



From habitual sleep hours to morbidity and mortality: existing evidence, potential mechanisms, and future agenda



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ABSTRACT

Epidemiological studies consistently show a strong U-shaped association between sleep duration and health outcomes. That is, both short and long sleepers are exposed to greater risks of death and diseases than normal length sleepers. Moreover, long sleep is often demonstrated as a stronger predictor of mortality than short sleep. While there is some experimental evidence in favor of a causal connection between short sleep and health, no such evidence exists to explain why excessive sleep might be associated with poor health. One possible explanation is that long duration sleep, instead of being a real cause of illness, is merely a marker of poor sleep quality or some unmeasured risk factor that confounds the association of long habitual sleep with mortality and other health outcomes. As for short sleep, the effect is said to be mediated via the hormones that alters glucose metabolism and appetite regulation as well as via an overactivity of the stress systems that causes increased heart rate and blood pressure. The mechanisms, however, are still poorly understood and future investigations should take into account sleep quality, objective and longitudinal sleep measures, more confounding biases, and the broad social context that influences the length and quality of sleep.

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Introduction

The amount of time spent in day-to-day sleep represents an important health behavior that received considerable empirical attention in the past few decades. Epidemiological studies of both cross-sectional and longitudinal designs, in general, show a U-shaped association between sleep duration and adverse health outcomes including mortality.^{1–11} This means that both short sleep and long sleep are associated with elevated health risks relative to the optimal mid-range sleep which is usually defined as 7–8 hours of sleep duration per day, although the definition varies from one study to another. Interestingly, habitual long-duration sleepers are found to be at greater risk of mortality than habitual short-duration sleepers.^{6,7} Not much is known, however, about the exact mechanisms linking sleep durations to mortality and health outcomes.

There are a few experimental studies documenting the physiologic mechanisms between short sleep and negative health effects,^{12–15} but no such evidence has emerged to date to demonstrate how long duration sleep might affect health. Available evidence indicates that sleep insufficiency may lead to metabolic dysregulation^{12,13} and changes in the fundamental properties of the neuro-endocrine stress

systems.¹⁶ These effects of sleep insufficiency may gradually accumulate over time and result in a variety of diseases including type 2 diabetes,^{8–10} obesity,^{17–21} hypertension,^{22–29} cardiovascular diseases (CVD),^{11,28–31} and so on. Thus, sleep duration is a crucial public health issue that, when it deviates from the normal range, takes a heavy toll in terms of morbidity and mortality outcomes. Based on a comprehensive review of existing literature, the present paper aims to revisit the U-shaped association between sleep duration and adult health, discuss the potential pathways and mechanisms driving this association, and suggest directions for future studies.

Sleep duration and health: epidemiological evidence

Sleep duration and mortality

There is a mounting body of epidemiological studies showing that sleep duration is independently associated with mortality even after statistically controlling for a wide array of covariates.^{1–5} Most of these studies provide evidence in support of a robust U-shaped association where both too little sleep and too much sleep significantly interferes with mortality. The evidence generally holds true for both women and men, younger and older adults, and across all geographic locations.⁷ Although a handful of studies are not entirely in agreement with the U-shaped association,^{32–34} nearly all of the studies

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demonstrate long sleep as a stronger predictor of mortality than short sleep.

The relationship between sleep duration and mortality, however, varies depending on age and sex and such variations are rather inconsistent and complex. The Older Finnish Twin Cohort Study, a large population-based prospective study of participants older than 18 years, shows that compared to a sleep duration of 7 hours, short sleep duration (<7 h) significantly increased the risk of all-cause mortality by 26% in men and 21% in women, whereas long sleep (>8 h) increased the risk by 31% and 39% in men and women, respectively. This was after adjustment had been made for the sociodemographic and lifestyle factors known to affect mortality.² While the association between sleep duration and mortality is more consistent for all-cause mortality, studies focusing on cause-specific mortality yield somewhat divergent results. Ikehara and colleagues,⁵ for example, investigated sex-specific associations of sleep duration with cause specific mortality in approximately 98,000 Japanese men and women 40–79 years old. The study findings reveal that relative to the average sleep duration of 7 hours, sleeping 4 hours or less is associated with a 2.32 times increased risk of mortality from coronary heart diseases in women and an approximately 1.5-fold increased risk of mortality from non-CVDs in both men and women. As for long sleep, sleep duration of ≥ 10 hours was associated with 1.5 to 2 times increased mortality from total stroke, ischemic stroke, total CVD, non-CVD, and all causes in both women and men. Mortality from cancer showed no significant association with sleep duration in either sex. Heslop and colleagues,³⁵ however, associated sleep duration with mortality from CVDs in men only. Prospectively examining sleep duration, the British Whitehall II cohort study³ found that a decrease in sleep duration from the regular sleep of 6, 7, or 8 hours increased the risk of mortality from CVD (hazard ratio [HR] 2.4, 95% confidence interval [CI] 1.4–4.1) while an increase in sleep duration from the regular sleep duration of 7 or 8 hours increased the risk of mortality from non-CVD causes (HR 2.1, 95% CI 1.4–3.1).

