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Title

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Permalink

<https://escholarship.org/uc/item/2wq4692q>

Journal

Sleep Medicine Clinics, 18(4)

ISSN

1556-407X

Authors

Full, Kelsie M

Johnson, Dayna A

Kaufmann, Christopher N

et al.

Publication Date

2023-12-01

DOI

10.1016/j.jsmc.2023.06.015

Peer reviewed



HHS Public Access

Author manuscript

Sleep Med Clin. Author manuscript; available in PMC 2024 June 01.

Published in final edited form as:

Sleep Med Clin. 2023 December ; 18(4): 415–422. doi:10.1016/j.jsmc.2023.06.015.

An Update on Sleep Duration, Obesity, and Mortality Risk in Women

Kelsie M. Full, PhD, MPH^{a,*}, Dayna A. Johnson, PhD, MPH, MSW, MS^b, Christopher N. Kaufmann, PhD, MHS^c, Atul Malhotra, MD^d

^aDivision of Epidemiology, Department of Medicine, Vanderbilt University Medical Center, 2525 West End Avenue, Suite 600, Nashville, TN 37203, USA;

^bDepartment of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Road, Atlanta, Georgia, 30322, USA;

^cDepartment of Health Outcomes and Biomedical Informatics, College of Medicine, University of Florida, 2004 Mowry Road, Gainesville, Florida, 32603, USA;

^dDivision of Pulmonary, Critical Care and Sleep Medicine, School of Medicine, University of California San Diego, 9500 Gilman Drive, La Jolla, California, 92093, USA

Keywords

Cardiometabolic; Sleep disorders; Sleep disparities; Sex differences

INTRODUCTION

Sleep is increasingly recognized as an essential factor to overall health and well-being. Diet, exercise, and sleep are often discussed as the 3 lifestyle pillars of health, with the dogma being that if one is ignored the other two will suffer. However, because of the pressures of today's 24/7 society, sleep is often viewed as a luxury. In fact, US population estimates indicate that the proportion of adults with short sleep durations has been increasing over the past 40 years.¹ Further, several recent epidemiologic studies have shown historically marginalized populations have shorter sleep duration in comparison to non-Hispanic White populations.² With the increase in the availability of the Internet and mobile devices, individuals can be constantly engaged throughout the 24-hour day. In addition, employment trends have led to increases in work hours, flexible or alternative work schedules, and demand for work travel, all contributing to the risk for inadequate sleep.^{3–5}

Women are a group of particular interest in the context of a discussion on sleep. This focus is for several reasons: first, women have been traditionally understudied in the context of sleep research.⁶ Second, women may be given disproportionate family responsibilities to balance with their own careers, including childcare, meal planning, and other household activities. As an example, women bore the unbalanced burden of household responsibilities during the COVID-19 pandemic that resulted in job loss, delays in career advancement,

*Corresponding author. k.full@vumc.org.

and employment dissatisfaction as compared with their male counterparts.⁷⁻⁹ These responsibilities may be a chronic burden or stress that may result in less time available to sleep as well as directly impairing sleep duration.^{10,11} Third, despite being understudied, the limited existing evidence suggests women are at increased risk of certain sleep disorders including insomnia, mood disturbance, and restless legs syndrome.⁶ Although obstructive sleep apnea (OSA) is more prevalent among men,¹² the prevalence of OSA is still high in women, potentially even greater with likely missed diagnosis.¹³ Research indicates that the stereotypical phenotype of OSA leads to disproportionate diagnosis of OSA in men, above and beyond the epidemiologic differences in occurrence.¹³ Specific to sleep duration, as women age they report increasing difficulty with getting sufficient sleep.¹⁴⁻¹⁶ In general, obtaining adequate healthy sleep poses a unique challenge to aging women.

EVIDENCE ON SLEEP DURATION, OBESITY, AND MORTALITY

The impact of abnormal sleep duration on various health outcomes has been well investigated. Highlights from the literature on the link between sleep duration, obesity, and mortality in women will be succinctly reviewed here. However, it is important to note that many studies have not focused specifically on sleep duration among women or sex differences in the associations. Several conclusions on abnormal sleep duration and obesity among women can be drawn from the existing epidemiologic literature.

