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Irregular sleep and all-cause mortality: a large prospective cohort study

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Corresponding Author:	Teruhide Koyama Kyoto Prefectural University of Medicine Kyoto, JAPAN
First Author:	Chie Omichi
Order of Authors:	Chie Omichi
	Teruhide Koyama
	Hiroshi Kadotani
	Etsuko Ozaki
	Satomi Tomida
	Tamami Yoshida
	Jun Otonari
	Hiroaki Ikezaki
	Megumi Hara
	Keitaro Tanaka
	Takashi Tamura
	Mako Nagayoshi
	Rieko Okada
	Yoko Kubo
	Isao Oze
	Keitaro Matsuo
	Yohko Nakamura
	Miho Kusakabe
	Rie Ibusuki
	Kenichi Shibuya
	Sadao Suzuki
	Miki Watanabe
	Kiyonori Kuriki
	Naoyuki Takashima
	Aya Kadota
	Sakurako Katsuura-Kamano
	Kokichi Arisawa
	Kenji Takeuchi
	Kenji Wakai
	the J-MICC Study Group

Abstract:	Objectives: Previous studies using objective parameters have shown that irregular sleep is associated with the disease incidence, progression, or mortality. This study aimed to determine the association between subjective sleep duration and sleep regularity, with mortality in a large population. Methods: Participants were from the Japan Multi-Institutional Collaborative Cohort study. We obtained information from each participant on sleep duration, sleep regularity, and demographics and overall lifestyle using self-administered questionnaires. We defined sleep regularity according to participants' subjective assessment of sleep/wake time regularity. Participants (n=81,382, mean age : 58.1±9.1years, males: 44.2%) were classified into six groups according to sleep duration and sleep regularity. Hazard ratios (HR) for time-to-event of death were calculated using the Cox proportional hazards model. Results: The mean follow-up period was 9.1 years and the mean sleep duration was 6.6 h/day. Irregular sleep significantly increased the risk of all-cause mortality in all models compared with regular sleep (HR 1.30, 95% confidence interval; CI, 1.18-1.44), regardless of sleep duration. Multivariable analysis of the six groups by sleep pattern (sleep regularity and duration) showed irregular sleep and sleep durations of <6 h/day, 6 to <8 h/day, or ≥8 h/day were associated with a 1.2-1.5-fold increases in mortality, compared to regular sleep and sleep duration of 6 to <8 h/day. Conclusions: Our study shows an association between sleep irregularity and all-cause mortality in a large Japanese population. Our findings provide further confirmation of the need to consider not only sleep duration, but also the regularity aspect of sleep schedules.
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Chie Omichi[1,2,3], PhD, Teruhide Koyama[1], PhD, Hiroshi Kadotani[2], PhD, MD, Etsuko Ozaki[1], PhD, Satomi Tomida[1,4], PhD, MD, Tamami Yoshida[1], MS, Jun Otonari[5,6], PhD, MD, Hiroaki Ikezaki[7,8], PhD, MD, Megumi Hara[9], PhD, MD, Keitaro Tanaka[9], PhD, MD, Takashi Tamura[10], PhD, Mako Nagayoshi[10], PhD, Rieko Okada[10], PhD, MD, Yoko Kubo[10], BA, Isao Oze[11], PhD, MD, Keitaro Matsuo[11,12], PhD, MD, Yohko Nakamura[13], PhD, Miho Kusakabe[13], DVM, Rie Ibusuki[14], PhD, Kenichi Shibuya[14,15], MD, Sadao Suzuki[16], PhD, MD, Miki Watanabe[16], PhD, Kiyonori Kuriki[17], PhD, Naoyuki Takashima[18,19], PhD, MD, Aya Kadota[18], PhD, MD, Sakurako Katsuura-Kamano[20], PhD, Kokichi Arisawa[20], PhD, MD, Kenji Takeuchi[10], PhD, DDS, Kenji Wakai[10], PhD, MD, and the J-MICC Study Group

[1]Department of Epidemiology for Community Health and Medicine, Kyoto Prefectural University of Medicine, Kyoto 602-8566, Japan

[2]Department of Psychiatry, Shiga University of Medical Science, Shiga 520-2192, Japan

[3]Department of Hygiene and Public Health, Osaka Medical and Pharmaceutical University, 20-7, daigaku-machi, Takatsuki, 569-8686, Japan.

