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Original Contribution

Sleep Duration and Total and Cause-Specific Mortality in a Large US Cohort: Interrelationships With Physical Activity, Sedentary Behavior, and Body Mass Index

Qian Xiao*, Sarah K. Keadle, Albert R. Hollenbeck, and Charles E. Matthews

* Correspondence to Dr. Qian Xiao, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 9609 Medical Center Drive, Rockville, MD 20850 (e-mail: qian.xiao@nih.gov).

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Both short and long durations of sleep are associated with higher mortality, but little is known about the interrelationship between sleep and other modifiable factors in relation to mortality. In the National Institutes of Health-AARP Diet and Health Study (1995–1996), we examined associations between sleep duration and total, cardiovascular disease (CVD), and cancer mortality among 239,896 US men and women aged 51–72 years who were free of cancer, CVD, and respiratory disease. We evaluated the influence of moderate-to-vigorous physical activity, television viewing, and body mass index (BMI; weight (kg)/height (m)^2) on the sleep-mortality association and assessed their combined association with mortality. During an average of 14 years of follow-up, we identified 44,100 deaths. Compared with 7–8 hours of sleep per day, both shorter and longer sleep durations were associated with higher total and CVD mortality. We found a greater elevation in CVD mortality associated with shorter sleep among overweight and obese people, suggesting a synergistic interaction between sleep and BMI. People in the unhealthy categories of all 4 risk factors (sleep <7 hours/day, moderate-to-vigorous physical activity ≤1 hour/week, television viewing ≥3 hours/day, and BMI ≥25) had significantly higher all-cause (relative risk (RR) = 1.42, 95% confidence interval (CI): 1.34, 1.52), CVD (RR = 1.90, 95% CI: 1.67, 2.17), and cancer (RR = 1.21, 95% CI: 1.09, 1.34) mortality. Short sleep duration may predict higher mortality, particularly CVD mortality, among overweight and obese people.

body mass index; mortality; physical activity; sedentary behavior; sleep; sleep duration

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; MVPA, moderate-to-vigorous physical activity; NIH, National Institutes of Health; RR, relative risk; TV, television.

Sleep has been increasingly recognized as an important determinant of human health. Many studies show elevated total mortality among both short- and long-duration sleepers when compared with persons who get approximately 7–8 hours of sleep per day (1), although the causality of this relationship has been hotly debated (2, 3). Studies focusing on cause-specific deaths have found a similar U-shaped relationship between sleep and cardiovascular disease (CVD) mortality (4–6), while the association of sleep with cancer mortality is less clear (6–11).

Like sleep, physical activity and sedentary behavior are fundamental activities of daily life and are crucially involved in overall health. People with low levels of physical activity (12) or prolonged sitting (13) experience higher mortality. The 3 behaviors are also closely related with and sometimes interdependent on one another. Studies have shown that both short- and long-duration sleepers have decreased activity levels (14–18), and some argue that this relationship may partially explain the observed health effects of sleep (19). Additionally, obesity, another important modifiable risk factor for various diseases and premature death (20), is positively associated with short sleep duration (21) and has been suggested to mediate the pathways that link sleep deficiency with higher mortality (3). Moreover, physical activity, sedentary behavior, and obesity may act as effect modifiers, and the sleep-mortality relationship may differ among people with different levels of activity and body size.

Given the intertwined relationship of sleep with physical activity, sedentary behavior, and obesity, it is important to understand whether and how the sleep-mortality relationship is influenced by these 3 factors. Doing so would help researchers to elucidate the mechanisms through which sleep exerts its health impact and health professionals to identify populations most vulnerable to adverse effects related to short or long sleep duration. Moreover, the positive associations among sleep deficit, physical inactivity, and obesity and their frequent coexistence within the same individual warrant a further examination of their combined health effects. Unfortunately, because of the limited amount of information about relevant behavioral exposures and the limited numbers of deaths in many earlier studies, little has been done to explore the interrelationship of sleep with other modifiable lifestyle factors and their joint association with mortality.

Thus, we examined the relationship between sleep duration and total, CVD, and cancer mortality in the National Institutes of Health (NIH)-AARP Diet and Health Study. To minimize the potential impact of confounding, we focused on healthy men and women who were free of chronic conditions at baseline. We put special emphasis on describing the interaction between sleep and moderate-to-vigorous physical activity (MVPA), television (TV) viewing, and body mass index (BMI), as well as their combined associations with mortality.