Mixed Results of Observational Studies Assessing Abnormal Sleep Duration and Weight Change in Women

In a 2006 landmark study among more than 68,000 women in the Nurses' Health Study, over 16 years of follow-up Patel and colleagues reported women sleeping less than 5 hours had a 1.15 relative risk of incident obesity compared with those sleeping 7 hours or more. At the baseline examination, the nurses were asked a single question on the number of hours they slept in a typical 24-hour period. In addition, over the 16-year period, women reporting short sleep duration (<6 hours) gained more weight over time as compared with women with adequate sleep duration (7-8 hours). Of note, women who reported long sleep duration (>8 h/d) also had increased body weight over time as compared with adequate sleepers, although these findings have been controversial.¹⁷ Although this study used only a 1-item self-report to assess usual sleep duration, the item was later validated with sleep diaries.¹⁸ Since then, several studies have reported associations between self-reported abnormal sleep duration and obesity.^{19,20} Although the evidence suggests an association, conflicting results have also been reported, particularly among women. In 2013, Appelhans and colleagues prospectively assessed sleep duration and weight change in midlife women in the Study of Women's Health Across the Nation, using 7-day actigraphy. There were no meaningful associations reported between objective short or long sleep durations with incident obesity.²¹

Data from Randomized Trials Supports Mechanisms and Causality

To investigate potential mechanisms linking sleep to weight gain, investigators have studied leptin and ghrelin: leptin is a satiety hormone made by adipocytes, whereas ghrelin stimulates appetite. In a physiologic clinical crossover study by Spiegel and colleagues, adult men underwent 2 days of sleep restriction (4 hours sleep restriction) followed by 2

days of sleep extension to investigate whether sleep duration curtailment altered appetite regulation. The investigators observed a reduction in leptin levels and an increase in ghrelin levels during sleep restriction days as compared with adequate sleep duration days. Both hormones changed in a direction to stimulate appetite.²² These findings were among the first to provide potential mechanisms explaining why short sleep duration might stimulate appetite and thus contribute to increases in body weight over time. The findings were followed by another crossover randomized trial by Nedeltcheva and colleagues among overweight adults at midlife to investigate if sleep restriction affected the effect of diet on weight loss. The investigators observed an impairment in loss of fat-free body mass with reduced dietary intake during the period of reduced sleep duration (5.5 hours) versus adequate sleep duration (8.5 hours).²³

Studies Have Helped to Rule Out Confounding by Genetics

Among nearly 120,000 participants in the UK Biobank, Celis-Morales and colleagues investigated the interaction of sleep duration and genetic predisposition to obesity.²⁴ Self-reported sleep characteristics, including short (<7 hours) and long sleep duration (>9 hours), were shown to modify the association of the genetic predisposition to obesity and anthropometric measurements including waist circumference, suggesting that abnormal sleep duration may exacerbate one's genetic risk of obesity.²⁴ By incorporating genetic predictors of obesity, these results partially rule out potential confounding and reverse causality and speak to how abnormal sleep duration itself may contribute to obesity.

Abnormal Sleep Duration Is Associated with Chronic Health Conditions and Mortality

A growing body of evidence supports that beyond obesity, and potentially by contributing to obesity, abnormal sleep duration increases the risk of chronic cardiovascular health conditions and increased mortality risk. Given this evidence, in 2022 the American Heart Association added sleep health to their list of the key factors that are essential to improving and maintaining cardiovascular health, as a part of "Life's Essential 8".²⁵ In the Massachusetts Male Aging Study, Yaggi and colleagues observed an impact of abnormal sleep duration on incident diabetes over the course of 15 years.²⁶ Of note, short sleepers (<6 hours) were twice as likely to develop clinical diabetes as compared with those with adequate sleep durations.²⁶ Long sleepers (>8 hours) were again at risk with a 3-fold increased risk of incident diabetes during follow-up.²⁶ Again in the Nurses' Health Study, abnormal sleep duration was linked with incident coronary artery disease in more than 71,000 women.²⁷ Ayas and colleagues observed an 82% increased risk of incident coronary artery disease in women reporting less than or equal to 5 hours of sleep per night as compared with those sleeping the recommended 8 hours per night.²⁷ The findings were followed by an important study by King and colleagues, assessing sleep duration and 5-year incident coronary artery calcification as a subclinical marker of atherosclerosis.²⁸ The investigators observed that short sleep duration (assessed via actigraphy) was predictive of incident coronary artery calcification; however, short sleep by self-report did not have the same predictive value regarding calcification risk.²⁸ Of note, the investigators did not observe an increase in calcification risk with long sleep durations as seen in prior studies. A higher cardiovascular burden has been consistently documented among racial/ethnic minorities, and numerous studies have connected abnormal sleep duration and poor

sleep health with adverse cardiovascular outcomes, including resistant hypertension, among Black adults.^{29–32} Lastly, several large cohort studies have reported an increased risk of cardiovascular and all-cause mortality associated with both short and long habitual sleep durations.^{18,33–35}

