ORIGINAL ARTICLE

Short Sleep Duration Increases Metabolic Impact in Healthy Adults: A Population-Based Cohort Study

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Objectives: The metabolic impact of inadequate sleep has not been determined in healthy individuals outside laboratories. This study aims to investigate the impact of sleep duration on five metabolic syndrome components in a healthy adult cohort.

Methods: A total of 162 121 adults aged 20–80 years (men 47.4%) of the MJ Health Database, who were not obese and free from major diseases, were recruited and followed up from 1996 to 2014. Sleep duration and insomnia symptoms were assessed by a self-administered questionnaire. Incident cases of five metabolic syndrome components were identified by follow-up medical examinations. Cox proportional hazard ratios (HRs) were calculated for three sleep duration categories "< 6 hours/day (short)," "6–8 hours/day (regular)," and "> 8 hours/day (long)" with adjustment for potential confounding factors. Analyses were stratified by insomnia symptoms to assess whether insomnia symptoms modified the association between sleep duration and metabolic syndrome.

Results: Compared to regular sleep duration, short sleep significantly ($p < .001$) increased the risk for central obesity by 12% (adjusted HR 1.12 [1.07–1.17]), for elevated fasting glucose by 6% (adjusted HR 1.06 [1.03–1.09]), for high blood pressure by 8% (adjusted HR 1.08 [1.04–1.13]), for low high-density lipoprotein–cholesterol by 7% (adjusted HR 1.07 [1.03–1.11]), for hypertriglyceridemia by 9% (adjusted HR 1.09 [1.05–1.13]), and for metabolic syndrome by 9% (adjusted HR 1.09 [1.05–1.13]). Long sleep decreased the risk of hypertriglyceridemia (adjusted HR 0.89 [0.84–0.94]) and metabolic syndrome (adjusted HR 0.93 [0.88–0.99]). Insomnia symptoms did not modify the effects of sleep duration.

Conclusions: Sleep duration may be a significant determinant of metabolic health.

Keywords: diabetes, dyslipidemia, hypertension, metabolic syndrome, obesity, sleep duration.

Statement of Significance

There has been a long-standing debate whether sleep duration is a determinant of cardiometabolic disease or a sign of comorbid conditions because previous studies did not exclude participants with pre-existing diseases that can affect both sleep duration and metabolic health, such as hyperthyroidism and hypothyroidism. To our knowledge, this is the first and largest prospective study reporting the metabolic impact of inadequate sleep duration in healthy individuals beyond the impact of comorbidities. Our findings provide strong evidence that short sleep duration is a significant risk factor of cardiometabolic disease, which emphasize the necessity for including sleep recommendations in future guidelines for optimal health.

INTRODUCTION

We spend one-third of our lifetime sleeping. Sleep is functionally important for cognitive performance[1] and homeostasis of the cardiovascular,[2] endocrine,[3] and immune systems.[3] However, the length of sleep has been significantly reduced due to the 24-hour lifestyle in modern society. Over the past 40 years, the prevalence of sleep shorter than 6 hours per day increased by more than 20% in the United States. The National Health and Nutrition Examination Survey 2005–2008 reported more than one-third of adults slept less than 7 hours per night.[4] Similar phenomenon was observed in Taiwan. The average sleep duration of adults was 6.3 hours per day according to the National Health Interview Survey in 2009.[5] Short sleep duration has been associated with poor quality of life, injuries, and death.[6] Sleep curtailment has become a growing public health problem.

Nevertheless, the impact of sleep curtailment on metabolic health has not been examined longitudinally across the lifespan in a large cohort. Previous epidemiological studies[7–11] estimating adverse metabolic effects of inadequate sleep were conducted in relatively small samples and did not screen their participants for comorbid conditions that can affect both sleep duration and metabolic health, such as hyperthyroidism and hypothyroidism. Inclusion of participants with these conditions created a significant amount of uncontrolled confounding, and thus made it difficult to ascertain whether inadequate sleep is a determinant of metabolic disorders or a sign of comorbid disease. Insomnia symptoms were also reported to be associated with an increased risk of cardiometabolic disease[12]; however, the effects of insomnia symptoms have also not been considered in previous studies that assessed the association between sleep duration and metabolic health. Therefore, we investigated the prospective association of sleep duration with the incidence of five metabolic syndrome components in a healthy population, taking insomnia symptoms into account.

METHODS

Study Population

Health information were collected from an ongoing population-based cohort of 570 414 adults (up to December 2014) who participated in a standard medical screening programme conducted by the MJ Health Management Institution in Taiwan. Through a paid membership, every participant was encouraged to visit the Institution periodically and received a comprehensive screening for obesity (general and central), impaired fasting glucose (IFG) and diabetes, dyslipidemia, hypertension and other cardiovascular disease, stroke, thyroid disease (hyperthyroidism or hypothyroidism), asthma and chronic obstructive pulmonary disease, chronic kidney disease, hepatitis and liver cirrhosis, and

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cancer. The detailed information of the MJ Health Database has been published previously[13] and can be accessed through the website of the MJ Health Research Foundation.[14] From 1996 to 2014, 162 121 participants aged 20–80 years (men 47.4%), who did not have any of the aforementioned conditions determined by their first medical screening, were included in this study. These participants visited the MJ Health Management Institute and received medical screening for at least two times. All participants provided information on sleep. Most participants (98.7%) visited the Institution for medical screening on a yearly basis. The number of visits ranged from 2 to 19.

