

Original Contribution

Sleep Duration and Coronary Heart Disease Mortality Among Chinese Adults in Singapore: A Population-based Cohort Study

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While some studies have found a positive association between both short and long sleep durations and cardiovascular disease (CVD), others have found an association only with a long or short sleep duration. In addition, there are limited data from non-Western populations on this topic. The authors examined the association between sleep duration and coronary heart disease (CHD) mortality among Chinese adults in Singapore (1993–2006), performing a prospective cohort study among 58,044 participants aged \geq 45 years (55.9% women) without preexisting CVD. The main outcome of interest was CHD mortality (n = 1,416). The authors found both short and long sleep durations to be positively associated with CHD mortality, independent of smoking, alcohol intake, and body mass index. Compared with persons with a sleep duration of 7 hours (referent), the multivariable relative risk of CHD mortality for a sleep duration of \leq 5 hours was 1.57 (95% confidence interval: 1.32, 1.88); for a sleep duration of \geq 9 hours, it was 1.79 (95% confidence interval: 1.48, 2.17). This association persisted in subgroup analyses by sex and body mass index. In a population-based cohort of Chinese adults from Singapore, sleep durations of \leq 5 hours and \geq 9 hours (versus 7 hours) were modestly associated with CHD mortality. These results suggest that sleep duration may be an important marker for CVD.

Asian continental ancestry group; cardiovascular diseases; coronary disease; mortality; Singapore; sleep

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease.

Sleep loss, long-term sleep deprivation, and alterations in sleep duration are common in modern society (1, 2). Nearly one-third of adults report sleeping less than 6 hours per night, leading some people to suggest that we live in a sleep-deprived society (2). Factors responsible for this change may include increases in environmental light, longer workdays/commuting time, an increase in shift work and night work, and the advent of television, radio, and the Internet (3).

Experiments have demonstrated that short-term sleep deprivation in healthy subjects results in adverse physiologic changes, including decreased glucose tolerance and increased insulin resistance, sympathetic tone, and blood pressure (4, 5). Short-term sleep deprivation results in elevations in levels of C-reactive protein, an inflammatory marker that is independently related to cardiovascular disease (CVD) (6). In contrast, the long-term cardiovascular consequences of sleep deprivation are less clear. Both long and short usual sleep durations are found to be associated with snoring, metabolic disturbances, abnormalities in lipid profile, and elevated markers of inflammation (7, 8). It is possible that long and short sleep durations may be related to underlying sleep-disordered breathing and obstructive sleep apnea (9), a syndrome independently related to hypertension (10) and increased CVD risk (11). In epidemiologic studies, compared with persons reporting 7 hours of sleep per night, shorter or longer sleep durations were found to be related to increased body mass index (BMI) (12–14), diabetes mellitus (15, 16), and hypertension (17–20)—all strong predictors of subsequent development of CVD (21).

However, relatively few epidemiologic studies have examined the association between sleep duration and CVD morbidity or mortality, and several questions regarding this putative association remain unanswered. First, while

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investigators in some previous studies reported a positive association with both short and long sleep durations and CVD or total mortality (22-28), others found an independent association only with either a short (29, 30) or a long (31, 32) duration. Second, in some previous studies, researchers found a significant association between sleep duration and CVD mortality in men only, not in women (24, 32). Third, none of the previous studies provided results stratified by BMI, an important potential confounder. Furthermore, other than studies from Japan (24, 27, 28), there is a limited amount of prospective data from Asian populations, who may have lower BMIs and different lifestyles and dietary exposures in relation to CVD risk than traditional Western populations. In this context, we examined the association between usual sleep duration and coronary heart disease (CHD) mortality in a large population-based study of Chinese adults in Singapore who were free of selfreported CVD at baseline.

