

## Relationship between Duration of Sleep and Hypertension in Adults: A Meta-Analysis

Yan Wang, MD<sup>1</sup>; Hao Mei, PhD<sup>2</sup>; Yan-Rui Jiang, MD<sup>1</sup>; Wan-Qi Sun, MD<sup>1</sup>; Yuan-Jin Song, MD<sup>1</sup>; Shi-Jian Liu, PhD<sup>3</sup>; Fan Jiang, MD, PhD<sup>1</sup>

<sup>1</sup>Department of Developmental and Behavioral Pediatrics, Institute of Pediatric Translational Medicine, Shanghai Children's Medical Center affiliated Shanghai Jiaotong University School of Medicine, Ministry of Education Shanghai Key Laboratory of Children's Environmental Health, Shanghai, China; <sup>2</sup>Department of Epidemiology, Tulane University, New Orleans, LA; <sup>3</sup>Department of Bioinformatics and Clinical Epidemiology, Institute of Pediatric Translational Medicine, Shanghai Children's Medical Center affiliated Shanghai Jiaotong University School of Medicine, Shanghai, China

**Objectives:** Epidemiologic studies have shown that chronic short sleep may be associated with the development of hypertension; however, the results are controversial. This meta-analysis was conducted to determine whether the duration of sleep is associated with hypertension.

**Methods:** Reference databases (PubMed, EmBase, the Cochrane Library, Chinese Biological Medicine database) were searched for studies related to sleep duration and hypertension. Sleep duration categories ( $\leq 5$  h, 6 h, 7 h, 8 h,  $\geq 9$  h) and prevalence or incidence of hypertension in each sleep category were extracted. A general analysis and subgroup analyses stratified by gender, age, study design, and different definitions of sleep duration were conducted to evaluate the relationship between sleep duration and hypertension.

**Results:** Thirteen articles out of a total of 1,628 articles involving 347,759 participants met the inclusion criteria. A U-shaped change in pooled odds ratios (ORs) for hypertension due to

the change of sleep duration was observed. The unadjusted OR for hypertension of individuals who slept  $\leq 5$  h vs 7 h was 1.61, 95% CI = 1.28–2.02; those who slept  $\geq 9$  h vs 7 h was 1.29, 95% CI = 0.97–1.71. The pooled ORs were still significant after adjusted by age and gender. Women deprived of sleep (sleep time  $\leq 5$  h vs 7 h, OR = 1.68, 95% CI = 1.39–2.03) had a higher risk of hypertension than men (OR = 1.30, 95% CI = 0.93–1.83).

**Conclusion:** Excessively longer and shorter periods of sleep may both be risk factors for high blood pressure; these associations are stronger in women than men.

**Keywords:** sleep duration, hypertension, meta-analysis, sleep deprivation, epidemiologic study

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Sleep is an important physiological process and it takes up approximately one third of our lives. Due to the accelerated pace of modern life, the average duration of nightly sleep has decreased considerably. In Finland, the self-reported duration of sleep has decreased by about 18 min over the last 33 years.<sup>1</sup> National surveys in the U.S. have shown a 1.5- to 2-hour decline in self-reported sleep duration over the past 50 years.<sup>2</sup> The National Sleep Foundation has reported an increase from 12% to 16% of subjects sleeping less than 6 hours on workdays between 1998 and 2005.<sup>3</sup> These data suggest an emerging trend of reduced sleep, which leads to a growing sleep debt among the general population.

Sleep deprivation has long been associated with neurocognitive impairment, attenuation of physical strength and skill, and increased impaired judgment.<sup>4–7</sup> However, excessively long of sleep may also leads to injury of health. Several studies have reported an association between the duration of sleep and chronic conditions, including type 2 diabetes, obesity, atherosclerosis, and hypertension.<sup>8–10</sup> The associations between the duration of sleep and hypertension, in particular, have stimulated debate. One U.S. investigation showed that short periods of sleep led to hypertension in middle-aged adults,<sup>11</sup> but a British study on a middle-aged population showed this influence