The ethics approval of the present study was obtained from the Joint Chinese University of Hong Kong and New Territories East Cluster Clinical Research Ethics Committee in Hong Kong (No. 2015.672). All participants gave written informed consent when they joined the medical screening programme at the MJ Health Management Institution. Personal identification was removed and remained anonymous when data were released for the purpose of research.

Data Collection

All participants were asked to report their demographic information, sleep condition, physical activity levels, cigarette smoking, alcohol consumption, and history of physician-diagnosed diseases through a self-administered questionnaire at every visit. Information from the first visit was used to investigate the association between sleep and metabolic health. There were two questions regarding sleep in the questionnaire. One question asked the participants to report the usual amount of time they slept per day ("How many hours do you usually sleep a day?") with answer categories "<4 hours," "4–6 hours," "6–8 hours," and ">8 hours." Since only a small number of participants (n = 1173, 0.7% of study population) slept less than 4 hours per day, these participants were grouped with those slept for 4–6 hours per day. All results were reported in the three categories of sleep duration; that is, "< 6 hours/day," "6–8 hours/day," and "> 8 hours/day." The other question asked the participants to describe their sleep quality ("How is your sleep condition in the last month?") using one or more of the following response options: "Difficulty initiating sleep," "Difficulty maintaining sleep," "Feeling of non-restorative sleep," "Use of sleeping pills," and "Sleep well". According to the diagnostic criteria by the American Psychiatric Association,[15] participants were considered as having insomnia symptoms if they reported one or more of the symptoms above.

Baseline status of IFG and diabetes, dyslipidemia, hypertension, thyroid disease (hyperthyroidism or hypothyroidism), asthma, chronic obstructive pulmonary disease, chronic kidney disease, hepatitis, liver cirrhosis, and cancer was determined through both self-reported physician diagnosis in the questionnaire and objective medical assessment. Physical and biomedical examinations were conducted by trained professionals. Height and weight were measured with participants wearing light indoor clothing without shoes using an anto-anthropometer (Nakamura KN-5000A, Tokyo, Japan). The waist circumference was measured at the midway between the top of hip bone and the bottom of ribs. The body mass index (BMI) was calculated as body weight (in kilograms) divided by the square of body height (in meters). After sitting for at least 5 minutes, systolic (SBP) and diastolic blood pressures (DBP) were measured on the right arm using an auto-sphygmomanometer (Citizen CH-5000, Tokyo, Japan). If the SBP was greater than or equal to 140 mmHg or DBP was greater than or equal to 90 mmHg, a second measurement was conducted after 10 minutes, and the data from the second measurement were used for data analysis. Blood, urine, and stool samples were collected and tested after an overnight fasting for 12 hours. Fasting plasma glucose (FPG), total cholesterol (TC), high (HDL-C) and low density lipoprotein–cholesterols, and triglycerides (TGs) were measured in plasma enzymatically with autoanalyzer (Hitachi 7150, Tokyo, Japan). Thyroid stimulating hormone, creatinine, liver enzymes, markers of hepatitis, and cancer were tested in plasma to exclude participants with hyperthyroidism, hypothyroidism, chronic kidney disease, liver disease, or cancers. Urinary protein was tested to exclude participants who were susceptible to impaired kidney function. Fecal occult blood was tested to exclude participants who were susceptible to colorectal cancer. Lung function test was used to exclude participants with asthma or chronic obstructive pulmonary disease. Ultrasonography of carotid artery, breast, and abdomen was conducted to exclude participants who were susceptible to atherosclerosis, cirrhosis, or tumor in breast or abdomen.

Outcome Ascertainment

There were a total of six outcomes (metabolic syndrome and its five components) in the present study. Central obesity, high blood pressure, elevated fasting glucose (IFG and diabetes), low HDL-C, high TGs, and metabolic syndrome were defined according to the Joint Interim Statement of the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute on Metabolic Syndrome.[16] Central obesity was defined as waist circumference over 80 cm in women and over 90 cm in men. High blood pressure was defined as SBP greater than or equal to 130 mmHg and/or DBP greater than or equal to 85 mmHg. Participants were classified as normal (FPG < 5.6 mmol/L), IFG (5.6 ≤ FPG < 7.0 mmol/L), and diabetes (FPG ≥ 7.0 mmol/L). Low HDL-C was identified with HDL-C levels lower than 1.3 mmol/L in females and less than 1.0 mmol/L in males. TGs higher than or equal to 1.7 mmol/L were classified as high TGs. Presence of any three of the above five components constitutes a diagnosis of metabolic syndrome. After the baseline assessment at their first visit, all participants were followed up, and the outcomes were identified by medical assessments during the subsequent visits. Censoring took place as the first occurrence of the outcomes or the last visit if the outcomes did not occur.