[4]Department of Endocrine and Breast Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan

[5]Department of Psychosomatic Medicine, Graduate School of Medical Sciences, Kyushu University

[6]Department of Psychosomatic Medicine, International University of Health and Welfare Narita Hospital

[7]Department of General Internal Medicine, Kyushu University Hospital

[8]Department of Comprehensive General Internal Medicine, Kyushu University Faculty of Medical Sciences

[9]Department of Preventive Medicine, Faculty of Medicine, Saga University

[10]Department of Preventive Medicine, Nagoya University Graduate School of Medicine

[11]Division of Cancer Epidemiology and Prevention, Aichi Cancer Center Research Institute

[12]Division of Cancer Epidemiology, Nagoya University Graduate School of Medicine

[13]Cancer Prevention Center, Chiba Cancer Center Research Institute

[14]Department of International Island and Community Medicine, Kagoshima University Graduate School of Medical and Dental Sciences

[15]Department of Emergency, Kagoshima Prefectural Oshima Hospital

[16]Department of Public Health, Nagoya City University Graduate School of Medical Sciences

[17]Laboratory of Public Health, Division of Nutritional Sciences, School of Food and Nutritional Sciences, University of Shizuoka

[18]Department of Public Health, Shiga University of Medical Science

[19]Department of Public Health, Kinki University Faculty of Medicine

[20]Department of Preventive Medicine, Tokushima University Graduate School of Biomedical Sciences

*Corresponding author: Teruhide Koyama

Department of Epidemiology for Community Health and Medicine, Kyoto Prefectural University of Medicine

465 Kajii-cho, Kamigyo-ku, Kyoto 602-8566, Japan

E-mail: tkoyama@koto.kpu-m.ac.jp

Tel: +81-75-251-5789

Fax: +81-75-251-5799

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Abstract

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Methods: Participants were from the Japan Multi-Institutional Collaborative Cohort study. We obtained information from each participant on sleep duration, sleep regularity, and demographics and overall lifestyle using self-administered questionnaires. We defined sleep regularity according to participants' subjective assessment of sleep/wake time regularity. Participants (n=81,382, mean age: 58.1±9.1years, males: 44.2%) were classified into six groups according to sleep duration and sleep regularity. Hazard ratios (HR) for time-to-event of death were calculated using the Cox proportional hazards model.

Results: The mean follow-up period was 9.1 years and the mean sleep duration was 6.6 h/day. Irregular sleep significantly increased the risk of all-cause mortality in all models compared with regular sleep (HR 1.30, 95% confidence interval; CI, 1.18-1.44), regardless of sleep duration. Multivariable analysis of the six groups by sleep pattern (sleep regularity and duration) showed irregular sleep and sleep durations of <6 h/day, 6 to <8 h/day, or ≥8 h/day were associated with a 1.2-1.5-fold increases in mortality, compared to regular sleep and sleep duration of 6 to <8 h/day.

Conclusions: Our study shows an association between sleep irregularity and all-cause mortality in a large Japanese population. Our findings provide further confirmation of the need to consider not only sleep duration, but also the regularity aspect of sleep schedules.

Keywords

sleep regularity, all-cause mortality, sleep duration

Introduction

Sleep duration and timing are considered components of sleep health. Buysee et al. defined sleep health as a multidimensional pattern of sleep-wakefulness, that was adapted to individual, social, and environmental demands. Sleep health promotes physical and mental well-being and good sleep health is characterized by subjective satisfaction, appropriate timing, adequate duration, high efficiency, and sustained alertness during waking hours[1].