METHODS

Study population

The NIH-AARP Diet and Health Study is a prospective study that was established in 1995–1996. Details of the study were reported previously (22). Briefly, participants were recruited from members of AARP (formerly the American Association of Retired Persons) who were aged 50–72 years and resided in one of 6 US states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). In total, 566,399 people satisfactorily completed the baseline questionnaire. Within 6 months of baseline, a second questionnaire, the risk factor questionnaire, was mailed to the baseline cohort. Of the 334,905 participants who completed both questionnaires, we excluded those who had missing information on sleep duration ($n = 1{,}532$), MVPA ($n = 4{,}596$), or sedentary behavior ($n = 1{,}643$) and those who reported an unknown or extreme (<15 or >50) BMI (unknown, $n = 6{,}522$; extreme, $n = 1{,}337$). We also excluded people who reported a prior diagnosis of heart disease ($n = 44{,}667$), stroke ($n = 4{,}062$), emphysema ($n = 6{,}159$), or cancer ($n = 16{,}405$) or had poor self-rated health ($n = 1{,}352$). We further excluded people who had at least 1 questionnaire filled out by a proxy respondent ($n = 6{,}687$) or who died, asked to be withdrawn, or moved out of the study area before the risk factor questionnaire data could be recorded ($n = 18$). The final analytical cohort consisted of 239,896 men and women. The study was approved by the National Cancer Institute Special Studies Institutional Review Board.

Assessment of sleep duration, MVPA, sedentary behavior, and BMI

On the risk factor questionnaire, participants were asked to report the usual amount of time they had slept at night (<5 hours, 5–6 hours, 7–8 hours, or ≥9 hours) and had napped during the day (none, <1 hour, 1–2 hours, 3–4 hours, or ≥5 hours) in a typical 24-hour period over the past 12 months. They were also given a list of examples of "moderate" and "vigorous" physical activities (MVPA) and were asked to indicate how often (never, rarely, weekly but <1 hour/week, 1–3 hours/week, 4–7 hours/week, or >7 hours/week) they had engaged in these activities during the past 10 years. Participants reported the amount of time they had spent in a typical day sitting overall (<3 hours, 3–4 hours, 5–6 hours, 7–8 hours, or ≥9 hours) and watching TV or videos (none, <1 hour, 1–2 hours, 3–4 hours, 5–6 hours, 7–8 hours, or ≥9 hours) during the past year. Because, in a previous study in this cohort, Matthews et al. (13) reported that TV viewing was a stronger predictor of mortality than overall sitting time, we considered TV viewing time our main indicator of sedentary behavior. Current height (in inches and feet) and weight (in pounds) were reported on the baseline questionnaire, and we calculated BMI at baseline as weight (kg) divided by height squared (m^2).

We further created dichotomous variables for sleep, MVPA, sedentary behavior, and BMI for interaction analysis and to calculate the combined association of all 4 variables with mortality. We chose cutoff values with physiological or clinical significance on the basis of existing literature, and we assigned 0 to "healthy" categories and 1 to "unhealthy" categories of sleep duration (1 for <5 hours and 5–6 hours; 0 for 7–8 hours and ≥9 hours) (1), MVPA (1 for never/rarely or <1 hour/week; 0 for 1–3 hours/week, 4–7 hours/week, and ≥7 hours/week) (13), TV viewing (1 for 3–4 hours/day, 5–6 hours/day, 7–8 hours/day, and ≥9 hours/day; 0 for none, <1 hour/day, and 1–2 hours/day) (13), and BMI (1 for ≥25; 0 for <25) (20). A total risk factor score was calculated by combining all values for each individual.

Mortality ascertainment

The vital status of study participants was ascertained through annual linkage to the Social Security Administration Death Master File. Cause-of-death information was obtained through follow-up searches of the National Death Index Plus. A previous study found that 95% of deaths can be identified using this method (23). The endpoints of our analysis were total mortality, CVD mortality (*International Classification of Diseases, Tenth Revision*, codes I00–I78), and cancer mortality (*International Classification of Diseases, Tenth Revision*, codes C00–C79).

Covariate assessment

The baseline and risk factor questionnaires also collected information on a broad range of covariates, including demographic characteristics; lifestyle factors, such as smoking history; medical history, such as hypertension, hypercholesterolemia, and diabetes; dietary intake, including intakes of total calories, total fat, fruits and vegetables, red meat, whole grains, coffee, and alcohol; and the use of dietary supplements, nonsteroidal antiinflammatory drugs, and menopausal hormone therapy (in women).

