A Prospective Study of Sleep Duration and Mortality Risk in Women

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Study Objectives: It is commonly believed that 8 hours of sleep per night is optimal for good health. However, recent studies suggest the risk of death is lower in those sleeping 7 hours. We prospectively examined the association between sleep duration and mortality in women to better understand the effect of sleep duration on health.
Design: Prospective observational study.
Setting: Community-based.
Participants: Women in the Nurses Health Study who answered a mailed questionnaire asking about sleep duration in 1986.
Interventions: None.
Measurements and Results: Vital status was ascertained through questionnaires, contact with next of kin, and the National Death Index. During the 14 years of this study (1986-2000), 5409 deaths occurred in the 82,969 women who responded to the initial questionnaire. Mortality risk was lowest among nurses reporting 7 hours of sleep per night. After adjusting for age, smoking, alcohol, exercise, depression, snoring, obesity, and history of cancer and cardiovascular disease, sleeping less than 6 hours or more than 7 hours remained associated with an increased risk of death. The relative mortality risk for sleeping 5 hours or less was 1.15 (95% confidence interval [CI], 1.02-1.29) for 6 hours, 1.01 (95% CI, 0.94-1.08), for 7 hours, 1.00 (reference group), for 8 hours, 1.12 (95% CI, 1.05-1.20), and for 9 or more hours 1.42 (95% CI, 1.27-1.58).
Conclusions: These results confirm previous findings that mortality risk in women is lowest among those sleeping 6 to 7 hours. Further research is needed to understand the mechanisms by which short and long sleep times can affect health.
Key Words: Sleep, sleep deprivation, proportional hazards models, women, survival rate
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INTRODUCTION

THE IMPORTANCE OF SLEEP TO A SENSE OF WELL-BEING IS EVIDENT TO ANYONE WHO HAS SPENT A SLEEPLESS NIGHT. However, the amount of sleep necessary for good health is unclear. Most sleep professionals, as well as the National Sleep Foundation, recommend that adults obtain 8 hours of sleep per night.[1] However, with the increasing demands placed on individuals in Western society, the time adults in the United States spend asleep has steadily fallen. The average sleep duration among American adults in a recent poll was only 6.9 hours per night, and 39% of respondents slept less than 7 hours.[1] The health effects of these changes in sleep habits are only beginning to be elucidated. Recent work suggests that beyond the deleterious neurocognitive effects of sleep restriction,[2] a short-term reduction in sleep time may lead to increased sympathetic tone and worsened glucose tolerance.[3] Epidemiologic studies suggest that those who sleep less may be at greater risk for developing cardiovascular disease and diabetes.[4,5]

An even more intriguing finding has been that increased time spent asleep may also result in adverse health outcomes. A recent, large, prospective study of American Cancer Society volunteers found an increased risk of death among those reporting sleeping more than 7 hours per night.[6] The mechanism by which increased sleep results in a higher mortality risk is unclear. Although many confounders, such as amount of physical activity and degree of obesity, were adjusted for in this study, the effects of other factors, including depressed mood, alcohol consumption, snoring, and shift working, were not investigated. All of these variables have been associated with increased mortality risk, and all have the potential to affect sleep habits. We sought to more-closely investigate the effects of both short and long sleep duration on the risk of death using a large prospective cohort of women.

Disclosure Statement
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METHODS

Study Population

The Nurses' Health Study (NHS) cohort was established in 1976 when 121,700 female married registered nurses, aged 30 to 55 years and residing in 11 large U.S. states, completed a mailed questionnaire on their medical history and lifestyle. The original sampling strategy for this cohort has been previously described.[7] Every 2 years, follow-up questionnaires are sent to update information on potential risk factors and identify newly diagnosed illnesses. The protocol for the study was approved by the Human Research Committee of Brigham and Women's Hospital. In 1986, subjects were asked to "Indicate total hours of actual sleep in a 24-hour period." Respondents chose from 1 of the following options: 5 hours or less, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, or 11 hours or more. A total of 83,417 women were still participating in the Nurses Health Study in 1986 and returned the questionnaire mailed that year. Of these, 448 did not provide a response to the question regarding sleep duration. All 82,969 women who did answer the sleep duration question were included in this study.