In recent years, many studies have shown that either too little or too much sleep increases the risk of mortality from all-causes[2] , cardiovascular disease (CVD)[3,4] and cancer[2,5]. In addition, several studies have shown that greater variability in sleep duration and timing is associated with an abnormal metabolic profile, including elevated blood pressure, dysregulation of blood lipids, and insulin resistance[6,7]. A meta-analysis of prospective cohort studies suggested a U-shaped curvilinear association with the lowest risk of all-cause mortality when sleep duration was about 7 h/day; both shorter and longer sleep duration were associated with an increased risk of all-cause mortality[8].

One factor affecting health is disruption of circadian rhythms. Recent reports indicate that chronic circadian rhythm disturbances are ubiquitous exposures that affect health that accumulate over time[9,10, 11]. Social and environmental factors that disrupt circadian rhythms include shift work, which has been linked to CVD[12,13] and breast cancer[14].

Previous studies have shown that irregular sleep pattern is as detrimental to health as inadequate sleep[15-18]. Taylor et al. examined the relationship between variability in sleep timing and metabolic health in non-shift workers in a cohort study in women[17]. They assessed sleep behaviors in midlife women (aged 48–58 years) using diary-reported bedtimes and wake times. They showed frequent shifts in sleep timing may be related to metabolic health among non-shift working midlife women. Thus, irregular sleep/wake timing may affect metabolic health, even in individuals who have never worked the night shift[15,17]. In addition, we reported from the Japan Multi-Institutional Collaborative Cohort (J-MICC) Study that irregular sleep was associated with metabolic syndrome. The study showed that irregular sleep was more strongly associated with metabolic syndrome than sleep duration or bedtime[19].

Tianyi H et al. found from a cohort study using actigraphy that irregular sleep might be a new risk factor for CVD, independent of traditional CVD risk factors and the quantity and quality of sleep[12]. Thus, although an association between CVD and irregular sleep has been shown, there are still only a few epidemiological studies on the association between regularity in sleep, other diseases, and mortality, as assessed by subjective.

To objectively assess sleep regularity, the timing and duration of sleep over multiple nights must be assessed, often quantified by the use of actigraphy over several days[6,17]. However, few large cohort studies have investigated the association between subjective regular sleep timing and mortality. The aim of this study was to determine the association between subjective sleep time and sleep regularity, respectively or in combination, with mortality in a large Japanese population.

Participants and Methods

Study participants

We included participants from the J-MICC Study, a large cohort study designed to identify and evaluate gene-environment interactions in the context of lifestyle-related diseases[20]. The participants were individuals aged 35 through 69 years, living in Japan. At the time of the baseline survey, from 2004–2014, the participants completed questionnaires and provided peripheral blood samples. The baseline study participants were recruited from 14 different regions throughout Japan. The study participants were enrolled from the community by mailing invitation letters or distributing leaflets (3 areas), or by recruiting patients at their first visit to a cancer hospital (1 area) or at health checkups (6 areas) [20,21] . Information of participants' deaths were collected from the baseline visit (2004–2014) through December 2017 or December 2018. The dataset used in the present study was fixed on September 1st, 2021, "ver.20210901".

In total, 92,527 individuals participated across 14 cities in Japan. Those with complete information on age, sex, body mass index (BMI), drinking and smoking status, physical activity, history of ischemic heart disease, cancer and stroke, average sleep duration, regularity of sleeping pill use (once a week), and sleep regularity were selected (n = 85,845). Those with a follow-up period of 365 days or less (n = 1,497) and those who regularly used sleeping pills (n = 2,966) were excluded, resulting in 81,382 participants across 13 cities for analysis (35,965 men and 45,417 women). Participants in the analytic sample did not differ significantly to those in the full dataset.

Written informed consents were obtained from all study participants. The study protocol was approved by the ethics committees at the Nagoya University Graduate School of Medicine (IRB No. 2010-939) and other institutions participating in the J-MICC study. This study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki.

Data collection and measurements

At enrollment, a self-administered questionnaire was distributed to all subjects and included questions common to all study areas; a table summarizing common questions covering basic characteristics, lifestyle, and clinical characteristics was provided in the article by Takeuchi et al [20] . We used a standardized self-administered questionnaire to obtain information about each participant's sleep duration (h/day), sleep regularity, education (high school graduate or less, beyond high school, missing), smoking and drinking status (never, former, or current), and daily physical activity duration. Physical activity was assessed in terms of metabolic equivalents (METs), as previously reported[22]. METs-hours per day of activity was estimated by multiplying the reported daily time spent in each activity by the relevant MET intensity.