In aggregate, the data consistently support the association and potential contribution of short sleep duration to poor metabolic health, obesity risk, chronic cardiovascular conditions, and mortality. In addition, long sleep is consistently linked with similar poor health outcomes, although the mechanism remains unclear. Despite the overwhelming collection of evidence, clarity on the underlying mechanisms and a lack of effective interventions remain missing from the literature.

AREAS FOR GREATER DISCUSSION

Given the substantial data available on the topic of sleep duration and cardiometabolic health, the authors have opted not to provide an exhaustive review of the existing literature. Instead, they have chosen to focus on 3 major areas deserving of more extensive discussion: (1) long sleep duration, (2) underlying mechanisms, and (3) racial/ethnic disparities.

Long Sleep

Although sleep deprivation has many known health effects, several large cohort studies have shown associations between long sleep duration and poor cardiometabolic health outcomes, including obesity. The observed association is consistent across different populations and different outcome measures.^{26,27,32,34} Despite this evidence, there has been greater societal concern of not getting enough sleep rather than getting too much sleep. The potentially detrimental effect of long sleep is often dismissed due to study design bias, possible residual confounding, or in some cases reverse causation; however, the authors believe further investigation is imperative. Evidence supports that long sleepers have increased risk of depression and certain inflammatory disorders.³⁶ However, the magnitude of these associations is quite modest as compared with the documented cardiometabolic risk associated with long sleep. Given the overwhelming emphasis on increasing sleep duration at the population level, it is also critically important to better understand the mechanisms that may explain the increased risk for poor cardiometabolic health in long sleepers. A few mechanisms have been proposed that warrant further investigation. First, sleep architecture has not been adequately assessed in habitual long sleepers.³⁷ The possibility exists that poor sleep quality and/or undiagnosed sleep disorders may be contributing to the need for long sleep. Second, it is possible that some adults have more irregular sleep patterns that are not well captured by self-report measures, including those composed of periods of sleep deprivation followed by long periods of recovery sleep. Sleep irregularity, defined as substantial variation in sleep durations throughout the week, has recently been associated with obesity and several cardiometabolic conditions.^{38–42} Third, the authors' clinical experience suggests that habitual long sleepers often have overall suboptimal health behaviors. For example, it has been observed that many individuals who sleep more than 10 hours per night experience social isolation, lack daily physical activity, have poor quality diets, and struggle with inconsistent employment. These lifestyle factors individually

contribute to cardiometabolic health and may be difficult to capture with traditional measurements and cut points when measuring confounders. Finally, several medications also contribute to the propensity for long sleep duration and may not be adequately captured in epidemiologic cohorts (eg, over-the-counter hypnotics).

The Underlying Mechanisms of Abnormal Sleep Duration

Numerous studies have investigated the physiologic effects of sleep deprivation to explain the connection between short sleep duration and adverse cardiometabolic health outcomes. Clinically, patients who are short sleepers fall into 3 distinct categories: those with insomnia who have trouble falling asleep or staying asleep, those with short sleep duration due to societal pressures (eg, mothers with young children, women working multiple jobs), and those who sleep short durations and do not perceive a biological need for more sleep. Although some debate exists regarding the deleterious effects of short sleep based on why it is occurring, our view is that sleep duration per se is the predominant variable; however, further work is needed in this area. In addition to the metabolic disturbances described earlier, short sleep duration has been shown to produce sympathoexcitation, or stimulation of the sympathetic nervous system, as well as increased cortisol concentration, increased inflammatory biomarkers, and increased markers of oxidative stress.^{36,43–46} In a small 22-day study by Yang and colleagues the investigators assessed micro-vascular and inflammatory responses during periods of sleep restriction (3 days of 4 hours). Although no significant differences were observed in macrocirculation, microcirculation, cell adhesion molecules, or markers of inflammation between the sleep-restricted group and healthy sleepers, in sex-stratified models, female participants were more likely to have increased inflammatory markers (interleukin-6) during sleep restriction period than men.⁴⁷ Calvin and colleagues investigated the effect of sleep restriction (5 hours) compared with healthy sleep (7 hours) on endothelial function, a potential mediator in cardiovascular disease risk. Participants in the sleep restriction group experienced significant endothelial impairment as compared with healthy controls.⁴⁸ In aggregate, the data suggest major physiologic effects of short sleep duration on physical health that may over time contribute to cardiometabolic outcomes. Although the mechanisms are still being delineated, the adverse effects are likely multifactorial and include metabolic, autonomic, inflammatory, and oxidative stress mechanisms. These complex causal pathways and relationships likely explain why short sleep has been connected to multiple different organ systems and outcomes. Thus, overall mortality is likely affected by short sleep duration due to multiple underlying mechanisms; however, thoughtfully designed studies are needed to confirm and clarify these mechanisms.

