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Insufficient and excessive amounts of sleep increase the risk of premature death from cardiovascular and other diseases: the Multiethnic Cohort Study

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Abstract

Objective—To explore an independent association between self-reported sleep duration and cause-specific mortality.

Methods—Data were obtained from the Multiethnic Cohort Study conducted in Los Angeles and Hawaii.

Results—Among 61,936 men and 73,749 women with no history of cancer, heart attack or stroke, 19,335 deaths occurred during an average 12.9 year follow-up. Shorter (≤5 h/day) and longer (≥9 h/day) sleepers of both sexes (vs. 7 h/day) had an increased risk of all-cause and cardiovascular disease (CVD) mortality, but not of cancer mortality. Multivariable hazard ratios for CVD mortality were 1.13 (95% CI 1.00-1.28) for ≤5 h/day and 1.22 (95% CI 1.09-1.35) for ≥9 h/day among men; and 1.20 (95% CI 1.05-1.36) for ≤5 h/day and 1.29 (95% CI 1.13-1.47) for ≥9 h/day among women. This risk pattern was not heterogeneous across specific causes of CVD death among men (P_{hetero} 0.53) or among women (P_{hetero} 0.72). The U-shape association for all-cause and CVD mortality was observed in all five ethnic groups included in the study and by subgroups of age, smoking status, and body mass index.

Conclusion—Insufficient or excessive amounts of sleep were associated with increased risk of mortality from CVD and other diseases in a multiethnic population.

Keywords

Sleep; mortality; cardiovascular disease; ethnic groups; prospective studies

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Conflict of Interest Statement
The authors declare that there are no conflicts of interest.

Introduction

A number of prospective studies have shown that longer or shorter sleep times are positively associated with all-cause mortality (Chien et al., 2010; Ferrie et al., 2007; Gangwisch et al., 2008; Hammond, 1964; Heslop et al., 2002; Hublin et al., 2007; Ikehara et al., 2009; Kripke et al., 2002; Kripke et al., 1979; Mallon et al., 2002; Mesas et al., 2010; Patel et al., 2004; Shankar et al., 2008; Wingard and Berkman, 1983), or with cardiovascular mortality as a group (Burazeri et al., 2003; Ferrie et al., 2007; Ikehara et al., 2009; Lan et al., 2007; Patel et al., 2004; Shankar et al., 2008; Stone et al., 2009; Suzuki et al., 2009). However, only two previous investigations examined the relation of sleep duration to specific causes of death and these were limited to stroke and coronary heart disease (Amagai et al., 2004; Ikehara et al., 2009). Furthermore, no prospective investigation has considered consistency of findings across different ethnic groups or within strata defined by potential confounders, such as sedentary behavior.

Our objective was to improve the understanding of the association of sleep duration with cause-specific mortality while accounting for confounders and mediators of this relation.

Materials and Methods

Study Population

The Multiethnic Cohort (MEC) is a prospective study including 215,000 men and women, aged 45–75 years, who answered a mailed survey form in Hawaii and Los Angeles in the 1990s (Kolonel et al., 2000). A self-administered questionnaire was used to collect information on demographic characteristics, lifestyle factors (smoking, diet, physical activity, hours of sitting and sleeping), medical history and anthropometric measures. The study was approved by the institutional review boards of the University of Hawaii and the University of Southern California.

Several exclusions were applied to the analysis as follows: 13,989 participants who did not self-identify as African American, Japanese American, Latino, Native Hawaiian or white, and 8,263 participants with implausible dietary data based on total energy intake or its components. Subjects with missing or incomplete information on hours engaged in sleeping and physical activity (n=18,874), or on height or weight (n=2,343), and smoking history (n=5,224) were also excluded. Additionally, men and women were excluded who reported a personal history of heart attack, stroke, or cancer at baseline, or if a history of malignancy was obtained from a cancer registry (n=30,869), or who died within the first year of cohort entry (n=535). A total of 135,685 participants were included in the analysis.

The excluded subjects were similar to the analytical sample with regard to median follow-up time, BMI, energy intake, hours spent sleeping per day, and prevalence of smoking (see Table S1). The excluded subjects were somewhat older (by 4.9 years on average), consumed more fruits and vegetables, drank an average of 2.6 fewer grams of alcohol per day, were more likely to have a history of hypertension and/or diabetes, and were less likely to have a college education.. We were careful to adjust for these factors in our analyses.

Ascertainment of Mortality

Deaths were ascertained largely through linkage to state death-certificate (Curb et al., 1985). A total of 19,335 deaths were identified through December 31, 2007, with an average 12.9 years of follow-up. Causes of deaths were assigned according to the International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10) (Table 1).

Data Description

Sleep duration including naps (h/day) in the year prior to cohort entry was ascertained using six categories: five hours or less, six, seven, eight, nine, and ten hours or more. For this analysis, the two longest sleeping groups were collapsed as ≥9 h/day. Participants were also asked to record hours spent in sitting activities, including transportation, work, meals, watching television; and other leisure activities, such as reading, playing cards and sewing, as well as hours spent engaging in physical activity. Physical activity was categorized in three domains, including 'strenuous sports', 'vigorous work', and 'moderate activity'. Metabolic equivalents (METs) for physical activity were computed by assigning 4.0 METs for moderate activities and 7.2 for vigorous work and strenuous sports (Institute of Medicine, 2005). Body mass index (weight divided by height (kg/cm^2)) was computed from self-reported weight and height.

Statistical Analysis

We compared sleep duration with respect to several demographic characteristics and lifestyle factors of interest. Age-adjusted means and percentages for basic characteristics and lifestyle factors were calculated through age standardization across 5-year age groups. Cox proportional hazard models with age as the time metric was used to examine the association of sleep duration with mortality after adjustment for potential confounders. Analysis of sleep duration and mortality was stratified by sex since cause-specific mortality was distributed differently among men and women. Age at cohort entry (grouped as 45-49, 50-54, 55-60, 60-64, 65-69, ≥70 years) and ethnicity (African American, Japanese American, Latino, Native Hawaiian, white) were adjusted as strata variables. Smoking adjustment included the average number of cigarettes/day, average number of cigarettes squared, indicator variables for former and current smokers, number of years smoked (time dependent), number of years since quitting (time dependent), and interaction terms consisting of race/ethnicity with the following variables: average number of cigarettes, average number of cigarettes squared, smoking status, and number of years smoked (Haiman et al., 2006).

The following variables were considered as potential confounders: education level (less than college, college graduate or higher, missing), marital status (married, else, missing), prevalent diabetes at baseline (no, yes), prevalent hypertension at baseline (no, yes), energy intake (above and equal or below the median: 2,184 Kcal/day for men, and 1,747 Kcal/day for women), alcohol intake (above and equal or below the median: 2.8 g/day for men and 0 g/day for women), physical activity (quartiles; 0.1-15.3, 15.4-33.3, 33.4-63.9, and ≥64.0 METs/week for men, 0.1-9.9, 10.0-20.7, 20.8-45.9, ≥46.0 METs/week for women), and hours sitting watching television (<1 hour, 1-4 hours, ≥5 hours, missing).