Information on endpoints such as death was collected through resident cancer registries, if available, lists of patients at major hospitals in the study area, mailed questionnaires to participants, questionnaires at checkups at physical examination facilities, death certificate notes, information from health insurance data, and secondary survey questionnaires[23]. The causes of death were confirmed by vital statistics data based on death certificates, with permission from the Ministry of Health, Labour and Welfare, Japan. Participants who moved out of the study region were excluded from the follow-up at the time of their exit.

Groups by sleep duration and regularity

Detailed information regarding sleep was collected using a questionnaire. Habitual sleep duration was assessed by asking the following question: “How many hours do you usually sleep? With regard to sleep regularity, the question “Are your bedtimes and wake times regular?” was asked, and the answer was either “regular” or “irregular.”

Participants were classified into six groups according to sleep duration (<6 h/day, 6 to <8 h/day, ≥8 h/day) and sleep regularity (regular, irregular). We additionally performed stratified analyses by sex and age (≥ 60, < 60 years old).

Statistical analyses

Differences in baseline characteristics between the sleep duration and regularity groups were assessed using the chi-squared test or analysis of variance (ANOVA). Hazard ratios (HRs) by sleep duration or regularity (and their 95% confidence intervals) were calculated using the Cox proportional hazards model. Using the 6 to <8 h/day and regular sleep group as a reference, the HRs for the other five groups were calculated.

Model 1 was adjusted for age, sex, BMI, and study city. Model 2 was adjusted for age, sex, BMI, study city, education, physical activity, alcohol consumption, and smoking status. Model 3 was adjusted for age, sex, BMI, study city, education, physical activity, alcohol consumption, smoking status, history of ischemic heart disease, history of stroke, and history of cancer. Statistical significance was set at $p < 0.05$. All data were analyzed using the SPSS version 25 (IBM Corp, Armonk, NY).

Results

Baseline characteristics

Of the 92,527 participants, 81,382 were analyzed. Their mean sleep duration was 6.6 (standard deviation [SD] 1.0) h/day. The total follow-up period was 736,319 person-years, with a mean follow-up of 9.01 years. The mortality rate was 4.59 (cases per 1000 person-years).

The baseline characteristics of the participants, stratified by sleep regularity and sleep duration, are shown in Table 1. The age (mean: 58.1 years, SD: 9.1) and proportion of males (54.9%) were significantly higher in the regular and ≥8 h/day sleep group ($p<0.001$). Mortality rate (per 1,000 person-years) was highest in the irregular and ≥8 h/day sleep group.

The highest proportion of current smokers was observed in the irregular and ≥8 h/day sleep group (28.8%, $p<0.001$), and the highest proportion of people with regular alcohol consumption was observed in the regular and ≥8 h/day sleep group (59.2%, $p<0.001$).

Association of sleep duration and sleep regularity with mortality

The results of the multivariable analysis of all-cause mortality according to the variables in the three models (adjusted HR [95%CI]) are shown in Table 2. The results showed that irregular sleep significantly increased the risk of all-cause mortality in all models, compared with regular sleep (Model 3, HR 1.30, 95%CI: 1.18-1.44). Similarly, there was a significantly increased risk of all-cause mortality with a sleep duration ≥8 h/day in all models, compared with a duration of 6 to <8 h/day (Model 3, HR 1.15, 95%CI: 1.05-1.25). By gender, male had a significantly increased risk of all-cause mortality in all models, regardless of age (Model 3, All age: HR 1.31, 95%CI: 1.16-1.48). Female had a significantly increased risk of all-cause mortality in all models only if they were under 60 years of age (Model 3, HR 1.35, 95%CI: 1.06-1.73).