to be real only in females and not statistically significant in males.<sup>10</sup> An investigation by Robillard showed that sleep deprivation led to hypertension in the elderly, but there were also other studies that showed no association between the duration of sleep and hypertension in the elderly.<sup>12,13</sup> There are also several studies showing that long periods of sleep are also associated with a higher risk for hypertension.<sup>14,15</sup> This is in contrast to the conclusion that long periods of sleep may be a protective factor with respect to metabolic syndrome.<sup>16</sup> It is difficult to reach a consensus using existing studies because they were performed on individuals of different races and used different sample sizes. For this reason, we conducted a meta-analysis to assess whether the evidence supports the existence of a relationship between the duration of sleep and hypertension.

Most recently, we found an article describing a meta-analysis of the association between short sleep duration and hypertension.<sup>17</sup> However, they defined short sleep duration as a duration  $\leq 5$ , 4–5,  $\leq 6$ , or  $< 7$  h per night and this discordant definition of short sleep duration might not be able to show any clear association between a specific sleep duration and hypertension. In addition, they only assessed nighttime sleep duration in their study rather than 24-h sleep duration which might be an important parameter for elderly population with

regular naps.<sup>18</sup> In the present study, we used uniform standards and more meticulous analysis to determine whether the evidence supports the presence of a relationship between duration of sleep and hypertension using data collected from a large population, to determine whether individuals of different ages and genders have different susceptibilities; whether nighttime and 24-h sleep duration have different relationships with hypertension in general population; and to obtain an overall risk estimate.

## METHODS

### Identification of Eligible Studies

The PubMed (1966 to September 12, 2012), EmBase (1950 to September 12, 2012), Cochrane Library (1993 to September 12, 2012), and Chinese Biological Medicine (1978 to September 12, 2012) databases were searched using “sleep duration,” “sleep deprivation,” and “sleep quality” as keywords or major descriptors. The results were then crossed with the keywords “hypertension” and “high blood pressure.” There were no further restrictions regarding language or age. We tried our best to search more related literature. Grey literatures and reference lists of relevant articles were also carefully retrieved.

### Included and Excluded Criteria

Reliable assessment of sleep duration is a challenging task that is made more difficult by the usage of different methods, instruments, and definitions in the various studies. Subjective measure of sleep duration included self-reports of average sleep during the day and night over the course of one week. We have followed previous studies that reported sleep duration categories of  $\leq 5$  h, 6 h, 7 h, 8 h, and  $\geq 9$  h. Seven hours was treated as a baseline.<sup>19,20</sup> Objective methods in large population mainly included polysomnography. Assessment criteria for hypertension were as follows: individuals who had systolic blood pressure readings  $\geq 140$  mm Hg or diastolic readings  $\geq 90$  mm Hg or who had been diagnosed with hypertension and used antihypertensive drugs.

Studies were excluded if they did not meet the definitions of hypertension or if there were no available sleep duration data or suitable reference sleep times in the article. If the duration and sources of study population recruitment overlapped more than 30% in two or more papers by the same authors, we only included one of the studies.

### Data Extraction

Data were independently extracted by two investigators (Wang Y. and Liu S.) and checked by the other authors of this manuscript. In the case of discrepancies in confirming the study design or effect size calculations, results were carefully discussed until both investigators agreed or the third author participated. Sample characteristics included study design, country or area, study population, number of included patients, sleep duration categories, diagnostic criteria for hypertension, participants' mean age, gender, method of collection of sleep duration and high blood pressure data, and risk-effect odds ratio (OR) or adjusted OR by age, sex, or adjusted OR by age, sex, physical activity, body mass index, smoking, alcohol

consumption, coffee consumption, educational level, number of social ties, depression, depressive symptoms, diabetes mellitus, and other risk factors in different model according to available variables in individual study.

Study design included cross-sectional, case-control, and prospective techniques. In other studies that did not describe their specific study design type, this was inferred from the study methods. The method of assessment of sleep time included self-reports and polysomnography. The most common question was, “How many hours of sleep do you usually get in a day or at night, on average?” As for the age group, we referenced the original articles. The elderly group was defined as  $> 60$  years, while the middle aged was referenced 45–60 years.