To examine whether the association pattern between sleep duration and cause-specific mortality differed between causes, the heterogeneity of the sleep effect was tested in case-only models. The category with the largest number of deaths was used as the comparison group, with competing risk models in which each cause of death was considered as a separate event (Therneau and Grambsch, 2000). A Wald test was used to compare the parameters between causes with degrees of freedom equal to 4(g-1) where g is the number of case groups and 4 represents the number of parameters being tested.

Stratified analyses of participant characteristics were conducted for all-cause and CVD mortality. Men and women were combined in the stratified analyses to retain study power, as no statistical interaction was found between sex and sleep duration on the risk of all-cause mortality or CVD mortality (P's >0.1). The Wald statistic for cross-product terms was used to test the significance of interaction.

All tests were two-sided, and $P < 0.05$ was considered statistically significant. Software SAS version 9.2 software was used (SAS Institute, Inc., Cary, North Carolina).

Results

The majority of participants (83%) reported sleeping between 6 and 8 h/day (Table 2). White and Japanese men and women were more likely than other ethnic groups to sleep between 6 and 8 h/day; whereas, African-Americans and Native Hawaiians averaged fewer hours of sleep. Men and women older than 70 years of age were more likely than younger men and women to sleep ≥ 9 h/day or ≤ 5 h/day. Men and women sleeping ≤ 5 h/day or ≥ 9 h/day were more likely than average sleepers to be married, have prevalent diabetes or hypertension, be a current smoker, obese and less physically active or more sedentary, and to consume more calories. Light alcohol drinkers and nondrinkers tended to sleep fewer hours than alcohol drinkers.

The association of sleep duration with all-cause mortality and cause-specific mortality including at least 100 deaths is presented in Tables 3 and 4. All-cause mortality showed a U-shaped association with sleep times in men (Table 3) and women (Table 4) (see also Figure 1). The four hazard ratios were simultaneously compared across the four major causes of mortality (malignant neoplasms, cardiovascular disease, respiratory disease and all others) and found to be significantly different in men (p =0.02) and women (p<0.01): sleep was not associated with mortality from malignant neoplasms, but sleep duration had a U-shaped association with mortality from CVD, respiratory disease and all other causes.

Multivariable HRs for CVD mortality were 1.13 for men and 1.20 for women sleeping ≤5 h/day; and 1.22 for men and 1.29 for women sleeping ≥ 9 h/day. This risk pattern for mortality was not heterogeneous across specific causes of death among men or among women within either the CVD category or the ‘all others’ category.

Stratification by various characteristics known to influence the risk of death had little influence on the U-shaped association between sleep duration and all-cause mortality (Table 5). A significant interaction was found between body mass index and sleep duration on all-cause mortality (P*int* 0.03).

Stratification analyses had little effect on the association between sleep duration and CVD mortality (P's for interaction >0.05), with the exception of a significant interaction with education (P_{int} 0.02) (Table 6). Longer sleepers (8 or ≥9 hr/day) among more highly educated subjects had a greater risk of CVD mortality compared to the reference group (7 h/day). The U-shaped associations of CVD mortality with sleep duration were robust to exclusion of participants who were current smokers, obese, or had a history of hypertension or diabetes.

Restricting the sample to participants with at least 10 yrs of follow-up attenuated the HRs for mortality in the shortest sleeping group, but in general the patterns of risk were consistent with results that included participants with less follow-up time (Table 7).

Discussion

In this study, men and women in the extremes of sleep duration faced higher risk of death, particularly from CVD. Moreover, the consistency of the U-shaped association of all cause and CVD mortality with sleep duration in analyses by subgroups of demographic and lifestyle factors, adds to the public health significance of our observations. A unique aspect of the current analysis was the consistency of the major findings among diverse ethnic groups.

Recent meta-analyses of results from prospective studies found that the risk of all-cause mortality was increased by 10-12% in short sleepers and 23-30% in long sleepers (Cappuccio et al., 2010; Gallicchio and Kalesan, 2009). Our result for all-cause mortality is consistent with the results from large cohort studies (Kripke et al., 2002; Patel et al., 2004; Tamakoshi and Ohno, 2004), namely a U-shaped relation of all-cause mortality with sleep duration.

We observed a U-shaped association of CVD mortality with sleep duration, in contrast to inconsistent results from previous studies (Burazeri et al., 2003; Heslop et al., 2002; Ikehara et al., 2009; Lan et al., 2007; Mallon et al., 2002; Patel et al., 2004; Shankar et al., 2008; Stone et al., 2009; Suzuki et al., 2009). While some investigators report null associations (Heslop et al., 2002; Mallon et al., 2002), others report significant positive associations of CVD mortality specific to longer sleepers (Burazeri et al., 2003; Ikehara et al., 2009; Lan et al., 2007; Patel et al., 2004; Stone et al., 2009; Suzuki et al., 2009). Meta-analyses found that the risk of all CVD mortality was increased by 23-41% in longer sleepers, but no association was observed in shorter sleepers (Cappuccio et al., 2011; Gallicchio and Kalesan, 2009). However, consistent with our result, men and women who decreased their sleep hours had a 2-fold higher risk of CVD mortality compared to men and women who had no change in their sleeping time in the Whitehall II Cohort (Ferrie et al., 2007).

The relatively large size of the Multiethnic Cohort allowed us to examine the relation of sleep duration to specific CVD outcomes. In accord with our findings, Japanese investigators reported significantly increased mortality from stroke among longer sleeping (≥10 h/day vs. 7 h/day) men (66% increased risk) and women (69% increased risk) (Ikehara et al., 2009). While risk of CHD death among shorter sleeping (≤4 h/day) women was increased 2.32-fold compared to average sleepers, CHD death was not associated with sleeping duration among men (Ikehara et al., 2009). However, the number of deaths from CHD in the extreme sleeping group was small (Ikehara et al., 2009). Another study of specific CVD outcomes showed non-significant relations to sleep, but this investigation had a small number of deaths (63 deaths from stroke, and 54 deaths from heart diseases) (Amagai et al., 2004). Finally, increased risks of CHD mortality in shorter and longer sleepers (≤5 h/day and ≥10 h/day vs. 7 h/day) were observed in a cohort of Singapore Chinese (Shankar et al., 2008).

We observed an increased risk of death from hypertension in extreme sleepers among women, but not men, although heterogeneity in risk across cardiovascular outcomes was not statistically significant in either sex. This result is consistent with findings from a large cross-sectional study showing increased hypertension among shorter sleeping (<6 h/day) women only (Stranges et al., 2008); as well as the Whitehall II study which reported that shorter sleeping women (≤5 h/day vs. 7 h/day), but not men, had a 19% increased risk of incident hypertension (Cappuccio et al., 2007). Mechanisms are not fully understood, but sex-specific differences in the activity of the angiotensin and renin-angiotensin systems might contribute to poorer control of hypertension in women than in men (Guarner-Lans et al., 2011; Ramírez-Expósito and Martínez-Martos, 2008; Yanes and Reckelhoff, 2011).