The results of multivariable analysis in the six groups by sleep pattern (sleep regularity and duration) are shown in Table 3. In models 1 and 2, the HRs for all groups were significantly higher than that for the regular and 6 to <8 h/day sleep group. In model 3, the HRs for the regular and ≥8 h/day sleep group (HR 1.14, 95%CI: 1.04-1.24), irregular and <6 h/day sleep group (HR 1.21, 95%CI 1.02-1.44), irregular and 6 to <8 h/day sleep group (HR 1.23, 95%CI 1.09-1.40), and irregular and ≥8 h/day sleep group (HR 1.52, 95%CI 1.18-1.96) were significantly increased, compared with the regular and 6 to ≥8 h/day sleep group.

Discussion

In this large prospective study of approximately 80,000 adult Japanese men and women, it was confirmed that irregular sleep and sleep duration ≤6 h/day, irregular sleep and sleep duration 6 to <8 h/day, or irregular sleep and sleep duration ≥8 h/day were associated with a 1.2-1.5-fold increases in mortality, compared to a regular and sleep duration of 6 to <8 h/day. To the best of our knowledge, our study is the first to demonstrate an association between subjective irregular sleep and all-cause mortality.

There has been a great deal of research on sleep duration and health. Shorter sleep duration has been associated with cognitive decline[24], obesity[25], type 2 diabetes[25], increased risk of CVD, motor vehicle accidents and early death[26], as well as psychiatric disorders[27].

In some large-scale prospective studies of adult men and women, there was a robust U-shaped relationship between sleep duration and all-cause mortality, with a nadir at 7 hours of sleep per day[4,28]. According to a systematic review and meta-analysis of prospective studies of sleep duration and mortality, short sleepers (commonly <7 h per night, often <5 h per night) have a 12% greater risk, and long sleepers (commonly >8 or 9 h per night) have a 30% greater risk of dying than those sleeping 7 to 8 h per night[29].

In other studies, only short sleep duration was associated with mortality. Several cohort studies objectively measured sleep duration using polysomnography (PSG) to assess the association between short sleep, insomnia and mortality. The Sleep Heart Health Study reported that short sleep duration only, not insomnia or poor sleep as defined using PSG, was significantly associated with all-cause mortality[30]. Also, the Penn State Cohort previously reported that insomnia with objective short sleep duration was associated with increased mortality in men[31].

Although many studies have reported that short sleep duration is associated with all-cause mortality, our study showed sleep duration of >8 h/day had a risk for mortality. Our study shows that sleep regularity and sleep duration were independently associated with all-cause mortality. It also shows that, when only sleep duration was considered, sleep duration ≥8 h/day was associated with all-cause mortality, while sleep duration <6 h/day was not associated. Our report is consistent with results of another recent Japanese cohort study by Svensson T et al. which found that all-cause mortality was associated with sleep duration ≥8 h/day but not with <7h/day in both men and women in the multivariable adjusted analysis[32] . The reasons why these results are different from those of others might be due to methodological differences[32], such as population, size, and adjusting covariates.

Sleep is multidimensional, and it is not limited to sleep duration, which is important for health and performance. The components of sleep depend not only on sleep duration but also sleep-wake cycle [27,33]. A previous study of sleep regularity indexes suggested that sleep timing and regularity were as important to health and performance as sleep duration[34]. Thus, consistent associations have been reported between irregular sleep and adverse mental and physical health outcomes, such as increased BMI, weight gain, affective disorders, insomnia, and general sleep deprivation [35]. Furthermore, it has been reported that irregular sleep may cause CVD, metabolic syndrome, and diabetes risks, independent of the effect of insufficient sleep[19,36,37]. In summary, regularity of sleep-wake patterns is also considered important in health promotion independent of sleep duration. In this study, a similar trend was confirmed by showing the relationship between all-cause mortality and sleep irregularity using a subjective assessment of sleep regularity.