If different periods of sleep were measured but no information regarding the association between sleep time and hypertension was reported, we contacted the authors and requested the missing information. If there was no response or the authors could not supply the data, then these studies were excluded.

### Data Synthesis and Effects

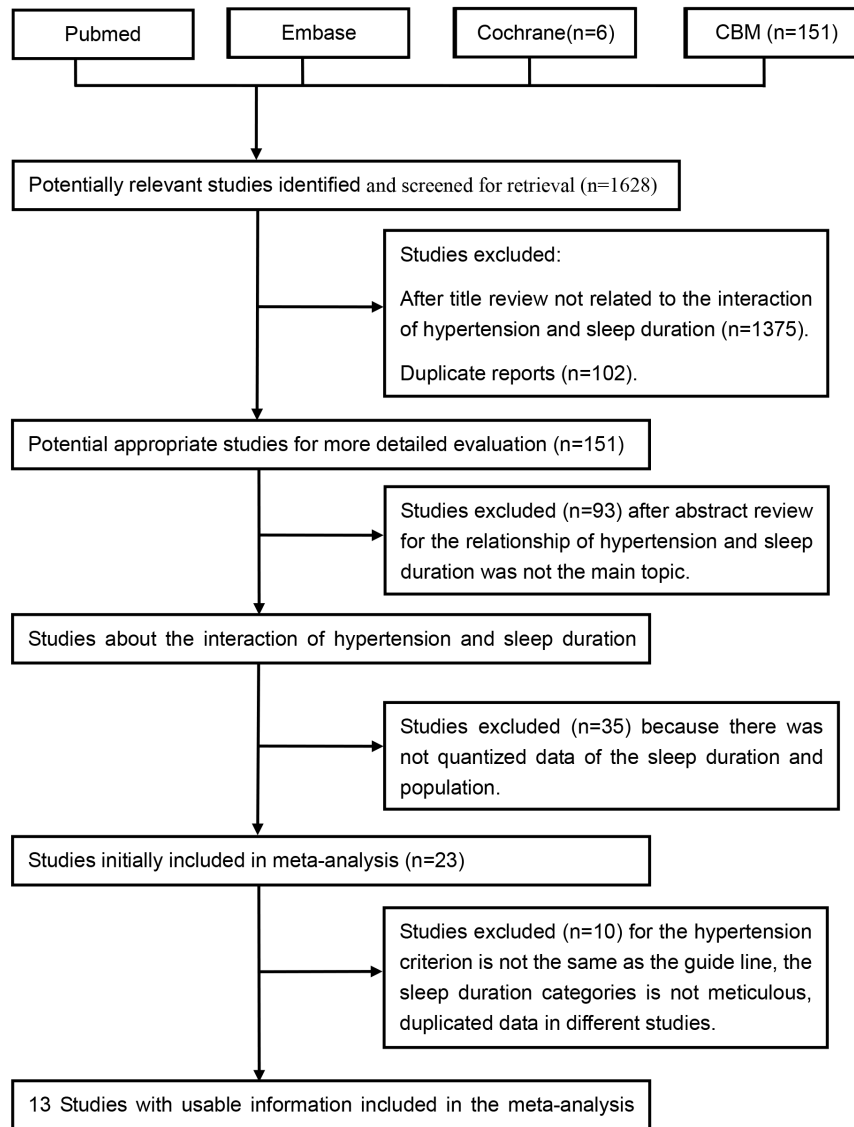
The effects of measures of interest were odds ratios (OR) for case-control studies and relative risks (RR) for cohort studies, using the corresponding 95% confidence intervals. Random and fixed-effects models were computed. The differences between fixed and random effect models were profoundly affected by the way significance testing was conducted. Significance testing in fixed-effects models is based on the total number of participants. This allows great statistical power but limited generalizability. Significance testing in the random-effects models is based on the total number of studies included in the meta-analysis, resulting in lower statistical power but greater generalizability. In view of the higher generalizability, we preferred the random-effects model.