This is the first prospective study, to our knowledge, which examined the association of sleep duration with various specific non-CVD causes of death. Although false-positive results are a concern, longer sleeping women, but not men, had an increased risk of death from diabetes; whereas, shorter and longer sleeping men, but not women, had an increased risk of death from mental/behavioral disease and kidney disease. Differences between sexes in insulin resistance (Yanes et al., 2005) or the hypothalamic-pituitary-adrenocortical axis (Pesonen et al., 2012) may provide a partial explanation for our sex-specific findings for death from diabetes and from kidney disease. It is likely that unadjusted confounders such as

sleep disturbances, insomnia or mood disorders, might have inflated the association for deaths due to mental/behavioral disease among men (Dew et al., 2003; Pollak et al., 1990; Rod et al., 2011).

In accordance with other studies (Basner et al., 2007; Chaput et al., 2008; Krueger and Friedman, 2009; López-García et al., 2008; Lauderdale et al., 2006; Magee et al., 2009; Nishiura and Hashimoto, 2010; Stamatakis et al., 2007; Stranges et al., 2008), we observed multiple demographic, lifestyle and co-morbid conditions that were associated with sleep duration. Older people, who are at greater risk of death, tend to sleep longer than younger people (Ferrie et al., 2007; Gangwisch et al., 2008), although it is unclear if this association is causal (Patel et al., 2012). Consistent with our results, African Americans had greater variability in sleep duration than other ethnic groups, and Hispanics had a greater tendency to sleep ≥9 hr/day (Hale and Do, 2007). Shorter (Hasler et al., 2004; Kohatsu et al., 2006; Nishiura and Hashimoto, 2010) and longer duration of sleep (Chaput et al., 2008; Hairston et al., 2010; López-García et al., 2008) have been associated with greater body mass, as well as with greater accumulation of abdominal fat (Hairston et al., 2010). A more pronounced impact of short sleep on all-cause mortality in obese compared to non-obese participants is worrisome, but may have resulted from residual confounding resulting from the strong correlation of energy intake, sitting hours, and physical activity with both sleep time and obesity (Horne, 2008; Marshall et al., 2008). Shorter sleepers and longer sleepers engage in less physical activity (Tu et al., 2012) and watch more television than average sleepers (Basner et al., 2007). It is reassuring that the increased risk of all-cause and CVD mortality among shorter and longer sleepers was generally consistent across various subgroups in our study.

Strengths of the study include the large number of subjects from a multiethnic population with long-term follow-up and multiple cause-specific outcomes. Accordingly, we were able to restrict the analyses of sleep duration and mortality to a healthy population and to a long-term followed population. One potential limitation of our study design was the absence of information concerning sleep quality, such as insomnia and sleep disturbance, or medical conditions/diseases that could affect sleep duration which might also influence risk of death. Because sleep was measured by self-administered questionnaire and not by objective tools, we cannot rule out the possibility that sleep duration may have been misclassified. Sleep duration was over-reported in a study comparing self-reported sleep to actinographic measurement (Lauderdale et al., 2008), implying that the association of higher mortality in the shortest sleeping group may be an underestimate of the true risk of death.

Conclusion

Men and women who have insufficient or excessive amounts of sleep are at increased risk of premature mortality from cardiovascular and other chronic diseases in a representative multiethnic populations.

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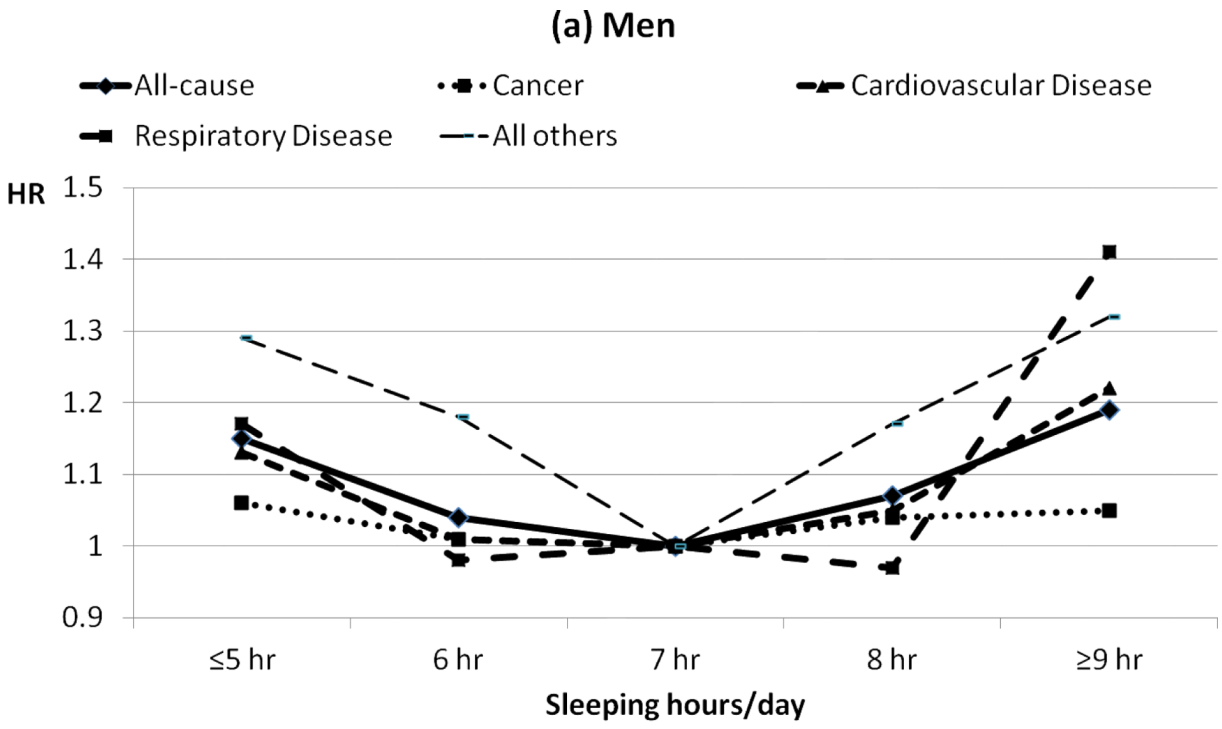
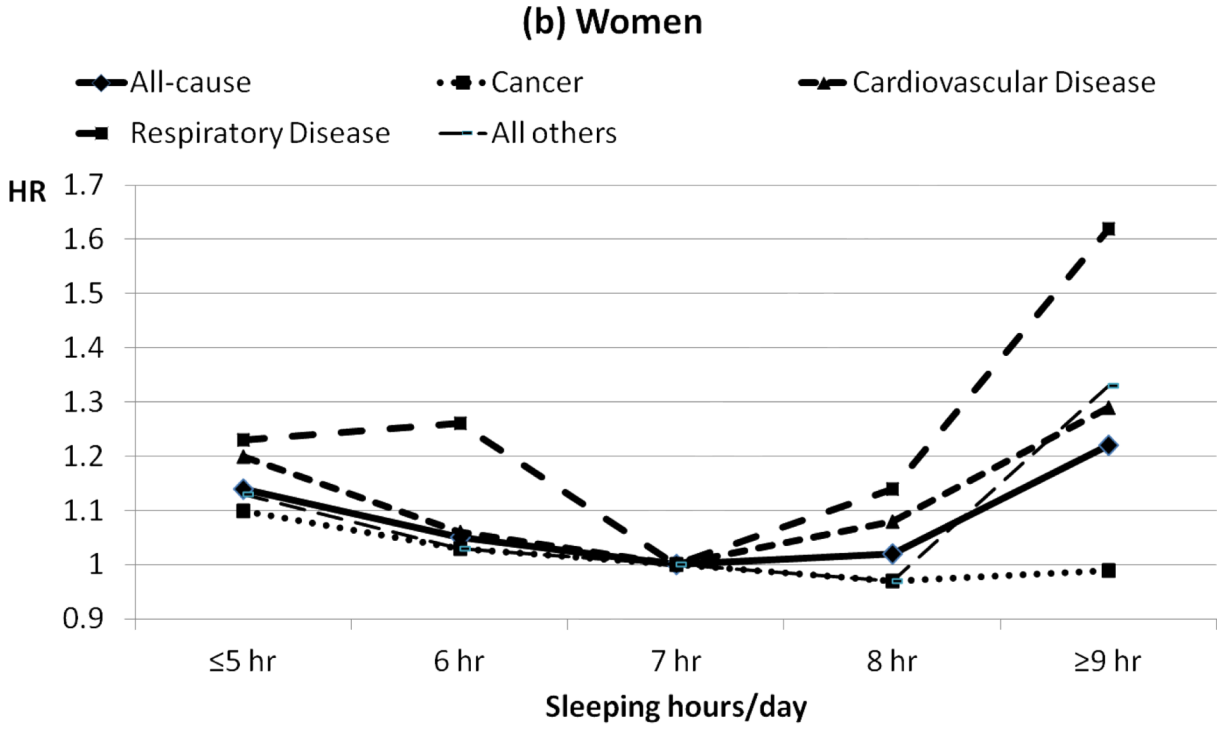
Highlights