Subjective assessment of sleep, along with objective assessment, is considered an important indicator and is essential in clinical practice[38]. No significant differences were reported between subjective sleep duration asked in the questionnaire and sleep diary[39] or even objective sleep duration measured by sleep encephalography[40]. Our study was an epidemiological study of a large population, and the outcome was mortality. Therefore, we needed a large sample size, and we considered that a simple subjective assessment using a questionnaire would be beneficial. In our study, we could not determine the cause of their irregular sleep, but asked a broad question, “Are your bedtimes and waking times regular?” Therefore, this irregularity includes those due to shift work, discrepancies in sleep time between work and free days, and subjective judgments by individuals in lifestyles that do not have such forms. We observed an association between a simple self-assessment of “not regular” and mortality.

Our study has several strengths, including the use of a prospective design, a large sample of about 80,000 men and women, mortality as outcome, comprehensive baseline information, and variables that are adjustable for lifestyle and activity levels. There has been no cohort study of this size investigating the association between sleep regularity and mortality; the study covered 13 cities in Japan.

There are several limitations that merit consideration. First, the study was limited to a single ethnic group and the findings may not be generalizable to others. Second, we did not investigate the degree or frequency of irregularities. We used subjective questions whether waking and sleeping times were regular. On the other hand, subjective question was also an advantage because it did not require a device and can be used for a large number of participants. Third, the validity of the information concerning sleep irregularity, which was acquired using subjective questionnaires, has not been established; in addition, we did not have data on individual timing preference or morningness-eveningness and we could not determine the cause of their irregular sleep. However, we consider that their versatility, including their many meanings, makes them suitable for application in future epidemiological studies. Forth, we did not have the history of sleep disorders and other chronic illnesses (i.e., HIV, Alzheimer's) and did not use these items in the analysis. Finally, our study is still ongoing, and the number of deaths was small at this stage. We were not able to report the causes of death at this time due to the small number of deaths, but we will be following this population and analyzing the causes of death in the future.

Conclusions

The findings of our study revealed an association between sleep irregularity and all-cause mortality in a large Japanese population. Our findings provide further confirmation of the need to assess not only sleep duration, but also the regularity aspect of sleep schedules in evaluating mortality risk.

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The authors declare that they have no conflicts of interest.

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Table 1. Baseline characteristics and follow-up data according to sleep pattern

	Regular sleep						Irregular sleep						
Sleep duration	<6 h/day		6 to <8 h/day		≥8 h/day		<6 h/day		6 to <8 h/day		≥8 h/day		p-value
n (%)	9,458	11.6	50,618	62.2	11,538	14.2	3,112	3.8	5,775	7.1	881	1.1	
Age, years, mean (SD)	54.6	9.5	55.1	9.2	58.1	9.1	53.1	9.6	53.4	9.4	54.6	10.0	<0.001
Sex, man, n (%)	3,727	39.4%	21,571	42.6%	6,336	54.9%	1,221	39.2%	2,642	45.7%	468	53.1%	<0.001
Death	379		1,858		662		142		274		61		
Person-years	85,082		457,795		105,242		27,939		52,279		7,982		
Mortality rate (per 1,000 person-years)	4.5		4.1		6.3		5.1		5.2		7.6		
BMI, kg/m^2 (SD)	23.0	3.5	22.8	3.2	23.0	3.2	23.7	3.7	23.5	3.5	23.5	3.5	0.121
Smoking status, n (%)													
Current	1,481	15.7%	7,795	15.4%	2,164	18.8%	729	23.4%	1,440	24.9%	254	28.8%	
Past	1,944	20.6%	11,183	22.1%	3,217	27.9%	567	18.2%	1,174	20.3%	213	24.2%	<0.001
Never	6,033	63.8%	31,640	62.5%	6,157	53.4%	1,816	58.4%	3,161	54.7%	414	47.0%	
Alcohol consumption, n (%)													
Current	4,951	52.3%	27,256	53.8%	6,834	59.2%	1,540	49.5%	3,137	54.3%	518	58.8%	
Past	267	2.8%	1,238	2.4%	361	3.1%	108	3.5%	173	3.0%	37	4.2%	<0.001
Never	4,240	44.8%	22,124	43.7%	4,343	37.6%	1,464	47.0%	2,465	42.7%	326	37.0%	
Physical activity (METs・hours/day)(SD)	15.1	13.6	14.1	12.4	15.7	13.8	15.5	13.9	14.9	13.5	13.5	13.0	1.000
Education, n (%)													
Missing	3,688	12.1%	19,939	65.3%	3,448	11.3%	1,099	3.6%	2,076	6.8%	280	0.9%	
High school graduate or less	2,316	12.1%	11,548	60.2%	3,089	16.1%	723	3.8%	1,258	6.6%	233	1.2%	<0.001
Beyond high school	3,454	10.9%	19,131	60.4%	5,001	15.8%	1,290	4.1%	2,411	7.7%	368	1.2%	
History of ischemic heart disease, n (%)													
Current	147	1.6%	697	1.4%	236	2.0%	60	1.9%	76	1.3%	22	2.5%	<0.001