We accessed the quality of each subgroup effects using GRADEprofiler 3.6 (GRADE Working Group).<sup>21,22</sup> GRADE offers 4 levels of evidence quality: high, moderate, low, and very low. Randomized trials begin as high quality evidence and observational studies as low quality evidence. Quality may be downgraded as a result of limitations in study design or implementation, inconsistency of evidence (heterogeneity), indirectness of evidence, imprecision of estimates (wide confidence intervals), or publication bias. Quality may be upgraded because of a very large magnitude of effect, a dose-response gradient, and if all plausible biases would reduce an apparent treatment effect.

### Heterogeneity Meta-Regression and Subgroup Analysis

Statistical heterogeneity among studies was estimated using a  $\chi^2$  test, Q statistics with corresponding p values, and  $I^2$  statistics. If the p value was  $> 0.10$  or  $I^2 \leq 50\%$ , statistical heterogeneity among studies was not considered apparent and a fixed-effects model was applied. When heterogeneity was present, meta-regression analysis was undertaken to determine the association between predictor variables and the effect size. Subgroups were established according to potential confounding variables. A random-effects model was used to determine pooled odds ratios and relative risks. We stratified the sleep

Figure 1—Flow chart of study selection.



participants by age, gender, and study design type, and then calculated the summary risk of sleep time for hypertension. The heterogeneity of each subgroup was also been evaluated.

### Sensitivity Analysis

When heterogeneity was observed, we conducted a sensitivity analysis in which one study was removed and the effects of the remaining studies were pooled to determine whether the results were affected in any statistically significant way. The effects of pooled individual studies were evaluated through both fixed and random-effects models.

### Publication Bias

Publication bias was evaluated using funnel plots and Egger test.  $p$  values  $< 0.10$  were considered to be statistically significant. The Duval and Tweedie Trim and Fill test was used because it estimates the number of theoretically missing studies and computes the combined effect estimate. If the meta-analysis captured all relevant studies, then these studies were

also included in the analysis. The meta-analyses and subgroup analyses were performed using Review Manager Version 5.1.7 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark). Adjusted odds ratios of sleep time for hypertension, meta-regression analysis, sensitivity analysis, and publication bias were performed using Stata software version 12.0 (Stata Corp, College Station, TX, U.S.). All statistical tests were two-tailed.

## RESULTS

### Search Results

We identified 1,628 potentially relevant articles from our search of the published literature (Figure 1). We excluded 1,615 articles, including 102 duplicated articles: 1,375 articles were excluded after title review. Another 93 articles were excluded after abstract review; then 58 full-text articles were retrieved and carefully evaluated, and 35 of these studies were

excluded because of a lack of available data regarding the duration of sleep and hypertension, including 7 articles related to pediatric hypertension because of various diagnostic criteria.<sup>23–29</sup> The remaining 23 studies were carefully analyzed, and 4 studies were excluded because of a lack of suitable sleep time categorization.<sup>30–33</sup> Three studies were excluded because the diagnostic criteria for hypertension did not meet the WHO guideline criteria.<sup>6,34,35</sup> Two studies were excluded because of a lack of suitable hypertension population data.<sup>36,37</sup> One study was excluded as an approximate duplicate (the same author published 2 related papers on the same population).<sup>38</sup> Thus 10 studies were excluded (**Table S1**, supplemental material), and 13 articles were ultimately included in the meta-analysis.

## Study Characteristics

Summary characteristics of the 13 included studies are given (**Table 1**). Of the 13 included studies, 4 were from the United States and one each from Australia, Brazil, France, Germany, South Korea, Mainland China, Spain, Taiwan, and the United Kingdom.<sup>10,11,13–15,39–46</sup> These studies included 347,759 participants, of whom 115,007 had hypertension. The cases and total participants for each sleep duration category were as follows: 7,452 of 19,695 had  $\leq 5$  h of sleep; 17,524 of 53,603 had 6 h; 26,648 of 92,895 had 7 h; 41,073 of 126,544 had 8 h; and 22,310 of 54,534 had  $\geq 9$  h. All participants were  $> 18$  years old. There were 6 cross-sectional studies and 7 prospective cohort studies. Two studies included both cross-sectional surveys and prospective cohort investigation.<sup>10,13</sup>

## Relationship of Sleep Duration and Hypertension

We evaluated the quality of included literature: the quality of all studies was low because study design type of included literature was observational study (**Figure S3A–S3D**, supplemental material). Some pooled effects was downgraded because of heterogeneity leading to serious inconsistency.