MATERIALS AND METHODS

Study population

The design of the Singapore Chinese Health Study has been described previously (33). Briefly, the cohort was recruited between 1993 and 1998, drawn from permanent residents or citizens of Singapore who lived in governmentbuilt housing (86% of the Singapore population resided in such facilities during the enrollment period). Men and women of Chinese ethnicity (restricted to the 2 major dialect groups, Cantonese and Hokkien) aged 45-74 years were eligible. A total of 63,257 persons (approximately 85% of eligible subjects) were enrolled. At recruitment, a face-toface interview was conducted in the subject's home by a trained interviewer using a structured, scanner-readable questionnaire. The questionnaire collected information on demographic factors, educational attainment, lifetime use of tobacco, current use of alcohol, current level of physical activity, medical history, family history of cancer, and usual sleep duration. The questionnaire included a validated, semiquantitative food frequency section listing 165 food items commonly consumed in the study population (33). The Singapore Food Composition Table (33), which we developed in conjunction with this cohort study, allowed for the estimation of intake levels of approximately 100 nutritive/ nonnutritive food components per study subject.

The study protocol followed the recommendations of the Declaration of Helsinki and was approved by the institutional review boards at the National University of Singapore and the University of Minnesota, Minneapolis, Minnesota. Written informed consent was obtained from all participants.

Exposure assessment

At the baseline examination, usual sleep duration was assessed by asking participants the following question: "On the average, during the last year, how many hours in a day did you sleep?", with the following response categories: 5 hours or less, 6 hours, 7 hours, 8 hours, 9 hours, and

10 hours or more. Age was defined as age in years at the time of the baseline examination. Education was categorized into no formal education, primary school, and secondary school or above. Cigarette smoking was classified into never smoker, former smoker, and current smoker based on the participant's choice of 3 possible responses to the question, "Have you ever smoked at least 1 cigarette a day for 1 year or longer?" Subjects who answered "no" were classified as nonsmokers; those who answered "yes, but I quit smoking" were classified as former smokers; and those who answered "yes, and I currently smoke" were classified as current smokers. Alcohol intake was assessed as grams of daily ethanol consumption. BMI was calculated as weight (kilograms) divided by the square of height (meters). Moderate physical activities included brisk walking, bowling, bicycling on level ground, tai chi, or chi kung; amounts of time spent in such activities were categorized as none, 1/2-3 hours/week, and >4 hours/week. Hypertension and diabetes mellitus were defined as a positive questionnaire response regarding a physician diagnosis of the condition. Dietary intakes of total calories, fruits, vegetables, fiber, total fat, and cholesterol were determined by means of the validated food frequency questionnaire (33). Using the questionnaire, we also collected information on weekly use of vitamin/ mineral supplements, menopausal status, and ever use of hormone replacement therapy.

CHD mortality

Deaths were identified through record linkage with the Singapore Registry of Births and Deaths. For the current analysis, we updated mortality data through December 31, 2006.

In a recent follow-up telephone/in-person interview conducted between 1999 and 2004, among the 61,685 subjects (97.5%) from whom we had contact or follow-up information (either from themselves, their next of kin, or death records), only 17 subjects (0.03%) had migrated out of Singapore. This suggests that emigration among these subjects was negligible and that vital statistics follow-up was virtually complete. Underlying causes of death were coded according to the *International Classification of Diseases*, Ninth Revision; codes 410–414, 427.5, 429.2, and 798 were used to define CHD deaths.

Out of 63,257 persons who participated in the baseline examination, we excluded subjects with cancer (n = 1,936), self-reported physician-diagnosed CHD (n = 2,402), and stroke (n = 875). This resulted in 58,044 participants who were free of cancer and clinical CVD at baseline. Among these subjects, 1,416 CHD deaths occurred by December 31, 2006.

