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Mortality Associated with Short Sleep Duration: The Evidence, The Possible Mechanisms, and The Future

Michael A. Grandner, PhD[1], **Lauren Hale, PhD**[2], **Melisa Moore, PhD**[1,3], and **Nirav P. Patel, MD**[1,4]

[1] Center for Sleep and Respiratory Neurobiology, Division of Sleep Medicine, Department of Medicine, University of Pennsylvania, Philadelphia, PA

[2] Graduate Program in Public Health, Department of Preventive Medicine, State University of New York, Stony Brook, NY

[3] The Sleep Center, Division of Pulmonary Medicine, Children's Hospital of Philadelphia, Philadelphia, PA

[4] Division of Allergy and Respiratory Critical Care, Department of Medicine, University of Pennsylvania, Philadelphia, PA

Abstract

This review of the scientific literature examines the widely observed relationship between sleep duration and mortality. As early as 1964, data have shown that 7-hour sleepers experience the lowest risks for all-cause mortality, whereas those at the shortest and longest sleep durations have significantly higher mortality risks. Numerous follow-up studies from around the world (e.g., Japan, Israel, Sweden, Finland, the United Kingdom) show similar relationships. We discuss possible mechanisms, including cardiovascular disease, obesity, physiologic stress, immunity, and socioeconomic status. We put forth a social-ecological framework to explore five possible pathways for the relationship between sleep duration and mortality, and we conclude with a four-point agenda for future research.

SLEEP DURATION AND MORTALITY: THE EVIDENCE

Over 40 years of evidence indicate a strong association between nightly sleep duration and mortality risk[1–2]. In general, sleep duration is associated with mortality in a U-shaped fashion, such that the lowest risk is most often found in the group who report sleep durations of 7–8 hours (See Tables 1 and 2 for a summary of their findings). Nearly uniformly, mortality risk increases with further deviation from the 7–8hr range.

Early Studies

The first study to examine the relationship between sleep duration and mortality risk in the population was reported in 1964[3]. Those reporting 7 hours of sleep demonstrated the lowest mortality rate. A follow-up analysis of the same sample[4] found that 7-hour sleepers were at

Corresponding Author: Michael A. Grandner Ph.D., University of Pennsylvania Center for Sleep and Respiratory Neurobiology, 125 South 31st Street, Philadelphia, PA 19104, P: (215) 746-4815 | F: (215) 746-4814, Michael.Grandner@uphs.upenn.edu.

the lowest risk, and those at the extreme ends (≤4 and ≥10 hours) were at the highest for both men and women.

A series of subsequent investigations analyzed data from adults from the Alameda County Study[5–9]. Mortality rates were calculated for a 9-year follow-up period adjusted for up to 14 covariates in addition to age. These studies reported that short (≤6 hours) and long (≥9 hours) sleepers had higher mortality rates than 7–8hr sleepers, even after adjustment for covariates[5–9]. In a later analysis, Kaplan and colleagues[8] analyzed age groups separately with a 17 year follow-up. In this analysis, a significant increase in mortality for the <7hr and >8hr sleepers was only present for those aged 50–59 at the time of follow-up.

Studies in the Elderly

In general, studies that have focused on elderly populations have supported findings from earlier research. Branch and Jette[10] observed findings similar to the Alameda County Study. Among the elderly, both short (<7 hours) and long (>8 hours) sleepers were at increased mortality risk. Another study in a sample of nursing home residents found that age-adjusted mortality rates were highest in women sleeping ≤4 hours and ≥9 hours and men sleeping ≤5 hours and ≥9 hours[11]. However, these risks became non-significant after adjusting for covariates. In a study of the elderly in the UK, significant increased mortality risk was found for those reporting ≥10 hours of sleep, and for those who reported "insomnia often.[12]" However, this study did not account for gender and the reference group had a very broad range of sleep duration (4.0–9.9 hours). Gale and Martyn[13] examined data from adults aged ≥65 years in the UK and found that, compared to 9-hour sleepers, those sleeping ≥10 hours were at increased risk of mortality. Conversely, analyses of health survey data from Spain (Barcelona) did not find significantly increased risk in elderly short or long sleepers, compared to the reference group (7–9 hours), though a non-significant increase for long sleep was observed[14].

While there is some variation, taken together, these results reveal that in the elderly, increased mortality is associated with both short and long sleep.

Sleep and Mortality: A Global Issue

Following earlier studies, scientists have explored this association around the world. Several of these studies occurred in Japan[15–19]. One study found increased mortality risk in those reporting sleep ≥9 hours, as compared to 7–8 hours in the farming town of Wakuya[15]. An analysis of the general population of Gifu prefecture aged 20–67 found that in age-adjusted analyses, increased mortality risk was associated with short (<7 hours) and long (10 hours) sleep compared to the reference group (7.0–8.9 hours), but after adjusting for covariates, only the short sleep association remained significant[16]. In a study of elderly residents from the village of Ohgimi, increased mortality was seen among those sleeping <6 and >7 hours in a model adjusted for age and health behaviors, but when physiological measures of health and functional status were entered into the model, only the relationship with short sleep remained statistically significant[17].

More recently, two large-scale studies have examined these relationships in samples representative of the general population of Japan. In one study[18], compared to the reference group (7.0–7.9 hours), men were at increased risk of mortality if they reported <6 hours of sleep, and women were at increased risk if they reported ≥9 hours. The largest sleep duration and mortality study in Japan investigated over 100,000 adults from 45 areas of Japan[19]. Compared to the reference group (7.0–7.9 hours), both men and women were at increased risk of mortality of they slept 8.0–8.9 hours or ≥9 hours on average. Further analysis of this dataset[20] reported that in men, ≥9 hours of sleep was associated with

increased risks of all-cause mortality, cardiovascular mortality, esophageal cancer, and pancreatic cancer, but decreased risk of prostate cancer; <7 hours of sleep was associated with a decreased risk of stomach cancer. In women, ≥9 hours of sleep was associated with increased all-cause mortality, cardiovascular mortality, urothelial cancer and non-Hodgkins lymphoma; <7 hours of sleep was associated with a decreased risk of lung cancer and cardiovascular disease.

A 10-year study of adults over 60 in Taiwan[21] found increased mortality risk (relative to 7 hours) associated with ≥10 hours of sleep in men, and all categories ≥8.0 hours of sleep in women. Analysis of the Singapore Chinese Health Study of ethnic Cantonese and Hokkien adults aged 45–74 found significant increases in mortality risk (relative to 7 hours) associated with ≤5, 6, 8, and ≥9 hours, though after adjusting for covariates, only the relationships in the most extreme categories remained significant[22].

In Israel, Burazeri and colleagues[23] examined data from adults ≥50 years old. Adjusted analyses found that in men, increased mortality risk was associated with sleep >8 hours, compared to a 6hr reference group. For women, mortality risk was lower for those reporting 6–8 hours of 24-hour sleep, compared to those sleeping <6 hours.