The unadjusted summary risk estimates of every sleep duration group for hypertension are shown (**Figures 2A–2D**). Overall, we observed statistically significant associations between pooled ORs of sleep duration and hypertension. In groups of individuals who slept  $\leq 5$  h vs those who slept 7 h, the combined OR was 1.61, 95% CI = 1.28–2.02; those who slept 6 h vs those who slept 7 h the combined OR was 1.24, 95% CI = 1.20–1.28; those who slept 8 h vs those who slept 7 h, the combined OR was 1.12, 95% CI = 1.10–1.14 and those who slept  $> 9$  h vs those who slept 7 h, the combined OR was 1.29, 95% CI = 0.97–1.71. We applied the random-effects model to all groups because of heterogeneity ( $p < 0.10$ ,  $I^2 > 50\%$ ).

## Meta-regression

We conducted meta-regression analysis in order to determine the source of this heterogeneity. Risk factors included study design (cross-sectional, case-control, or cohort design), sleep duration ( $\leq 5$  h, 6 h, 7 h, 8 h,  $\geq 9$  h), different definitions of sleep duration (night sleep time only or 24-h total), age (middle aged or elderly), and country or area. The result of meta-regression demonstrated study design in sleep 5 h vs 7 h ( $p = 0.02$ ) and sleep duration in 9 h vs 7 h ( $p = 0.01$ ) contributed to the heterogeneity. Statistical comparisons with

regard to specific sleep indices follow (**Table 2**). The heterogeneity of each subgroup was shown in (**Table S2**, supplemental material).

## Stratified Analysis

We then conducted subgroup analyses and stratified the pooled risk estimate by gender, age, study design, and different definitions of sleep duration, and compared the different subgroup summary risk estimates and trends (**Figure 3**). In the sex subgroup analyses, women deprived of sleep (sleep time  $\leq 5$  h, OR = 1.68, 95% CI = 1.39–2.03, random-effects model) had a higher risk of hypertension than men (OR = 1.30, 95% CI = 0.93–1.83, random-effects model), and either men or women who slept longer (sleep time  $\geq 8$  h versus 7 h) had an increased risk of hypertension. With respect to study design, the risk estimate and confidence interval of the prospective cohort study were found to be smaller than those of the cross-sectional studies among individuals who slept for different periods. Relative risk of sleep time  $\leq 5$  h in prospective cohort studies was found to be 1.31 (95% CI = 1.15–1.49, random-effects model); and the OR was 1.81 (95% CI = 1.56–2.10, random-effects model) in cross-sectional studies. In the age subgroup analyses, the pooled OR (OR = 1.61, 95% CI = 1.27–2.04, random-effects model) for short sleep duration (sleep time  $\leq 5$  h) for hypertension in middle-aged people was higher than in older people (OR = 1.25, 95% CI = 0.94–1.68, random-effects model); conversely, long periods of sleep (sleep time  $\geq 9$  h, OR = 1.30, 95% CI = 1.04–1.63, random-effects model) in older people were associated with a greater risk of hypertension than in middle-aged people (OR = 1.16, 95% CI = 0.73–1.85, random-effects model). In the different sleep duration definition subgroups, only sleep duration  $\leq 5$  h was accompanied with high risk of hypertension in nighttime sleep analysis, while in 24-h sleep duration analysis, all short and long sleep durations groups were related to hypertension compared with 7-h reference group.

## Sensitivity Analysis

We also conducted a sensitivity analysis to evaluate whether removal of a study from this analysis significantly affected remaining pooled results. Two studies performed on individuals who slept  $\leq 5$  h vs 7 h (those by Fang et al. and Magee et al.) were omitted, and the remaining pooled effects were statistically significant. When one study of those individuals who slept 8 h vs 7 h and  $\geq 9$  h vs 7 h (Magee et al.), was omitted, the remaining pooled effects were statistically significant (**Figures S1A–S1C**, supplemental material).