Although older adults are more likely to report both short and long sleep durations than younger adults,^{36,37} relatively few studies on sleep and mortality specifically focused on the older age populations and yielded less definite conclusions. A population-based cohort study conducted among the 65–85 years old in Japan shows that long sleep is strongly associated with all-cause and CVD mortality but no significant association was observed between short sleep and mortality.³⁸ A recently published population-based study in China shows higher risk of mortality in both short and long sleepers, with longer sleep being associated with a higher risk of cause-specific CVD mortality than shorter sleep among the elderly.³⁹ The age-stratified analyses carried out in an earlier study in a large sample in the USA revealed that the U-shaped association between sleep duration and mortality is reserved for the elderly only, with no significant relationship found in the middle-aged subjects (HR 0.67, 95% CI 0.43–1.05).⁴ This is in contrast with some other studies that demonstrate the effect of sleep on mortality is more strongly pronounced in young adults.^{2,40}

The U-shaped association of habitual sleep duration with mortality was further confirmed by two independent systematic reviews and meta-analyses covering men and women of both general adult and older ages across various geographic regions.^{5,7} The first meta-analysis, conducted in 2009, was based on 23 prospective cohort studies that investigated the self-reported sleep durations with both all-cause and cause-specific mortality. The pooled relative risk (RR) estimates revealed that long sleep duration carried 23% additional risk of all-cause mortality relative to the average sleep duration while the corresponding excess risk for short sleep duration was 10%. The pooled effects for specific types of mortality, however, were less conclusive. Long sleepers were at greater risk of mortality from both cancer and CVD than medium sleepers whereas short sleepers

showed an increased, albeit nonsignificant, risk of mortality from CVD only (RR 1.06, 95% CI 0.94, 1.18).⁶ One year later, another meta-analysis covering more than 1.3 million participants came up with roughly similar patterns of associations between sleep duration and all-cause mortality. In the pooled analyses, a 30% increased risk of death was detected in long sleepers while the increased risk of death in short sleepers was 12%, which, if causally linked, would be equivalent to 25 million deaths of people aged over 20 in the US alone.⁷

Sleep duration and adverse health outcomes

In common with mortality, a heightened risk of obesity, type 2 diabetes, CVDs, including hypertension, coronary heart disease and stroke, are also frequently shown on either end of sleep duration indicating the presence of a U-shaped association,^{29,41} although the evidence of a positive association of long sleep with these health outcomes appears to be less compelling compared to mortality. The quantitative pooled estimates of a meta-analysis conducted by Cappuccio et al⁸ indicate that the RR of developing type 2 diabetes is 1.28 for people who reported a short habitual sleep of ≤ 5 –6 h/night and 1.48 for those with a long habitual sleep of ≥ 8 –9 h/night. These findings were also confirmed by a recently published meta-analysis that found a U-shaped dose-response relationship between sleep duration and risk of type 2 diabetes.⁹ Similarly, a meta-analysis of longitudinal population studies examining the associations between sleep durations and CVDs linked both extremes of sleep duration with developing coronary heart disease and stroke but not total CVD.¹¹ Data on CVDs from the Jichi Medical School Cohort Study in Japan, however, demonstrated that sleeping less than 6 hours was significantly associated with an elevated risk of the incidence of CVDs in men only (HR 2.14, 95% CI 1.11–4.13) while sleeping more than 9 hours showed no statistical significance (HR 1.33, 95% CI 0.93–1.92).³¹

Research also associates short sleep and, to a lesser degree, long sleep with hypertension^{22–29} and obesity.^{17–21} Much of this evidence, however, came from cross-sectional studies, which do not allow one to claim causal connections. On the other hand, the pooled analyses of the longitudinal studies examining the association between sleep duration and hypertension indicates that only short sleep increases the risk of developing hypertension (RR 1.23, 95% CI 1.06–1.42) among the adult populations.²⁸ For obesity, too, only short sleep is found to consistently show statistical association in prospective cohort studies.^{18,19} Emerging evidence, however, is suggestive of an attenuating effect of sleep duration on hypertension and obesity with age.^{28,42} A prospective analysis from the English Longitudinal Study of Ageing shows that short sleep predicts incident hypertension among men and women aged ≤ 60 years but not in older adults.²⁸ Examining data from the National Health and Nutrition Examination Survey, a recently published study in the USA⁴² also reported significant interactions between age and sleep duration, used both as continuous and categorical variables, with regard to the body mass index (BMI). The study found: a negative linear relationship in young adulthood, with more sleep being linked to lower BMI; a U-shaped relationship in middle adulthood, with relatively high BMI in both short and long sleepers; and an attenuated relationship in older adulthood, with only very short sleepers having minimally higher BMI.

Beyond sleep duration

In addition to sleep duration, sleep quality (ie, trouble falling asleep, trouble staying asleep, early awakening, etc.) is also found to be an important risk factor for mortality and other health outcomes. For instance, a French GAZEL cohort study with a total of 16,989 male and female participants examined the effects of sleep

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