In Sweden, an analysis of survey data from adults aged 45–65 years found that age-adjusted mortality risk was increased in male long sleepers (>8 hours) compared to the reference group (6–8 hours), though this result became non-significant after adjusting for all covariates[24]. No relationships were seen for women.

In Finland, sleep duration data for adults (age 24–101) comprising all twins born before 1958 was analyzed[25]. When compared to the reference group (7–8 hours), increased mortality risk was found for men and women who reported <7 or >8 hours of sleep.

In the United Kingdom, three studies have investigated non-elderly, general population samples[26–28]. Huppert and Whittington[26] found that sleep duration was not related to mortality in women, but long sleep duration (>8 hours) predicted mortality in men. Heslop and colleagues[27] examined a sample representing the general population of Glasgow, Scotland. This study investigated sleep duration at multiple times. Women reporting <7 hours at second screening were at increased risk of all-cause and cardiovascular mortality when adjusting for covariates, but this relationship became non-significant when stress level was introduced in the model. For men, age-adjusted analyses showed increased risk in those who were <7hr sleepers at both time points compared to those 7–8hr sleepers at both time points, but this became non-significant when marital status and social class were included. Men and women who were always <7hr sleepers demonstrated increased risk for all-cause mortality in models adjusting for age, marital status, social class and health risk factors. Inclusion of stress level significantly attenuated the short sleep-mortality association to the null.

Other studies have also measured sleep duration at multiple points in time. Ferrie and colleagues[28] longitudinally examined mortality risk for sleep durations measured during two time periods. The data came from the ongoing Whitehall II cohort. For the first time period, only ≤5 hours of sleep was associated with increased all-cause and cardiovascular mortality risk in adjusted analyses, and only in models that adjusted only for age. For the second time period, increased all-cause mortality was associated with ≤5 or ≥9 hours of sleep and increased cardiovascular mortality was associated with ≤5 hours of sleep. Those reporting having slept 7–8 hours at baseline were protected if they remained in that category at the second time period. Interestingly, mortality risk increased if they deviated above or below that duration category. Those reporting 6 hours of sleep benefitted from an increase to 7

hours, but not 8 hours. Subjects reporting ≤5 hours were subject to decreased mortality risk if they reported 6 hours at the second time point.

Finally, there have been several studies in U.S. population samples[29–35]. Qureshi and colleagues[29] examined data from the National Health and Nutrition Examination Survey (NHANES) and found an increased risk of mortality in long sleepers (>8 hours). Chen and Foley found that mortality was associated with <6 or >9 hours of sleep, but only in those over 60 years of age[36]. A recent reanalysis of the NHANES data[35] found that even after controlling for a variety of covariates, short sleep of ≤5 hours, as well as longer sleep of 8 and ≥9 hours, was associated with increased mortality, relative to 7 hours. However, analysis of age sub-groups (<60 versus >60 years), revealed that only subjects aged >60 demonstrated showed a significant mortality relationship with short and long sleep duration.

Data from the well-known cohorts of the Framingham Study[30] and Nurses' Health Study[32, 34] also support the elevated mortality risks associated with short and long sleep. The former study found the highest mortality risk in subjects reporting <6 hours and >9 hours. The latter reported increased all-cause age-adjusted mortality risk (relative to the 7 hours) in all short (≤5 and 6 hours) and long (8 and ≥9) groups.[34] Ayas and colleagues[32] also examined this dataset in another publication and found similar results.

Dew and colleagues[33] reviewed data from several studies to conduct the first electroencephalographic study of sleep and mortality risk. In their sample of 184 individuals, short sleepers (<6 hours) did not have significantly higher mortality risks than the rest of the sample. However, increased mortality risk was associated with sleep latency >30 minutes, sleep efficiency <80%, and slow wave sleep <1%.

Kripke and colleagues conducted the largest study of sleep duration and mortality using over 1 million records from the Cancer Prevention Study II[31]. After adjustment for demographic risk factors, health habits, status, history, and medications, they found distinct U-shaped curves across sleep duration categories, demonstrating increased mortality risk the further the deviation from 7 hours. Thus, those who reported sleep of 7 hours (6.5–7.4 hours before coding) were at the lowest risk of mortality and those sleeping <6.5 or >7.4 hours were at increasingly greater risk, the further from the nadir of the U curve. Depression and stress were not included in these analyses.

Meta-Analysis

Gallicchio and Kalesan[37] present the first meta-analysis of data from the studies described above (see Table 1 for included studies). Using random-effects meta-analysis, the authors report that the pooled RR for all-cause mortality for short sleep was 1.10 (95%CI=[1.06, 1.15]), with cardiovascular-related RR at 1.06 (95%CI=[0.94,1.30]) and cancer-related RR at 0.99 (95%CI=[0.88,1.13]). For long sleep, RR for all-cause mortality was 1.23 (95%CI=[1.16,1.30]), with cardiovascular RR at 1.38 (95%CI=[1.13,1.69]) and cancer RR at 1.21 (95%CI=[1.11,1.32]). Thus, while short sleep carries an increased mortality risk, this is not explained by cardiovascular disease or cancer. For long sleep, the increased risk was significant for all-cause, cancer, and cardiovascular mortality. The methodology of this study has been reviewed elsewhere[38]. Although there are a number of limitations to the included studies (described below), the meta-analysis meets many of the guidelines proposed by the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Working Group[39]. The pooled relative risks reported in this paper are small, but even small shifts in mean effects are of significant population value[40].

Limitations of previous epidemiological studies

Despite the valuable contributions of prior research, there are several limitations of this literature. One important limitation of prior epidemiological studies is that definitions of "short" and "long" sleep vary across studies, thus preventing adequate comparisons. For example, while the study by Kripke and colleagues[31] contained groups representing every hour of duration within the sample, the study by Rumble and Morgan[12] measured only three groups, with the reference group reporting 4–9.9 hours of sleep. Additionally, while the various survey questions used in these studies may have face validity, it is unclear that they are reliable and valid measures of sleep duration. These surveys employed questions which have not been validated against objective sleep recordings; thus, it is unclear what precisely they are measuring. It may be the case that factors such as time in bed, demand characteristics, social desirability, paradoxical insomnia (i.e., sleep state misperception), and other factors covary with these self reports of sleep duration.

Another important source of heterogeneity is the inclusion of covariates. Many studies found relationships only when adjusting for age and in most cases, gender. This suggests that there is an age (or cohort) effect, and a difference between men and women. Other covariates, including indicators of health status and history, sociodemographic and socioeconomic factors, functioning, medication use, and psychological morbidity, varied between studies, with a range of 0[3], [7]-32[31] covariates besides age. Both under adjustment and over adjustment present concerns. Not adjusting for enough variables could mean that psome relationships are driven by third factors, and not by sleep duration. Over adjusting may remove some of the causal effects of sleep, if the covariate is on the causal pathway between sleep and mortality.