We extracted adjusted odds ratios from 4 included studies.<sup>13,40,41,43</sup> The summary odds ratio simultaneously adjusted by age and gender for  $\leq 5$  h vs 7 h was 1.23, 95% CI = 1.01–1.49; for 6 h vs 7 h was 1.13, 95% CI = 1.02–1.25; for 8 h vs 7 h was 1.06, 95% CI = 0.96–1.17; and for  $\geq 9$  h vs 7 h was 1.18, 95% CI = 1.03–1.36. The first, second, and fourth comparisons above were statistically significant.

## Publication Bias

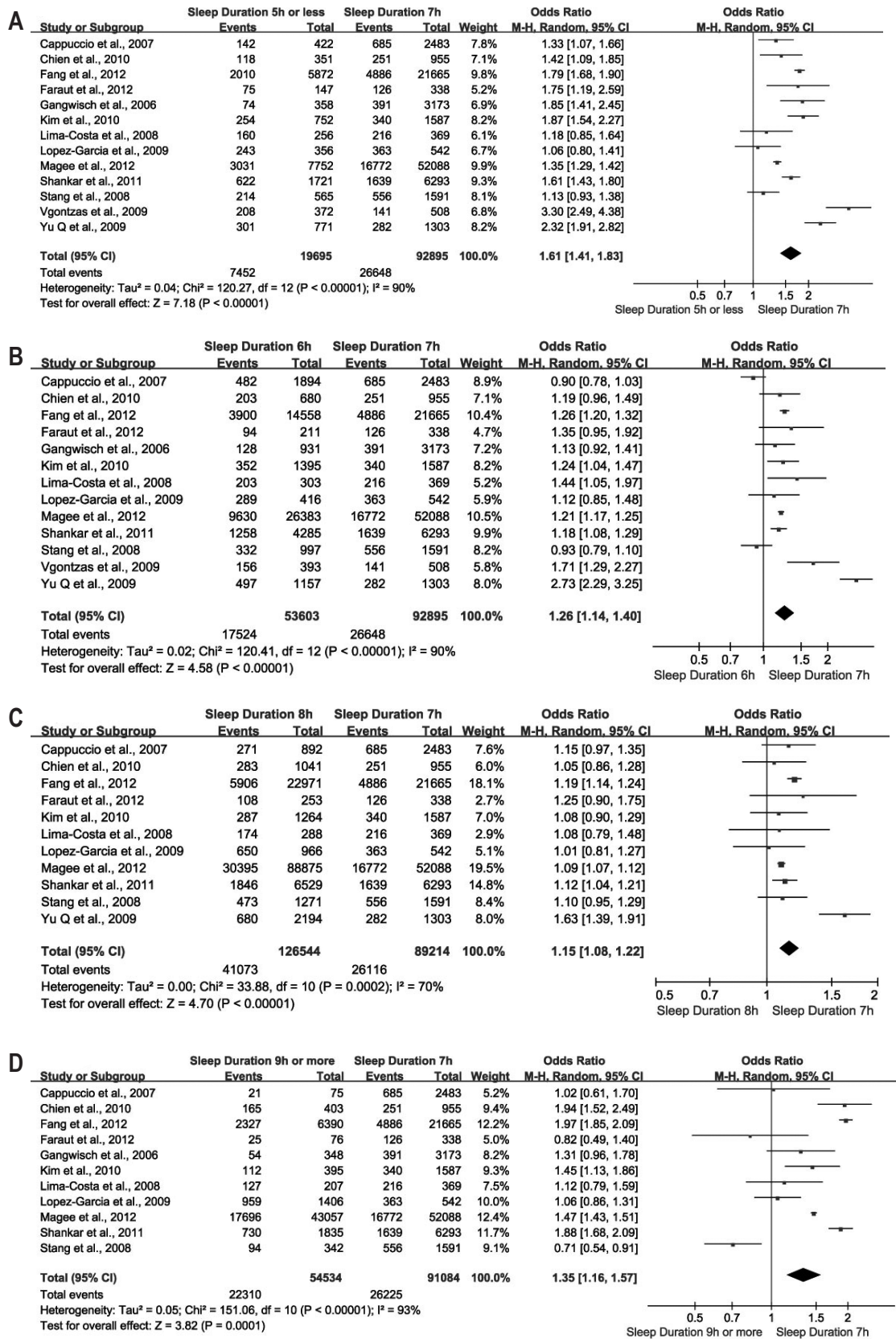
We then evaluated publication bias using a funnel plot (**Figure S2A–S2D**, supplemental material) and Egger's test. No groups showed publication bias (for those who slept  $\leq 5$  h