Questionnaire Validation

As part of the biennial follow-up questionnaire in 2000, the surviving cohort was asked, "How many hours of actual sleep do you get in a 24-hour period?" with identical choices for response as on the 1986 questionnaire. In 2002, we mailed a supplemental questionnaire to 480 women who had responded to the 2000 question. Women were randomly selected from within each sleep-duration response category (the categories of 9, 10, and 11+ hours were combined because of small numbers) to provide equal numbers for each response. On the supplemental questionnaire, we asked the same question as on the 2000 NHS questionnaire and invited the participants to maintain a sleep diary for 1 week. Each morning, subjects were instructed to record their recalled sleep duration from the previous night as well as any time spent in daytime naps. Daily sleep durations were averaged over the week of data collection, including only those women who had completed at least 6 days of diaries.

From the 480 supplemental questionnaires mailed, 260 (54%) were returned with a response to the question on sleep duration and 179 (37%) with at least 6 days of the sleep diary. The mean (SD) age of the respondents in 2002 was 67.6 (7.1) years. The Spearman correlation between average time spent sleeping by sleep diaries and time reported on the 2002 sleep duration question was 0.79 ($P < .0001$). We also observed those reporting 5 and 6 hours of sleep on the questionnaire to actually sleep slightly longer, sleeping an average of 5.2 hours and 6.2 hours respectively (as assessed by sleep diaries). Those reporting 8 and 9 or more hours, on the other hand, actually slept slightly less based on sleep diaries (an average of 7.7 and 8.5 hours, respectively). Average sleep time was 7.0 hours in those reporting 7 hours of sleep. We found good reproducibility of the sleep-duration question asked on the 2000 and 2002 questionnaires with Cohen's κ statistic of 0.39 ($P < .0001$). When a deviation of 1 hour was allowed, the correlation became even stronger ($\kappa = 0.81$).

Identification of Deaths

All deaths occurring up to June 2000 were included in the primary analysis. Deaths were reported by next of kin and the postal system or ascertained through the National Death Index. We estimate that follow-up for deaths was more than 98% complete.[8] For all deaths, we sought death certificates and, when appropriate, requested permission from the next of kin to review medical records (subject to state regulations). Underlying cause of death was assigned according to the *International Classification of Diseases, Eighth Revision (*ICD-8*)*. The primary endpoint in this analysis was death from any cause. We also conducted secondary analyses based on cause of death. Deaths were divided into those due to cancer (ICD-8 codes 140.0-207.9), cardiovascular disease (ICD-8 codes 390.0-458.9 and 795.0-795.9), and all other causes.

Statistical Analysis

Cox proportional hazards regression modeling was used to estimate the rate ratio (RR) of death for each sleep-duration category relative to the reference group with adjustment made for important covariates. We chose a reference category of 7 hours per night because that is the median and modal sleep duration in both the United States and the NHS.[1] Because only 0.7% of participants reported 10 or 11+ hours of sleep, we combined these categories with 9 hours. Each woman contributed person-time from the time of the initial questionnaire until the end of follow-up (June 1, 2000), death, or loss to follow-up.

Covariates that were simultaneously adjusted for in the model included age (in 5-year categories), body mass index (BMI)(in quintiles), smoking status (never, past, current smoking of 1 to 14, 15 to 24, and ≥ 25 cigarettes per day), alcohol consumption (0, 1-4, 5-14, ≥ 15 g per day), physical activity (weekly energy expenditure in quartiles), snoring history (never, occasionally, regular), a history of cancer (excluding non-melanoma skin cancer), a history of cardiovascular disease (defined as a history of angina, myocardial infarction, stroke, or coronary artery bypass graft surgery), and depressed mood (defined as a 36-Item Short-Form Health Survey mental health index of ≤ 52 from 1992). Information regarding age, BMI, physical activity, and smoking was updated based on questionnaire results every 2 years, while information regarding alcohol use and depression was updated every 4 years. Because sleep restriction may lead to development of hypertension and diabetes, these covariates may lie on the causal pathway linking sleep duration and mortality and, therefore, were not included in initial models. Similarly, we excluded working rotating shifts as a covariate from our main models because it is unclear whether the effect of shift working is mediated through sleep restriction or an independent pathway. We did, however, consider these variables as confounding factors in supplemental analyses.