Table 1. Baseline Characteristics of 239,896 Healthy[a] Participants According to Sleep Duration in the NIH-AARP Diet and Health Study, 1995–1996

Characteristic	Sleep Duration, hours/day							
	<5 (*n* = 6,054)		5–6 (*n* = 75,223)		7–8 (*n* = 150,966)		≥9 (*n* = 7,653)	
	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)
Female sex	52.2		45.3		42.6		44.6	
Age, years		62.1 (5.4)		62.1 (5.4)		62.6 (5.3)		63.4 (5.2)
White, non-Hispanic race/ethnicity	83.3		89.5		94.5		95.0	
College or postcollege education	27.3		38.3		45.2		43.8	
Married	54.8		63.8		70.4		68.1	
Excellent self-reported health	13.5		18.9		23.0		20.2	
Current smoker	15.0		12.4		10.2		9.9	
Former smoker	42.0		46.8		48.5		49.6	
No napping during the day	44.2		49.0		55.2		52.7	
MVPA <1 hour/week	30.5		25.0		22.4		28.6	
Television viewing ≥3 hours/day	71.8		64.2		61.6		65.3	
Body mass index[b]		28.3 (5.6)		27.1 (4.8)		26.5 (4.4)		26.8 (4.8)
Personal history of diabetes	10.3		7.4		6.0		7.8	
Personal history of hypertension	42.4		36.6		34.0		38.7	
Use of nonsteroidal antiinflammatory drugs	67.0		71.2		72.2		69.9	
Ever use of menopausal hormone therapy[c]	44.6		52.2		57.4		58.8	
Dietary intake								
Alcohol, g/day		12.2 (44.2)		11.6 (34.7)		13.5 (34.2)		22.6 (54.2)
Fruits and vegetables, servings/kcal/day		4.1 (2.2)		4.0 (1.9)		3.9 (1.8)		3.7 (1.8)
Whole grains, servings/kcal/day		0.6 (0.6)		0.7 (0.5)		0.7 (0.5)		0.7 (0.5)
Total fat, g/kcal/day		0.3 (0.1)		0.3 (0.1)		0.3 (0.1)		0.3 (0.1)
Red meat, g/kcal/day		34.3 (22.8)		34.0 (21.4)		34.0 (20.8)		34.4 (21.6)
Total energy, kcal/day		2,011 (1,264)		1,845 (924)		1,826 (842)		1,967 (1,039)

Abbreviations: MVPA, moderate-to-vigorous physical activity; NIH, National Institutes of Health; SD, standard deviation.

[a] Defined as reporting fair or better health and no cancer, heart disease, stroke, or emphysema.

[b] Weight (kg)/height (m)^2.

[c] Percentage of women.

Statistical analysis

We found no evidence for interaction between sleep duration and sex in all-cause mortality (*P* for interaction = 0.95); therefore, we present our findings with males and females combined. Relative risks and 2-sided 95% confidence intervals were estimated with the Cox proportional hazards model, using SAS (SAS Institute, Inc., Cary, North Carolina). Person-years of follow-up time were calculated from baseline to the date of death or the end of follow-up (December 31, 2011), whichever came sooner. Covariates considered as confounders included age, sex, race/ethnicity, marital status, education, self-reported health, smoking status, smoking dose (cigarettes/day), years since quitting smoking (including 0 for current smoking), and alcohol drinking. Additional adjustment for napping, use of nonsteroidal antiinflammatory drugs, histories of hypertension, hypercholesterolemia, and diabetes, and intakes of total calories, red meat, total fat, whole grains, coffee, and fruits and vegetables had little impact on the results (<5% change in effect estimates), so these variables were not retained in our final models. MVPA, TV viewing, and BMI were considered as potential confounders and mediators; therefore, we included these variables in separate models. A test for linear trend was performed by modeling a numerical value for each sleep category (1 for <5 hours, 2 for 5–6 hours, 3 for 7–8 hours, and 4 for ≥9 hours). We also performed sensitivity analysis by excluding deaths that occurred within the first 3 years of follow-up.

To evaluate whether there was multiplicative interaction between sleep and MVPA, TV viewing, and BMI, we conducted subgroup analysis of sleep and mortality stratified according to these 3 variables. Tests for multiplicative interaction were performed using the likelihood ratio test, comparing the fit of models that had a cross-product term between sleep duration and the covariate of interest with that of models without this term. To evaluate additive interaction, we calculated the joint influences of sleep duration (<7 hours/day and ≥7 hours/day) and MVPA (<1 hour/week and ≥1 hour/week), TV viewing (>3 hours/day and ≤3 hours/day), or BMI (<25 and ≥25). We also calculated the relative excess risk due to interaction, a measure of additive interaction, and its associated 95% confidence interval (24, 25). Finally, to evaluate the combined association of all 4 variables with mortality, we examined the association between mortality and the total score for sleep, MVPA, TV viewing, and BMI.

RESULTS

During 3,363,604 person-years of follow-up, we identified a total of 44,100 deaths, including 11,635 CVD deaths and 16,644 cancer deaths. Compared with people in the 7- to 8-hour sleep category, shorter sleepers were more likely to be female, to currently smoke, and to have a history of diabetes or hypertension but were less likely to be white, college-educated, or married, to use nonsteroidal antiinflammatory drugs or hormonal therapy (if women), or to report excellent health (Table 1). Moreover, compared with 7–8 hours of sleep, both shorter and longer durations of sleep were associated with less MVPA and prolonged TV viewing, while only shorter sleep was associated with higher BMI.