RACIAL/ETHNIC DISPARITIES

Given the long-lasting disparities in sleep health and the need to address these sleep disparities, deserved attention has been given to socioeconomic and racial/ethnic differences in the context of sleep duration. Adults with low socioeconomic status may be particularly susceptible to societal and economic pressures described earlier and thus sleep duration may be compromised as a direct result.⁵ It is also well documented that racial/ethnic minority groups are at a greater risk for suboptimal sleep health, including particularly abnormal sleep durations. In the racially/ethnically diverse MESA study, Chen and colleagues reported

sleep durations varied significantly across racial/ethnic groups. As compared with 20% of non-Hispanic Whites, 40% of Black and African American participants and 30% of Hispanic/Latinx participants had habitual sleep durations less than 6 hours per night.⁴⁹ Evidence supports that racial/ethnic differences in sleep may be explained by socioeconomic status, racism, discrimination, neighborhood environments, and access to care,^{2,50,51} but they are also in part explained by cultural differences in sleep-related beliefs. Historically, sleep has been stigmatized among Black and African American populations, contributing to the underreporting of poor sleep among Black and African American adults, and similarly, because of these stigmas around sleep, there tends to be a culture emphasis on work as opposed to sleep.⁵² In a study composed of predominately older women, Grandner and colleagues found that Black older women were more likely to believe sleepiness was related to laziness and bad habits and were less likely to report motivation to make enough time for sleep or believe sleep was related to one's health than the White older women.⁵³ Within racial/ethnic subgroups, differences in sleep have been reported, stressing the importance of developing a better understanding of the multiple layers of social determinants that contribute to disparities in sleep health. Using NHANES data collected among 5160 US adults, Seicean and colleagues observed that Mexico-born US immigrants were less likely to report short habitual sleep durations than Mexican-Americans born in the United States, highlighting differences that exist within the US Hispanic Latino community.⁵⁴ The investigators hypothesized the differences between the US and foreign born Hispanic Latinos may in part be related to differences in cultural beliefs and values toward sleep health.⁵⁴ Within the US Hispanic Latino community there are unique barriers to obtaining adequate sleep including the stress and lifestyle changes caused by acculturation.⁵⁵ In the HCHS/SOL study including 16,415 US Hispanic Latinos, large differences were reported in both OSA prevalence (13.7% for moderate-to-severe sleep disturbed breathing) and diagnosis (1.3%), as well as OSA risk across subgroups of Hispanic backgrounds. These results suggest the proportion of undiagnosed sleep disorders may be even greater in some racial/ethnic population subgroups and may explain a larger burden of disease in these groups, including obesity.⁵⁶

In summary, there is a need to address the multilevel social determinants of health that contribute to sleep disparities.^{50,52,57} At the individual level, an opportunity exists through advocacy and educational efforts to improve health literacy, knowledge, and perceptions regarding the importance of adequate sleep to overall health and well-being. There is a need to develop culturally tailor sleep interventions. For example, racially tailoring interventions has shown participants to be more engaged and more likely to complete the intervention,⁵⁸ and increases in OSA self-efficacy have been observed.⁵⁹ In addition to individual-level targets, contextual factors are also of importance. The literature supports that the neighborhood environment explains a large portion of documented sleep disparities.⁶⁰ Thus, designing interventions and targeting policy to address adverse environments could potentially improve sleep duration at the community level.⁵⁰ Data from a natural experiment illustrated that living closer to a neighborhood investment was associated with better sleep outcomes,⁶¹ thus investing in neighborhoods could potentially have a positive effect on sleep health. Based on the evidence, targeting the multilevel determinants of sleep disparities is a promising avenue for accomplishing sleep equity.