Additional analyses were conducted stratifying on a history of chronic disease at baseline both to address the possibility that chronic illness confounded the relationship between sleep duration and mortality risk and to assess for modification of the effect of sleep duration on mortality risk. Preexisting illness was defined as a history of cancer (other than non-melanoma skin cancer), coronary artery disease (angina, myocardial infarction, or coronary artery bypass surgery), stroke, diabetes, hypertension, or obesity (BMI ≥ 30 kg/m^2) in 1986. Finally, secondary analyses were performed for specific causes of death.

All statistical analyses were conducted using SAS version 8.2 (SAS Institute, Inc., Cary, NC).

RESULTS

Baseline characteristics of the 82,969 women are shown in Table 1 stratified by sleep-duration response. Women reporting both long and short sleep durations tended to be older and heavier and to have more illnesses. Alcohol use was greater and exercise lower with increasing sleep duration. A history of working night shifts was most common in nurses reporting sleeping 5 hours or less, with nearly a third of this group reporting 5 or more years of shift working.

The primary analysis used all-cause mortality as the endpoint. We documented 5409 deaths during the 14 years of follow-up. After adjustment for age, we found a significant increase in mortality risk associated with both short and long sleep durations (Table 2). For women sleeping less than or equal to 5 hours per night, the RR of death was 1.41 (95% CI, 1.25-1.58) compared to those sleeping 7 hours. In long sleepers, the RRs were 1.18 (95% CI, 1.10-1.26) and 1.72 (95% CI, 1.55-1.91) for those sleeping 8 and 9 or more hours, respectively. After adjustment for potential confounders, the effects of extreme sleeping habits were attenuated but remained significant (Model 1, Table 2). Physical activity, depression, and alcohol consumption were the largest confounders of

Table 1—Baseline Characteristics Stratified by Self-Reported Sleep Duration in 1986

	Hours of Sleep per Day				
	≤ 5	6	7	8	≥ 9
Number of Subjects (%)	3887 (4.7)	21,226 (25.6)	34,132 (41.1)	19,752 (23.8)	3972 (4.8)
Age, y*	53.8 (6.9)	53.1 (7.0)	52.8 (7.2)	53.4 (7.3)	53.8 (7.4)
BMI, kg/m2*	26.4 (5.7)	25.7 (5.0)	25.1 (4.6)	25.2 (4.7)	25.7 (5.2)
Alcohol, g/day*	4.9 (9.9)	5.6 (10.2)	6.1 (10.2)	6.7 (11.6)	7.9 (13.9)
Physical activity, METs/wk*	14.0 (22.9)	14.1 (20.7)	14.4 (21.5)	13.9 (20.7)	12.1 (16.6)
SF-36 Mental Health Index†	73.1 (16.6)	76.1 (14.6)	77.3 (13.8)	77.2 (14.3)	75.2 (15.8)
Hypertension, %	32.4	27.0	23.8	25.9	30.5
Diabetes, %	6.4	4.0	3.3	4.2	5.7
Cardiovascular disease, %	8.6	5.9	4.7	5.6	8.4
Cancer, %	8.6	6.5	6.1	7.1	7.9
Current smoking, %	23.6	23.4	20.6	19.7	22.4
Regular snoring, %	10.7	10.3	8.7	10.2	11.8
Night-shift work > 5 y, %‡	32.1	22.6	16.7	16.3	17.5

*Data are presented as mean (SD).
†Reported in 1992.
‡Reported in 1988.
All variables are significantly different across sleep duration categories ($P < .05$).
BMI refers to body mass index; MET, metabolic equivalent; SF-36; 36-Item Short-Form Health Survey.