Also, the stability of sleep as a trait in relation to health outcomes has not been established. The studies that only measure sleep at one time point assume that self-reported sleep duration at one time represents a stable exposure.

Finally, the majority of studies reviewed in this paper use datasets that were not designed to evaluate relationships with sleep. Frequently, analyses are constrained to use the only sleep question available in the survey (usually an estimate of habitual sleep duration), which limits the reliability and validity of the findings.

SLEEP DURATION AND MORTALITY: THE POSSIBLE MECHANISMS

While previous literature clearly describes an association between mortality and both short and long sleep, the remainder of this review will focus on mechanisms and pathways primarily associated with only short sleep, as short and long sleepers seem to represent distinct groups[41]. Effects for long sleep may be larger, but we chose to focus on short sleep for two reasons. First, shorter sleep appears to be a more salient issue in our society where insufficient sleep is a major public health concern[42]. Furthermore, large numbers of laboratory studies support mechanisms that may explain a direct link between short sleep and mortality. Thus, short sleep is a more wide-reaching problem with a larger base of research from which to draw conclusions. Second, a fairly comprehensive review of mortality associated with long sleep, and possible mechanisms, was recently published[1]. We wished to avoid redundancy with that publication, taking advantage of limited space by only addressing short sleep..

While prior research has broadly investigated the relationship between short sleep duration and mortality risk, any association is unlikely to be exclusive or singularly present. Furthermore, it is possible that some or all conditions may be antecedent (but undetected) to the development of short sleep duration. Finally, as described earlier, the link between sleep

duration and various conditions may be a result of a common underlying mechanism, leading to an inflated association. Notwithstanding, short sleep duration has been linked with 7 of the 15 leading causes of death in the US (cardiovascular disease, malignant neoplasm, cerebrovascular disease, accidents, diabetes, septicemia, and hypertension)[43].

Short Sleep & Cardiovascular Disease

Cardiovascular disease leads as the top cause of death in the United States[43]. Several[18–19, 22, 28, 32, 44–45], but by no means all[21, 23–24, 27, 29, 31, 34] population-based studies report increased risk of cardiovascular disease or mortality for short sleep duration in men and/or women from various continents (e.g., North America, Asia, and Europe). Most adjusted for potential confounders including socio-demographic, socio-economic and health factors. All employed a self-reported measure of sleep duration. More recent studies have linked short sleep duration with carotid artery intima-media thickness (a marker of atherosclerotic disease)[46] and coronary artery calcification (a risk factor for coronary events)[47]. Sleep was measured using actigraphy in the latter.

Two prospective studies failed to show consistent independent associations between short sleep duration and stroke[29, 48]. Other important cardiovascular factors that have been investigated for their associations with short sleep duration include hyperlipidemia and hypertension. Data are suggestive of a correlation between unfavorable triglyceride and high-density lipoprotein profiles in female short sleepers[49] (<6 hours) and people with diabetes[50].

Two cross-sectional studies suggest ≥60% increased likelihood of hypertension in short sleepers[51–52]. Longitudinal data support this relationship, but it is unknown if this will be consistently independent of confounders[52–53] and whether there are gender-specific associations[52]. Laboratory data support shorter-term effects of sleep deprivation on blood pressure and sympathetic activity in normotensive[54] and hypertensive subjects[55]. Short sleep may act as a stressor in the acute and chronic setting. The downstream consequences may lead to elevated blood pressure equilibrium.

Emerging work investigating the mechanisms linking sleep deprivation and cardiovascular outcomes has included biomarkers. C-reactive protein (CRP), an acute phase reactant, is a marker of cardiovascular risk[56]. Elevated CRP concentrations have been reported in healthy subjects exposed to total and partial short-term sleep deprivation[57–58]. Cytokines (especially interleukin-6 and tumor necrosis factor alpha) levels are also elevated in response to acute total and partial sleep restriction[59]. It appears, therefore, that sleep deprivation, at least in the acute setting, initiates a response akin to inflammation as evidenced by biomarkers such as CRP and cytokines. It has been suggested that CRP may be a link between sleep restriction and cardiovascular disease[60]; however, it remains unclear whether CRP is a risk factor or predictor for cardiovascular disease. Further, Taheri and colleagues[61] recently reported that there was no relationship between CRP levels and sleep duration in the Wisconsin Sleep Cohort Study. Therefore, it is challenging on several counts to deduce that CRP accounts for the link between chronic short sleep and cardiovascular disease.

It is important to note that the meta-analysis found no significant risk of cardiovascular mortality associated with short sleep[37]. While we feel that the meta-analysis represents a significant contribution to this literature, there are many reasons why there may have been no significant effect. For example, the measurement of short sleep is imprecise. Second, many of the proposed mechanisms for cardiovascular pathways were not directly assessed in mortality studies. Third, the meta-analysis did not include enough studies, with appropriate covariates, to definitively rule out cardiovascular causes of death.

In summary, while a variety of cardiovascular outcomes have been investigated, results showing independently increased cardiovascular risks for subjects reporting short sleep are inconsistent.

Short Sleep & Obesity

Significant public, media, and scientific attention has focused on the link between short sleep and obesity[62]. Recent reviews and meta-analyses[63–64] have assessed this link in great detail. Cross-sectional (19 adult, 11 pediatric) and longitudinal (5 adult, 4 pediatric) studies have investigated the short sleep-obesity association (references in cited reviews). In adults, most studies report relationships between short sleep and obesity. The association appears to more uniform in the pediatric population. Interestingly, the nature of the relationship may differ between adults and children, with a U-shaped association in adults compared with a negative linear relationship in children. It may be challenging to expose children to sleep in excess of need on account of their increased need for longer sleep times during development and less variability in individual sleep need during childhood and adolescence. Additionally, societal constraints (e.g. school) curtail sleep opportunity.

The mechanisms supportive of the obesogenic effects of short sleep are several, including upregulation of appetite, increased time to eat, lower energy expenditure, and altered glucose metabolism. The relationship between short sleep and reduced leptin and elevated ghrelin has been observed in both epidemiological and laboratory studies[65–66]. Such perturbations in leptin and ghrelin profiles may culminate in a powerful stimulus to food intake which can ultimately lead to obesity[66]. Other metabolic hormones have also been implicated in the short sleep-weight gain association including cortisol, insulin, and growth hormone (see detailed review[67]).

Short Sleep and Obstructive Sleep Apnea

Sleep apnea may partially explain the relationship between short sleep duration and mortality. This disorder is associated with sleep disruption and is associated with increased mortality risk[68–70]. However, it is largely unaddressed by the current studies. Several researchers have suggested that the relationship between long sleep duration and mortality risk may be the result of patients with sleep apnea compensating for the large degree of fragmentation associated with the disorder by spending more time asleep or excessive amounts of time in bed[1]. Conversely, the fragmentation associated with sleep apnea may lead individuals to report less overall sleep[71]. Thus, it may be that mortality is related to variables associated with sleep apnea, rather than long or short sleep per se. However, there is not sufficient evidence to suggest that those with sleep apnea sleep more or less than the average[72]. Additionally, many predictors of sleep apnea, including age, gender, and body mass index, were controlled for in some of the epidemiological studies. Thus, it is possible that the relationship between sleep duration and mortality may overlap somewhat with that of sleep apnea and mortality, but it is unlikely that these relationships are collinear.