In Table 2, we present the associations between sleep duration and all-cause, CVD, and cancer mortality. Compared with persons reporting 7–8 hours of sleep per day, <5 hours of sleep was associated with 16% and 25% higher total mortality and CVD mortality, respectively, while ≥9 hours of sleep was associated with an 11% increase in total mortality, after adjustment for covariates and MVPA, TV viewing, and BMI. The sleep-mortality association was attenuated only slightly after adjustment for each of the individual risk factors. Excluding deaths that occurred in the first 3 years of follow-up had little impact on the results. Because daytime napping may influence the relationship between nighttime sleep and mortality, we performed an analysis restricting the data to participants who reported no napping during the day, and the results were similar (see Web Table 1, available at http://aje.oxfordjournals.org/).

We first examined the 2-way joint association of short sleep and MVPA, TV viewing, and BMI with mortality, each as a dichotomous variable (Table 3). Because the relationship between sleep and mortality was U-shaped, we excluded people who reported ≥9 hours of sleep per day. Overall, higher mortality was observed among people with <7 hours of sleep per day and <1 hour/week of MVPA, ≥3 hours/day of TV viewing, or BMI ≥25. Additionally, we found a statistically significant synergistic interaction between sleep duration and BMI in relation to CVD mortality. Compared with people who reported ≥7 hours of sleep per day and BMI <25, people with <7 hours of sleep and BMI ≥25 had a 33% increase in risk of dying from CVD (95% confidence interval (CI): 1.26, 1.40). The relative excess risk due to interaction associated with this relative risk was 0.14 (95% CI: 0.06, 0.22), which indicates that about one-third (14%) of the 33% excess risk can be attributed to the coexistence of short sleep and higher BMI, above the risk attributable to the individual factors. In contrast, we did not detect any other statistically significant interaction between sleep and MVPA or TV viewing.

We then examined the sleep-mortality association in more refined subgroups defined by different categories of BMI (Table 4), MVPA (Web Table 2), and TV viewing (Web Table 3). Among participants with BMI ≥35, getting fewer than 5 hours of sleep per day was associated with 42% higher CVD mortality (for <5 hours vs. 7–8 hours, relative risk (RR) = 1.42, 95% CI: 1.12, 1.79), while among people with BMI <25, there was no association between CVD mortality and sleep duration. In contrast, in analysis stratified by MVPA and TV viewing, we observed elevated all-cause and CVD mortality associated with <5 hours of sleep in almost all subgroups, with relative risks ranging from 1.13 to 1.46. The only exception was the subgroup reporting ≤2 hours of TV watching, among whom <5 hours of sleep was not associated with increased CVD mortality; however, the number of deaths was small.

Finally, among participants reporting <5, 5–6, and 7–8 hours of sleep per day, we estimated the mortality risk associated with the presence of an increasing number of "unhealthy" risk factors (i.e., less sleep (<7 hours/day), less MVPA (<1 hour/week), more TV viewing (≥3 hours/day), and elevated BMI (≥25)) (Table 5). We found that there was a highly significant trend between a higher (less healthy) risk factor score and greater mortality (all *P*'s < 0.0001). For each 1-point increase in the total risk factor score, there were 8%, 14%, and 4% increases in all-cause, CVD, and cancer mortality, respectively. People who were "unhealthy" with regard to all 4 risk factors had significantly higher all-cause (RR = 1.42, 95% CI: 1.34, 1.52), CVD (RR = 1.90, 95% CI: 1.67, 2.17), and cancer (RR = 1.21, 95% CI: 1.09, 1.34) mortality than people who were unhealthy with regard to none of the factors.

DISCUSSION

In this large cohort, we confirmed a U-shaped association between sleep duration and all-cause and CVD mortality among healthy middle-aged and older US men and women. The sleep-mortality association appeared to be independent of MVPA and sedentary behavior. In contrast, short sleep duration had a stronger relationship with CVD mortality among overweight or obese people, and we estimated that about one-third of the excess risk was due to the synergistic interaction between short sleep and high BMI.

