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ORIGINAL ARTICLE

Modeling the cardiometabolic benefits of sleep in older women: exploring the 24-hour day

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Abstract

Study Objectives: Activities throughout the day, including sleep, sedentary behavior (SB), light-intensity physical activity (LIPA), and moderate to vigorous physical activity (MVPA) are independently associated with cardiometabolic health. Few studies have examined interrelationships between sleep and 24-hour activity and associations with cardiometabolic risk. The objective of this study is to understand how replacing time in SB, LIPA, or MVPA with sleep impacts cardiometabolic risk.

Methods: Women's Health Initiative OPACH Study participants ($N = 3329$; mean age = 78.5 ± 6) wore ActiGraph GT3X+ accelerometers 24 hours/7 days. Adjusted linear regression estimated the relationship between sleep duration and cardiometabolic markers. Separately for shorter (<8 hours) and longer (≥8 hours) sleepers, isotemporal substitution models estimated the cross-sectional associations with cardiometabolic markers with reallocating time in daytime activities to or from sleep.

Results: Longer sleep duration was associated with higher insulin, HOMA-IR, glucose, total cholesterol, and triglycerides (all $p < 0.05$). The associations between sleep duration and C-reactive protein, waist circumference, and body mass index (BMI) were U-shaped (both $p < 0.05$). For shorter sleepers, reallocating 33 minutes of MVPA to sleep was associated with *higher* values of insulin, HOMA-IR, glucose, triglycerides, waist circumference, and BMI (0.7%–11.5%). Replacing 91 minutes of SB time with sleep was associated with *lower* waist circumference and BMI (−1.3%, −1.8%). For long sleepers, shifting 91 minutes of sleep to SB was associated with *higher* waist circumference and BMI (1.3%, 1.4%).

Conclusions: This is one of the first isotemporal analyses to include objectively measured sleep duration. Results illuminate possible cardiometabolic risks and benefits of reallocating time to or from sleep.

Statement of Significance

This is the first study to provide support of the association between accelerometer-measured sleep duration and markers of cardiometabolic health in older women. This evidence contributes to the understanding of the mechanisms through which sleep may influence cardiometabolic health. We investigated the associations in a large racially-ethnically diverse cohort of participants from a Women's Health Initiative (WHI) ancillary study. Sleep extension studies may be a worthy and feasible cardiometabolic risk reduction strategy. Results of isotemporal substitution models provide insight on the potential benefits of reallocation of 24-hour activity to increase sleep duration. The research questions explored support the public health importance of sleep and cardiometabolic health, and inform lifestyle prevention strategies for cardiometabolic risk reduction.

Key words: sleep duration; aging; accelerometers; cardiovascular

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Introduction

Throughout the 24-hour day, time is spent in activities that can be distinctly categorized as sleep, sedentary behavior (SB), or physical activity (light physical activity and moderate to vigorous physical activity [MVPA]). Individually, these 24-hour activities are linked to cardiometabolic health. Both MVPA and light-intensity physical activity (LIPA) are beneficially associated with cardiometabolic health, including reduced risk of incident cardiovascular disease (CVD) [1, 2]. SB is linked with markers of poor cardiometabolic health and with increased risk of incident CVD, even after adjusting for PA [3–6]. Evidence suggests short sleep durations (<7 hours) predict incident cardiometabolic conditions such as type 2 diabetes, obesity, and cardiovascular events [7–12]. Only a few studies have used wearable devices to examine associations between sleep duration and cardiometabolic risk factors. Findings from these studies support associations between both short and long sleep durations and cardiovascular biomarkers (such as fasting glucose and C-reactive protein [CRP]), systolic blood pressure (BP), and obesity [13–17].

Despite the increasing evidence that short and long sleep durations increase risk for cardiometabolic health, epidemiologic studies show that over 30% of Americans are not meeting the recommended 8 hours of sleep per night [18]. For older adults, achieving optimal hours of quality sleep may be even more difficult. As adults age, they report poorer sleep quality, more restless sleep, and more nocturnal awakenings [19–22]. Older women report poorer sleep quality than older men [23]. Thus for aging women, health interventions that aim to extend or decrease sleep time for cardiometabolic risk reduction may be a feasible CVD intervention strategy [18, 24, 25].

The high incidence of CVD among older women in the United States suggests that we need to identify more feasible strategies to target CVD risk reduction in this population. Many lifestyle interventions focus on increasing daily MVPA. However, it is estimated that only 10%–30% of older adults currently meet PA guidelines [26, 27]. Sleep extension interventions may be a more feasible alternative to PA interventions particularly in older populations where PA may be difficult to achieve due to health or environmental barriers. Pilot sleep extension studies have found that increasing sleep duration may not only feasible, but effective in decreasing cardiovascular risk [28, 29]. As clinical recommendations and sleep research support increasing sleep time among short sleepers, more research is needed to understand from where this time should come within the 24-hour day.

Recently, researchers have used isotemporal substitution modeling [30] to examine 24-hour behavior, estimating the beneficial associations if a fixed amount of time spent in one activity is shifted to another activity. Several of these studies have demonstrated that the amount of time allocated to daily activities is significantly related to cardiometabolic health [31–34]. However, previous isotemporal analyses have focused on daytime activity and most have not included sleep in their analyses. The isotemporal studies that included sleep relied solely on self-reported sleep measures [30–34], which over-estimate sleep duration when compared to more objective estimates from polysomnography or actigraphy [35, 36].