Short Sleep & Diabetes

Nearly all of the epidemiologic (5 longitudinal[73–77] and 2 cross-sectional[78–79]) and laboratory studies[80] to date have reported associations between habitual/imposed short sleep and risk of diabetes. Furthermore, glycemic control appears to be worse in people with diabetes who report poorer subjective sleep quality and short sleep duration[79]. Formal intervention studies are required to assess sleep's role in the genesis and course of diabetes in the longer term. Of note, significant attenuation of the relationship has been observed upon including BMI and/or hypertension in the multi-variable models, indicating that a significant proportion of the link between short sleep and diabetes risk could be explained by such comorbid risks or conditions.

Short Sleep & Physiologic Stress

Stress affects our sleep and, conversely, sleep deprivation is itself a stressor. Investigators have demonstrated that sleep deprivation or restriction can increase the activity of the neuroendocrine stress systems (hypothalamic-pituitary-adrenal axis and autonomic sympatho-adrenal axis) and also the reactivity of these systems to downstream stressors[80]. Chronic activation of these systems, and the consequent perturbation in the regulation of serum glucocorticoid levels, may lead to disease, neuronal damage, and earlier aging[81].

Short Sleep & Immunity

The impact of sleep deprivation on the immune system has been challenging to study. It is exceedingly difficult to isolate effects of sleep as an independent variable as physiologic processes change relative to wakefulness[82]. Parameters of cellular and humoral immune systems have been investigated for their associations with differing durations of sleep deprivation. Results have been inconsistent and at times contradictory. A recent analysis of 153 adults found that those who slept <7 hours/night trended towards increased likelihood to develop a cold after rhinovirus exposure compared to those who slept 8 hours (OR=2.94[95%CI=1.18–7.30])[83]. Interestingly, immune incompetence has been reported with sub-optimal antibody titer responses following vaccination amidst periods of sleep deprivation[82]. Finally, correlative evidence supports a significant association between NREM sleep and recovery from infection[82].

Short Sleep & Socioeconomic Status

A growing interest in the socioeconomic disparity in sleep has emerged with investigators examining the influence of factors such as income, poverty, education, and employment upon sleep duration and/or sleep quality[84–86]. Findings have been broadly similar: disadvantaged groups have higher likelihood of less/poorer sleep. The challenges of interpreting these associations are similar to other dilemmas in the SES-health literature: First, the influence of socioeconomic status upon health occurs throughout the life-course. Second, this influence depends on the life stage. Third, SES is challenging to measure. Fourth, cross-sectional analyses hinder the ability to discern the direction of the association. It is conceivable that sleep curtailment may lead to socioeconomic disparity which, in and of itself, confers increased risk for mortality[87]. However, it may be more plausible that socioeconomic status is a proximal cause of short sleep. This would suggest that sleep could be an innocent bystander-- a mediator, moderator or confounder, or it could be in the causal pathway of the SES-mortality relationship. Thus, investigators have begun to examine the influence of sleep quality and sleep duration on the SES-health gradient[88–89].

SLEEP DURATION AND MORTALITY: THE POTENTIAL PATHWAYS

In Figure 1, we present a social-ecological model[90] of the determinants of sleep. This model allows for multiple levels of effects, namely the microsystem, the mesosystem, and macrosystem. Specific components of each layer are listed in detail in the diagram, and range from individual characteristics and health behaviors in the microsystem, school and work environments in the mesosystem, and policy and physical environments in the macrosystem. This theoretical pathway has considerable implications for policies and interventions. It suggests that in order to reduce sleep-related mortality, interventions should occur at the individual, social, environmental, and policy levels. Here we introduce the social-ecological model and explore five theoretical pathways through which the relationships between sleep and mortality may be observed. The five pathways are outlined on Figure 1 with letters A-E:

A: Short Sleep Causes Mortality Directly

The pathway (A) in which short sleep causes mortality directly provides the simplest model – a direct relationship between short sleep and mortality. Evidence from animal models that support this pathway show that sleep deprivation in rats leads to death within 2 weeks[91]. As described in many of the studies above, epidemiologic data support this pathway with large-scale analyses that adjust for a variety of confounders and still finding that short sleep duration is associated with increased mortality[19, 31]. This crude depiction suggests that merely altering (e.g., extending) sleep is sufficient to alter mortality risk, yet it oversimplifies the problem. Four more realistic and complex pathways are described below, all of which need to be considered when translating the widely observed relationship between short sleep and mortality into clinical and population-based interventions.

B: Short Sleep is a Mediating or Moderating Factor

In the second potential pathway (B1 and 2), short sleep duration is a mediating (B1) and/or moderating (B2) factor. This perspective provides a more contextual picture of the observed relationship between short sleep duration and mortality. That is, short sleep may result from variety of social, environmental, and physiological changes that lead to increased mortality risk. This pathway is supported by literature examining social determinants of health[92–93]. The same populations that are at risk for poor health are also at risk for poor sleep[93]. Those who live in urban environments, are racial minorities, or have low levels of education are generally more likely to be short sleepers[93–94]. In Pathways B1 and B2, short sleep duration is a behavioral intermediary along the pathway of increased morbidity and mortality[88–89, 93].

C: Short Sleep is Mediated or Moderated by Social and Physiologic Factor(s)

Pathway (C) indicates short sleep itself causes physiological and social outcomes that may lead to increased mortality. Again, the challenge with this pathway is that the array of physiological and social outcomes is large, and it is not clear which are the most relevant mechanisms to understanding the sleep/mortality relationship. Some of these potential pathways (e.g. cardiovascular, immune, obesity) are discussed above. For example, short sleep may lead to hormonal and behavioral patterns that are conducive to weight gain or reduced productivity that then lead individuals on a pathway toward heightened mortality risk. These examples show how the effects of short sleep on health may be mediated or moderated by the social determinants of health[95].

D: Short Sleep is Associated with Other Characteristics Causally Linked to Mortality

The fourth potential pathway (D) is one in which short sleep is associated with other characteristics causally linked to mortality but is not itself related to mortality. An example here is age, which is independently associated with mortality (i.e., after surviving early life, the risk of mortality increases with age). Also, sleep duration decreases as one ages[96], yet the role of short sleep in explaining the high mortality rates among the elderly compared to younger people is a very minor one at best. Statistically, a common strategy to accommodate these types of pathways is to use multivariate models to adjust for confounding factors such as age when looking for a correlation between sleep and mortality. This effectively removes the effect of the D type pathways. Unfortunately, not all characteristics that follow along the D pathway are as easily observable as age, and consequently it is difficult to adjust for their effects. Thus, when discussing the relationship between sleep and mortality, we must consider that other factors may be driving both outcomes.