A meta-analysis by Cappuccio et al. (1) summarized findings from 16 studies of 27 independent cohort samples and concluded that both short and long sleep duration are significant

Table 2. Association Between Baseline Sleep Duration and Mortality Among 239,896 Healthy[a] Participants in the NIH-AARP Diet and Health Study, 1995–1996

Model	Sleep Duration, hours/day											
	<5			5–6			7–8			≥9		
	No. of Deaths	Multivariate RR	95% CI	No. of Deaths	Multivariate RR	95% CI	No. of Deaths	Multivariate RR	95% CI	No. of Deaths	Multivariate RR	95% CI
All-Cause Mortality												
	1,420			14,130			26,827			1,723		
Base model[b]		1.21	1.15, 1.28		1.05	1.03, 1.07		1.00	Referent		1.14	1.08, 1.19
Base model + MVPA		1.20	1.14, 1.27		1.05	1.03, 1.07		1.00	Referent		1.12	1.07, 1.18
Base model + TV viewing		1.19	1.13, 1.25		1.05	1.03, 1.07		1.00	Referent		1.13	1.07, 1.18
Base model + BMI[c]		1.19	1.13, 1.25		1.04	1.02, 1.07		1.00	Referent		1.13	1.07, 1.18
Full model[d]		1.16	1.10, 1.23		1.04	1.02, 1.06		1.00	Referent		1.11	1.06, 1.19
Full model, excluding deaths occurring within 3 years after baseline		1.18	1.11, 1.26		1.05	1.02, 1.07		1.00	Referent		1.13	1.07, 1.20
Cardiovascular Disease Mortality												
	426			3,798			6,968			443		
Base model		1.35	1.22, 1.49		1.07	1.03, 1.12		1.00	Referent		1.10	1.00, 1.22
Base model + MVPA		1.33	1.21, 1.47		1.07	1.03, 1.12		1.00	Referent		1.08	0.98, 1.19
Base model + TV viewing		1.31	1.19, 1.45		1.07	1.03, 1.11		1.00	Referent		1.09	0.99, 1.20
Base model + BMI		1.29	1.17, 1.42		1.06	1.02, 1.10		1.00	Referent		1.09	0.99, 1.20
Full model		1.25	1.13, 1.38		1.06	1.02, 1.10		1.00	Referent		1.07	0.97, 1.17
Full model, excluding deaths occurring within 3 years after baseline		1.29	1.13, 1.47		1.04	0.98, 1.09		1.00	Referent		1.14	1.01, 1.30
Cancer Mortality												
	464			5,176			10,414			590		
Base model		1.09	1.00, 1.20		1.01	0.97, 1.04		1.00	Referent		1.03	0.95, 1.12
Base model + MVPA		1.09	0.99, 1.20		1.01	0.97, 1.04		1.00	Referent		1.03	0.94, 1.11
Base model + TV viewing		1.09	0.99, 1.19		1.01	0.97, 1.04		1.00	Referent		1.03	0.95, 1.12
Base model + BMI		1.08	0.99, 1.19		1.00	0.97, 1.04		1.00	Referent		1.03	0.95, 1.12
Full model		1.07	0.98, 1.18		1.00	0.97, 1.04		1.00	Referent		1.02	0.94, 1.11
Full model, excluding deaths occurring within 3 years after baseline		1.07	0.95, 1.21		1.00	0.95, 1.04		1.00	Referent		1.02	0.91, 1.13

Abbreviations: BMI, body mass index; CI, confidence interval; MVPA, moderate-to-vigorous physical activity; NIH, National Institutes of Health; RR, relative risk; TV, television.

[a] Defined as reporting fair or better health and no cancer, heart disease, stroke, or emphysema.

[b] Results were adjusted for sex (male or female), age at baseline (years; continuous), race/ethnicity (non-Hispanic white; non-Hispanic black; Hispanic; or Asian, Pacific Islander, American Indian/Alaskan Native, or other), marital status (married, widowed, divorced, separated, or never married), education (<12 years, 12 years, post–high school, some college, or college/postgraduate), self-reported health (excellent, very good, good, or fair), smoking (never, former, or current smoker), smoking dose (0, 1–10, 11–20, 21–30, 31–40, 41–50, 51–60, or >60 cigarettes/day), years since quitting smoking (never quit (0 years), ≥10 years, 5–9 years, 1–4 years, or <1 year), and alcohol drinking (g/day; continuous).

[c] Weight (kg)/height $(m)^2$.

[d] Results were adjusted for all variables in the base model plus MVPA (never, rarely, <1 hour/week, 1–3 hours/week, 4–7 hours/week, or >7 hours/week), TV viewing (none, <1 hour/day, 1–2 hours/day, 3–4 hours/day, 5–6 hours/day, 7–8 hours/day, or ≥9 hours/day), and baseline BMI (<18.5, 18.5–<25, 25–<30, 30–<35, or ≥35).