Statistical Analysis

Baseline characteristics of participants were presented as number with percentage for categorical variables and mean with standard deviation for continuous variables. The incidence rate of metabolic syndrome and its five components was reported as the number of new cases per 1000 person-years. The following three Cox proportional hazards models were used to estimate the impact of sleep duration on metabolic health, and the results were reported as hazard ratios (HRs) (95% confidence

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intervals): Model 1 was adjusted for sex (female, male) and age (continuously); Model 2 was additionally adjusted for socioeconomic and lifestyle factors, including education levels (with or without Bachelor degree), marital status (single, married/cohabiting, divorced/widowed), smoking (never, ever), alcohol drinking (frequency: <1/week, ≥1/week), and leisure-time physical activity (no/light activity, moderate activity, vigorous activity); and Model 3 was additionally adjusted for biomedical risk factors, including BMI (continuously), waist circumference (continuously), SBP (continuously), DBP (continuously), FPG (continuously), TC to HDL-C ratio (continuously), and TG (continuously). Stratified analyses by insomnia symptoms were conducted to assess the influence of insomnia symptoms on the association between sleep duration and metabolic health. The proportional hazard assumption was examined by plotting the Kaplan-Meier survival curves and by Schoenfeld residuals. There was no evidence against the proportionality assumption. We examined whether the association of sleep duration and metabolic health varied between women and men by adding sex interaction term to the fully adjusted models (Model 3). No evidence of effect modification by sex was found (all p values for interaction terms >.05), and combined results for both sexes were presented. All statistical analyses were performed using STATA version 14.0 software (Stata Corporation, College Station, TX). A two-tailed p value <.05 was considered to be statistically significant.

We also conducted two sensitivity analyses to evaluate the robustness of our findings: (1) we excluded cases identified in the first 3 years of follow-up and repeated the analyses to address potential reverse causality; and (2) we restricted the analyses to participants aged 50 years or younger at their first visit to test if the observed association of sleep duration and metabolic health was due to aging.

RESULTS

Participant Characteristics

Table 1 shows the baseline characteristics of the study population across three categories of sleep duration. From 1996 to 2014, 85 255 women (52.6%) and 76 866 men (47.4%) participated in this study, which contributed to 787 983 person-years of observation. Among them, 18.6 % were short sleepers (<6 hours/day), 72.8% were regular sleepers (6–8 hours/day, referent), and 8.6% were long sleepers (>8 hours/day). More than half of the participants (57.6%) reported that they had insomnia symptoms. More short sleepers took sleeping pills (1.2%) compared to regular sleepers (0.5%). There was no significant difference in demographic and cardiovascular risk factors among participants of the three categories of sleep duration at baseline.

Sleep Duration and Metabolic Health

Among the 162 121 participants, 15 834 became overweight and obese (BMI ≥ 25 kg/m^2), and the incidence rate of overweight and obesity in the entire cohort was 23.1 (22.7–23.4) per 1000 person-years. The incidence rate increased by more than 20% in short sleepers (28.4 [27.5–29.5] per 1000 person-years). Compared with regular sleep duration, short sleep duration was associated with an increase of 18% (adjusted HR 1.18 [1.12–1.23]) in risk of overweight and obesity and led to a 12% (adjusted HR 1.12 [1.07–1.17]) increase in risk of becoming centrally obese during the follow-up period (Table 2). Furthermore, short sleepers were more likely to develop high blood pressure (adjusted HR 1.08 [1.04–1.13]), IFG and diabetes (adjusted HR 1.06 [1.03–1.09]), low HDL-C (adjusted HR 1.07 [1.03–1.11]), hypertriglyceridemia (adjusted HR 1.09 [1.05–1.13]), and metabolic syndrome (adjusted HR 1.09 [1.05–1.13]) compared to regular sleepers (all p < .001). Sleep duration longer than 8 hours was associated with a decreased risk of hypertriglyceridemia (adjusted HR 0.89 [0.84–0.94]) and metabolic syndrome (adjusted HR 0.93 [0.88–0.99]).

We conducted a stratified analysis to determine whether the association between sleep duration and metabolic health was modified by insomnia symptoms (Table 3). About two-thirds of short sleepers reported that they had insomnia symptoms at baseline. The unadjusted incidence rates of central obesity, IFG and diabetes, hypertriglyceridemia, and metabolic syndrome appeared to be a bit higher in short sleepers without insomnia symptoms than those with insomnia symptoms. After adjusting for sex, age, and other covariates (Model 3), the HRs of short sleep duration for metabolic syndrome and its five components were similar among participants with and without insomnia symptoms. The association of short sleep duration and metabolic syndrome was not modified by insomnia symptoms (All p for homogeneity of HRs >.05). However, long sleep duration appeared to be protective against metabolic syndrome only in participants without insomnia symptoms.

Sensitivity Analysis

Two sensitivity analyses were conducted to assess whether the association between short sleep duration and metabolic syndrome was due to reverse causality. First, we excluded incident cases in the first 3 years of follow-up and found that short sleep duration remained significantly associated with elevated risk of developing overweight/obesity (adjusted HR 1.15 [1.08–1.23]), central obesity (adjusted HR 1.12 [1.05–1.19]), high blood pressure (adjusted HR 1.10 [1.03–1.17]), IFG and diabetes (adjusted HR 1.06 [1.01–1.10]), low HDL-C (adjusted HR 1.07 [1.00–1.14]), hypertriglyceridemia (adjusted HR 1.07 [1.01–1.14]), and metabolic syndrome (adjusted HR 1.10 [1.04–1.16]) (Table 4). Second, we excluded participants older than 50 at baseline (21 953 participants, 13.5% of study population) and also found that the association of short sleep duration and the risk of metabolic syndrome was similar to those observed in the entire study population (Table 5). Long sleep duration remained to be associated with a decreased risk of hypertriglyceridemia, but there was no effect on metabolic syndrome after excluding participants older than 50.

DISCUSSION

Metabolic health is largely dependent on behavioral factors and their interactions with the genetic makeup. Sleep represents another important modifiable behavioral factor in addition to diet and physical activity. Investigating the prospective association between sleep duration and major metabolic traits in a healthy population helps us understand to what extent the length of sleep is able to modulate the accumulation of metabolic impact with minimum interference from reverse causality and residual confounding due to comorbidities. To the best of

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Table 1—Baseline Characteristics of All Participants, by Sleep Duration.