Past	109	1.2%	560	1.1%	139	1.2%	44	1.4%	68	1.2%	17	1.9%	
Never	9,202	97.3%	49,361	97.5%	11,163	96.7%	3,008	96.7%	5,631	97.5%	842	95.6%	
History of cancer, n (%)													
Current	222	2.3%	1,308	2.6%	376	3.3%	110	3.5%	167	2.9%	28	3.2%	
Past	334	3.5%	1,723	3.4%	430	3.7%	87	2.8%	153	2.6%	33	3.7%	<0.001
Never	8,902	94.1%	47,587	94.0%	10,732	93.0%	2,915	93.7%	5,455	94.5%	820	93.1%	
History of stroke, n (%)													
Current	70	0.7%	273	0.5%	107	0.9%	14	0.4%	32	0.6%	7	0.8%	
Past	98	1.0%	471	0.9%	150	1.3%	26	0.8%	55	1.0%	14	1.6%	<0.001
Never	9,290	98.2%	49,874	98.5%	11,281	97.8%	3,072	98.7%	5,688	98.5%	860	97.6%	

SD, standard deviation; BMI, body mass index; METs, metabolic equivalents

Table 2. Hazard ratios and their confidence intervals for mortality according to sleep regularity and sleep duration

							<60 years			≥60 years		
				HR	95%CI	p-value	HR	95%CI	p-value	HR	95%CI	p-value
All												
	Model 1	Irregular sleep		1.39	1.26-1.54	<0.001	1.37	1.18-1.60	<0.001	1.24	1.09-1.42	<0.001
			<6 h/day	1.10	1.00-1.22	0.830	0.88	0.75-1.03	0.100	0.94	0.83-1.06	0.300
		Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
			≥8 h/day	1.25	1.15-1.36	<0.001	1.21	0.99-1.48	0.070	1.04	0.91-1.20	0.560
	Model 2	Irregular sleep		1.31	1.19-1.45	<0.001	1.29	1.11-1.50	0.001	1.16	1.02-1.33	0.030
			<6 h/day	1.09	0.99-1.20	0.085	1.12	0.95-1.31	0.170	1.05	0.93-1.19	0.440
		Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
			≥8 h/day	1.17	1.08-1.28	<0.001	1.36	1.16-1.59	<0.001	1.08	0.98-1.19	0.140
	Model 3	Irregular sleep		1.30	1.18-1.44	<0.001	1.33	1.14-1.55	<0.001	1.15	1.00-1.31	0.044
			<6 h/day	1.08	0.98-1.19	0.133	1.14	0.97-1.33	0.110	1.03	0.91-1.17	0.600
		Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
			≥8 h/day	1.15	1.05-1.25	0.002	1.31	1.11-1.53	0.001	1.06	0.96-1.17	0.260
Male												
	Model 1	Irregular sleep		1.40	1.23-1.58	0.001	1.34	1.11-1.63	0.003	1.42	1.21-1.65	<0.001
			<6 h/day	0.82	0.73-0.92	0.001	0.13	0.62-0.95	0.770	0.85	0.74-0.99	0.035
		Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
			≥8 h/day	0.93	0.81-1.07	0.301	0.95	0.74-1.24	0.730	0.93	0.79-1.09	0.360
	Model 2	Irregular sleep		1.31	1.16-1.47	<0.001	1.26	1.04-1.53	0.020	1.32	1.13-1.54	0.001
		Sleep duration	<6 h/day	1.20	1.06-1.35	0.003	1.25	1.02-1.54	0.030	1.15	0.99-1.33	0.070
			6 to <8 h/day	Reference			Reference			Reference		