The primary aim of this study was to use 24-hour accelerometry data to (1) examine the associations between accelerometer-measured sleep duration and markers of cardiometabolic health in a sample of older women and (2) construct isotemporal substitution models to assess the cardiometabolic associations of redistributing SB, LIPA, and MVPA time to or from sleep time. This modeling will answer the following key questions: (1) what is the potential cardiometabolic benefit of increasing sleep duration, in short sleepers, if time spent in SB is decreased? and (2) what is the potential benefit of decreasing sleep duration, in long sleepers, if time spent in LIPA or MVPA is increased? This study will provide a better understanding of how 24-hour activity is related to cardiometabolic health for older adult women and may highlight opportunities for the development of novel cardiovascular lifestyle interventions for this population.

Methods

Study sample

Our study included older women enrolled in the Objective Physical Activity and Cardiovascular Health (OPACH) study, an ancillary study to the Women's Health Initiative Long Life Study aimed at examining the relationship between accelerometer-measured physical activity and incidence of CVD in older women (ages 63–99 years). More detailed information on the OPACH study objectives, recruitment, and methodology are published [37]. Participants were consented for OPACH (n = 7048) between 2012 and 2013 and in-home visits were conducted to obtain fasting blood draws, health and lifestyle questionnaires, anthropometric measurements, and BP readings. At the home visit, participants received a GT3x accelerometer to wear on their waist for 24 hours per day and were asked to concurrently complete a daily sleep log over the 7-day period. Of the consented OPACH participants, 6489 women returned their device; 6114 of these women also completed sleep logs for at least 1 day. The study sample consisted of 3329 women with at least two 24-hour periods of valid accelerometer data, a completed sleep log that overlapped with accelerometer data, and fasting CVD biomarker results (Figure 1).

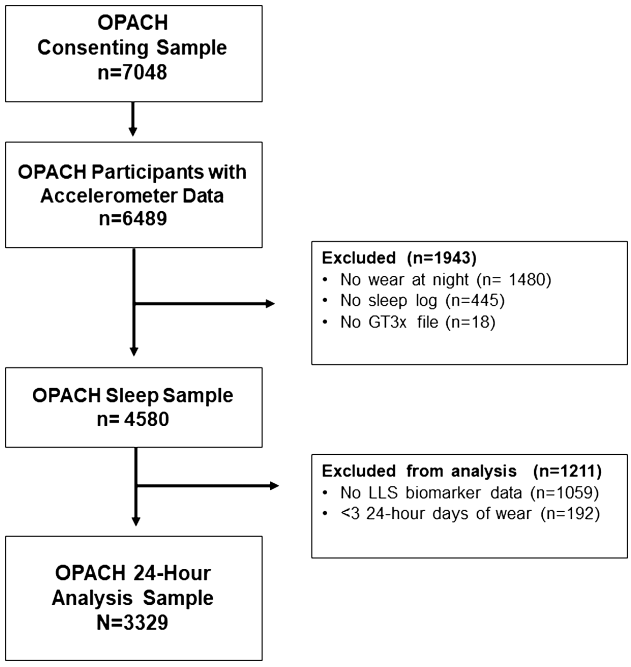

Figure 1. OPACH study participant flow diagram.

24-hour activity

24-hour activity was assessed with a hip-worn triaxial accelerometer (Actigraph GT3X+; Pensacola, FL). The ActiGraph device, worn on the hip, has been validated for physical activity, SB and sleep duration estimates [38, 39]. Data were recorded at 30 Hertz (Hz). After devices were returned, data were processed using ActiLife version 6.11 software, separately for sleep duration and the daytime activity variables. Once sleep duration and daytime activity variables were created, data were merged on the epoch level to create a 24-hour dataset for each participant. A 24-hour day was defined as in-bed time to in-bed time and a wear period must be at least 16 hours (1000 minutes) including the primary sleep period to be considered valid.

Sleep duration

Sleep duration data were processed using the 30 Hz data condensed to 60-second Agilegraph Data File (AGD) with the low-frequency extension filter applied. AGD files were scored using a standard protocol. A trained member of the research team identified the primary sleep period for each night, by determining the participant's in-bed time and out of bedtime, using the participant sleep logs and a visual review of the data for each night the participant wore the device. This procedure is aligned with the Society of Behavioral Sleep Medicine actigraphy methods guidelines and draws from a protocol shown to have high interrater reliability [40, 41]. The validated Cole-Kripke algorithm [42] was applied to the identified primary sleep period and classified each minute of the period as sleep or wake time. Estimates of nightly sleep duration were derived from the summing of epochs classified as sleep by the Cole-Kripke algorithm (minutes/night) during the defined primary sleep period.

Physical activity and SB

PA data were processed as previously described [37]. Age-appropriate PA-intensity cut points were used to classify SB (<19 counts/15 seconds), LIPA (19–518 counts/15 seconds), and MVPA (≥519 counts/15 seconds) [43]. Minutes of in bedtime not classified as sleep by the Cole-Kripke sleep-wake algorithm were classified as minutes of SB.

Markers of cardiometabolic health

Resting BP was measured after a 5-minute rest period using an aneroid sphygmomanometer and cuff size based on measured arm circumference. The average of two BP readings was recorded. Participant height (cm), weight (kg), and waist circumference were measured by trained staff using a portable scale, stadiometer, and measuring tape. Participants' body mass index (BMI; kg/m^2) was computed with the measured height and weight. Fasting blood draws were obtained by staff according to standard protocol and serum samples were sent to the University of Minnesota Fairview Advanced Research and Diagnostic Laboratory (ARDL) to be assayed for cardiometabolic biomarkers as previously described [44].