- Shorter and longer sleep increased the risk of all-cause and CVD mortality.
- Risk pattern for CVD mortality was not heterogeneous across specific causes.
- The association for all-cause and CVD mortality was consistent across subgroups.
- Sleep duration was not associated with cancer mortality.



a



b

Figure 1.

Hazard ratios of all-cause and cause specific mortality as a group among men (a) and women (b) in the Multiethnic Cohort Study, 1993-2007.

Table 1

The coding assignments and number of deaths for cause-specific mortality among 135,685 men and women in the Multiethnic Cohort Study, 1993-2007

	Codes		Deaths	
Cause of death	**ICD-9**	**ICD-10**	**No.**	**%**
All Causes			19,335	
Malignant Neoplasms	140-239	C00-C97	6,772	35.0
Cardiovascular disease			6,610	34.2
Coronary Heart Dis	410-414, 429	I20-I25	3,476	18.0
Myocardial Infarction	410	I21, I22	1,188	6.1
Ischemic Heart Disease	411-414, 429	I20, I23-25	2,288	11.8
Stroke	430-438	I60-I69	1,259	6.5
Cardiomyopathy	425	I42	252	1.3
Cardiac Arrest	427	I46	250	1.3
Hypertensive Heart Disease	402-404	I11-13	267	1.4
Hypertension	401-405	I10, I12	235	1.2
Congestive Heart Failure	428	I50	201	1.0
Aortic Aneurysm	441	I71	130	0.7
All other major cardiovascular disease	394-398, 410-429, 440-447	I05-I09, I26-I28, I30-I52, I70-I79	540	2.8
Respiratory disease			1,340	6.9
Pneumonia	480-488	J10-J18	508	2.6
Emphysema	492	J43	127	0.7
Asthma	493	J45-J46	56	0.3
All other chronic lower respiratory disease	464-496	J40-J47	649	3.4
All Others			4,613	23.9
Infectious/Parasitic Dis	001-139	A,B	354	1.8
Disease of blood & blood-forming organs & certain disease involving immune mechanism	279, 282-89	D58, D61-86	62	0.3
Diabetes	250	E10-E14	667	3.4
Mental/Behavioral Disease	298-299, 303	F01-50	239	1.2
Alzheimer's Disease	331	G30	172	0.9
Parkinson's Disease	332	G20-G21	266	1.4
Motor Neuron Disease	335	G12	92	0.5
Peptic Ulcer	531-533	K25-K27	52	0.3
Liver Disease	571	K70-K76	324	1.7
Vascular Insufficiency of Intestine	557	K55	74	0.4
Musculoskeletal Disease	710-730	M00-86	136	0.7
Kidney Disease	581-586	N03-05, N17-19, N26	246	1.3
Accidents	800-929	V01-X59, Y85-89	381	2.0
Suicide	950-956	X60-X84	131	0.7
In situ, benign neoplasms	227, 230-239	D10-D36, D37-D48	121	0.6

Abbreviation: ICD-9, Ninth Revision of the International Classification of Diseases; ICD-10, Tenth Revision of the International Classification of Diseases.

Table 2

Distribution of self-reported daily sleeping hours (row percentage) by selected characteristics among 135,685 men and women in the Multiethnic Cohort Study, 1993-1996[a]

Variable	Age-adjusted row percentage					
	Daily sleeping					
	≤5 hr	6 hr	7 hr	8 hr	≥9 hr	P-value[b]
Number of subjects (Row %)	11,841 (8.7%)	33,711 (24.8%)	44,711 (33.0%)	34,110 (25.1%)	11,312 (8.3%)	
Ethnicity						<0.01
White	4.7	18.9	35.9	30.9	9.7	
African American	14.5	26.7	26.4	22.7	9.8	
Native Hawaiian	13.4	27.3	28.2	22.2	8.9	
Japanese American	7.9	30.2	36.4	20.6	5.0	
Latino	9.4	22.2	30.3	27.5	10.7	
Age at entry, years						<0.01
45-64	8.6	25.7	33.8	24.3	7.6	
65-69	8.8	22.8	31.6	27.0	9.9	
70+	9.4	22.8	30.2	27.2	10.3	
Sex						<0.01
Men	7.8	25.0	33.2	25.4	8.5	
Women	9.5	24.8	32.7	24.9	8.1	
Education						0.82
High school or some college	9.7	24.8	31.2	25.2	9.1	
College graduate/postgraduate	6.3	24.9	36.8	25.3	6.8	
Married						<0.01
Yes	11.3	26.2	30.6	23.5	8.4	
No	7.5	24.2	34.0	25.9	8.3	
Diabetes						0.12
Yes	11.8	24.9	28.1	24.4	10.7	
No	8.5	24.9	33.4	25.2	8.1	
Hypertension						<0.01
Yes	10.2	26.1	30.8	24.1	8.8	