the effect of short sleep times, while physical activity was the primary confounder of long sleep times. Additional adjustment for hypertension and diabetes (Model 2, Table 2) as well as shift-working history (Model 3, Table 2) resulted in a further reduction in the excess mortality risk among short sleepers to a level not significantly different from those sleeping 7 hours. On the other hand, additional adjustment for hypertension, diabetes, and shift working had little effect on the mortality risk of sleeping more than 7 hours. When the long sleepers were further subdivided, a clear dose-response relationship was observed with continued increase in mortality risk associated with longer sleep times. In the fully adjusted model, the RRs were 1.36 (95% CI, 1.21-1.52) for those reporting 9 hours of sleep, 1.51 (95% CI, 1.19-1.92) for 10 hours of sleep, and 1.85 (95% CI, 1.06-3.21) for 11 or more hours of sleep.

To minimize the potential of confounding by the presence of illnesses that might affect sleep habits and increase mortality risk, we also conducted analyses stratified by the presence of preexisting illness (history of cancer, coronary artery disease, stroke, hypertension, diabetes, or obesity) at the onset of the study period. There were 1953 deaths in the 49,408 disease-free women and 3456 deaths in the 33,561 women with preexisting illness. In both groups, there was a trend toward increased mortality risk in those sleeping 5 hours or less compared to sleeping 7 hours (Table 3). Sleeping more than 7 hours was also was associated with increased mortality risk in both groups, but the magnitude of increase was greater in those with preexisting illness.

Sleep duration may have been influenced by early symptoms associated with undiagnosed morbidity. We therefore repeated our analysis excluding deaths occurring in the first 4 years of follow-up. We analyzed the relationship between sleep duration assessed in 1986 and mortality from 1990 through 2000. A total of 81,864 women and 4304 deaths were available for this analysis (Table 3). Despite the 4-year latency period, no substantial difference in the point estimates of the risk attributable to short and long sleep durations was found. Similar to our primary analyses, the RR of death increased with sleep durations of more than 7 hours.

We also conducted analyses restricted to specific causes of death (Table 4). Cancer and cardiovascular disease were the 2 most common causes, with 2642 and 1084 deaths, respectively. The next most frequent causes of death included respiratory disease (n = 314), accidents and injuries (n = 187), neuropsychiatric disorders (n = 134), and gastrointestinal disease (n = 133). Because of the small numbers, noncancer noncardiovascular deaths were grouped together for the purposes of these analyses. In general, the effect of short sleep durations was minimal for cancer and cardiovascular disease although evident for death from other causes. This increase in risk for noncancer noncardiovascular death was largely attributable to respiratory deaths. The RR of 5 or fewer hours of sleep for a respiratory death was 1.70 (95% CI, 1.07-2.69). The RR of 5 or fewer hours of sleep for death from an accident or injury, on the other hand, was only 1.07 (95% CI, 0.56-2.02). In contrast, for all major causes of death, we found a clear rise in the mortality risk with increasing sleep times above 7 hours.

Table 2—Relative Risks (95% Confidence Intervals) of Death by Self-Reported Sleep Duration

	Hours Of Sleep Per Day				
	≤ 5	6	7	8	≥ 9
Number of deaths	331	1317	1950	1398	413
Age-adjusted relative risk	**1.41 (1.25-1.58)**	1.07 (1.00-1.15)	1	**1.18 (1.10-1.26)**	**1.72 (1.55-1.91)**
Multivariate model #1*	**1.15 (1.02-1.29)**	1.01 (0.94-1.08)	1	**1.12 (1.05-1.20)**	**1.42 (1.27-1.58)**
Multivariate model #2†	1.12 (0.99-1.26)	1.00 (0.94-1.08)	1	**1.11 (1.03-1.19)**	**1.39 (1.25-1.55)**
Multivariate Model #3‡	1.08 (0.96-1.22)	0.99 (0.92-1.06)	1	**1.11 (1.03-1.19)**	**1.40 (1.25-1.55)**

Bold print indicates statistically different from 7 hours of sleep.
*Adjusted for age, smoking status, alcohol consumption, physical activity, depression, history of snoring, body mass index, and history of cancer and cardiovascular disease.
†Adjusted for above plus history of hypertension and diabetes mellitus.
‡Adjusted for above plus shift-working history.