Table 3. Interactions Between and Joint Effects of Sleep Duration and Moderate-to-Vigorous Physical Activity, Television Viewing, and Body Mass Index in Relation to Mortality Among 239,896 Healthy[a] Participants in the NIH-AARP Diet and Health Study, Excluding People Reporting ≥9 Hours of Sleep per Day, 1995–1996

Lifestyle Factor	Sleep Duration, hours/day				Relative Excess Risk due to Interaction	
	7–8		<7			
	Multivariate RR[b]	95% CI	Multivariate RR[b]	95% CI	Multivariate RR[b]	95% CI
Total Mortality						
MVPA, hours/week					−0.01	−0.07, 0.05
≥1	1.00	Referent	1.07	1.04, 1.09		
<1	1.18	1.13, 1.23	1.23	1.20, 1.28		
TV viewing, hours/day					−0.01	−0.06, 0.05
≤3	1.00	Referent	1.07	1.03, 1.11		
>3	1.11	1.06, 1.15	1.17	1.14, 1.20		
BMI[c]					−0.002	−0.06, 0.06
<25	1.00	Referent	1.06	1.03, 1.10		
≥25	1.05	1.01, 1.10	1.11	1.08, 1.15		
Cardiovascular Disease Mortality						
MVPA, hours/week					−0.04	−0.13, 0.05
≥1	1.00	Referent	1.11	1.06, 1.17		
<1	1.27	1.22, 1.32	1.35	1.26, 1.43		
TV viewing, hours/day					0.01	−0.11, 0.12
≤3	1.00	Referent	1.09	1.01, 1.17		
>3	1.14	1.08, 1.20	1.25	1.18, 1.32		
BMI					0.14	0.06, 0.22
<25	1.00	Referent	1.01	0.94, 1.08		
≥25	1.18	1.13, 1.23	1.33	1.26, 1.40		
Cancer Mortality						
MVPA, hours/week					−0.03	−0.11, 0.05
≥1	1.00	Referent	1.02	0.98, 1.06		
<1	1.13	1.09, 1.18	1.12	1.06, 1.19		
TV viewing, hours/day					−0.02	−0.09, 0.06
≤3	1.00	Referent	1.02	0.96, 1.09		
>3	1.05	1.01, 1.10	1.06	1.01, 1.11		
BMI					−0.06	−0.14, 0.01
<25	1.00	Referent	1.05	1.00, 1.11		
≥25	1.06	1.02, 1.11	1.05	1.00, 1.10		

Abbreviations: BMI, body mass index; CI, confidence interval; MVPA, moderate-to-vigorous physical activity; NIH, National Institutes of Health; RR, relative risk; TV, television.

[a] Defined as reporting fair or better health and no cancer, heart disease, stroke, or emphysema.

[b] Adjusted for age, sex, race/ethnicity, marital status, education, self-reported health, smoking status, smoking dose, years since quitting smoking, and alcohol drinking.

[c] Weight (kg)/height (m)^2.

predictors of higher risk of death (RR = 1.12 (95% CI: 1.05, 1.18) for short sleep and RR = 1.30 (95% CI: 1.22, 1.38) for long sleep). However, there is still a lively debate on whether the observed association reflects a true causal relationship between sleep duration and mortality or is a product of residual confounding due to chronic conditions (2, 3). In a recent systematic review, Kurina et al. (26) argued that people with poor health and hence at higher risk of death may be more likely to report shortened or prolonged sleep, and therefore the observed sleep-mortality relationship may be caused by preexisting diseases. In support of this view, Magee et al. (10) reported in a large Australian study that a significant U-shaped relationship was found only among "unhealthy" participants (i.e., those with 1 or more chronic conditions or low physical function), not among healthy participants. Bias due to chronic conditions is a valid concern; therefore, in our

Table 4. Association Between Baseline Sleep Duration and Mortality, According to Body Mass Index, Among 239,896 Healthy[a] Participants in the NIH-AARP Diet and Health Study, 1995–1996