Statistical analysis

We categorized sleep duration into 5 categories: ≤ 5 hours, 6 hours, 7 hours, 8 hours, and ≥ 9 hours. We compared selected baseline characteristics of the cohort by sleep duration categories using chi-square tests or analysis of variance, as appropriate. Cox proportional hazards regression modeling was used to estimate the relative risk and 95%

Chavastavistis	Sleep Duration, hours						
Characteristic	≤5	6	7	8	≥9		
No. of persons at risk	5,450	13,605	19,179	15,961	3,849		
Age, years	58.6 (0.10)	56.6 (0.1)	55.7 (0.1)	55.8 (0.1)	58.1 (0.1)		
Women, %	61.0	55.5	55.6	53.4	55.4		
No formal education, %	34.0	28.1	26.0	24.8	29.4		
Smoking, %							
Current smoker	19.3	19.1	19.0	20.4	22.4		
Former smoker	11.7	11.3	9.8	10.9	13.6		
Never smoker	69.0	69.6	71.2	68.7	64.0		
Alcohol intake, g/day	2.2 (0.1)	1.8 (0.1)	1.6 (0.1)	1.9 (0.1)	2.2 (0.1)		
Alcohol intake, nondrinker, %	81.9	80.6	81.4	80.2	81.9		
Body mass index ^b	23.3 (0.04)	23.1 (0.03)	22.8 (0.02)	23.1 (0.03)	23.1 (0.05)		
No weekly moderate physical activity, % ^c	77.8	77.9	79.1	78.2	77.7		
Hypertension, %	28.4	23.4	22.3	23.1	27.6		
Diabetes mellitus, %	10.8	8.6	7.6	8.9	13.3		
Total calories, kcal/day	1,515.4 (7.3)	1,554.9 (4.7)	1,548.8 (3.9)	1,575.9 (4.4)	1,580.9 (8.7)		
Fruit intake, g/day	190.0 (2.2)	204.9 (1.4)	206.3 (1.2)	203.2 (1.3)	192.7 (2.6)		
Vegetable intake, g/day	109.9 (0.8)	109.0 (0.5)	112.7 (0.4)	111.4 (0.5)	108.4 (0.8)		
Dietary fiber intake, g/day	12.4 (0.08)	12.6 (0.04)	12.8 (0.04)	12.8 (0.04)	12.5 (0.09)		
Total fat intake, g/day	43.2 (0.3)	44.1 (0.2)	43.7 (0.1)	44.5 (0.2)	44.8 (0.3)		
Cholesterol intake, mg/day	171.6 (1.4)	172.8 (0.9)	171.6 (0.7)	176.3 (0.8)	182.4 (1.6)		
Weekly use of vitamin/ mineral supplements, %	6.4	6.4	6.4	6.1	5.6		
Women only							
Menopausal, %	81.6	74.0	69.9	67.9	73.2		
Ever use of hormone replacement therapy, %	5.8	5.5	5.1	5.7	6.0		

Table 1. Baseline Characteristics of the Study Cohort, by Usual Sleep Duration, Singapore Chinese Health Study,1993–2006^a

^a Data presented are mean values (with standard deviations in parentheses) or row percentages, as appropriate.

^b Weight (kg)/height (m)².

^c Moderate physical activities included brisk walking, bowling, bicycling on level ground, tai chi, or chi kung. Amounts of time spent in such activities were categorized as none, $\frac{1}{2}$ -3 hours/week, or \ge 4 hours/week.

confidence interval for CHD mortality in each sleep duration category relative to the reference group, with adjustment made for important covariates. We chose a reference category of 7 hours per night because that is the median and modal sleep duration in the Singapore Chinese Health Study, and also to be consistent with previous research in the field (23, 31). We used 2 Cox proportional hazards models: the age- and sex-adjusted model and the multivariableadjusted model, which was additionally adjusted for dialect group (Cantonese, Hokkien), education (no formal education, primary school or below, secondary school, above secondary school), year of recruitment, BMI, smoking (current smoker, former smoker, never smoker), alcohol intake (g/day), moderate physical activity (absent, 1/2-3 hours/ week, ≥ 4 hours/week), dietary intakes of total calories (kcal/day), fruits (g/day), vegetables (g/day), fiber (g/day), total fat (g/day), and cholesterol (mg/day), weekly use of vitamin/mineral supplements (absent, present), and, among

women, menopausal status (yes, no) and ever use of postmenopausal hormone replacement therapy (never use, former use, current use). To examine the consistency of the observed association between sleep duration and CHD mortality, we performed subgroup analyses by sex and by BMI categories that were consistent with the World Health Organization BMI classification (34) for CVD risk stratification in Asian populations (<23, \geq 23).