The following markers of cardiometabolic health were included in these analyses: fasting insulin, CRP, homeostatic model assessment of insulin resistance (HOMA-IR), fasting glucose, HDL cholesterol, total cholesterol, triglycerides from the cardiometabolic assays, and systolic BP, waist circumference, and BMI from the in-home visit measurements.

Covariates

The baseline WHI lifestyle survey was used to measure participant age, race/ethnicity (categorized as black, white, or Hispanic), and education (categorized into high school/GED or less, some college, college graduate or more).

At OPACH baseline, participants completed the WHI lifestyle questionnaire and medical history survey that measured current smoking status (yes/no), self-reported sleep disturbances, sleep medication use, comorbid conditions, self-rated heath, hypertension status, and diabetes status. The WHI Insomnia Rating Scale (WHIIRS) was used to assess self-reported sleep disturbances [45]. The five-item scores (0–4) are summed to create a scale score ranging from 0 to 20. A higher WHIIRS score is reflective of greater presence of sleep disturbances and has been shown to predict CVD [46]. Self-reported sleep medication use was assessed with 1-item asking women "in the last 4 months, how many times per week a participant used sleep medications?" Response options ranged from "None in the past 4 weeks" to "5 or more times per week". Sleep medication use was categorized as no use in past 4 weeks, some use (≤2 times per week), frequent use (>2 times per week). The number of self-reported non-CVD chronic conditions were assessed in the survey and were used to create a comorbidity index score [47]. The index included self-reported history of cerebrovascular disease, cancer, depression, hip fractures, osteoarthritis, chronic obstructive pulmonary disease (COPD), cognitive impairment, sensory impairment, history of frequent falls, and urinary incontinence. The number of conditions was summed to create a comorbidity index score (0–10). Participants were categorized as having no comorbid conditions, 1 condition, or 2 or more conditions. Self-rated health was derived from 1-item from the WHI lifestyle questionnaire: "In general would you say your health is…". Response options ranged from "excellent" to "poor". Self-reported hypertension status was derived from reported use of medications used to manage high BP. Diabetes status was derived from the WHI medical history questionnaire item, "Did a doctor ever say that you had sugar diabetes or high blood sugar when you were not pregnant?" or who, reported being treated with insulin or oral hypoglycemic medication at any annual medical update conducted during the WHI follow-up. The WHI self-reported diabetes item has been shown to have strong agreement with physician medical chart review [48].

Statistical analysis

Average daily minutes of sleep, MVPA, LIPA, and SB were included in a series of regression models to assess the associations with markers of cardiometabolic health. Prior to analysis, all cardiometabolic marker variables were log-transformed. All of the activity variables were adjusted for device wear time using the residuals method [49] to account for variation in wear time across individuals that may impact estimates of 24-hour activity categories. Daily activity variables were summed to create a 24-hour total wear time variable.

Single activity variable models.

As one of the aims of the current analyses was to examine the effect of reallocation of time to or from sleep duration, the primary focus was on the independent associations of sleep duration with cardiometabolic markers as the first step. Adjusted linear regression models for each marker of cardiometabolic health and sleep duration were run, adjusting for multiple covariates and total wear time, but not for the other types of activity. Models included adjustment for age, race/ethnicity, education, sleep disturbances, sleep medication use, self-rated health, smoking status, and comorbid conditions. Estimated mean values for each cardiometabolic marker were compared according to sleep durations of 6, 8, and 10 hours. Evidence demonstrates that the relationship between sleep duration and cardiometabolic biomarkers may be U-shaped, with both short and long durations significantly associated with various cardiometabolic biomarkers [49, 50]. A quadratic term was therefore included in the sleep single activity variable models to explore the possible U-shape in the relationships. When the quadratic term was not significant, it was removed, and the model was rerun with only a linear term for sleep duration. The single activity variable models for MVPA, LIPA, and SB were also performed adjusting for covariates.

Sensitivity analysis

The associations between sleep duration and the cardiometabolic markers of interest could be influenced by medications used to regulate chronic conditions such as hypertension and diabetes. We did not adjust for hypertension status or diabetes status because of the potential for these conditions to be part of the causal pathway. To test the extent to which associations were sensitive to possible medication use, interactions were tested for hypertension (hypertension status*sleep) and diabetes (diabetes status*sleep) in the single variable models.

Isotemporal substitution models

When significant associations were observed for a cardiometabolic marker in the sleep single activity variable models, isotemporal substitution models were performed on that marker stratified by sleep duration (<8 hours, ≥8 hours) to test the reallocation of time to sleep for short sleepers and from sleep for long sleepers.

Isotemporal substitution models estimated the association with the cardiometabolic markers of reallocating daytime activity to or from sleep [30]. The substitution model for each cardiometabolic marker included a variable for each daily activity besides sleep duration (SB, LIPA, and MVPA), the 24-hour total wear time variable as a linear term, and the aforementioned covariates. Including a total wear time variable in the model holds time constant and allows interpretations to be made about the cross-sectional associations of cardiometabolic marker levels with reducing the mean time spent in one activity by equivalently increasing the mean time spent in another activity. Not including the sleep variable in the models allows for interpretation of increasing or decreasing sleep time by shifting it from or to another daily activity [30]. Results are reported for one standard deviation unit substitution of each of the daytime activity behaviors to or from sleep.