		≥8 h/day	1.10	0.99-1.22	0.078	1.21	0.99-1.48	0.070	1.04	0.93-1.18	0.480
Model 3	Irregular sleep		1.31	1.16-1.48	<0.001	1.30	1.07-1.58	0.007	1.31	1.12-1.52	0.001
		<6 h/day	1.18	1.05-1.33	0.007	1.27	1.03-1.56	0.027	1.12	0.97-1.30	0.120
	Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
		≥8 h/day	1.08	0.97-1.19	0.160	1.16	0.95-1.42	0.150	1.03	0.91-1.16	0.650
Female											
Model 1	Irregular sleep		1.12	0.94-1.34	0.200	1.39	1.09-1.78	0.008	0.91	0.70-1.18	0.480
		<6 h/day	1.11	0.94-1.31	0.240	1.04	0.82-1.33	0.750	1.18	0.93-1.49	0.170
	Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
		≥8 h/day	1.49	1.21-1.83	<0.001	1.70	1.23-2.34	0.001	1.40	1.07-1.84	0.015
Model 2	Irregular sleep		1.08	0.91-1.29	0.370	1.34	1.05-1.71	0.021	0.89	0.68-1.15	0.360
		<6 h/day	0.90	0.76-1.06	0.200	0.96	0.75-1.22	0.720	0.84	0.66-1.06	0.140
	Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
		≥8 h/day	1.32	1.13-1.54	<0.001	1.61	1.25-2.09	<0.001	1.16	0.96-1.41	0.120
Model 3	Irregular sleep		1.06	0.89-1.27	0.510	1.35	1.06-1.73	0.016	0.86	0.66-1.11	0.250
		<6 h/day	0.90	0.76-1.07	0.240	1.00	0.79-1.28	0.970	0.83	0.66-1.05	0.120
	Sleep duration	6 to <8 h/day	Reference			Reference			Reference		
		≥8 h/day	1.28	1.10-1.49	0.020	1.59	1.23-2.05	<0.001	1.13	0.93-1.36	0.230

HR, hazard ratio; CI, confidence interval

Model 1 was adjusted for age, sex, body mass index, sleep duration, study city

Model 2 was adjusted for age, sex, body mass index, sleep duration, study city, education, physical activity, alcohol consumption, smoking status

Model 3 was adjusted for age, sex, body mass index, sleep duration, study city, education, physical activity, alcohol consumption, smoking status, history of ischemic heart disease, history of stroke, history of cancer

Table 3. Hazard ratios and their confidence intervals for mortality according to sleep pattern

		Regular sleep			Irregular sleep	
Sleep duration	<6 h/day	6 to <8 h/day	≥8 h/day	<6 h/day	6 to <8 h/day	≥8 h/day
Model 1, HR	1.14	Reference	1.19	1.33	1.34	1.71
95%CI	1.02-1.28		1.09-1.30	1.12-1.57	1.18-1.52	1.33-2.21
Model 2, HR	1.12	Reference	1.16	1.23	1.24	1.55
95%CI	1.00-1.27		1.06-1.27	1.03-1.46	1.09-1.40	1.20-2.00
Model 3, HR	1.11	Reference	1.14	1.21	1.23	1.52
95%CI	0.99-1.24		1.04-1.24	1.02-1.44	1.09-1.40	1.18-1.96

HR, hazard ratio; CI, confidence interval

Model 1 was adjusted for age, sex, body mass index, study city

Model 2 was adjusted for age, sex, body mass index, sleep duration, study city, education, physical activity, alcohol consumption, smoking status,

Model 3 was adjusted for age, sex, body mass index, sleep duration, study city, education, physical activity, alcohol consumption, smoking status, history of ischemic heart disease, history of stroke, history of cancer