We also performed several supplementary analyses. First, we examined the association between sleep duration and CHD mortality after excluding the first 4 years of followup, since early deaths are more likely to be biased. Second, because the observed association between sleep duration and CHD mortality may be explained by the effect of diabetes mellitus or hypertension, we performed a subgroup analysis among relatively "healthy" study subjects (n = 42,758), after excluding subjects with baseline diabetes mellitus or hypertension. Third, to examine whether the

Usual Sleep Duration, hours	No. of Persons at Risk (<i>n</i> = 58,044)	No. of Coronary Heart Disease Deaths (<i>n</i> = 1,416)	Age- and Sex-Adjusted RR	95% CI	Multivariable- Adjusted RR ^a	95% CI
≤5	5,450	177	1.74	1.49, 2.03	1.57	1.32, 1.88
6	13,605	318	1.19	1.05, 1.36	1.13	0.98, 1.31
7	19,179	402	1 (referent)		1 (referent)	
8	15,961	373	1.18	1.04, 1.33	1.12	0.97, 1.29
≥9	3,849	146	1.98	1.68, 2.33	1.79	1.48, 2.17

Table 2. Association Between Sleep Duration and Coronary Heart Disease Mortality, Singapore Chinese Health Study, 1993–2006

Abbreviations: CI, confidence interval; RR, relative risk.

^a Relative risks were adjusted for age (years); sex (men, women); dialect group (Cantonese, Hokkien); education (no formal education, primary school or below, secondary school, above secondary school); year of recruitment; body mass index (weight (kg)/height (m)²); smoking (current smoker, former smoker, never smoker); alcohol intake (g/day); moderate physical activity (none, $\frac{1}{2}$ -3 hours/week, \geq 4 hours/week); dietary intakes of total calories (kcal/day), fruits (g/day), vegetables (g/day), total fat (g/day) and cholesterol (mg/day); weekly use of vitamin/mineral supplements (absent, present); and, among women, menopausal status (yes, no) and ever use of postmenopausal hormone replacement therapy (never use, former use, current use).

observed association between sleep duration and CHD mortality is partially mediated by diabetes mellitus and hypertension, factors that are associated with both sleep duration (15, 17) and mortality (35), we additionally adjusted for these variables (absent, present) in the multivariable model and noted the effect of adjustment on the magnitude of association. Finally, we performed a stratified analysis by age category (≤ 60 years, > 60 years) to examine the consistency of the observed association by age. All analyses were conducted using SAS, version 9.2 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Among 58,044 adults aged \geq 45 years without prevalent cancer or self-reported CVD who were included in the current analysis, there were 1,416 CHD deaths. Table 1 presents the baseline characteristics of the population by sleep duration category. Thirty-three percent of eligible subjects reported sleeping 7 hours per night. Compared with persons with a 7-hour sleep duration, those with both short $(\leq 5 \text{ hours})$ and long $(\geq 9 \text{ hours})$ durations of sleep were more likely to be older, smokers, hypertensive, diabetic, postmenopausal (women only), and users of hormone replacement therapy (women only) and more likely to have no formal education, greater alcohol consumption (g/day), higher BMI, higher dietary intakes of calories, total fat, and cholesterol, and lower dietary intakes of fruits, vegetables, and fiber.

Table 2 presents the relative risk of CHD mortality by sleep duration category. Compared with persons with a sleep duration of 7 hours (referent category), both shorter and longer sleep durations were positively associated with CHD mortality in the age- and sex-adjusted model. In the multivariable-adjusted model, compared with a sleep duration of 7 hours, statistically significant associations with CHD mortality were observed for sleep durations of ≤ 5 hours and ≥ 9 hours.