Interpretation of the Isotemporal models (and the reallocation of time) requires the assumption of a linear relationship among exposure variables and the outcome variables, and therefore cannot model nonlinear (e.g. U-shaped) associations, which are expected in studies of sleep duration. To address this, we stratified the sample into short (<8 hours) and long (≥8 hours) sleepers using the median sleep duration (8.17 hours/night). The isotemporal analyses were implemented separately on the stratified samples to allow for proper interpretation of cardiometabolic associations of sleep duration was increased for short sleepers or decreased for long sleepers. Sensitivity analyses included repeating isotemporal models after re-categorizing short sleep (<7 hours) and long sleep (>9) hours.

Importantly, because these data are cross-sectional, the resulting coefficients cannot be interpreted as causal effects; instead, they should be viewed as estimated associations from the reallocation of 24-hour time. All tests were 2-tailed with alpha set to 0.05. All analyses were performed R statistical software version 3.1.1 [51].

Results

Of the 6489 women in the OPACH sample with accelerometer data, 4580 had valid sleep data. One hundred ninety-two had less than 3 complete days of 24-hour wear, and 1059 did not have LSS blood draws, leaving data from 3329 women available for this analysis. There were statistically significant differences in the age and race/ethnicity distributions between the current analytic sample and the full OPACH study cohort with accelerometer data. The 3329 women included in the sleep sample were slightly older (mean age: 78.9 vs 78.5 years, $p < 0.01$), and the included participants had a larger proportion of white women (53% vs 45%), and a smaller proportion of Black women (30% vs 38%, $p < 0.001$) than the original OPACH cohort.

Descriptive statistics including socio-demographic and health status characteristics stratified by sleep duration category are presented in Table 1. Participants had an average age of 78.9 (*SD* = 6.7) years. Over half of the participants were white (53.3%) and college-educated (78.9%). Only 2.3% of the sample were currently smokers and 29.3% were classified as obese. Participants self-reported an average sleep disturbance score of 6.3 (*SD* = 4.5) out of 20. The average nightly accelerometer-measured sleep duration for the sample was 490 minutes (*SD* = 70.7) or 8 hours 10 minutes.

Women with longer sleep durations (≥8 hours) were significantly more likely to be older and White. Additionally, longer sleepers were more likely to report higher sleep disturbance scores. Women with shorter sleep durations were more likely to be Black or Hispanic and had significantly higher BMIs. On average, long sleepers had more minutes of daily wear time, and sleep time, but fewer minutes of MVPA, LIPA, and SB.

Sleep duration was significantly associated with several cardiometabolic markers. The results of the single activity variable sleep models are presented in Table 2. Models adjusted for age, race/ethnicity, education, sleep disturbances, sleep medication use, self-rated health, smoking status, and comorbidity index. In addition to the adjusted linear regression model results, estimated mean values for each cardiometabolic marker at 6 hours, 8 hours, and 10 hours of sleep are presented.

Results for all models examining insulin, HOMA-IR, and glucose are presented for the sample excluding women with diabetes based on the results of our sensitivity analysis showing

Table 1. Participant characteristics for the OPACH Cohort by sleep duration categories (*N* = 3329)

	Full sample *N* = 3329	Short sleepers <8 hours *n* = 1486	Long sleepers ≥8 hours *n* = 1843	
	Mean ± *SD* *N* (%)	Mean ± *SD* *N* (%)	Mean ± *SD* *N* (%)	*p*
Age, years	78.9 ± 6.7	78.0 ± 6.6	79.7 ± 6.7	**<0.001**
63–69	330 (9.9)	179 (12.0)	151 (8.2)	**<0.001**
70–79	1275 (38.3)	623 (42.0)	652 (35.4)	
80–89	1576 (47.3)	635 (42.7)	941(51.1)	
≥90	148 (4.4)	49 (3.3)	99 (5.4)	
Race-ethnicity				**<0.001**
White	1782 (53.5)	734 (49.4)	1048 (56.9)	
Black	991 (29.8)	482 (32.4)	509 (27.6)	
Hispanic	556 (16.7)	270 (18.2)	286 (15.5)	
Education				0.71
High school or less	686 (20.6)	310 (20.9)	376 (20.5)	
Some college	1285 (38.6)	563 (38.0)	722 (39.4)	
College graduate	1340 (40.3)	607 (41.0)	733 (40.0)	
Current smoker	78 (2.3)	43 (2.9)	35 (1.9)	0.08
Sleep Disturbance Score	6.3 ± 4.5	6.0 ± 4.4	6.5 ± 4.5	**<0.01**
Sleep medication use				
More than 2 times per week	199 (6.0)	71 (4.8)	128 (7.0)	**<0.01**
Comorbidity index				
≥2 comorbidities	1646 (49.4)	702 (47.2)	944 (51.2)	**<0.01**
Self-rated health				
At least good	2792 (83.9)	1277 (92.9)	1515 (89.0)	**<0.001**
Hypertension	2360 (70.9)	1031 (69.4)	1329 (72.1)	0.09
Diabetes	649 (19.5)	296 (19.9)	353 (19.1)	0.61
24-hour activity variables				
Wear time (minutes/day)	1380.3 (44.5)	1370.3 (44.2)	1388.3 (43.1)	**<0.001**
MVPA (minutes/day)	49.3 (33.8)	54.4 (36.7)	45.1 (30.7)	**<0.001**
LIPA (minutes/day)	276.0 (74.0)	295.0 (74.6)	260.8 (69.8)	**<0.001**
SB (minutes/day)	564.9 (90.4)	589.8 (93.0)	544.9 (83.0)	**<0.001**
Sleep (minutes/day)	490.1 (70.7)	431.1 (42.6)	537.6 (50.2)	**<0.001**

Numbers do not sum to total due to missing data.
Bold value represents $p < 0.05$.

that diabetes status interacted with sleep duration in relation to insulin, HOMA-IR, and glucose (all *p* values <0.05). Sleep by hypertension status interaction effects were not statistically significant in relation to any outcome. Results of all models stratified by diabetes status are presented in Supplementary Table 1.