Variable	Age-adjusted row percentage					
	Daily sleeping					
	≤5 hr	6 hr	7 hr	8 hr	≥9 hr	P-value[b]
No	8.0	24.4	34.0	25.6	8.1	
Smoking						<0.01
Nonsmoker	9.0	25.4	33.7	24.4	7.5	
Former smoker	7.9	24.3	33.2	26.0	8.6	
Current smoker	9.5	24.3	30.4	25.5	10.3	
Body mass index, kg/m^2						0.22
Non-obese (<25.0)	7.4	24.6	35.4	25.2	7.4	
Overweight (25.0-29.9)	9.1	25.2	31.8	25.3	8.6	
Obese (≥30.0)	11.8	24.4	28.2	24.7	10.9	
Physical activity, METs/week[c]						<0.01
<15.4 (men), <10.0 (women)	11.1	24.8	29.4	24.9	9.8	
15.4-33.3 (men), 10.0-20.7 (women)	9.2	26.2	32.7	24.2	7.7	
33.4-63.9 (men), 20.8-45.9 (women)	7.7	25.2	34.7	24.8	7.7	
≥64.0 (men), ≥46.0 (women)	7.5	23.4	34.2	26.6	8.3	
Sitting watching television, h/day						<0.01
< 1	10.2	25.0	32.4	24.8	7.6	
1-4	8.1	25.0	33.6	25.3	8.0	
≥5	11.7	23.8	26.9	24.6	12.9	
Calorie intake, Kcal/day						<0.01
<2,184 (men), <1,747 (women)	8.4	25.4	34.2	24.8	7.2	
≥2,184 (men), ≥1,747 (women)	9.0	24.3	31.7	25.5	9.4	
Alcohol intake, g/day						<0.01
<2.8 (men), zero (women)	9.7	26.0	32.0	24.2	8.1	
≥2.8 (men), >0 (women)	7.5	23.5	34.0	26.2	8.8	

Abbreviation: METs, metabolic equivalent of task.

[a] Data are presented as row percentage unless otherwise indicated. Row percentage are adjusted for age through age standardization across 5 year age groups.

[b] *P* Value for the difference of mean between subgroups adjusted for age based on analysis of variance.

[c] METs for moderate activity, vigorous work and strenuous sports.

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Table 3

Hazard ratios for all-cause and cause specific mortality in relation to self-reported sleep duration among 61,936 men in the Multiethnic Cohort Study, 1993-2007[a,b]

Outcome[c]	Deaths		Daily sleeping				
			≤5 hr	6 hr	7 hr	8 hr	≥9 hr
	No.	%	HR (95% CI)	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)
All Causes	10,738	-	1.15 (1.06-1.23)*	1.04 (0.99-1.10)	1.00	1.07 (1.01-1.12)*	1.19 (1.12-1.27)*
Malignant Neoplasms	3,717	34.6	1.06 (0.94-1.21)	1.01 (0.92-1.10)	1.00	1.04 (0.96-1.13)	1.05 (0.94-1.18)
Cardiovascular disease	3,772	35.1	1.13 (1.00-1.28)	1.01 (0.92-1.11)	1.00	1.05 (0.96-1.14)	1.22 (1.09-1.35)*
Coronary Heart Disease	2,096	19.5	1.21 (1.04-1.42)*	0.96 (0.85-1.08)	1.00	1.00 (0.89-1.12)	1.16 (1.00-1.34)*
Myocardial Infarction	667	6.2	1.24 (0.94-1.64)	0.92 (0.74-1.15)	1.00	0.98 (0.80-1.20)	1.16 (0.89-1.50)
Ischemic Heart Disease	1,429	13.3	1.20 (0.99-1.45)	0.98 (0.84-1.13)	1.00	1.01 (0.88-1.16)	1.16 (0.98-1.39)
Stroke	627	5.8	1.02 (0.74-1.40)	1.10 (0.88-1.37)	1.00	1.13 (0.91-1.39)	1.35 (1.03-1.75)*
Cardiomyopathy	163	1.5	0.68 (0.32-1.47)	1.46 (0.95-2.25)	1.00	1.40 (0.91-2.14)	1.62 (0.95-2.75)
Cardiac Arrest	162	1.5	1.61 (0.93-2.78)	0.98 (0.62-1.54)	1.00	1.08 (0.71-1.65)	1.48 (0.89-2.48)
Hypertensive Heart Disease	137	1.3	0.75 (0.38-1.47)	1.18 (0.76-1.84)	1.00	1.01 (0.64-1.58)	0.72 (0.37-1.41)
Hypertension	129	1.2	1.14 (0.61-2.13)	0.72 (0.42-1.23)	1.00	1.16 (0.74-1.82)	1.22 (0.68-2.18)
Congestive Heart Failure	116	1.1	1.42 (0.74-2.70)	0.80 (0.45-1.43)	1.00	1.23 (0.76-2.02)	1.43 (0.79-2.60)
Respiratory disease	725	6.8	1.17 (0.89-1.55)	0.98 (0.80-1.22)	1.00	0.97 (0.79-1.18)	1.41 (1.12-1.78)*
Pneumonia	295	2.7	1.09 (0.70-1.71)	0.98 (0.70-1.37)	1.00	0.96 (0.71-1.31)	1.36 (0.95-1.96)
All others	2,524	23.5	1.29 (1.11-1.50)*	1.18 (1.05-1.31)*	1.00	1.17 (1.05-1.30)*	1.32 (1.15-1.51)*
Infectious/Parasitic Disease	210	2.0	1.26 (0.77-2.04)	0.72 (0.47-1.09)	1.00	1.29 (0.91-1.83)	1.38 (0.87-2.19)
Diabetes	355	3.3	0.89 (0.59-1.35)	0.95 (0.71-1.28)	1.00	1.03 (0.78-1.36)	1.03 (0.72-1.48)
Mental/Behavioral Disease	119	1.1	3.25 (1.65-6.38)*	2.43 (1.37-4.29)*	1.00	1.82 (1.03-3.22)	2.91 (1.54-5.49)*
Alzheimer's Disease	111	1.0	2.07 (1.00-4.29)	1.67 (0.95-2.92)	1.00	1.63 (0.96-2.78)	1.64 (0.82-3.25)
Parkinson's Disease	108	1.0	1.39 (0.60-3.18)	2.14 (1.21-3.76)*	1.00	1.87 (1.08-3.24)*	1.82 (0.93-3.57)
Liver Disease	202	1.9	1.19 (0.69-2.04)	1.39 (0.95-2.02)	1.00	1.07 (0.73-1.57)	1.05 (0.64-1.74)
Kidney Disease	140	1.3	1.81 (0.98-3.34)	1.10 (0.64-1.90)	1.00	1.81 (1.13-2.90)*	1.99 (1.13-3.51)*
Accidents	226	2.1	1.47 (0.94-2.32)	0.97 (0.68-1.41)	1.00	0.92 (0.64-1.31)	1.18 (0.75-1.86)

Abbreviation: CI, Confidence Intervals; HR, Hazard Ratio

*HR (95% CI) which not includes 1.00.

[a]Hazard ratios were calculated with age as the time metric, adjusted for 5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity (METs per week for moderate activity, vigorous work and strenuous sports), hours spent daily watching television, and smoking history by inclusion of the following variables: [smoking status, average number of cigarettes, average number of cigarettes squared, number of years smoked (time dependent), number of years since quitting (time dependent), and interactions between ethnicity and the smoking variables].