Characteristic	Sleep duration, hours/day			
	All	<6	6–8	>8
All participants	162 121	30 092 (18.6%)	118 023 (72.8%)	14 006 (8.6%)
Sex				
Women	85 255 (52.6%)	15 573 (51.8%)	61 117 (51.8%)	8565 (61.2%)
Men	76 866 (47.4%)	14 519 (48.3%)	56 906 (48.2%)	5441 (38.9%)
Age				
20–30 years	54 449 (33.6%)	9307 (30.9%)	40 103 (34.0%)	5039 (36.0%)
31–40 years	59 245 (36.5%)	9433 (31.4%)	44 983 (38.1%)	4829 (34.5%)
41–50 years	26 474 (16.3%)	5269 (17.5%)	19 124 (16.2%)	2081 (14.9%)
>50 years	21 953 (13.5%)	6083 (20.2%)	13 813 (11.7%)	2057 (14.7%)
Education				
Primary school or lower	15 397 (9.5%)	4266 (14.2%)	9370 (7.9%)	1761 (12.6%)
Secondary school	41 837 (25.8%)	7543 (25.1%)	29 238 (24.8%)	5056 (36.1%)
Tertiary or above	104 787 (64.6%)	18 259 (60.7%)	79 352 (67.3%)	7176 (51.3%)
Marital status				
Single	51 608 (32.7%)	9743 (33.4%)	37 884 (32.9%)	3981 (29.2%)
Married or cohabited	99 383 (63.0%)	17 592 (60.4%)	72 812 (63.3%)	8979 (65.8%)
Divorced or widowed	6806 (4.3%)	1817 (6.2%)	4301 (3.7%)	688 (5.0%)
Physical activity				
No or light activity	117 830 (72.7%)	22 130 (73.5%)	84 732 (71.8%)	10 968 (78.3%)
Moderate activity	28 408 (17.5%)	5004 (16.6%)	21 512 (18.2%)	1892 (13.5%)
Vigorous activity	15 883 (9.8%)	2958 (9.8%)	11 779 (10.0%)	1146 (8.2%)
Ever smokers	41 870 (26.8%)	8367 (28.9%)	29 585 (26.0%)	3918 (29.4%)
Regular drinkers	29 578 (19.2%)	5987 (21.0%)	20 651 (18.3%)	2940 (22.3%)
Insomnia symptoms				
No	67 467 (42.4%)	11 050 (37.6%)	50 383 (43.4%)	6034 (44.0%)
Yes	91 585 (57.6%)	18 305 (62.4%)	65 591 (56.6%)	7689 (56.0%)
Body mass index (kg/m^2)	22.7 ± 3.5	23.2 ± 3.6	22.6 ± 3.4	22.2 ± 3.5
Waist circumference (cm)				
Women	70 ± 7.8	71.3 ± 8.3	69.7 ± 7.6	69.7 ± 8.1
Men	81.7 ± 8.8	82.3 ± 9.2	81.5 ± 8.6	81.2 ± 9.1
Systolic blood pressure (mmHg)	116.0 ± 15.8	117.4 ± 16.5	115.8 ± 15.6	114.7 ± 16.2
Diastolic blood pressure (mmHg)	70.5 ± 10.6	70.9 ± 10.8	70.4 ± 10.6	70.2 ± 10.6
Pulse (bpm)	73.3 ± 10.2	71.7 ± 10.1	72.3 ± 10.2	73.4 ± 10.3
Fasting plasma glucose (mmol/L)	5.3 ± 0.8	5.4 ± 0.9	5.3 ± 0.7	5.3 ± 0.9
Total cholesterol (mmol/L)	4.9 ± 0.9	5.0 ± 0.9	4.9 ± 0.9	4.9 ± 0.9
HDL-C (mmol/L)				
Women	1.5 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	1.5 ± 0.4
Men	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3

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Table 1—*Continued*

Characteristic	Sleep duration, hours/day			
	All	<6	6–8	>8
LDL-C (mmol/L)	3.0 ± 0.8	3.1 ± 0.8	3.0 ± 0.8	3.0 ± 0.8
Triglycerides (mmol/L)	1.2 ± 1.0	1.3 ± 1.0	1.2 ± 1.0	1.2 ± 0.9

Baseline characteristics of participants are presented as number (%) for categorical variables and mean ± standard deviation for continuous variables.
HDL-C = high density lipoprotein–cholesterol; LDL-C = low density lipoprotein–cholesterol.

our knowledge, this is the largest prospective cohort study of healthy individuals that has addressed this topic. After 787 983 person-years of follow-up, we observed that sleep duration less than 6 hours per day significantly increased the risk of developing general obesity, central obesity, IFG and diabetes, high blood pressure, low HDL-C, hypertriglyceridemia, and metabolic syndrome. The risk of metabolic syndrome associated with short sleep was essentially the same between participants with and without insomnia symptoms and was not attenuated by excluding either early cases identified in the first 3 years of follow-up or participants older than 50. Additionally, we also found that sleep duration longer than 8 hours in healthy adults was associated with reduced risks of hypertriglyceridemia and metabolic syndrome.