In women without diabetes, longer sleep duration was associated with higher values of insulin (*p*: <0.001) HOMA-IR (*p*: <0.001), and glucose (*p*: 0.027). In the entire cohort, longer sleep duration was significantly associated with higher values of total cholesterol (*B*: 0.230, *p*: 0.024) and triglycerides (*B*: 0.005, *p*: <0.001). The relationship between sleep duration and CRP total sleep time [TST]^2: *B*: 0.001, *p*: 0.030), waist circumference (TST^2: *B*: 0.001, *p*: 0.061), and BMI (TST^2: *B*: 0.001, *p*: 0.041), was U-shaped, with larger values of CRP, waist circumference, and BMI in both shorter and longer sleep durations.

In the single variables models for MVPA, LIPA, and SB, each activity was significantly related to every cardiometabolic marker after adjustment (Supplementary Table 2). Model results for insulin, HOMA-IR, and glucose are presented for the sample excluding women with diabetes based on the results of our sensitivity analysis.

The results of the Isotemporal substitution models for short sleepers and long sleepers are displayed in Figures 2 and 3.

For the short sleepers, model results estimate the association (percent change) of reallocating 1 *SD* of activity to sleep. Reallocating one SD (33 minutes/day) of MVPA to sleep was detrimental across most of the cardiometabolic markers, including higher values of insulin (11.5%, 95% confidence interval [CI]: 6.0–17.2), HOMA-IR (6.1%, CI: 3.5–8.8), glucose (1.3%, CI: 0.6–2.0), triglycerides (4.3%, CI: 1.2–7.6), waist circumference (1.0%, CI: 0.6–1.4), and BMI (0.7%, CI: 0.2–1.2). For LIPA, a similar detrimental association was observed in some markers when one standard deviation of LIPA (74 minutes/day) was reallocated to sleep. Reallocating 74 minutes/day of LIPA to sleep was significantly associated with higher values of insulin (9.1%, CI: 1.2–17.6), HOMA-IR (4.0%, CI: 0.1–7.9), triglycerides (9.0%, CI: 4.1–14.0), and BMI (0.9%, CI: 0.1–1.7). Isotemporal results for reallocating one standard deviation of SB (91 minutes/day) to sleep were mixed. Significant beneficial associations were observed for waist circumference (–1.3%, CI: –2.0 to –0.6) and BMI (–1.8%, CI: –2.7 to –1.0).

For the long sleepers, model results estimate the association (percent change) of reallocating 1 *SD* from sleep to MVPA, LIPA, and SB. In long sleepers, reallocating time from sleep to MVPA (33 minutes/day) had beneficial associations across almost all cardiometabolic markers. Reallocating 33 minutes/day

Table 2. OPACH Cohort: single variable models for sleep duration and estimated cardiometabolic markers

	6 hours	8 hours	10 hours		B[a]	SE[a]	p
Insulin (mmol/L)[b,c]							
	52.03	60.32	69.92	Linear term	0.012	0.002	**<0.001**
				Quadratic term	—	—	—
C-Reactive Protein (mg/L)[c]							
	1.81	1.80	2.06	Linear term	-0.041	0.023	0.068
				Quadratic term	0.001	0.001	**0.030**
HOMA-IR[b,c]							
	1.33	1.43	1.53	Linear term	0.006	0.001	**<0.001**
				Quadratic term	—	—	—
Glucose (mg/dL)[b]							
	91.26	92.45	93.65	Linear term	0.100	0.045	**0.027**
				Quadratic term	—	—	—
HDL cholesterol (mmol/L)							
	61.07	60.78	60.48	Linear term	-0.024	0.039	0.526
				Quadratic term	—	—	—
Total cholesterol (mmol/L)							
	194.24	197.00	199.76	Linear term	0.230	0.102	**0.024**
				Quadratic term	—	—	—
Triglycerides (mg/dL)[c]							
	90.86	96.86	103.27	Linear term	0.005	0.001	**<0.001**
				Quadratic term	—	—	—
Systolic blood pressure (mmHg)							
	125.88	125.56	125.25	Linear term	-0.026	0.037	0.481
				Quadratic term	—	—	—
Waist circumference (cm)							
	90.66	89.19	89.29	Linear term	-0.581	0.293	**0.047**
				Quadratic term	0.001	0.001	0.061
BMI (kg/m^2)							
	28.40	27.75	27.79	Linear term	-0.259	0.120	**0.030**
				Quadratic term	0.001	0.001	0.041

Models adjusted for weartime, age, race-ethnicity, education, smoking status, sleep disturbances, sleep medication use, and comorbidity index, and self-rated health.
[a]Beta coefficients and standard errors reflect associations for 10 minutes of sleep duration.
[b]Women with diabetes excluded from analysis for this biomarker.
[c]Beta coefficients are log-transformed.
Bold value represents $p < 0.05$.