[b]The test of heterogeneity across causes of death was performed using competing risk techniques, where each cause was a different event. A Wald test was used to compare the parameters between causes. P for heterogeneity (degrees of freedom = 12) across malignant neoplasms, cardiovascular disease, respiratory disease, and all others was 0.02. P for heterogeneity (degrees of freedom = 32) across specific cardiovascular disease was 0.53. P for heterogeneity (degrees of freedom = 60) across cause-specific disease within ‘All others’ was 0.42.

[c]Hazard ratios are given only for conditions with 100 cases or more.

Table 4

Hazard ratios for all-cause and cause specific mortality in relation to self-reported sleep duration among 73,749 women in the Multiethnic Cohort Study, 1993-2007[a,b]

Outcome[c]	Deaths		Daily sleeping				
			≤5 hr	6 hr	7 hr	8 hr	≥9 hr
	No.	%	HR (95% CI)	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)
All Causes	8,597	-	1.14 (1.06-1.23)*	1.05 (0.99-1.12)	1.00	1.02 (0.96-1.08)	1.22 (1.13-1.31)*
Malignant Neoplasms	3,055	35.5	1.10 (0.97-1.25)	1.03 (0.94-1.14)	1.00	0.97 (0.88-1.07)	0.99 (0.87-1.14)
Cardiovascular disease	2,838	33.0	1.20 (1.05-1.36)*	1.06 (0.96-1.18)	1.00	1.08 (0.98-1.20)	1.29 (1.13-1.47)*
Coronary Heart Disease	1,380	16.1	1.18 (0.98-1.42)	1.13 (0.97-1.31)	1.00	1.12 (0.96-1.29)	1.23 (1.02-1.49)*
Myocardial Infarction	521	6.1	1.18 (0.87-1.59)	1.23 (0.96-1.56)	1.00	1.10 (0.86-1.40)	1.29 (0.94-1.75)
Ischemic Heart Disease	859	10.0	1.18 (0.94-1.49)	1.06 (0.88-1.29)	1.00	1.13 (0.94-1.36)	1.20 (0.95-1.53)
Stroke	632	7.4	1.16 (0.88-1.52)	0.99 (0.79-1.23)	1.00	1.07 (0.87-1.33)	1.39 (1.06-1.83)*
Cardiomyopathy	89	1.0	---	---	---	---	---
Cardiac Arrest	88	1.0	---	---	---	---	---
Hypertensive Heart Disease	130	1.5	1.45 (0.81-2.58)	1.34 (0.81-2.20)	1.00	1.13 (0.67-1.89)	1.72 (0.95-3.09)
Hypertension	106	1.2	2.21 (1.09-4.46)*	2.03 (1.11-3.72)*	1.00	2.05 (1.13-3.71)*	2.46 (1.22-4.97)*
Respiratory disease	615	7.2	1.23 (0.92-1.65)	1.26 (1.00-1.58)	1.00	1.14 (0.91-1.43)	1.62 (1.25-2.11)*
Pneumonia	213	2.5	0.87 (0.49-1.52)	1.45 (0.98-2.15)	1.00	1.45 (0.98-2.13)	2.08 (1.32-3.26)*
All others	2,089	24.3	1.13 (0.97-1.31)	1.03 (0.91-1.16)	1.00	0.97 (0.86-1.10)	1.33 (1.15-1.55)*
Infectious/Parasitic Disease	144	1.7	1.59 (0.94-2.71)	0.93 (0.58-1.51)	1.00	1.04 (0.66-1.66)	1.90 (1.11-3.26)*
Diabetes	312	3.6	1.24 (0.84-1.84)	1.22 (0.87-1.69)	1.00	1.15 (0.83-1.59)	1.57 (1.09-2.28)*
Mental/Behavioral Disease	120	1.4	0.92 (0.46-1.83)	1.33 (0.83-2.11)	1.00	0.93 (0.56-1.54)	0.90 (0.44-1.86)
Alzheimer's Disease	155	1.8	0.93 (0.34-2.53)	0.98 (0.48-2.02)	1.00	1.36 (0.72-2.59)	1.70 (0.73-3.97)
Parkinson's Disease	64	0.7	---	---	---	---	---
Liver Disease	122	1.4	1.55 (0.83-2.88)	1.20 (0.71-2.04)	1.00	1.29 (0.77-2.14)	1.97 (1.09-3.54)*
Kidney Disease	106	1.2	0.71 (0.34-1.45)	0.73 (0.42-1.27)	1.00	0.92 (0.55-1.53)	1.36 (0.74-2.49)
Accidents	155	1.8	0.74 (0.39-1.40)	1.10 (0.73-1.66)	1.00	0.86 (0.55-1.35)	1.41 (0.82-2.44)

Abbreviation: CI, Confidence Intervals; HR, Hazard Ratio.

*HR (95% CI) which not includes 1.00

[a]Hazard ratios were calculated with age as the time metric, adjusted for 5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity (METs per week for moderate activity, vigorous work and strenuous sports), hours spent daily watching television, and smoking history by inclusion of the following variables: [smoking status, average number of cigarettes, average number of cigarettes squared, number of years smoked (time dependent), number of years since quitting (time dependent), and interactions between ethnicity and the smoking variables].

[b]The test of heterogeneity across causes of death was performed using competing risk techniques, where each cause was a different event. A Wald test was used to compare the parameters between causes. P for heterogeneity (degrees of freedom = 12) across malignant neoplasms, cardiovascular disease, respiratory disease, and all others was <0.01. P for heterogeneity (degrees of freedom = 32) across specific cardiovascular disease was 0.72. P for heterogeneity (degrees of freedom = 60) across cause-specific disease within ‘All others’ was 0.54.

[c]Hazard ratios are given only for conditions with 100 cases or more.

Table 5

Hazard ratios for all-cause mortality in relation to self-reported sleep duration by several characteristics among 135,685 men and women in the Multiethnic Cohort Study, 1993-2007[a]