Comparison With Previous Studies

The associations between sleep duration and obesity, high blood pressure, dyslipidemia, hyperglycemia, and metabolic syndrome were examined separately in various populations but the evidence remained inconclusive. Short sleep duration was associated with obesity in most cross-sectional[9,17] and longitudinal studies,[18] while five cohort studies found no effect of sleep duration on weight gain.[18] A summary of 17 cross-sectional and six prospective studies reported that short sleep duration (≤5–7 hours per night) was associated with a higher risk of both prevalent and incident hypertension in participants younger than 65 years but not in older participants.[19] Although China Health and Nutrition Survey reported short sleep duration (<6 hours/day) was associated with higher prevalence of hypertriglyceridemia in women,[20] another survey of 7100 healthy adults in Taiwan did not observe any association between sleep and dyslipidemia.[21] Both short and long sleep duration were linked to an increased risk of diabetes[22] and metabolic syndrome,[7–11] but some investigations suggested that long sleep duration was an indication rather than a determinant of underlying disease.[23,24]

Compared to the aforementioned studies, the present study has the following strengths. First, many previous studies were conducted in a cross-sectional manner which might be prone to reserve causality. Prospective cohort design with a large sample size enables the present study to determine the temporal direction of sleep-disease association with sufficient power to yield an unbiased result by adjusting for a comprehensive set of potential confounders. Second, previous studies did not exclude participants with pre-existing comorbidities. This limited their ability to dissect the role of sleep from the influence of comorbid conditions such as hyperthyroidism that affects both sleep and metabolic health. The present study screened all participants for major chronic disease and only included participants without these conditions and thus was able to evaluate the effects of sleep duration beyond the impact of comorbid disorders. As a result of selecting a healthy population and modeling with comprehensive adjustments for confounding factors, the HRs of sleep duration in the present study were lower than those in the previous studies. Our results remained unchanged after excluding early cases identified in the first 3 years of follow-up, which further confirmed that these findings were not due to reverse causality or affected by residual confounding. Third, many of the previous studies did not take into account insomnia symptoms and sleep medications. Insomnia symptoms are highly prevalent in individuals with short sleep duration. More than half of participants in the present study had insomnia symptoms. The association between sleep duration and metabolic syndrome cannot be properly interpreted without taking insomnia symptoms into account. In the present study, stratified analyses by insomnia symptoms demonstrated that the association between short sleep duration and metabolic syndrome were similar among participants with and without insomnia symptoms.

Potential Mechanisms for the Observed Associations

Several potential mechanisms underlying how curtailed sleep contributes to the impact of metabolic health have been suggested by many experimental studies. Sleep curtailment may contribute to obesity, diabetes, dyslipidemia, hypertension, and metabolic syndrome via pathophysiological changes in neuroendocrine and autonomous nervous systems as well as via behavior alterations in food intake and physical activity.[25,26] The pathophysiological responses to acute sleep reduction were first demonstrated by Spiegel et al.[25,27] who showed that sleep restriction led to decrease of glucose tolerance. Restriction of sleep to 4 hours per night was associated with a reduction of 30% in glucose clearance[25] and an elevation of 22% in endogenous hepatic glucose production.[27] Later studies conducted by Cedernaes et al.[28,29] showed that sleep restriction impaired both fasting and postprandial insulin sensitivity. Potential underlying mechanisms include alterations in gut microbiota,[29] epigenetic, and transcriptional profile of core circadian clock genes.[30] Spiegel et al.[31] also reported that sleep restriction to 4 hours per night led to a 28% increase in ghrelin and an 18% decrease in leptin in healthy men, resulting in reduced fat oxidation.[32,33] Overactive sympathetic nervous system and high levels of catecholamines due to sleep restriction can also increase blood pressure and heart rate.[34] In addition to these pathophysiological changes, sleep curtailment contributes to adverse

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Table 2—Hazard Ratios (95% CI) of Incident Metabolic Syndrome by Sleep Duration.

Metabolic component	Sleep duration, hours/day					
	<6		6–8		> 8	
Central obesity						
Case/person-years	4336/126 873		14 509/564 526		1780/70 649	
Incidence rate	34.2	(33.2–35.2)	25.7	(25.3–26.1)	25.2	(24.1–26.4)
Model 1	1.20	(1.16–1.25) §	1.00		1.01	(0.97–1.07)
Model 2	1.21	(1.17–1.25) §	1.00		0.99	(0.94–1.04)
Model 3	1.12	(1.07–1.17) §	1.00		1.01	(0.94–1.08)
High blood pressure						
Case/person-years	3737/133 600		12 729/581 556		1476/72 827	
Incidence rate	28.0	(27.1–28.9)	21.9	(21.5–22.3)	20.3	(19.3–21.3)
Model 1	1.11	(1.07–1.15) §	1.00		0.95	(0.90–1.00)
Model 2	1.12	(1.07–1.16) §	1.00		0.95	(0.90–1.01)
Model 3	1.08	(1.04–1.13) §	1.00		1.02	(0.95–1.09)
IFG and diabetes						
Case/person-years	7566/102 319		28 888/449 398		3341/57 506	
Incidence rate	73.9	(72.3–75.6)	64.3	(63.5–65.0)	58.1	(56.2–60.1)
Model 1	1.07	(1.05–1.10) §	1.00		0.95	(0.92–0.98) ‡
Model 2	1.09	(1.06–1.12) §	1.00		0.96	(0.92–0.99) †
Model 3	1.06	(1.03–1.09) §	1.00		0.97	(0.93–1.02)
Low HDL-C						
Case/person-years	4803/80 665		18 455/343 436		2150/38 760	
Incidence rate	59.5	(57.9–61.3)	53.7	(53.0–54.5)	55.5	(53.2–57.9)
Model 1	1.05	(1.01–1.08) ‡	1.00		1.04	(1.00–1.09)
Model 2	1.05	(1.01–1.08) ‡	1.00		1.02	(0.97–1.06)
Model 3	1.07	(1.03–1.11) §	1.00		0.99	(0.94–1.05)
High triglycerides						
Case/person-years	4701/119 025		17 479/510 836		1952/64 308	
Incidence rate	39.5	(38.4–40.6)	34.2	(33.7–34.7)	30.4	(29.0–31.7)
Model 1	1.08	(1.05–1.12) §	1.00		0.97	(0.92–1.01)
Model 2	1.09	(1.05–1.12) §	1.00		0.94	(0.90–0.99) †
Model 3	1.09	(1.05–1.13) §	1.00		0.89	(0.84–0.94) §
Metabolic syndrome						
Case/person-years	5083/126 945		17 570/555 349		1984/69 659	
Incidence rate	40.0	(39.0–41.2)	31.6	(31.2–32.1)	28.5	(27.3–29.8)
Model 1	1.14	(1.11–1.18) §	1.00		0.95	(0.91–1.00) †
Model 2	1.15	(1.12–1.19) §	1.00		0.94	(0.89–0.98) ‡
Model 3	1.09	(1.05–1.13) §	1.00		0.93	(0.88–0.99) †