E: Characteristics that Lead to Mortality Lead to Short Sleep

The final pathway (E), sometimes referred to as reverse causality, is shown by the line labeled E. In this pathway, the same characteristics that eventually lead to increased mortality may also be causally associated with shortened sleep. While it is important to discern the roles of intermediate variables, this can be very challenging statistically. Reverse causality is best studied in very controlled experimental environments or prospective studies where causal sequencing can be readily observed.

SLEEP DURATION AND MORTALITY: THE FUTURE

Many questions remain regarding the sleep-mortality relationship. A better understanding the physiological/psychosocial connections between amount of sleep and shortened lifespan is critical. Simply documenting this relationship is no longer sufficient – we must explore possible mechanisms and pathways as well develop targeted interventions that can positively alter this relationship. We propose several directions for the future:

First, research programs should investigate long and short sleep separately, as both are associated with increased mortality risk but the pathways may vary[41]. Thus, increased research needs to phenotype habitual long and short sleepers, to better characterize these groups in terms of prospective and/or objective sleep, psychological functioning, performance, and health status, including obesity, cardiovascular functioning, glucose tolerance, etc. Further, sleep quality should be considered more carefully in addition to simply sleep duration. Sleep duration alone is an insufficient measure for characterizing sleep. For example, short sleep is not the same as sleep insufficiency. Studying sleep disturbance, alone and with sleep duration, will better elucidate the public health implications of sleep.

Second, potential mechanisms and pathways to mortality should be explored and clarified. We present a social-ecological model of sleep and mortality, which focuses on a number of potential factors that influence sleep duration at the micro-, meso- and macrosystem level, as well as ways in which the resultant sleep duration (and quality) may impact physiological and social outcomes which may be related to mortality. While this paper presents some evidence for some of these pathways, they need to be explored in greater detail. For example, studies exploring social determinants of sleep are necessary. Studies of attitudes and beliefs about sleep, passed through society, culture and family, will help clarify the components of a social-ecological model of sleep. Additionally, studies of health outcomes such as obesity, cardiovascular disease, and metabolic dysregulation, associated with habitual sleep parameters (verified with objective methods) will clarify which health outcomes are truly associated with habitual sleep.

Third, individual variation in sleep duration needs must be better understood. For some, 7 hours is insufficient, and for some, 7 hours is excessive. There has been little consideration of individual differences regarding sleep duration preferences and how these preferences are related to health outcomes. Current investigations into individual differences associated with susceptibility to sleep loss[97] are beginning to clarify this issue.

Fourth, community-based intervention studies are needed to better understand mechanisms that underlie this relationship and reduce mortality risk. For example, one intervention could include increasing sleep time to prevent obesity. We are not aware of any intervention studies that show weight loss in response to changes in sleep behavior, although current evidence has fueled lively discussions[40].

PRACTICE POINTS

1. Sleep duration and mortality are related in a U-shaped fashion with the lowest risk being about 7–8 hours and increasing risk associated with more or less sleep. This relationship holds true across the adult lifespan, various geographic regions, and with the inclusion of a variety of covariates.
2. Short sleep is related to cardiovascular disease, cancer, cerebrovascular accidents, diabetes, and hypertension. These associations may occur via metabolic or inflammatory processes, physiologic stress, or socioeconomic factors.
3. There are several pathways by which short sleep may be related to mortality: sleep may directly cause mortality, it may mediate/moderate a relationship, or may be unrelated to mortality but related to a variable that is responsible for the correlation.
4. A number of factors likely influence sleep duration at the micro-, meso-, and macro-level of the social-ecological model.

RESEARCH AGENDA

1. Examine short sleep and long sleep as separate pathways toward mortality risk. Also, include poor sleep as a factor that may influence this relationship.
2. Explore possible mechanisms and pathways of the sleep/mortality relationship. Cardiovascular disease, obesity, metabolic dysregulation, stress, immune dysfunction, psychological outcomes, cancer and coping difficulties may play a role. Also, determinants of sleep duration may include aspects of the social-ecological model, including micro-, meso- and macro-system.
3. Better understand the role of individual differences in the relationship between sleep duration and health outcomes in general, and mortality specifically.
4. Develop and evaluate community-based interventions that target aspects of these pathways and may reduce population-level mortality risk.

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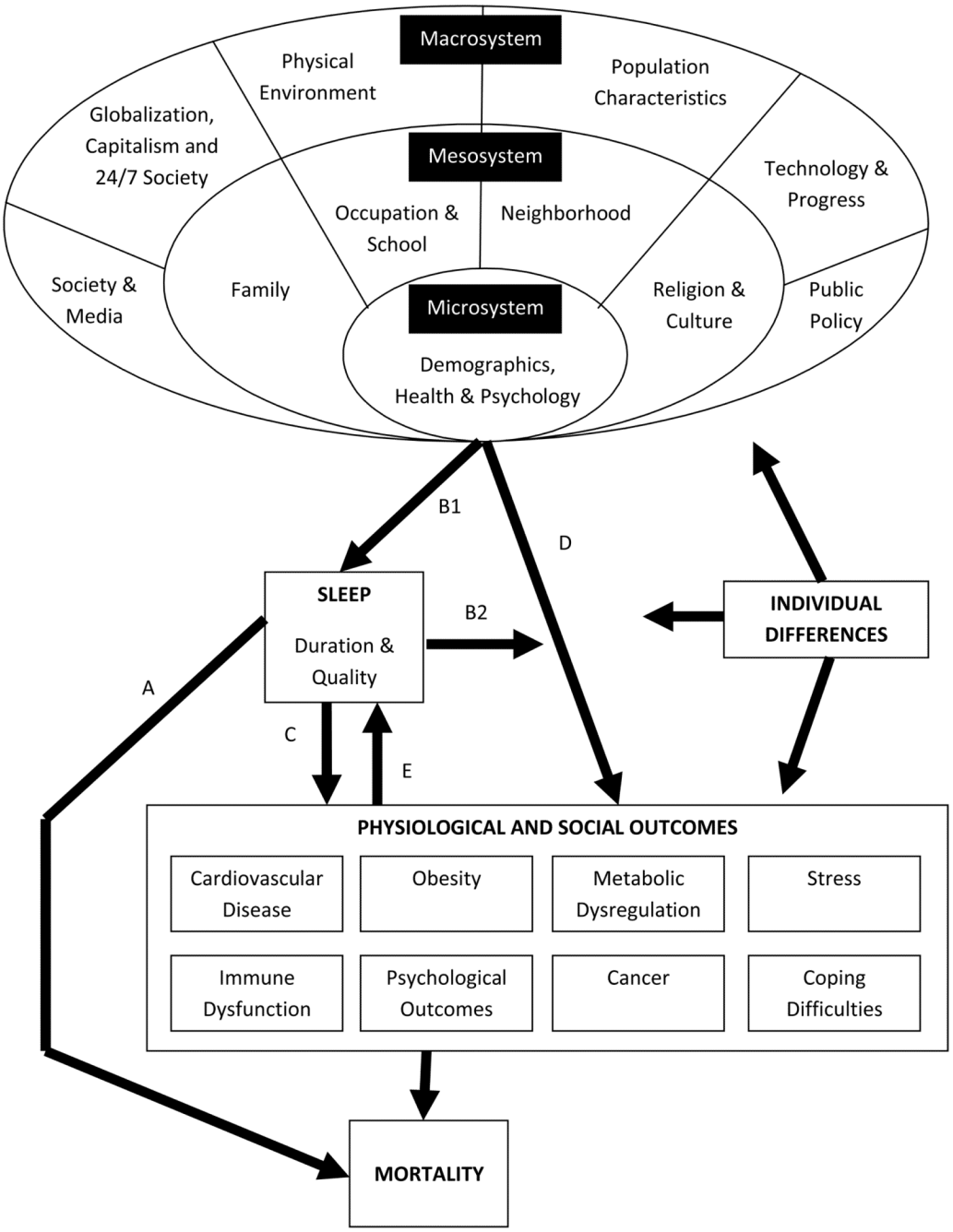