To examine the consistency of the observed associations, we performed subgroup analysis by sex (Table 3) and BMI category (Table 4). Similar to the findings for the whole cohort, compared with a sleep duration of 7 hours, a statistically significant multivariable association with CHD

Table 3.	Association Between Sleep	Duration and Coronary	Heart Disease Mortality, by	Sex, Singapore C	Chinese Health Study, 1993–2006
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Usual Sleep Duration, hours	Men ($n = 25,552$)				Women (<i>n</i> = 32,492)			
	No. of Persons at Risk	No. of CHD Deaths	Multivariable- adjusted RR ^a	95% CI	No. of Persons at Risk	No. of CHD Deaths	Multivariable- adjusted RR ^a	95% CI
≤5	2,097	100	1.70	1.35, 2.15	3,353	77	1.43	1.09, 1.88
6	5,975	194	1.20	0.99, 1.45	7,630	124	1.04	0.82, 1.31
7	8,444	236	1 (referent)		10,735	166	1 (referent)	
8	7,358	226	1.10	0.92, 1.32	8,603	147	1.15	0.92, 1.44
\geq 9	1,678	90	1.88	1.48, 2.40	2,171	56	1.67	1.24, 2.27

Abbreviations: CHD, coronary heart disease; CI, confidence interval; RR, relative risk.

^a Relative risks were adjusted for age (years); dialect group (Cantonese, Hokkien); education (no formal education, primary school or below, secondary school, above secondary school); year of recruitment; body mass index (weight (kg)/height (m)²); smoking (current smoker, former smoker, never smoker); alcohol intake (g/day); moderate physical activity (none, ½–3 hours/week, ≥4 hours/week); dietary intakes of total calories (kcal/day), fruits (g/day), vegetables (g/day), fiber (g/day), total fat (g/day) and cholesterol (mg/day); weekly use of vitamin/mineral supplements (absent, present); and, among women, menopausal status (yes, no) and ever use of postmenopausal hormone replacement therapy (never use, former use, current use).

 Table 4.
 Association Between Sleep Duration and Coronary Heart Disease Mortality, by Body Mass Index^a Category, Singapore Chinese Health

 Study, 1993–2006
 1993–2006

Usual Sleep Duration, hours	Body Mass Index <23 ^b ($n = 27,995$)				Body Mass Index ≥23 ^b (<i>n</i> = 30,049)			
	No. of Persons at Risk	No. of CHD Deaths	Multivariable- adjusted RR ^c	95% CI	No. of Persons at Risk	No. of CHD Deaths	Multivariable- adjusted RR ^c	95% CI
≤5	2,492	76	1.74	1.33, 2.29	2,958	101	1.45	1.15, 1.83
6	6,408	151	1.37	1.10, 1.71	7,197	167	0.98	0.80, 1.19
7	9,349	164	1 (referent)		9,830	238	1 (referent)	
8	7,866	163	1.19	0.95, 1.47	8,095	210	1.07	0.89, 1.29
\geq 9	1,880	69	2.00	1.51, 2.65	1,969	77	1.65	1.28, 2.14

Abbreviations: CHD, coronary heart disease; CI, confidence interval; RR, relative risk.

^a Weight (kg)/height (m)².

^b Cutoffs were based on the World Health Organization classification for cardiovascular risk stratification in Asian populations (34).

^c Relative risks were adjusted for age (years); sex (men, women); dialect group (Cantonese, Hokkien); education (no formal education, primary school or below, secondary school, above secondary school); year of recruitment; body mass index; smoking (current smoker, former smoker, never smoker); alcohol intake (g/day); moderate physical activity (none, $\frac{1}{2}$ -3 hours/week, \ge 4 hours/week); dietary intakes of total calories (kcal/day), fruits (g/day), vegetables (g/day), fiber (g/day), total fat (g/day) and cholesterol (mg/day); weekly use of vitamin/mineral supplements (absent, present); and, among women, menopausal status (yes, no) and ever use of postmenopausal hormone replacement therapy (never use, former use, current use).

mortality was observed for sleep durations of ≤ 5 hours and ≥ 9 hours.