Incidence rates were calculated as rates per 1000 person-years.
Model 1: adjusted for age and sex;
Model 2: adjusted for age, sex, education, marital status, smoking, alcohol drinking, leisure-time physical activity;
Model 3: adjusted for age, sex, education, marital status, smoking, alcohol drinking, leisure-time physical activity, body mass index, waist circumference, systolic and diastolic blood pressure, fasting plasma glucose, total- and HDL-cholesterol ratio, and triglycerides.
†$p < .05$; ‡$p < .01$; §$p < .001$.
CI = confidence interval; HDL-C = high density lipoprotein–cholesterol; IFG = impaired fasting glucose.

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Table 3—Hazard Ratios (95% CI) of Incident Metabolic Syndrome by Sleep Duration and Insomnia.

Metabolic component	Participants without insomnia symptoms						Participants with insomnia symptoms					
	Sleep duration, hours/day						Sleep duration, hours/day					
	<6		6–8		>8		<6		6–8		>8	
Central obesity												
Case/person-years	1718/47 175		6735/235 960		899/29 557		2532/77 519		7543/321 432		841/40 101	
Incidence rate	36.4	(34.7–38.2)	28.5	(27.9–29.2)	30.4	(28.5–32.5)	32.7	(31.4–34.0)	23.5	(22.9–24.0)	21.0	(19.6–22.4)
Hazard ratio	1.14	(1.06–1.21) §	1.00		1.09	(0.99–1.20)	1.10	(1.03–1.16) ‡	1.00		0.93	(0.84–1.03)
High blood pressure												
Case/person-years	1438/50 652		5799/245 891		721/30 921		2212/80 578		6732/328 201		717/40 878	
Incidence rate	28.4	(27.0–29.9)	23.6	(23.0–24.2)	23.3	(21.7–25.1)	27.5	(26.3–28.6)	20.5	(20.0–21.0)	17.5	(16.3–18.9)
Hazard ratio	1.09	(1.02–1.17) §	1.00		1.01	(0.92–1.12)	1.06	(1.00–1.13) †	1.00		1.04	(0.94–1.14)
IFG and diabetes												
Case/person-years	2917/38 092		13 041/185 411		1 518/23 719		4469/62 551		15 428/258 587		1755/32 967	
Incidence rate	76.6	(73.8–79.4)	70.3	(69.1–71.6)	64.0	(60.9–67.3)	71.4	(69.4–73.6)	59.7	(58.7–60.6)	53.2	(50.8–55.8)
Hazard ratio	1.05	(1.00–1.10) †	1.00		0.94	(0.88–1.00)	1.07	(1.03–1.11) ‡	1.00		1.00	(0.94–1.06)
Low HDL-C												
Case/person-years	1791/30 705		7935/145 759		945/16 605		2898/48 389		10 212/192 801		1170/21 524	
Incidence rate	58.3	(55.7–61.1)	54.4	(53.3–55.7)	56.9	(53.4–60.7)	59.9	(57.7–62.1)	53.0	(51.9–54.0)	54.4	(51.3–57.6)
Hazard ratio	1.08	(1.02–1.15) ‡	1.00		1.03	(0.95–1.12)	1.06	(1.01–1.11) †	1.00		0.96	(0.90–1.04)
High triglycerides												
Case/person-years	1901/44 100		7881/211 328		891/27 007		2709/72 766		9351/292 797		1025/36 410	
Incidence rate	43.1	(41.2–45.1)	37.3	(36.5–38.1)	33.0	(30.9–35.2)	37.2	(35.9–38.7)	31.9	(31.3–32.6)	28.2	(26.5–29.9)
Hazard ratio	1.11	(1.05–1.18) §	1.00		0.90	(0.83–0.98) †	1.06	(1.01–1.12) †	1.00		0.87	(0.81–0.95) ‡
Metabolic syndrome												
Case/person-years	2021/47 442		8279/232 167		992/29 264		2953/77 293		9019/316 100		950/39 448	
Incidence rate	42.6	(40.8–44.5)	35.7	(34.9–36.4)	33.9	(31.9–36.1)	38.2	(36.9–39.6)	28.5	(27.9–29.1)	24.1	(22.6–25.7)
Hazard ratio	1.08	(1.02–1.15) §	1.00		0.91	(0.84–0.99) †	1.09	(1.03–1.15) ‡	1.00		0.93	(0.85–1.01)