Table 3—Relative Risks (95% Confidence Intervals) of Death by Self-Reported Sleep Duration in Secondary Analyses

	Hours Of Sleep Per Day				
	≤ 5	6	7	8	≥ 9
Disease-free cohort*	1.14 (0.92-1.40)	0.94 (0.84-1.05)	1	1.05 (0.94-1.18)	**1.30 (1.07-1.58)**
Preexisting-illness cohort*	1.12 (0.97-1.29)	0.99 (0.91-1.08)	1	**1.17 (1.07-1.28)**	**1.45 (1.27-1.65)**
4-year lag†	1.06 (0.92-1.21)	1.01 (0.94-1.10)	1	**1.12 (1.04-1.21)**	**1.30 (1.15-1.47)**

Bold print indicates statistically different from 7 hours of sleep.
*Preexisting illness defined as history of cancer, cardiovascular disease, hypertension, diabetes, or obesity in 1986. Analyses adjusted for age, smoking status, alcohol consumption, physical activity, depression, history of snoring, body mass index, and shift-working history.
†Analysis of deaths occurring after June 1990 adjusted for age; smoking status; alcohol consumption; physical activity; depression; history of snoring; body mass index; history of cancer, cardiovascular disease, hypertension, diabetes; and shift-working history.

Table 4—Relative Risks (95% Confidence Intervals) of Cause-Specific Mortality by Self-Reported Sleep Duration*

	Hours Of Sleep Per Day				
	≤ 5	6	7	8	≥9
Cancer death (n = 2642)	0.96 (0.80-1.15)	0.96 (0.87-1.06)	1	1.08 (0.98-1.19)	**1.21 (1.03-1.43)**
Cardiovascular death (n = 1084)	1.04 (0.79-1.35)	1.06 (0.91-1.25)	1	1.12 (0.95-1.31)	**1.56 (1.25-1.96)**
Death from other causes (n = 1683)	**1.33 (1.09-1.61)**	0.97 (0.85-1.10)	1	1.14 (1.01-1.30)	**1.53 (1.27-1.84)**

Bold print indicates statistically different from 7 hours of sleep.
*Adjusted for age; smoking status; alcohol consumption; physical activity; depression; history of snoring; body mass index; history of cancer, cardiovascular disease, hypertension, or diabetes; and shift-working history.

DISCUSSION

We observed in this large, prospective cohort study a modest but significant association between self-reported sleep duration and mortality risk. Both short and long self-reported sleep durations were associated with an increased risk of death after adjustment for important confounding factors. The adjusted mortality risk for women sleeping 5 hours or less was 15% greater than for those sleeping 7 hours. Similarly, sleeping 9 or more hours was associated with a 42% increase in risk.

Prior studies have reported that both short and long sleepers have an increased mortality risk. In a study in Alameda County, California, middle-aged adults sleeping less than 7 hours or more than 8 hours had a 30% greater mortality risk than those reporting sleeping 7 or 8 hours, even after controlling for a variety of potential confounders.[9] Studying a cohort of 1.1 million American Cancer Society volunteers, Kripke et al also observed an association between sleep duration and mortality risk, with the minimum risk in those reporting 7 hours of sleep per night.[6] Similar to our findings, this study also found that the risk due to increased sleep times was much greater than the risk attributable to reduced sleep times. In addition, a prior analysis from the NHS identified the minimum risk for fatal cardiovascular events to be in those sleeping 7 hours.[4]