In a supplementary analysis, when we examined the association between sleep duration and CHD mortality after excluding the first 4 years of follow-up, the results were essentially similar. Compared with a sleep duration of 7 hours (referent), the relative risk was 1.10 (95% confidence interval (CI): 0.93, 1.31) for a duration of 6 hours, 1.54 (95% CI: 1.25, 1.90) for a duration of $\leq \! 5$ hours, 1.08 (95% CI: 0.91, 1.27) for a duration of 8 hours, and 1.77 (95% CI: 1.42, 2.22) for a duration of >9 hours. In a second supplementary analysis, when we reexamined the association between sleep duration and CHD mortality in the subgroup of relatively "healthy" study subjects (n = 42,758), defined as those without diabetes mellitus or hypertension, the results were essentially similar. Compared with a sleep duration of 7 hours (referent), the relative risk was 1.12 (95% CI: 0.91, 1.38) for a duration of 6 hours, 1.79 (95% CI: 1.40, 2.29) for a duration of <5 hours, 1.08 (95% CI: 0.88, 1.32) for a duration of 8 hours, and 1.62 (95% CI: 1.22, 2.16) for a duration of \geq 9 hours. In a third supplementary analysis, we additionally adjusted for diabetes mellitus and hypertension in the multivariable model; the magnitude of association was attenuated. Compared with a sleep duration of 7 hours (referent), the relative risk was 1.07 (95% CI: 0.94, 1.22) for 6 hours, 1.36 (95% CI: 1.19, 1.55) for \leq 5 hours, 1.10 (95% CI: 0.97, 1.25) for 8 hours, and 1.40 (95% CI: 1.18, 1.66) for >9 hours. Finally, we examined the association between sleep duration and CHD mortality by age. Among subjects aged ≤ 60 years (n = 40,722), compared with a sleep duration of 7 hours (referent), the relative risk was 1.17 (95% CI: 0.95, 1.44) for 6 hours, 1.62 (95% CI: 1.39, 1.88) for \leq 5 hours, 1.04 (95% CI: 0.83, 1.30) for 8 hours, and 1.43 (95% CI: 1.18, 1.73) for ≥ 9 hours. Among subjects over age 60 years (n = 17,322), compared with a sleep duration of 7 hours (referent), the relative risk was 1.06 (95% CI: 0.85, 1.32) for 6 hours, 1.39 (95% CI: 1.18, 1.64) for \leq 5 hours, 1.14

(95% CI: 0.94, 1.38) for 8 hours, and 1.82 (95% CI: 1.22, 2.72) for \geq 9 hours.

DISCUSSION

In this large, population-based cohort of Chinese adults from Singapore, we found that in comparison with a sleep duration of 7 hours, sleep durations of <5 hours and >9hours were modestly associated with CHD mortality. These associations appeared to be independent of major confounders and were consistently present in subgroup analyses by sex and BMI category. Our results contribute to the current literature on sleep duration and CVD and mortality by: 1) suggesting positive associations with both short and long sleep durations that are largely independent of sex, BMI, and other confounders and 2) demonstrating associations consistent with those of previous Western studies in an Asian population with a lower BMI and different lifestyle and dietary exposures in relation to CVD risk than Western populations. Our results also suggest that the observed association between sleep duration and CHD mortality is mediated, at least in part, by diabetes mellitus and hypertension, factors that are reported to be related to sleep duration (15, 17) and also CHD mortality (35).