Cause of Death and BMI[b] Category	Sleep Duration, hours/day												P for Interaction Between Sleep Duration and BMI
	<5			5–6			7–8			≥9			
	No. of Deaths	Multivariate RR[c]	95% CI	No. of Deaths	Multivariate RR[c]	95% CI	No. of Deaths	Multivariate RR[c]	95% CI	No. of Deaths	Multivariate RR[c]	95% CI	
All causes													0.48
15.0–24.9	388	1.19	1.07, 1.32	4,665	1.05	1.01, 1.09	9,811	1.00	Referent	601	1.08	1.00, 1.18	
25.0–29.9	518	1.15	1.05, 1.26	5,711	1.03	1.00, 1.07	11,223	1.00	Referent	682	1.13	1.05, 1.23	
30.0–34.9	290	1.19	1.06, 1.34	2,578	1.07	1.02, 1.12	4,126	1.00	Referent	294	1.18	1.05, 1.33	
35.0–50.0	224	1.32	1.15, 1.52	1,176	1.01	0.94, 1.09	1,667	1.00	Referent	146	1.17	0.99, 1.38	
Cardiovascular disease													0.03
15.0–24.9	78	0.98	0.78, 1.23	1,077	1.01	0.94, 1.09	2,336	1.00	Referent	132	0.98	0.82, 1.17	
25.0–29.9	175	1.46	1.25, 1.70	1,543	1.07	1.01, 1.14	2,890	1.00	Referent	187	1.20	1.03, 1.39	
30.0–34.9	90	1.28	1.03, 1.60	787	1.15	1.05, 1.25	1,180	1.00	Referent	75	1.05	0.82, 1.30	
35.0–50.0	83	1.42	1.12, 1.79	391	1.00	0.88, 1.14	562	1.00	Referent	49	1.14	0.85, 1.53	
Cancer													0.06
15.0–24.9	149	1.20	1.02, 1.42	1,798	1.03	0.98, 1.09	3,891	1.00	Referent	206	0.97	0.84, 1.11	
25.0–29.9	165	0.98	0.84, 1.14	2,162	0.99	0.94, 1.05	4,485	1.00	Referent	242	1.03	0.90, 1.17	
30.0–34.9	101	1.17	0.95, 1.43	885	0.99	0.91, 1.08	1,529	1.00	Referent	110	1.23	1.01, 1.49	
35.0–50.0	49	0.99	0.74, 1.34	331	0.95	0.83, 1.09	509	1.00	Referent	32	0.87	0.61, 1.25	

Abbreviations: BMI, body mass index; CI, confidence interval; NIH, National Institutes of Health; RR, relative risk.

[a] Defined as reporting fair or better health and no cancer, heart disease, stroke, or emphysema.

[b] Weight (kg)/height (m)^2.

[c] Adjusted for age, sex, race/ethnicity, marital status, education, self-reported health, smoking status, smoking dose, years since quitting smoking, and alcohol drinking.

Table 5. Relationship of a Total Risk Factor Score for Overall Sleep Duration, Moderate-to-Vigorous Physical Activity, Television Viewing, and Body Mass Index to Mortality Among 239,896 Healthy[a] Participants in the NIH-AARP Diet and Health Study, Excluding People Reporting ≥9 Hours of Sleep per Day, 1995–1996

Cause of Death and Total Risk Factor Score[b]	No. of Deaths	Multivariate RR[c]	95% CI	*P* for Trend
All causes				<0.0001
1	2,043	1.00	Referent	
2	7,939	1.08	1.03, 1.13	
3	11,863	1.16	1.11, 1.22	
4	7,552	1.25	1.19, 1.32	
5	2,109	1.42	1.34, 1.52	
Cardiovascular disease				<0.0001
1	555	1.00	Referent	
2	1,951	1.23	1.10, 1.37	
3	2,700	1.35	1.22, 1.51	
4	1,633	1.54	1.38, 1.72	
5	395	1.90	1.67, 2.17	
Cancer				<0.0001
1	612	1.00	Referent	
2	2,704	1.09	1.01, 1.17	
3	4,196	1.10	1.02, 1.19	
4	2,933	1.18	1.09, 1.27	
5	825	1.21	1.09, 1.34	

Abbreviations: CI, confidence interval; NIH, National Institutes of Health; RR, relative risk.

[a] Defined as reporting fair or better health and no cancer, heart disease, stroke, or emphysema.

[b] The total risk factor score was calculated for each participant by combing all of the numerical scores assigned to each category of sleep duration (1 for <5 hours/day and 5–6 hours/day; 0 for 7–8 hours/day and ≥9 hours/day), moderate-to-vigorous physical activity (1 for never/rarely or <1 hour/week; 0 for 1–3 hours/week, 4–7 hours/week, and ≥7 hours/week), television viewing (1 for 3–4 hours/day, 5–6 hours/day, 7–8 hours/day, and ≥9 hours/day; 0 for none, <1 hour/day, and 1–2 hours/day), and body mass index (weight (kg)/height (m)^2; 1 for ≥25, 0 for <25).

[c] Adjusted for age, sex, race/ethnicity, marital status, education, self-reported health, smoking status, smoking dose, years since quitting smoking, and alcohol drinking.

study we excluded people reporting histories of cancer, heart disease, stroke, and emphysema, as well as poor health. We still observed significantly greater total and CVD mortality among both short- and long-duration sleepers. Furthermore, we also excluded deaths that occurred during the first 3 years of follow-up in this already-healthy group. The exclusion did not affect the associations for either short sleep or long sleep, and it even strengthened the increased risk of CVD mortality among long-duration sleepers, suggesting it was unlikely that the results were driven by unreported medical conditions.