Figure 1. Model for socioecological influences upon sleep duration/behavior and associated outcomes

A – Direct causal relation between sleep duration and mortality
B1 & B2 – Intermediary role of sleep (mediator and moderator roles)
C – Cause of outcomes that, in turn, confer increased mortality
D – Linked with phenomena that are associated with increased mortality

Table 1

Studies Investigating Mortality Associated with Sleep Duration

First Author	Year	N	% Female	Age Range	Years Studied	Covariates besides age	Sleep Duration of Reference Group
Amagai	2004[18]	11325	61%	19–93	9	8	7–7.9 hours
Ayas	2003[32]	71617	100%	45–65	10	15	8 hours
Belloc	1973[9]	6928	39%	>18	5.5	0	None
Branch	1984[10]	1235	62%	66–98	4.75	6	7–8 hours
Breslow	1980[7]	6928	39%	>18	9.5	0	None
Burazeri	2003[23]	1842	54%	≥50	9–11	24	6 hours
Chen*	1994[36]	10287	Not reported	32–86	4	4	6–9 hours
Dew	2003[33]	184	54%	≥55	4.1–19.5	0	≥6 hours
Ferrie	2007[28]	10308	33%	35–55	11.8 and 17.1	13	7 hours
Gale	1998[13]	1299	Not reported	≥65	23	9	9 hours
Gangwisch	2008[35]	9789	63%	32–86	8–10	16	7 hours
Goto	2003[17]	724	65%	≥65	12	12	6–7 hours
Gottlieb*	2002[30]	4541	56%	nr	14	5	7–8 hours
Hammond	1964[3]	1064004	57%	<30–≥80	3	0	None
Heslop	2002[27]	3030	15%	Men <65 Women <60	3.25	10	Always 7–8 hours
Hublin	2007[25]	21268	52%	24–101	22	10	7–8 hours
Huppert	1995[26]	6096	56%	≥18	7	nr	6–9 hours
Kaplan	1987[8]	6928	36%	38–≥70	17	6	7–8 hours
Kojima	2000[16]	5322	54%	20–67	12	10	7–8 hours
Kripke	1979[4]	823065	56%	30–>90	3.6	5	7–7.9 hours
Kripke	2002[31]	1116936	57%	30–102	6	32	6.5–7.4 hours
Lan	2007[21]	3079	43%	≥64	10	11	7–7.9 hours

First Author	Year	N	% Female	Age Range	Years Studied	Covariates besides age	Sleep Duration of Reference Group
Mallon	2002[24]	1870	52%	45–65	12	17	6–8 hours
Patel	2004[34]	82969	100%	40–65	10	11	7 hours
Pollak	1990[11]	1855	81%	65–98	3.5	10	None
Qureshi	1997[29]	7844	64%	32–>72	10	9	6–8 hours
Ruigomez	1995[14]	1219	61%	≥65	5	7	7–9 hours
Rumble	1992[12]	1020	Not reported	≥65	5	2	4–9.9 hours
Shankar	2008[22]	58044	55.5%	45–74	5	17	7 hours
Suzuki	2008[20]	109778	60%	40–79	12.5(m) 12.9(w)	2	7–8 hours
Tamakoshi	2004[19]	104298	58%	40–79	10	14	7–7.9 hours
Tsubono	1993[15]	4318	60%	≥40	4	1	7–8 hours
Wingard	1982[6]	6928	36%	30–69	9	14	7–8 hours
Wingard	1983[5]	4713	53%	30–69	9	7	7–8 hours

*=not included in meta-analysis[37]

Table 2

Odds Ratios and Mortality Rates in Studies of Sleep Duration and Mortality Across the World

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
Amagai 2004 (Asia)	Men:	<6	**2.3**	1.3– 3.9	**2.4**	1.3–4.2	1.56
		6	1.1	0.7– 1.8	1.1	0.7–1.8	0.60
		7	1.0	*Reference*	1.0	*Reference*	0.59
		8	1.0	0.7–1.3	0.9	0.6–1.2	0.68
		≥9	1.3	0.9–1.8	1.1	0.8–1.6	1.27
	Women:	<6	0.8	0.3–2.2	0.7	0.2–2.3	0.19
		6	1.3	0.8–2.0	1.3	0.8–2.1	0.31
		7	1.0	*Reference*	1.0	*Reference*	0.26
		8	1.0	0.7–1.5	1.1	0.8–1.6	0.37
		≥9	1.5	1.0–2.3	1.5	1.0–2.4	0.79
Ayas 2003 (North America)	Men & Women:	≤5	**1.67**	1.02–2.74	1.12	0.68–1.84	
		6	1.05	0.75–1.46	0.91	0.65–1.28	
		7	0.80	0.58–1.09	0.83	0.60–1.14	
		8	1.0	*Reference*	1.0	*Reference*	
		≥9	**1.71**	1.05–2.77	1.45	0.89–2.36	
Belloc 1973 (North America)	Men:	≤6					0.09
		7					0.63
		8					0.57
		≥9					0.66
	Women:	≤6					0.04
		7					0.36
		8					0.46
		≥9					0.66
Branch 1984 (North America)	Men:	7–8	1.0	*Reference*			0.22
		<7 or >8	1.60	0.94–2.28			0.31