Incidence rates were calculated as rates per 1000 person-years.
Hazard ratios were adjusted for age, sex, education, marital status, smoking, alcohol drinking, leisure-time physical activity, body mass index, waist circumference, systolic and diastolic blood pressure, fasting plasma glucose, total- and HDL-cholesterol ratio, and triglycerides (Model 3).
†$p < .05$; ‡$p < .01$; §$p < .001$.
CI = confidence interval; HDL-C = high density lipoprotein–cholesterol; IFG = impaired fasting glucose.

modification of diet and physical activity. Sleep deprivation has been shown to increase food intake in order to compensate the energy needed for extended wakening time in a number of laboratories studies.[25,26] An increased level of the orexigenic hormone ghrelin and a decreased level of the anorexigenic hormone leptin were also associated with increased appetite and food consumption.[25,31,35] Moreover, individuals with sleep deprivation were more likely to consume larger portion of meals and high-energy foods.[25,36] Sleep restriction to roughly 4 hours per night was estimated to increase energy intake by 20%.[37,38] These behavioral changes may partially result in activation of brain reward and food-sensitive centers by sleep loss.[39,40] Meanwhile, short sleepers are less likely to engage in physical activity and more likely to have sedentary lifestyle.[41–43]

Mechanisms underlying the association between long sleep duration and metabolic health are unclear. Previous studies suggested comorbidity[23,24] is a key causal intermediate factor for the association between long sleep duration and adverse health events. In this study, we eliminated the impact of comorbidity by choosing healthy participants. We observed that sleep duration longer than 8 hours was protective against hypertriglyceridemia and metabolic syndrome. This is in contrast to most previous studies which found adverse effects or no associations. There may be different mechanisms that can explain the protective effects of long sleep duration. The recommended sleep duration for optimal health by the US National Sleep Foundation is 7–9 hours per night for people <65 years old. We speculated that a large proportion of the

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Table 4—Hazard Ratios (95% CI) of Incident Metabolic Syndrome by Sleep Duration With Exclusion of Early Cases Identified Within the First 3 Years.

Metabolic component	Sleep duration, hours/day					
	<6		6–8		>8	
Central obesity						
Case/person-years	1864/103 543		6862/474 602		856/60 245	
Incidence rate	18.0	(17.2–18.8)	14.5	(14.1–14.8)	14.2	(13.3–15.2)
Hazard ratio	1.12	(1.05–1.19) §	1.00		0.98	(0.90–1.08)
High blood pressure						
Case/person-years	1865/109 477		6783/490 004		786/62 434	
Incidence rate	17.0	(16.3–17.8)	13.8	(13.5–14.2)	12.6	(11.7–13.5)
Hazard ratio	1.10	(1.03–1.17) ‡	1.00		1.03	(0.94–1.12)
IFG and diabetes						
Case/person-years	3533/80 364		14 523/364 457		1772/47 548	
Incidence rate	44.0	(42.5–45.4)	39.0	(39.2–40.5)	37.3	(35.6–39.0)
Hazard ratio	1.06	(1.01–1.10) †	1.00		0.96	(0.90–1.02)
Low HLD-C						
Case/person-years	1624/61 800		6624/271 057		772/31 217	
Incidence rate	26.3	(25.0–27.6)	24.4	(23.9–25.0)	24.7	(23.9–26.5)
Hazard ratio	1.07	(1.00–1.14) †	1.00		0.97	(0.89–1.05)
High triglycerides						
Case/person-years	1978/96 154		8032/423 692		943/54 296	
Incidence rate	20.6	(19.7–21.5)	19.0	(18.5–19.4)	17.4	(16.3–18.5)
Hazard ratio	1.07	(1.01–1.14) †	1.00		0.87	(0.80–0.95) ‡
Metabolic syndrome						
Case/person-years	2271/102 562		8468/462 747		943/59 093	
Incidence rate	22.1	(21.3–23.1)	18.3	(17.9–18.7)	16.0	(15.0–17.0)
Hazard ratio	1.10	(1.04–1.16) ‡	1.00		0.87	(0.80–0.94) ‡

Incidence rates were calculated as rates per 1000 person-years.
Hazard ratios were adjusted for age, sex, education, marital status, smoking, alcohol drinking, leisure-time physical activity, body mass index, waist circumference, systolic and diastolic blood pressure, fasting plasma glucose, total- and HDL-cholesterol ratio, and triglycerides (Model 3).
†$p < .05$; ‡$p < .01$; §$p < .001$.
CI = confidence interval; HDL-C = high density lipoprotein–cholesterol; IFG = impaired fasting glucose.

participants defined as long sleepers at the present study (>8 hours/day) might be within the recommended range of sleep duration (8–9 hours/day), and thus, we could not distinguish the effects of duration greater than 9 hours. Besides, mental health conditions are closely related to long sleep duration, but we did not collect information on mental health in this study. Further studies that take mental health conditions into account are warranted.