of sleep to MVPA was significantly related to lower values for insulin (–10.8%, CI: –15.1 to –6.3), CRP (–7.6%, CI: –13.7 to –1.0), HOMA-IR (–5.8%, CI: –8.1 to –3.5), slightly lower levels of glucose (–1.1%, CI: –1.7 to –0.5), waist circumference (–1.0%, CI: –1.4 to –0.6) and BMI (–0.6%, CI: –1.1 to –0.1). Similar results were observed when sleep time was shifted and LIPA was increased by one standard deviation (74 minutes), with lower values for insulin (–9.6%, CI: –14.7 to –4.2), CRP (–15.0%, CI: –21.5 to –7.8), HOMA-IR (–5.2%, CI: –7.9 to –2.4), glucose (–0.9%, CI: –1.7 to –0.2), triglycerides (–6.6%, CI: –9.6 to –3.5), waist circumference (–1.0%, CI: –1.4 to –0.5), and BMI (–1.6%, CI: –2.1 to –1.0). Shifting time from sleep to increase SB time by 1 *SD* resulted in significantly higher values of waist circumference (1.3%, CI: 0.8–1.9) and BMI (1.4%, CI: 0.7–2.1). A very small, beneficial association was observed for total cholesterol (–1.1%, CI: –1.8 to –0.3) when one standard deviation of SB (91 minutes) was reallocated from sleep to SB.

The results of the sensitivity analyses for alternate sleep duration categories (<7 for short sleep and >9 for long sleep) demonstrated that although the percent change of associations increased in some markers, the direction of associations remained consistent (Supplementary Figures 1 and 2).

Discussion

To our knowledge, the current study is one of the first published studies to report on the relationship between accelerometer-measured sleep duration and cardiometabolic health in a large ethnically diverse cohort of older women. Previous single variable analyses and meta-analyses have demonstrated that sleep duration is significantly related to several markers of cardiometabolic health including measures of metabolic function, gluco-regulatory function, and adiposity, however the inclusion of objectively measured sleep duration in older samples has been limited in this previous research [14, 16, 17, 49, 52]. From our analysis, three key findings have emerged. First, in our sample, accelerometer-measured sleep duration was significantly related to several markers of cardiometabolic health, including insulin, triglycerides, and waist circumference. Second, the relationship between sleep duration and cardiometabolic risk varies across the cardiometabolic markers examined. Third, the results of our isotemporal models suggest that how time in MVPA, LIPA, and SB is reallocated to or from sleep duration is significantly related to cardiometabolic health, highlighting opportunities for the enhancement of current cardiovascular lifestyle interventions.

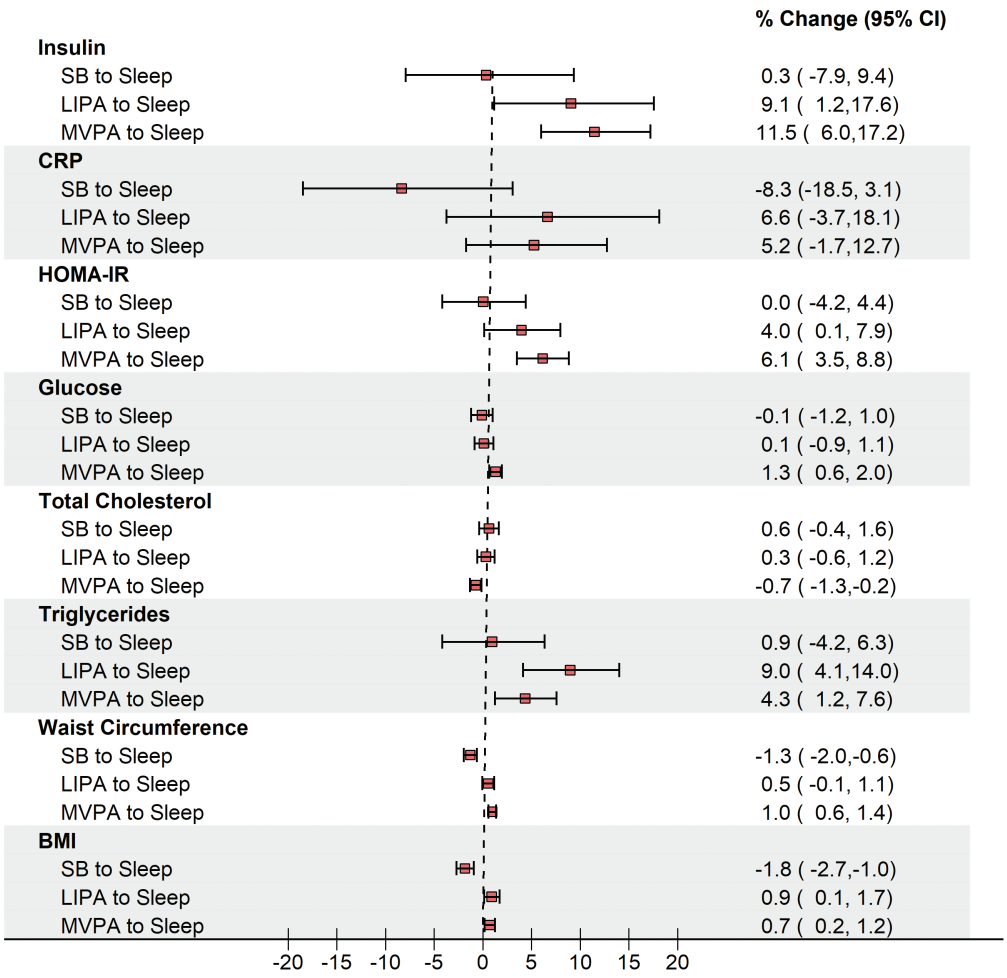

Figure 2. Short sleep (<8 hours): reallocation of 1 *SD* of activity to sleep and percent change to cardiometabolic markers.