Variable	No. Deaths	Daily sleeping					P int[b]
		≤5 hr	6 hr	7 hr	8 hr	≥9 hr	
		HR (95% CI)	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	
Ethnicity							0.34
White	4,417	1.30 (1.14-1.48)	1.07 (0.98-1.17)	1.00	1.07 (0.99-1.16)	1.26 (1.14-1.38)	
African American	4,391	1.06 (0.96-1.17)	1.01 (0.93-1.10)	1.00	0.99 (0.91-1.08)	1.17 (1.06-1.30)	
Native Hawaiian	1,515	1.22 (1.04-1.44)	0.96 (0.83-1.11)	1.00	1.10 (0.95-1.28)	1.26 (1.05-1.51)	
Japanese American	5,110	1.11 (1.00-1.23)	1.09 (1.01-1.17)	1.00	1.09 (1.01-1.18)	1.23 (1.10-1.37)	
Latino	3,902	1.10 (0.98-1.24)	1.01 (0.93-1.11)	1.00	1.01 (0.92-1.09)	1.12 (1.01-1.25)	
Age at enrollment							0.89
45-64	8,145	1.17 (1.08-1.26)	1.05 (0.99-1.12)	1.00	1.02 (0.96-1.09)	1.23 (1.14-1.33)	
65-69	4,746	1.13 (1.02-1.26)	1.07 (0.98-1.16)	1.00	1.05 (0.97-1.13)	1.25 (1.14-1.38)	
70+	6,444	1.09 (0.99-1.19)	1.02 (0.95-1.09)	1.00	1.07 (1.00-1.14)	1.14 (1.05-1.24)	
Education							0.14
High school or some college	15,447	1.12 (1.06-1.19)	1.05 (1.00-1.10)	1.00	1.03 (0.99-1.08)	1.19 (1.13-1.26)	
College graduate/postgraduate	3,836	1.21 (1.06-1.37)	1.03 (0.95-1.13)	1.00	1.10 (1.01-1.20)	1.23 (1.10-1.38)	
Diabetes							0.31
Yes	3,858	1.09 (0.97-1.22)	1.00 (0.91-1.10)	1.00	1.06 (0.97-1.15)	1.30 (1.17-1.44)	
No	15,477	1.15 (1.09-1.22)	1.06 (1.01-1.10)	1.00	1.04 (1.00-1.09)	1.17 (1.11-1.24)	
Hypertension							0.99
Yes	9,483	1.17 (1.09-1.25)	1.04 (0.99-1.11)	1.00	1.05 (0.99-1.11)	1.22 (1.14-1.31)	
No	9,852	1.11 (1.03-1.20)	1.05 (0.99-1.11)	1.00	1.04 (0.99-1.1)	1.19 (1.11-1.28)	
Smoking status							0.48
Nonsmokers	6,556	1.14 (1.04-1.24)	1.01 (0.95-1.08)	1.00	1.03 (0.96-1.10)	1.19 (1.09-1.30)	
Former smokers	7,900	1.19 (1.10-1.30)	1.09 (1.03-1.16)	1.00	1.10 (1.03-1.17)	1.23 (1.14-1.33)	
Current smokers	4,879	1.07 (0.96-1.19)	1.02 (0.95-1.11)	1.00	0.99 (0.92-1.07)	1.19 (1.08-1.31)	
Body mass index, kg/m^2							0.03
Non-obese (<25.0)	9,057	1.13 (1.04-1.22)	1.02 (0.96-1.08)	1.00	1.05 (0.99-1.11)	1.24 (1.15-1.33)	
Overweight (25.0-29.9)	6,753	1.13 (1.03-1.23)	1.05 (0.98-1.12)	1.00	1.07 (1.00-1.14)	1.25 (1.15-1.35)	
Obese (≥30.0)	3,525	1.19 (1.06-1.33)	1.12 (1.02-1.23)	1.00	1.00 (0.91-1.10)	1.08 (0.96-1.21)	
Physical activity, METs/week[b]							0.09
<15.4 (men), <10.0 (women)	6,162	1.17 (1.07-1.28)	1.12 (1.04-1.21)	1.00	1.13 (1.06-1.21)	1.28 (1.18-1.40)	
15.4-33.3 (men), 10.0-20.7 (women)	4,199	1.15 (1.03-1.28)	1.05 (0.96-1.14)	1.00	0.98 (0.91-1.07)	1.13 (1.01-1.26)	
33.4-63.9 (men), 20.8-45.9 (women)	5,259	1.06 (0.96-1.18)	1.00 (0.93-1.08)	1.00	1.01 (0.93-1.08)	1.19 (1.08-1.31)	
≥64.0 (men), ≥46.0 (women)	3,715	1.22 (1.08-1.38)	1.00 (0.91-1.09)	1.00	1.05 (0.96-1.14)	1.20 (1.07-1.34)	
Sitting watching television, h/day							0.10
< 1	2,073	1.17 (1.01-1.36)	1.11 (0.98-1.26)	1.00	1.13 (1.00-1.28)	1.38 (1.18-1.62)	
1-4	14,120	1.13 (1.06-1.20)	1.06 (1.01-1.11)	1.00	1.02 (0.98-1.07)	1.19 (1.12-1.26)	

Variable	No. Deaths	Daily sleeping					P int[b]
		≤5 hr	6 hr	7 hr	8 hr	≥9 hr	
		HR (95% CI)	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	
≥5	2,766	1.20 (1.06-1.37)	0.95 (0.85-1.07)	1.00	1.09 (0.99-1.22)	1.17 (1.04-1.32)	
Healthy population[c]	2,437	1.08 (0.93-1.25)	1.09 (0.98-1.21)	1.00	1.05 (0.94-1.17)	1.32 (1.14-1.53)	-

Abbreviation: CI, Confidence Intervals; HR, Hazard Ratio; METs, metabolic equivalent of task; Pint, P-value for interaction

[a]Hazard ratios were calculated with age as the time metric, adjusted for variables not relevant to the stratified variables: 5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity (METs per week for moderate activity, vigorous work and strenuous sports), hours spent daily watching television, and smoking history by inclusion of the following variables: [smoking status, average number of cigarettes, average number of cigarettes squared, number of years smoked (time dependent), number of years since quitting (time dependent), and interactions between ethnicity and the smoking variables].

[b]Calculated using the Wald statistic for cross-product terms.

[c]Restricted to men and women who are nonsmokers, non-obese, and who don't have hypertension nor diabetes at baseline (n=68,243).

Table 6

Hazard ratios for cardiovascular mortality in relation to self-reported sleep duration by several characteristics among 135,685 men and women in the Multiethnic Cohort Study, 1993-2007[a]