In the current study, the large sample size available for analysis, the magnitude of association between sleep duration and CHD mortality, the independence of the association from traditional risk factors (including smoking, alcohol intake, and BMI), and the consistency within subgroup analyses by sex and BMI suggest that these findings are less likely to be due to chance. In addition, our results are consistent with several previous reports (22–28) (though not all (29–32)) that examined an association between sleep duration and CVD risk. It could be argued that an observed association between long sleep duration (\geq 9 hours) and CHD mortality could be due to underlying disease that caused the subjects to sleep as much as they did, suggesting an increased need for sleep and indirectly suggesting a reduced physiologic reserve, reducing their ability to survive underlying serious illness (23). Our results from supplementary analyses 1) that excluded the initial 4 years of follow-up and 2) were carried out in the subgroup of relatively "healthy" subjects without diabetes or hypertension at baseline are important in this regard. The relatively consistent findings in these analyses also point towards a true association between short and long sleep durations and CHD mortality.

Several lines of recent evidence suggest that an association between short and long sleep durations and CVD and mortality are plausible. Experiments have demonstrated that short-term sleep deprivation in healthy subjects results in adverse physiologic changes relating to CVD risk (4-6). In large epidemiologic studies, both long and short usual sleep durations are reported to be associated with snoring and with metabolic disturbances, including insulin resistance, an abnormal lipid profile, and elevated markers of inflammation (7, 8). Short sleep may be associated with increased cortisol levels and abnormal growth hormone secretion (36). Similarly, mechanisms underlying an observed association between long sleep duration and CVD and mortality may include the relation of long sleep duration to depression, depressive symptoms, and low thyroid function and the relation between long sleep duration and low socioeconomic status, all of which are independently related to CVD and mortality (37, 38). In addition, it is possible that long and short sleep durations may be a marker for underlying sleep-disordered breathing and obstructive sleep apnea (9), a syndrome that is independently related to hypertension (10) and increased CVD risk (11). Finally, in recent epidemiologic studies, compared with persons reporting 7 hours of sleep, both shorter and longer sleep durations were found to be related to increased BMI (12-14), diabetes mellitus (15, 16), and hypertension (17-20)-all strong predictors of subsequent CVD development (21).

The main advantages of the current study include its large sample size, the longitudinal follow-up, and the availability of detailed lifestyle and dietary data with which to adjust for potential confounders. Furthermore, in contrast to previous studies (22, 23) that examined sleep duration in relation to CVD risk among particular occupational groups such as US nurses, among whom shift work is common, our study subjects were selected from a general-population sample base and thus were less affected by the potentially confounding effect of shift work, a predictor of CVD (39) that can also affect sleep duration. The main limitation of this study was the lack of information on depression and depressive symptoms, a potential confounder in the association between increased sleep and CHD mortality (40). Given that the magnitude of the observed association in the current study was modest-to-weak, it is possible that further adjustment for unmeasured potential confounders such as depression, socioeconomic status variables (other than education), or body fat distribution may have substantially attenuated these findings. Second, we measured sleep duration by self-report and only at a single time point. Ferrie et al. (26) recently examined the effect of changes in sleep duration over time on mortality in the large Whitehall II cohort and showed that short sleep duration was associated with CVD mortality,

a finding consistent with our results, while long sleep duration was associated only with non-CVD mortality, a finding that contrasts with our results. It is possible that single-point assessment of sleep exposure, as in our study, may be a poor indicator of sleep debt and that changes in sleep duration over time (as in Ferrie's et al.'s study (26)) would reveal a different pattern of association. In addition, self-reported sleep duration, as opposed to objective measures of sleep duration, is prone to misclassification and may under- or overestimate the observed findings.

In conclusion, in a large population-based cohort of Chinese adults from Singapore, we found that in comparison with a sleep duration of 7 hours, sleep durations of \leq 5 hours and \geq 9 hours were modestly associated with risk of CHD mortality. This association appeared to be independent of major confounders and was consistently present in subgroup analyses carried out by sex and BMI category. These results are consistent with the hypothesis that sleep duration may be an important indicator of CVD risk.

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