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
	Women:	7–8	1.0	*Reference*			0.17
		<7 or >8	1.34	0.85–1.83			0.22
Breslow 1980 (North America)	Men:	≤6					0.16
		7					0.12
		8					0.11
		≥9					0.14
	Women:	≤6					1.0
		7					0.7
		8					0.8
		≥9					1.0
Burazeri[a] 2003 (Asia and Africa)	Men (night):	<6	1.0	*Reference*	1.0	*Reference*	
		6–8	1.21	0.83–1.76	1.25	0.83–1.87	
		>8	**1.86**	1.19–2.91	**1.91**	1.16–3.13	
	Men (24h):	<6	1.0	*Reference*	1.0	*Reference*	
		6–8	1.03	0.65–1.64	1.41	0.83–2.39	
		>8	**1.81**	1.12–2.93	**2.13**	1.23–3.71	
	Women (night):	<6	1.0	*Reference*	1.0	*Reference*	
		6–8	0.82	0.57–1.17	0.80	0.54–1.17	
		>8	0.95	0.63–1.42	1.08	0.70–1.66	
	Women (24h):	<6	1.0	*Reference*	1.0	*Reference*	
		6–8	0.68	0.46–1.01	0.64	0.42–0.97	
		>8	0.84	0.56–1.27	0.80	0.51–1.24	
Chen 1994 (North America)	Age ≥60:	<6 or >9					0.20
		6–9					0.15
	Age <60:	<6 or >9					.02
		6–9					.02

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
Ferrie[b] 2007 (Europe)	Time 1:	≤ 5	**1.61**	1.20–2.15	1.24	0.92–1.67	9.54
		6	1.11	0.91–1.35	1.00	0.82–1.22	6.05
		7	1.0	*Reference*	1.0	*Reference*	5.24
		8	1.08	0.85–1.38	1.07	0.84–1.36	5.51
		≥9	1.77	0.84–3.76	1.54	0.72–3.28	7.87
	Time 2:	≤ 5	**2.07**	1.38–3.13	**1.78**	1.17–2.71	6.90
		6	1.21	0.89–1.66	1.13	0.83–1.55	3.75
		7	1.0	*Reference*	1.0	*Reference*	3.20
		8	1.13	0.85–1.52	1.11	0.82–1.48	3.79
		≥9	**2.00**	1.18–3.38	**1.95**	1.15–3.31	6.90
	Change from baseline:	No Chg	1.0	*Reference*	1.0	*Reference*	
		Incr. 5–6	0.88	0.60–1.28	0.92	0.63–1.5	4.14
		Incr. 7–8	**1.84**	1.31–2.58	**1.75**	1.24–2.47	5.09
		Decr. 6–8	**1.72**	1.25–2.38	**1.62**	1.17–2.25	4.65
Gale 1998 (Europe)	Men & Women:	≤7			1.0	0.7–1.4	
		8			0.8	0.7–1.0	
		9			1.0	*Reference*	
		10			1.2	1.0–1.4	
		11			1.3	1.0–1.7	
		≥12			**1.7**	1.2–2.5	
Gangwisch[c] 2008 (North America)	All Ages:	≤ 5			1.17	0.99–1.39	
		6			0.95	0.81–1.11	
		7			1.0	*Reference*	
		8			**1.23**	1.08–1.39	
		≥9			**1.34**	1.15–1.56	
	Age <60:	≤ 5			0.67	0.43–1.05	
		6			0.75	0.53–1.08	
		7			1.0	*Reference*	

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
		8			1.02	0.75–1.38	
		≥9			1.04	0.66–1.65	
	Age >60:	≤ 5			**1.26**	1.06–1.53	
		6			0.98	0.83–1.17	
		7			1.0	*Reference*	
		8			**1.25**	1.09–1.44	
		≥9			**1.36**	1.15–1.60	
Goto 2003 (Asia)	Men & Women:	<6	1.42	0.61–3.27	1.29	0.50–3.24	
		6–7	Ref	*Reference*	1.0	*Reference*	
		>7	1.62	0.99–3.26	1.54	0.97–2.58	
Gottlieb 2002 (North America)	Men:	<6			1.4	None reported	
		6			0.8		
		7–8			1.0		
		9			1.3		
		>9			1.5		
	Women:	<6			1.7	None reported	
		6			1.1		
		7–8			1.0		
		9			0.9		
		>9			1.8		
Hammond 1964[d] (North America)	Men, Time 1:	<4					6.70
		4					3.13
		5					2.08
		6					1.27
		7					0.96
		8					1.18
		9					1.54
		≥10					3.15

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
	Men, Time 2:	<4					5.17
		4					2.91
		5					1.99
		6					1.67
		7					1.44
		8					1.59
		9					1.91
		≥10					2.87
Heslop 2002 (Europe)	Men:	<7	**1.30**	1.06–1.61	1.15	0.93–1.42	
		7–8	1.0	*Reference*	1.0	*Reference*	
		>8	1.04	0.65–1.66	0.91	0.57–1.46	
	Women:	<7	**1.99**	1.16–3.41	1.73	0.99–3.03	
		7–8	1.0	*Reference*	1.0	*Reference*	
		>8	0.60	0.08–4.37	0.58	0.08–4.22	
Hublin 2007 (Europe)	Men:	<7	**1.34**	1.19–1.51	**1.26**	1.11–1.43	
		7–8	1.0	*Reference*	1.0	*Reference*	
		>8	**1.32**	1.17–1.48	**1.24**	1.09–1.41	
	Women:	<7	1.12	0.98–1.28	1.21	1.05–1.40	
		7–8	1.0	*Reference*	1.0	*Reference*	
		>8	**1.20**	1.06–1.35	**1.17**	1.03–1.34	
Huppert 1995 (Europe)	Men & Women:	<6	0.95				
		6–9	1.0				
		>9	2.25				
Kaplan 1987 (North America)	Age 38–49:	7–8	1.0	*Reference*			
		<7 or >8	1.23	0.88–1.70			
	Age 50–59:	7–8	1.0	*Reference*			
		<7 or >8	**1.44**	1.08–1.91			

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
	Age 60–60:	7–8	1.0	*Reference*			
		<7 or >8	0.95	0.73–1.24			
	Age ≥70:	7–8	1.0	*Reference*			
		<7 or >8	1.05	0.85–1.29			
Kojima 2000 (Asia)	Men:	<7	**1.9**	1.1–3.29	**1.93**	1.12–3.35	
		7–8.9	1.0	*Reference*	1.0	*Reference*	
		9–9.9	1.13	0.73–1.74	1.15	0.74–1.77	
		≥10	**1.94**	1.01–3.76	1.77	0.88–3.54	
	Women:	<7	0.92	0.53–1.62	0.90	0.50–1.61	
		7–8.9	1.0	*Reference*	1.0	*Reference*	
		9–9.9	1.10	0.61–2.00	1.07	0.58–1.95	
		≥10	0.42	0.06–3.02	0.40	0.06–2.92	
Kripke 1979 (North America) Mortality Ratios	Men:	<4	2.8	None reported			
		4–4.9	1.59				
		5–5.9	1.38				
		6–6.9	1.11				
		7–7.9	1.0				
		8–8.9	1.10				
		9–9.9	1.29				
		≥10	1.77				
	Women:	<4	1.48	None reported			
		4–4.9	1.40				
		5–5.9	1.20				
		6–6.9	1.13				
		7–7.9	1.0				
		8–8.9	1.13				
		9–9.9	1.27				
		≥10	1.82				