Variable	No. Deaths	Daily sleeping					P int[b]
		7 hr	6 hr	7 hr	8 hr	≥9 hr	
		HR (95% CI)	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	
Ethnicity							0.19
White	1,367	1.56 (1.25-1.95)	1.10 (0.94-1.29)	1.00	1.13 (0.99-1.30)	1.28 (1.08-1.53)	
African American	1,721	1.06 (0.91-1.25)	1.02 (0.89-1.17)	1.00	1.04 (0.91-1.19)	1.30 (1.11-1.53)	
Native Hawaiian	564	1.02 (0.78-1.34)	0.87 (0.69-1.11)	1.00	0.98 (0.77-1.24)	1.17 (0.88-1.56)	
Japanese American	1,608	1.10 (0.91-1.33)	1.06 (0.93-1.21)	1.00	1.16 (1.02-1.33)	1.41 (1.17-1.70)	
Latino	1,350	1.13 (0.94-1.37)	0.99 (0.85-1.16)	1.00	0.96 (0.84-1.11)	1.01 (0.84-1.21)	
Age at enrollment							0.64
45-64	2,507	1.12 (0.97-1.28)	1.00 (0.90-1.11)	1.00	0.99 (0.89-1.10)	1.18 (1.03-1.36)	
65-69	1,600	1.27 (1.06-1.52)	1.15 (1.00-1.33)	1.00	1.07 (0.93-1.22)	1.43 (1.22-1.68)	
70+	2,503	1.09 (0.94-1.26)	0.98 (0.88-1.10)	1.00	1.14 (1.03-1.27)	1.20 (1.05-1.37)	
Education							0.02
High school or some college	5,364	1.16 (1.05-1.27)	1.03 (0.95-1.11)	1.00	1.04 (0.96-1.12)	1.22 (1.11-1.33)	
College graduate/postgraduate	1,230	1.11 (0.88-1.39)	1.04 (0.88-1.21)	1.00	1.20 (1.04-1.39)	1.34 (1.10-1.63)	
Diabetes							0.25
Yes	1,618	0.98 (0.82-1.17)	0.95 (0.82-1.09)	1.00	0.97 (0.85-1.11)	1.21 (1.03-1.42)	
No	4,992	1.21 (1.10-1.34)	1.06 (0.98-1.14)	1.00	1.10 (1.02-1.19)	1.24 (1.13-1.37)	
Hypertension							0.73
Yes	3,826	1.11 (0.99-1.25)	1.00 (0.92-1.10)	1.00	1.07 (0.98-1.16)	1.24 (1.12-1.39)	
No	2,784	1.22 (1.07-1.40)	1.08 (0.97-1.19)	1.00	1.08 (0.97-1.19)	1.26 (1.11-1.43)	
Smoking status							0.65
Nonsmokers	2,359	1.17 (1.02-1.35)	1.00 (0.89-1.12)	1.00	1.07 (0.95-1.19)	1.21 (1.04-1.40)	
Former smokers	2,673	1.19 (1.03-1.37)	1.06 (0.95-1.18)	1.00	1.11 (1.00-1.23)	1.29 (1.13-1.47)	
Current smokers	1,578	1.08 (0.90-1.30)	1.05 (0.91-1.20)	1.00	1.00 (0.87-1.15)	1.22 (1.04-1.44)	
Body mass index, kg/m^2							0.10
Non-obese (<25.0)	2,861	1.12 (0.98-1.29)	1.03 (0.93-1.14)	1.00	1.03 (0.93-1.14)	1.30 (1.15-1.48)	
Overweight (25.0-29.9)	2,392	1.11 (0.95-1.29)	1.00 (0.89-1.12)	1.00	1.16 (1.04-1.29)	1.28 (1.12-1.47)	
Obese (≥30.0)	1,357	1.26 (1.05-1.50)	1.08 (0.93-1.26)	1.00	0.98 (0.84-1.14)	1.11 (0.93-1.34)	
Physical activity, METs/week[b]							0.96
<15.4 (men), <10.0 (women)	2,227	1.13 (0.98-1.31)	1.11 (0.99-1.26)	1.00	1.13 (1.01-1.27)	1.33 (1.15-1.53)	
15.4-33.3 (men), 10.0-20.7 (women)	1,494	1.24 (1.04-1.48)	1.00 (0.87-1.15)	1.00	0.96 (0.84-1.11)	1.15 (0.96-1.37)	
33.4-63.9 (men), 20.8-45.9 (women)	1,738	1.09 (0.91-1.30)	1.01 (0.88-1.15)	1.00	1.01 (0.89-1.15)	1.23 (1.05-1.45)	
≥64.0 (men), ≥46.0 (women)	1,151	1.21 (0.97-1.51)	0.96 (0.81-1.14)	1.00	1.18 (1.02-1.38)	1.25 (1.02-1.53)	
Sitting watching television, h/day							0.08
< 1	701	1.08 (0.83-1.40)	1.20 (0.97-1.48)	1.00	1.10 (0.89-1.36)	1.44 (1.10-1.87)	
1-4	4,800	1.20 (1.08-1.33)	1.04 (0.96-1.13)	1.00	1.07 (0.99-1.15)	1.26 (1.14-1.39)	

Variable	No. Deaths	Daily sleeping					P int[b]
		7 hr	6 hr	7 hr	8 hr	≥9 hr	
		HR (95% CI)	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	
≥5	977	1.08 (0.87-1.35)	0.86 (0.72-1.04)	1.00	1.02 (0.86-1.22)	1.11 (0.91-1.36)	
Healthy population[c]	673	1.30 (0.99-1.70)	1.13 (0.92-1.39)	1.00	1.05 (0.85-1.29)	1.35 (1.02-1.79)	-

Abbreviation: CI, Confidence Intervals; HR, Hazard Ratio; METs, metabolic equivalent of task; Pint, P-value for interaction

[a]Hazard ratios were calculated with age as the time metric, adjusted for variables not relevant to the stratified variables: 5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity (METs per week for moderate activity, vigorous work and strenuous sports), hours spent daily watching television, and smoking history by inclusion of the following variables: [smoking status, average number of cigarettes, average number of cigarettes squared, number of years smoked (time dependent), number of years since quitting (time dependent), and interactions between ethnicity and the smoking variables].

[b]Calculated using the Wald statistic for cross-product terms.

[c]Restricted to men and women who are nonsmokers, non-obese, and who don't have hypertension nor diabetes at baseline (n=68,243).

Table 7

Hazard ratios for all-cause and cause specific mortality as a group in relation to self-reported sleep duration among 123,628 men and women who were followed ≥10 years in the Multiethnic Cohort Study, 1993-2007[a,b]

Outcome	Deaths		Daily sleeping				
			≤5 hr	6 hr	7 hr	8 hr	≥9 hr
	No.	%	HR (95% CI)	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)
All Causes	7.517	-	1.08 (0.99-1.18)	1.07 (1.01-1.14)	1.00	1.00 (0.94-1.06)	1.18 (1.09-1.28)
Malignant Neoplasms	2.380	31.7	1.07 (0.92-1.24)	1.09 (0.98-1.21)	1.00	0.95 (0.85-1.05)	1.08 (0.93-1.25)
Cardiovascular disease	2,604	34.6	1.09 (0.95-1.26)	1.05 (0.94-1.17)	1.00	1.04 (0.93-1.15)	1.23 (1.07-1.40)
Respiratory disease	552	7.3	1.03 (0.75-1.42)	1.07 (0.85-1.35)	1.00	0.94 (0.75-1.18)	1.11 (0.83-1.48)
All others	1,981	26.4	1.09 (0.93-1.28)	1.11 (0.98-1.25)	1.00	1.04 (0.93-1.17)	1.26 (1.09-1.47)

Abbreviation: CI, Confidence Intervals; HR, Hazard Ratio.

[a] Hazard ratios were calculated with age as the time metric, adjusted for 5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity (METs per week for moderate activity, vigorous work and strenuous sports), hours spent daily watching television, and smoking history by inclusion of the following variables: [smoking status, average number of cigarettes, average number of cigarettes squared, number of years smoked (time dependent), number of years since quitting (time dependent), and interactions between ethnicity and the smoking variables].

[b] The test of heterogeneity across causes of death was performed using competing risk techniques, where each cause was a different event. A Wald test was used to compare the parameters between causes. P for heterogeneity (degrees of freedom = 12) across malignant neoplasms, cardiovascular disease, respiratory disease, and all others was 0.72.