Sleep duration and cardiometabolic health in older women

Evidence of the possible U-shaped relationship, with both short and long sleep durations associated with increased risk, and cardiometabolic health has been inconsistent in previous research [49]. Based on this evidence, we attempted to account for the possibility that the relationship between sleep duration and the cardiometabolic markers would be U-shaped in our sample of older women, and hypothesized that shorter sleep durations would be associated with increased cardiometabolic risk. Our results demonstrate that the relationship between sleep and cardiometabolic health differed across different cardiometabolic markers, with a linear relationship for some markers and a u-shaped relationship with CRP, waist circumference, and BMI. Further, longer sleep duration was associated with higher values of insulin, HOMA-IR, glucose, total cholesterol, and triglycerides. Our study results may differ from our hypotheses considering our unique sample. Our sample is composed of some of the oldest age groups of women in the United States. While our results differ from studies showing the relationship between short sleep duration and cardiometabolic risk, it is worth noting that these results, in a sample of older women, are concordant with previous findings that show increased risk for longer sleep durations [8, 53, 54]. Our study findings are especially novel considering the evidence supporting the differences in the gluco-regulatory processes in the oldest old [55, 56]. In the literature, there is a limited understanding of the mechanisms through which long sleep duration is related to cardiometabolic health; however, this relationship continues to emerge. It has been hypothesized that this relationship may be explained by other factors. In our analysis, we adjusted for comorbid conditions, sleep disturbances, and sleep medications, yet the relationship between long sleep duration and increased cardiometabolic risk persisted. This study provides more context on the possible role of daytime activity in the associations between long sleep duration and cardiometabolic health in older women.

Implications for cardiovascular lifestyle interventions

To increase or decrease sleep durations to improve cardiometabolic health, time would need to be reallocated to or from another behavior in the 24-hour day. While growing evidence demonstrates that sleep duration should be increased in short sleepers or decreased in long sleepers, it is not clear what shift in daytime activity must occur to provide the most benefit. Isotemporal modeling techniques allow for the exploration of the associated change in cardiometabolic risk of reallocating time spent sleeping when it is shifted to or from LIPA, MVPA, or SB [30, 31]. Our study results are consistent with a previous isotemporal

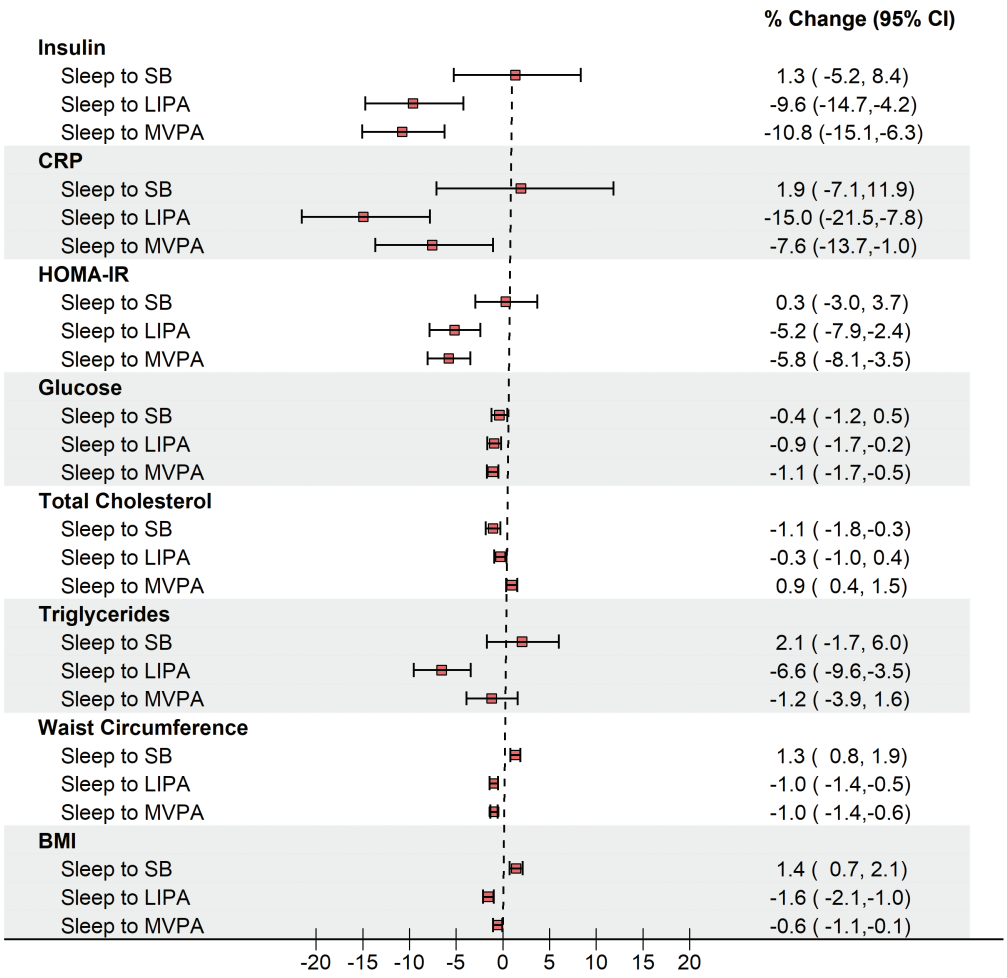

Figure 3. Long sleep (≥8 hours): reallocation of 1 *SD* of activity from sleep and percent change to cardiometabolic markers.