For short sleepers, after controlling for hypertension, diabetes, and shift working, the RR of death was attenuated and no longer significant. Several studies have begun to address the mechanisms by which short sleep may adversely affect health. Spiegel et al restricted sleep in 11 healthy young men to 4 hours per night for 6 nights and then allowed a sleep-recovery period for 6 nights.[3] Despite the short duration of partial sleep deprivation, the subjects demonstrated impaired glucose tolerance, higher evening cortisol levels, increased sympathetic nervous system activity, and a reduction in leptin secretion in the sleep-deprived versus the recovery state.[3,10] The reduction in insulin sensitivity, elevation in sympathetic activity, and suppression of leptin secretion may lead to a greater risk of diabetes, hypertension, and obesity, respectively, among the chronically sleep restricted. Recent work from the NHS suggesting a higher risk of diabetes and cardiovascular disease in short sleepers supports this hypothesis.[4,5] If this is the case, by controlling for diabetes, hypertension, and obesity in the current study, we may have underestimated the true effect of short sleep times on mortality risk. Nevertheless, we found little change in the RR estimate by adjusting for hypertension and diabetes, suggesting that the adverse health effect of short sleep may be independent of these diseases. The large effect of short sleep duration on risk of a respiratory death also suggests that alternative mechanisms may exist, since hypertension and diabetes are not major risk factors for pulmonary disease.

On the other hand, shift working is a common cause of insomnia and reduced sleep time as individuals try to sleep at adverse times because of both circadian influences and environmental cues. In addition, shift working may have adverse health consequences, including heart disease and breast cancer.[11-13] The loss of association between short sleep durations and mortality after adjusting for shift working may therefore be due to "overcontrolling," as reduced sleep duration may be the causal mechanism by which shift working causes disease. However, alternative etiologies, such as suppression of melatonin secretion by nocturnal light exposure, have also been proposed as an explanation for the effect of shift working on health outcomes.[14]

In contrast to our findings in short sleepers, long sleepers had an increased mortality rate that persisted even after controlling for potential confounders. In adjusted analyses, a 40% excess risk was observed in nurses reporting 9 or more hours of sleep per night. Although the potential mechanisms by which increased sleep time may lead to adverse health are not known, similar findings have been suggested in prior studies. The American Cancer Society study found the adjusted RR of increased sleep times to be 1.13, 1.23, and 1.41 in women sleeping 8, 9, and 10 or more hours per night.[6] Consistent with prior studies, the increased mortality risk among long sleepers did not appear to be limited to one cause of death.[6,9] We observed similar patterns in the effect of long sleep times on the various cause-specific (ie, cancer, cardiovascular disease, other) death rates, suggesting that the mechanism of elevated risk is not via damage to a single organ system.

The explanation of the association between increased self-reported sleep duration and mortality remains open to speculation. One possibility is that increased self-reported sleep duration is a marker of increased sleep need and that individuals with increased sleep needs may have a reduced physiologic reserve, reducing their ability to survive serious illness. In support of this theory, a prior study found that although sleeping 7 hours was associated with a 10% greater risk of myocardial infarction than was sleeping 8 hours, the risk of dying from myocardial infarction was 17% lower in those sleeping 7 hours.[4]

There are several strengths to our study. First, our measure of sleep time is likely a more-accurate measure of true sleep duration than was the measure used in previous questionnaire-based studies because of the formulation of our question. We asked about total amount of sleep over a 24-hour period, which would include naps or other daytime sleep. In contrast, the study performed by Kripke et al asked, "On the average, how many hours do you sleep each night?"[6] Depending on an individual's interpretation of such a question, substantial measurement bias may arise among those who nap, work night shifts, or sleep in the daytime for other reasons. In addition, we were able to validate our question about sleep duration. We found strong correlation between our sleep-duration question and sleep times as measured by 1 week of sleep diaries with little systematic bias. The bias that was found in using the sleep-duration question led to an overestimate of the departure of individual sleep times from the median of 7 hours. Thus, those categorized as sleeping 6 hours actually slept an average of 6.2 hours, while those categorized as sleeping 8 hours, slept only 7.7 hours. The effect of this bias would be, if anything, to cause an underestimation of the true biologic effect of sleep on mortality because estimates of the relative mortality risk of sleeping 8 hours relative to 7 hours actually compare sleeping 7.7 hours to 7 hours. It should be noted that our reference, sleep diaries have been previously validated against actigraphic measurements of sleep.[15] In addition, our measure of sleep duration was reproducible over 2 years, further validating the measure. Another strength of this study was the use of repeated measurements of potential confounders, allowing for better controlling for these factors. Third, verification of cause of death was performed by reviewing medical records whenever possible. Thus we believe there was less misclassification of cause of death than in prior studies, which relied solely on death certificates.