**Table 1**—Summary of the 13 studies included in the meta-analysis.

Study	Country or Area	Study Design	Study Population	Sample Size (n)	Age (y)	Data Collection	Hypertension Criteria	Categories of Sleep Duration	OR Adjusted Model and Adjusted Factors for OR
Cappuccio et al. 2007	British	CSS	The Whitehall II cohort 1997–1999	5,766	35–55	Sleep questionnaires	≥ 140/90 mm Hg, Drug	≤ 5, 6, 7, 8, ≥ 9 h; 7 h is for reference	LRM adjusted for age, employment, alcohol consumption, smoking, physical activity, BMI, SF36 Mental, SF36 Physical, depression cases, hypnotics use, CVD drugs.
		PCS	The Whitehall II cohort 2002–2003	3,691	35–55				
Chien et al. 2010	Taiwan China	PCS	The Chin-Shan Community Cardiovascular Cohort study	3,430	≥ 35	Sleep questionnaires	≥ 140/90 mm Hg, Drug	≤ 5, 6, 7, 8, ≥ 9h	
Fang et al. 2012	America	CSS	National Health Interview Surveys (NHISs) 2007–2009	71,455	≥ 18	Self-reported	Self response	< 6, 6, 7, 8, 9, ≥ 10; 8 h is for reference	LRM adjusted for race/ethnicity, education, smoking status, alcohol intake, physical activity, BMI, stroke, coronary heart disease, and diabetes status.
Faraut et al. 2012	France	CSS	French adults visited the general practitioners of Paris' primary care centers.	1,046	55.5	Self-reported	≥ 140/90 mm Hg, Drug	< 5, 6, 7, 8, ≥ 9 h; 7 h is for reference	LRM adjusted for demographic variables, clinical characteristics, biochemical features, lifestyle demographic variables, clinical variables, psychological characteristics and sleep disorders.
Gangwisch et al. 2006	America	PCS	The first National Health and Nutrition Examination Survey (NHANES I)	4,810	32–86	Self-reported	≥ 140/90 mm Hg, Drug	≤ 5, 6, 7–8, ≥ 9 h; 7–8 h is for reference	Cox proportional hazards models. Adjusted for daytime sleepiness, depression, physical activity, alcohol consumption, salt consumption, smoking, pulse rate, gender, education, age, ethnicity, overweight/obesity and diabetes.
Kim, J, Jo I. 2010	Korea	CSS	2005 Korean National Health and Nutrition Examination Survey	5,393	≥ 19	Self-reported	≥ 140/90 mm Hg, Drug	< 5, 6, 7, 8, ≥ 9 h; 7 h is for reference	LRM adjusted for overweight/obesity, diabetes smoking status, alcohol consumption, physical activity, depressive symptoms, diabetes mellitus, and stroke.
Lima-Costa et al. 2008	Brazil	PCS	Bambui Health Aging Study	1,423	68.9	Self-reported	≥ 140/90 mm Hg, Drug	< 6, 6–7, 7–8, 8–9; ≥ 7–8 h is for reference	LRM adjusted for age, gender, skin color, diabetes mellitus, depressive symptoms, BMI and hypnotic or sedative medications.
Lopez-Garcia et al. 2009	Spain	CSS	Spanish population recruited during 2001	3,686	≥ 60	Self-reported	≥ 140/90 mm Hg, Drug	4–5, 6, 7, 8, 9, 10–15 h; 7 h is for reference	LRM adjusted for sex, age, physical activity, BMI, smoking, alcohol consumption, coffee consumption, educational level, number of social ties, perceived health, depression, number of chronic diseases, arousal from sleep at night, and anxiolytic intake.
		PCS	Spanish population 2001–2003	890	≥ 60				
Magee et al. 2012	Australia	PCS	The Medicare Australia enrolment database	218,155	≥ 45	Self-reported	Self response	< 6, 6, 7, 8, ≥ 9; 7 h is for reference	LRM adjusted for age, sex, country of birth, marital status, education, employment status, remoteness, BMI, physical activity, smoking, alcohol and screen time.
Yu Qing et al. 2009	China	CSS	Workers in Lin nan cang mine	5,425	50.62 ± 13.19	Self-reported	≥ 140/90 mm Hg, Drug	< 6, 6–, 7–, ≥ 8 h	
Shankar et al. 2011	America	CSS	2008 National Health Interview Survey (NHIS)	20,663	≥ 18	Self-reported	Self-response	≤ 5, 6, 7, 8, ≥ 9 h	
Stang et al. 2008	Germany	PCS	Heinz Nixdorf Recall Study	4,766	45–74	Sleep questionnaires	≥ 140/90 mm Hg, Drug	≤ 5, 6, 7, 8, ≥ 9 h; 7 h is for reference	Adjusted for age.
Vgontzas et al. 2009	America	CSS	Randomly selected from central Pennsylvania	1,741	48.7	Self-reported	≥ 140/90 mm Hg, Drug	≤ 5, 6, 7, ≥ 7 h; ≥ 7 h is for reference	LRM adjusted for age, race, sex, BMI, diabetes, smoking status, alcohol consumption, depression, SDB, insomnia, and sampling weight.