FUTURE DIRECTIONS

Despite considerable progress in our understanding of how sleep duration and sleep health more generally are associated with cardiometabolic health, substantial unresolved questions remain.

For clinicians:

- Given the high prevalence and major impact of poor sleep and sleep disorders, should universal screening be implemented in clinics or in the community setting?
- With the major expansion in the use of wearable consumer products, should data from these devices be used to guide clinical decision-making?
- Based on the interdependence of diet, exercise, and sleep, a question often posed by patients is: “Should I get up early and sleep less to go to the gym?” The answer likely depends on total sleep time and individual characteristics; however, a greater understanding of the interdependence of these health behaviors is needed.
- Are women more susceptible biologically to the effects of poor sleep and sleep disturbances or are observed differences more related to societal factors?

For researchers:

1. How can we achieve more comprehensive evaluations of sleep health beyond self-reported sleep duration? Polysomnography and other limited channel sleep tests can be cumbersome, particularly when one considers trying to collect these data in large studies.
2. Given the uncertainty regarding underlying mechanisms, a need for further longitudinal studies with repeated assessments and the impact of interventions needs to be under-taken. Actionable targets could be identified to help to mitigate the adverse health effects associated with inadequate sleep.
3. Given the paucity of data from underrepresented minorities, further longitudinal data enriched for various subgroups are essential to evaluate and understand better within group and between group differences. Beyond just describing differences between groups, interventions focused on social and environmental determinants of health are needed to help achieve sleep health equity.

For policy makers:

1. Increasing public education regarding the importance of sleep to overall health could be achieved through educational curriculum, mass media, social media, and via strong advocates.
2. Given the disproportionate burden of family responsibilities that are often placed on women, there may be a need for further discussion regarding policies related to maternal leave, flexibility around childcare, and pay equity.

3. Given the ever-increasing numbers of shift workers in today's 24/7 society, optimizing schedules considering their impact on sleep and overall health needs to be considered further. Policies could be developed to optimize lighting, scheduling, and to prioritize safety (eg, avoiding drowsy driving or occupational accidents).

FUNDING

Dr Full receives funding from the Eunice Kennedy Shriver National Institute of Child and Human Development award for the Building Interdisciplinary Research Careers in Women's Health career development program (K12HD043483). Dr Johnson receives funding from the National Institutes of Health, National Institute for Heart Lung and Blood (Grant #R01HL157954). Dr Kaufmann receives funding from the National Institute on Aging (Grant #'s: K01AG061239, R01AG079391, P30AG028740), and Sleep Research Society Foundation (Grant #: 23-FRA-001). Dr Malhotra receives funding from the National Institutes of Health.

DISCLOSURE

Dr Malhotra is funded by the NIH. He reports income related to medical education from Livanova, Eli Lilly, Zoll and Jazz. Additionally, ResMed provided a philanthropic donation to UCSD. All other authors have nothing to disclose.

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KEY POINTS

- Because of the pressures of today's 24/7 society, an increasing number of adults in the United States are suffering from insufficient sleep, and unique social, occupational, and clinical factors make getting healthy sleep a challenge for women.
- Consistent evidence supports the association and potential contribution of short sleep duration to poor metabolic health, obesity risk, chronic cardiovascular conditions, and mortality.
- More research is needed to understand better the comprehensive sleep health of phenotypic short and long sleepers to understand the pathways underlying the observed associations with cardiometabolic health.
- To accomplish sleep equity across racial and ethnic minority populations, who disproportionately experience sleep disparities, there is a need to design research studies and interventions to address the multiple layers of social determinants that contribute to sleep disparities.

CLINICS CARE POINTS

- With the consistent data linking poor sleep to adverse cardiometabolic conditions and the documented high prevalence of poor sleep and sleep disorders, clinicians should consider briefly screening patients for sleep disorders.
- Clinicians should be aware that as women age, they are specifically at a greater risk for insufficient sleep and certain sleep disorders (eg, insomnia).
- More research is needed to understand better if women are more susceptible biologically to the adverse effects of poor sleep and sleep disturbances or if observed differences are due to societal factors.