Several potential limitations of this study should be noted. First, our population was limited to women, the vast majority of whom were Caucasian and who had a similar socioeconomic status. Although such homogeneity would reduce confounding by these factors, it may reduce the generalizability of our findings to other populations. Currently, however, we have no reason to suspect that the effect of sleep duration on mortality would be different in men or groups of different ethnicity, income, or education level. Because the cohort studied were nurses, shift working was very common. The importance of shift working on the relationship between sleep and mortality may not, therefore, be generalizable to other populations.

Second, our study was observational in design, and, thus, we cannot conclude that altering sleep duration will cause changes in mortality risk. In addition, we cannot exclude the presence of unrecognized confounders not accounted for in our analyses as a cause of the reported associations. The effects of recognized confounders may also not have been adequately accounted for in this analysis because of the inability to fully measure them with the questionnaire instruments used. For example, the effects of sleep apnea may not be fully accounted for by using self-reported snoring as the measure of apnea. Third, we cannot completely rule out the possibility of "reverse causation." Short or long sleep duration may be a symptom of early disease, predating the diagnosis. However, analyses restricted to those without a diagnosis of serious disease at the onset of the study, as well as analyses excluding deaths occurring within 4 years of self-reported sleep duration, did not yield appreciably different results, making this explanation of our findings unlikely.

Finally, factors influencing the amount of daily sleep were not ascertained in our study. The effect of a short or long sleep duration on mortality risk may be very different depending on whether the sleep behavior is due to intrinsic sleep needs (sleep drive), a sleep disorder, or external environmental pressures.

CONCLUSIONS

Our data suggest that self-reported sleep duration is an independent predictor of mortality. The minimum risk occurs in those sleeping 6 to 7 hours per night, with increased risk in those sleeping both shorter and longer hours. The mechanism of this increased risk remains unclear but could not be explained by controlling for a number of potential confounders. More research is required to study both the environmental and genetic factors that determine an individual's sleep duration and the physiologic changes associated with this variability.

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REFERENCES

1. National Sleep Foundation. 2002 Sleep in America Poll. Washington: National Sleep Foundation; 2002.
2. Van Dongen HA, Maislin G, Mullington J, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 2002;26:117-26.
3. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet 1999;354:1435-9.
4. Ayas NT, White DP, Manson JE, et al. A prospective study of sleep duration and coronary heart disease in women. Arch Intern Med 2003;163:205-9.
5. Ayas NT, White DP, Al-Delaimy WK, et al. A prospective study of self-reported sleep duration and incident diabetes in women. Diabetes Care 2003;26:380-4.
6. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry 2002;59:131-6.
7. Colditz GA, Manson JE, Hankinson SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. J Womens Health 1997;6:49-62.
8. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax Nationwide Death Search. Am J Epidemiol 1994;140:1016-9.
9. Wingard DL, Berkman LF. Mortality risk associated with sleeping patterns among adults. Sleep 1983;6:102-7.
10. Spiegel K, Leproult R, Copinschi G, Van Cauter E. Impact of sleep length on the 24-h leptin profile. Sleep 2001;24:A74.
11. Kawachi I, Colditz GA, et al. Prospective study of shift work and risk of coronary heart disease in women. Circulation 1995;92:3178-82.
12. Schernhammer ES, Laden F, Speizer FE, et al. Rotating night shifts and risk of breast cancer in women participating in the nurses' health study. J Natl Cancer Inst 2001;93:1563-8.
13. Davis S, Mirick DK, Stevens RG. Night shift work, light at night, and risk of breast cancer. J Natl Cancer Inst 2001;93:1557-62.
14. Hansen J. Light at night, shiftwork, and breast cancer risk. J Natl Cancer Inst 2001; 93:1513-5.
15. Lockley SW, Skene DJ, Arendt J. Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. J Sleep Res 1999;8:175-83.