modeling analysis conducted by Buman et al. that examined cardiometabolic risks associated with reallocation of time spent in self-reported sleep, and objectively measured SB and PA among an NHANES sample of 2185 adults (mean age 46.6) [31]. Congruent with the results of Buman et al., our results show cardiometabolic marker benefits among long sleepers who reallocated sleep time to MVPA. We found a similar pattern for reallocating time from sleep to LIPA, a result that was not observed in the NHANES sample, and is particularly meaningful for our sample of older women who may find achieving shifts to LIPA more feasible than shifts to MVPA. Further, when time was reallocated from SB to sleep in short sleepers it had beneficial associations with several of the cardiometabolic markers. Building upon the results of the NHANES study, our study used an objective assessment of sleep duration; measured using accelerometry with an average sleep duration calculated from 2 to 5 nights of sleep and focused on reallocation of time to sleep in short sleepers and from sleep in long sleepers. In contrast, the NHANES study assessed sleep duration with one item on a questionnaire.

Our study results provide support for sleep extension interventions in short sleepers [29], but suggest that how time is reallocated impacts cardiometabolic health. These findings have promising value for translation in clinical practice but require testing in randomized controlled trials. In cognitive behavior therapy interventions for sleep, individuals with poor sleep are encouraged to stay out of bed, but keep activity light [57]. Based on our results, interventions targeting sleep extension should consider providing recommendations that are both achievable and provide the most cardiometabolic benefits. For short sleepers, replacing SB time in the evening with sleep may be an achievable target with cardiometabolic benefits, or for long sleepers reducing SB time in bed and increasing LIPA throughout the day may provide benefits.

While our study results show benefits for increasing or decreasing sleep duration, replacing time in MVPA or LIPA with sleep in short sleepers and replacing sleep duration with SB in longer sleepers are shifts in 24-hour time that are not likely to reduce cardiometabolic risk. These findings indicate that it may be important to consider the allocation of time throughout the 24-hour day when designing cardiovascular lifestyle interventions to decrease cardiometabolic risk. When developing intervention strategies, it is worthwhile to consider time spent in other activities, regardless of the behavioral target of the intervention.

A primary strength of our study was the use of accelerometers to objectively measure 24-hour activity. The OPACH study employed hip accelerometers, the gold standard for assessment of daytime PA; however, wrist placement is considered superior for assessment of sleep [39, 58]. Hip-worn accelerometers provide a more accurate assessment of SB and sleep duration than

self-reported measures [36, 59, 60]. Additionally, we employed thoughtful data processing steps to ensure the accuracy of our behavior classification. The primary sleep period was defined using participant sleep logs and visual coding to enhance accuracy when defining the sleep period. Older women have lower levels of activity throughout the day, which may lead algorithms to misclassify SB as sleep. The visual inspection of in-bed and out-of-bed time to define the sleep period not only provided more accurate estimates of sleep duration, but also more accurate estimates of SB, by capturing in-bed sedentary time. In-bed sedentary time is often omitted when SB data processing protocols remove in-bed time from their analyses. Distinguishing between sleep and in-bed sedentary time is important as lying in bed in bed awake does not have the same benefits as sleeping.

Our study population includes only post-menopausal older women from the unique WHI sample, and therefore may not be generalizable to men, other age groups, or working adults (including shiftworkers). However, the study population included larger numbers of older Black and Hispanic women than previous studies that have assessed the relationship between sleep duration and cardiometabolic health. Further, this study is cross-sectional, limiting our ability to make causal inferences about the reallocation of time spent in one behavior to another. When using isotemporal modeling techniques, and when designing behavior change interventions, the feasibility of behavior change targets is important. Our analysis included calculations for a one standard deviation change in MVPA, LIPA, and SB, a magnitude of change that may not be realistic for all women in the sample. The isotemporal modeling approach can show us where a benefit can be expected to occur under an ideal shift in time, but the associated magnitude of change is often not realistic. Our study findings do not represent actual activity replacement, but the estimated results of modeling shifts in population-level data. In our analysis we were not able to completely address relevant medication use, such as antihypertensives, insulin sensitizers, or lipid-lowering drugs. However, we did address medication use through our sensitivity analyses in which we explored interaction between sleep duration and self-reported treated diabetes mellitus or hypertension and presented our results accordingly. It is possible that residual confounding by medication use could still have been present. Further, we did not have information on sleep disorder diagnoses, including diagnosis of obstructive sleep apnea, which is prevalent condition in the older adult population.

Cardiovascular interventions for older women should continue to target increasing LIPA and MVPA and reducing SB, but also consider sleep duration as a lifestyle risk factor worth targeting for cardiometabolic risk reduction. Including sleep behavioral targets in existing lifestyle interventions may provide a feasible target for older women who are short or long sleepers. Future research should continue to use 24-hour data to explore the interrelationships of activity throughout the day using novel statistical analyses. Moreover, future cardiovascular lifestyle interventions should examine further the possibility of multiple behavior targets, including more specific activity replacement targets, and tailoring intervention targets for feasibility.

Supplementary material

Supplementary material is available at *SLEEP* online.
Supplemental Table 1: Sleep duration and cardiometabolic markers by diabetes medication treatment status.
Supplemental Table 2: Single Variable Models for MVPA, LIPA, and SB and Cardiometabolic Markers.
Supplemental Figure 1: Short Sleep (<7 hours): Reallocation of 1 SD of Activity to Sleep and Associations to Markers (n=519).
Supplemental Figure 2: Long Sleep (>9 hours): Reallocation of 1 SD of Activity from Sleep and Associations to Markers (n=733).

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