. McMenamin TM. A time to work: recent trends in shift work and flexible schedules. *Monthly Lab Rev*. 2007;130:3–15.
57. Lauderdale DS, et al. Self-reported and measured sleep duration: how similar are they? *Epidemiology*. 2008;19(6):838–845.
58. Zinkhan M, et al. Agreement of different methods for assessing sleep characteristics: a comparison of two actigraphs, wrist and hip placement, and self-report with polysomnography. *Sleep Med*. 2014;15:1107–1114.
59. Knutson KL, et al. Role of sleep duration and quality in the risk and severity of type 2 diabetes mellitus. *Arch Intern Med*. 2006;166(16):1768–1774.