The discrepancy between the Australian study (10) and ours is intriguing and might be accounted for by several factors. First, the criteria used to define less healthy populations in both studies were similar but different. The Australian study not only included chronic conditions but also included functional capacity assessed by means of a physical function questionnaire; however, self-reported health was not a component in their assessment. Moreover, the shortest sleep category in our study (<5 hours/day) was shorter than theirs (<6 hours/day), and the elevation in mortality may become stronger as sleep duration further decreases. Finally, the follow-up period in the Australian study (5 years) was shorter than ours (14 years), and as suggested by the meta-analysis, studies with shorter follow-up time tended to find a weaker association between long sleep duration and mortality (1). Overall, our findings indicate that even in a population free of chronic conditions such as cancer, heart disease, and stroke, both short and long sleep durations are associated with a higher risk of death, supporting a genuine link between sleep duration and mortality.

We did not find an association between sleep duration and cancer mortality. The null association with cancer deaths was consistent with previous studies, all of which found statistically nonsignificant results (6–8, 10, 11). Cancer consists of many different types of malignancies with large heterogeneity in their development and progression, and it is possible that the effects of sleep could differ in different forms of cancer. Hence, future studies should examine the impact of sleep on specific cancer sites and cancer subtypes.

A unique contribution of our study, given our large sample size, is that we were able to examine the interaction of sleep with other modifiable factors, including obesity, physical activity, and sedentary behaviors. Short sleep duration has been linked to higher BMI in cross-sectional studies and to excess weight gain and risk of obesity in prospective cohort studies (21, 27), and some researchers have suggested that sleep deficiency may have contributed to the obesity epidemic in the United States (28). On the other hand, obese people are more likely to develop sleep disorders that lead to disturbed and insufficient sleep (29). In our study, we found that the association between sleep and CVD mortality was more apparent among overweight or obese participants, suggesting that these people may be more susceptible to the adverse effects associated with sleep alterations. Moreover, our analysis of additive interaction showed that short sleep and high BMI in combination conferred an excessively high risk of CVD death. This finding is particularly striking but needs to be confirmed in future studies. If confirmed, this could have important public health implications. Over two-thirds of the US population is overweight (BMI ≥25) or obese (BMI ≥30) (30), and more than one-third of Americans sleep less than 7 hours per night (31). The positive association between short sleep and elevated BMI indicates that the two conditions coexist in a substantial proportion of the population. These individuals may need more rigorous surveillance and interventions tailored to their special needs. Moreover, on a population level, public health initiatives are needed to break the vicious cycle of sleep deficiency and obesity.

We found that overall the U-shaped association between sleep duration and all-cause mortality was independent of MVPA or TV viewing and was not modified by these behaviors, although we could not rule out the possibility that the relationship between sleep and CVD mortality might be weaker among people with short TV viewing times. One of the proposed mechanisms relating short sleep duration to poor health, such as obesity, metabolic syndrome, and CVD, was reduced exercise due to fatigue caused by sleep deficiency (32, 33). Our finding that short sleep may still adversely affect health even among people who are relatively active was particularly intriguing, suggesting that additional mechanisms may be in play. Overall, these findings highlight the importance of sleep as a health behavior distinct from both physical activity and sedentary behavior, and they indicate that even among relatively active people, improving sleep hygiene may confer additional health benefits.

One of the major strengths of our study was its large sample size, which enabled us to analyze the interaction of sleep with other lifestyle factors and their combined association with mortality. In addition, it allowed us to exclude participants with preexisting conditions and poor health and still retain sufficient statistical power. However, our study also had several limitations. Information on sleep, physical activity, sedentary behavior, and BMI was all self-reported and was subject to error and misclassification. Moreover, we only had 1-time measures of these factors and were not able to determine cumulative exposure or fluctuations over time. For physical activity, participants were asked to report their usual levels in the past 10 years, and we assumed that their responses reflected their average activity levels during this longer period. We were not able to evaluate changes in physical activity that occurred during this time. The sleep categories provided in the questionnaire were somewhat broad, which did not allow us to evaluate the association of mortality with sleep duration in more refined categories—particularly the association with excessively long sleep duration (≥10 hours/day), which may be associated with further increase in mortality. We also did not have information on mental and sleep disorders that may lead to altered sleep duration and are associated with higher mortality, such as depression, insomnia, sleep apnea, and simple snoring. Such conditions may confound the sleep-mortality association (26). Moreover, the health behavior variables were dichotomized, which is somewhat arbitrary and may obscure some of the nuances in the dose-dependent relationship between individual behaviors and mortality. Lastly, because our study population included healthy middle-aged and older people who were free of major chronic conditions, the findings should not be generalized to populations of different ages or with different health status.

In summary, we confirmed that sleep duration is a powerful predictor of mortality. Our findings highlight the importance of encouraging healthy sleep behaviors in the general population, especially in persons who are already at elevated health risk due to obesity.

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