Limitations of the Present Study

Apart from the strengths highlighted above, there are several limitations in the present study. First, findings from a cohort study are not as robust as those from a randomized controlled trial. Since metabolic syndrome is a chronic condition that takes time to develop, it is neither practical nor ethically acceptable to put a group of healthy people under a hazard exposure (sleep curtailment) for years, let alone decades. For this reason, an observational prospective study in relatively young healthy individuals would be the closest to an ideal study design to evaluate the long-term health impact of sleep curtailment. Second, like other large-scale population studies, we used self-reported sleep duration rather than objective sleep measurement by actigraphy or polysomnography due to the high cost incurred and logistic difficulties of using sleep monitoring devices for over 100,000 individuals. Self-reported total sleep time recorded by a single question is correlated well with a 1-week sleep diary ($r = 0.79$),[44] moderately correlated with actigraphy record ($r = 0.48$–0.52)[45,46] but weakly correlated with polysomnography data ($r = 0.18$).[46] The discrepancy between

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Table 5—Hazard Ratios (95% CI) of Incident Metabolic Syndrome by Sleep Duration With Exclusion of Participants Older Than 50 Years.

Metabolic component	Sleep duration, hours/day					
	<6		6–8		>8	
Central obesity						
Case/person-years	3175/106 376		11 847/517 090		1330/64 174	
Incidence rate	29.8	(28.8–30.9)	22.9	(22.5–23.3)	20.7	(19.6–21.9)
Hazard ratio	1.13	(1.08–1.19) §	1.00		0.99	(0.92–1.07)
High blood pressure						
Case/person-years	2475/114 623		9838/538 096		1035/66 656	
Incidence rate	21.6	(20.8–22.5)	18.3	(17.9–18.6)	15.5	(14.6–16.5)
Hazard ratio	1.07	(1.02–1.13) †	1.00		1.04	(0.96–1.13)
IFG and diabetes						
Case/person-years	6000/87 829		25 303/416 417		2825/52 957	
Incidence rate	68.3	(66.6–70.1)	60.8	(60.0–61.5)	53.3	(51.4–55.3)
Hazard ratio	1.06	(1.03–1.10) §	1.00		0.98	(0.93–1.02)
Low HDL-C						
Case/person-years	3818/69022		16 222/315 437		1828/35 025	
Incidence rate	55.3	(53.6–57.1)	51.4	(50.6–52.2)	52.2	(49.9–54.6)
Hazard ratio	1.06	(1.02–1.11) ‡	1.00		0.98	(0.93–1.04)
High triglycerides						
Case/person-years	3687/98 428		15 098/465 101		1646/58 279	
Incidence rate	37.5	(36.3–38.7)	32.5	(31.9–33.0)	28.2	(26.9–29.6)
Hazard ratio	1.10	(1.05–1.14) §	1.00		0.92	(0.86–0.98) ‡
Metabolic syndrome						
Case/person-years	4004/66 323		16 726/304 862		1901/34 020	
Incidence rate	60.4	(58.5–62.3)	54.9	(54.0–55.7)	55.9	(53.4–58.4)
Hazard ratio	1.09	(1.04–1.13) §	1.00		0.99	(0.94–1.05)

Incidence rates were calculated as rates per 1000 person-years.
Hazard ratios were adjusted for age, sex, education, marital status, smoking, alcohol drinking, leisure-time physical activity, body mass index, waist circumference, systolic and diastolic blood pressure, fasting plasma glucose, total- and HDL-cholesterol ratio, and triglycerides (Model 3).
†$p < .05$; ‡$p < .01$; §$p < .001$.
CI = confidence interval; HDL-C = high density lipoprotein–cholesterol; IFG = impaired fasting glucose.

self-reported (sleep questionnaire and diary) and objective (actigraphy and polysomnography) measures of sleep may be ascribed to the small sample size and adaptation effects of polysomnography. More importantly, this discrepancy may reflect that psychological perception of sleep/awake state is somehow different from the physiological sleep/awake thresholds defined by body movements and electroencephalogram. Self-reported sleep duration may represent a combination of psychological and physiological estimation of sleep behavior and thus might be more useful for identifying individuals under both psychological and biological stress. Nevertheless, both self-reported and objective short sleep duration were associated with increased cardiometabolic risk.[47,48] Third, the prevalence of insomnia symptoms was assessed by a simple question that was useful for large-scale screening programme but did not account for severity, frequency, duration, or association with daytime functioning of the symptoms. Fourth, due to the lack of multiple assessments of sleep and insomnia symptoms, we were not able to capture the longitudinal changes of sleep condition and its immediate health impact. Fifth, our study did not evaluate the role of sleep apnea in the association between sleep duration and metabolic health. A previous study in adults with obstructive sleep apnea showed that short sleepers had higher risk for hypertension than regular sleepers (odds ratio: 1.66 [1.16–2.38]),[49] suggesting that short sleep duration contributes to extra risk in addition to sleep apnea. Further prospective investigation in large-population cohort is warranted to distinguish the effects of sleep duration and apnea. Finally, although we have adjusted for a large number of confounding factors in our models, some potential confounders were not included, such as variability in weekday-weekend sleep,

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contraceptive use, hormonal replacement therapy, household income, or number of children in the household.

CONCLUSIONS

This study demonstrates that short sleep duration is associated with increased risk of metabolic syndrome in healthy individuals. It supports sleep duration as a significant determinant of metabolic health. Identification of individuals with sleep curtailment and promotion of sleep hygiene with an emphasis on optimal sleep duration should be included in any population health strategy for reducing metabolic impact for an entire population.

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DISCLOSURE STATEMENT

The authors declare that they have no conflict of interest.

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