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
Kripke 2002 (North America) (Mortality Hazard Ratios)	Men:	3			1.19	0.96–1.47	
		4			**1.17**	1.06–1.28	
		5			**1.11**	1.05–1.18	
		6			**1.08**	1.04–1.11	
		7			1.0	*Reference*	
		8			**1.12**	1.09–1.15	
		9			**1.17**	1.13–1.21	
		≥10			**1.34**	1.28–1.40	
	Women:	3			**1.33**	1.08–1.64	
		4			**1.11**	1.01–1.22	
		5			**1.07**	1.01–1.13	
		6			**1.07**	1.03–1.11	
		7			1.0	*Reference*	
		8			**1.13**	1.09–1.16	
		9			**1.23**	1.17–1.28	
		≥10			**1.41**	1.34–1.50	
Lan 2007 (Asia)	Men:	<7	0.97	0.76–1.23	0.98	0.76–1.25	
		7–7.9	1.0	*Reference*	1.0	*Reference*	
		8–8.9	1.11	0.91–1.36	1.09	0.89–1.33	
		9–9.9	**1.33**	1.08–1.65	1.14	0.91–1.42	
		≥10	**1.86**	1.48–2.34	**1.51**	1.19–1.92	
	Women:	<7					
		7–7.9					
		8–8.9					
		9–9.9					
		≥10					
Mallon 2002 (Europe)	Men:	<6	1.1	0.6–7.0			
		7–8	1.0	*Reference*			

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
		>8	**2.0**	1.2–3.2			
	Women:	<6	1.0	0.6–1.8			
		7–8	1.0	*Reference*			
		>8	1.3	0.6–2.6			
Patel 2004 (North America)	Women:	≤5	**1.41**	1.25–1.58	1.08	0.96–1.22	
		6	1.07	1.0–1.15	0.99	0.92–1.06	
		7	1.0	*Reference*	1.0	*Reference*	
		8	**1.18**	1.1–1.26	**1.11**	1.03–1.19	
		≥9	**1.72**	1.55–1.91	**1.40**	1.25–1.55	
Pollak 1990 (North America)	Men:	≤4					0.24
		5					0.25
		6					0.16
		7					0.17
		8					0.22
		≥9					0.30
	Women:	≤4					0.19
		5					0.07
		6					0.14
		7					0.08
		8					0.13
		≥9					0.18
Qureshi 1997 (North America)	Stroke:	6–8	1.0	*Reference*	1.0	*Reference*	
		<6	1.0	0.7–1.5	1.0	0.70–1.5	
		>8	**1.5**	1.1–2.1	**1.5**	1.1–2.0	
	CV Disease:	6–8	1.0	*Reference*	1.0	*Reference*	
		<6	1.3	0.9–1.7	1.3	1.0–1.8	
		>8	1.2	0.9–1.6	1.2	0.8–1.5	

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
Ruigomez 1995 (Europe)	Men:	<7	1.06	0.61–1.83			
		7–9	1.0	*Reference*			
		>9	1.30	0.71–2.38			
	Women:	<7	0.66	0.37–1.16			
		7–9	1.0	*Reference*			
		>9	1.46	0.79–2.70			
Rumble 1992 (Europe)	Men & Women:	<4	1.12	0.47–2.69			
		≥10	1.60	0.74–3.47			
Shankar 2008 (Asia)	Men:	≤5			**1.7**	1.35–2.15	
		6			1.20	0.99–1.45	
		7			1.0	*Reference*	
		8			1.1	0.92–1.32	
		≥9			**1.88**	1.48–2.40	
	Women:	<5			**1.43**	1.09–1.88	
		6			1.04	0.82–1.31	
		7			1.0	*Reference*	
		8			1.15	0.92–1.44	
		≥9			**1.67**	1.24–2.27	
Suzuki 2008 (Asia)	Men:	<7	1.03	0.97–1.09			
		7–8	1.0	*Reference*			
		≥9	**1.32**	1.26–1.40			
	Women:	<7	0.99	0.94–1.05			
		7–8	1.0	*Reference*			
		≥9	**1.42**	1.22–1.52			
Tamakoshi 2004 (Asia)	Men:	≤4	**1.62**	1.26–2.09	0.88	0.44–1.78	
		5	**1.16**	1.01–1.33	1.07	0.83–1.38	
		6	1.09	1.0–1.19	1.11	0.95–1.28	

First Author	Stratum	Sleep Duration (hrs)	Odds Ratio (least adjusted)	95% CI	Odds Ratio (fully adjusted)	95% CI	Mortality rate (%)
		7	1.0	*Reference*	1.0	*Reference*	
		8	**1.11**	1.05–1.19	**1.19**	1.07–1.32	
		9	**1.26**	1.15–1.37	**1.27**	1.08–1.48	
		≥10	**1.73**	1.58–1.90	**1.75**	1.46–2.09	
	Women:	≤4	**1.60**	1.28–2.02	**1.83**	1.20–2.81	
		5	1.14	0.99–1.31	1.18	0.90–1.53	
		6	1.05	0.96–1.15	1.17	0.99–1.39	
		7	1.0	*Reference*	1.0	*Reference*	
		8	**1.23**	1.14–1.33	**1.35**	1.17–1.56	
		9	**1.35**	1.20–1.51	**1.57**	1.26–1.96	
		≥10	**1.92**	1.70–2.17	**2.12**	1.67–2.68	
Tsubono 1993 (Asia)	Men & Women:	≤6	1.26	0.81–1.97			
		7–8	1.0	*Reference*			
		>9	**1.58**	1.16–2.15			
Wingard 1982 (North America)	Men & Women:	≤6 or ≥9	**1.13**	1.1–1.7			
		7–8	1.0	*Reference*			
	Men:	≤6 or ≥9					0.14
		7–8					0.08
	Women:	≤6 or ≥9					0.09
		7–8					0.06
Wingard 1983 (North America)	Men:	≤6			**RR=1.3**[e]		**14.8**
		7–8					**8.2**
		≥9					**11.1**
	Women:	≤6					**9.0**
		7–8					**5.6**
		≥9					**8.5**

[a] risk was separately calculated for nighttime sleep (ngt) and total sleep across 24 hours (24h)

[b] risk reported at two time points (Time 1) and (Time 2) followed by risk associated with change in sleep duration from baseline (Change): no change (No chg), increase from 5–6 hours (Incr. 5–6), increase from 7–8h (Incr. 7–8), or decrease from 6, 7 or 8 hours (Decr. 6–8)

[c] risk was calculated for the total sample (total), as well as separately for those aged <60 years (Age <60) and those 60 or older (Age ≥60)

[d] rates were separately calculated for 9 age groups; those presented are means weighted based on number in each age group

[e] relative risk for males & females not sleeping 7–8 hrs= **1.3** (p=0.04)

Note: risks reported in **bold** font represent statistically significant risks