CSS, cross-sectional survey; PCS, prospective cohort study; LRM, logistic regression model; BMI, body mass index; CVD: cardiovascular diseases; SDB, sleep disordered breathing.

Figure 2—Forest plot of association between sleep duration and hypertension.



Odds ratios (ORs) in the individual study are presented as squares with 95% confidence intervals (CIs) presented as extended lines. The pooled OR with its 95% CI is shown as a diamond. (A) Those who slept ≤ 5 h versus those who slept 7 h. (B) Those who slept 6 h versus those who slept 7 h. (C) Those who slept 8 h versus those who slept 7 h. (D) Those who slept ≥ 9 h versus those who slept 7 h.

**Table 2**—Meta-regression analysis.

Risk Factors	5 h vs 7 h		6 h vs 7 h		8 h vs 7 h		9 h vs 7 h	
	t	p (95% CI)	t	p (95% CI)	t	p (95% CI)	t	p (95% CI)
Study design	-2.69	0.02 (-0.6–0.07)	-0.14	0.28 (-0.53–0.17)	-0.95	0.36 (-0.29–0.12)	-0.57	0.58 (-0.56–0.34)
Sleep duration	-0.76	0.46 (-0.52–0.25)	-0.70	0.50 (-0.48–0.25)	-0.66	0.53 (-0.27–0.15)	3.64	0.01 (0.19–0.79)
Night or 24-h sleep	1.52	0.16 (-0.13–0.71)	1.95	0.08 (-0.04–0.70)	0.30	0.77 (-0.21–0.27)	0.85	0.42 (-0.32–0.69)
Middle-aged or old	-1.82	0.11 (-1.09–0.14)	-0.27	0.80 (-0.77–0.61)	-0.48	0.65 (-0.55–0.37)	-0.76	0.48 (-0.73–0.40)
Country or area	-1.69	0.12 (-0.10–0.01)	-0.40	0.70 (-0.07–0.05)	0.08	0.94 (-0.04–0.03)	-0.15	0.88 (-0.08–0.07)

vs 7 h,  $t = 0.68$ ,  $p = 0.509$ , 95% CI =  $-2.18$ – $4.14$ ; for those who slept 6 h vs 7 h,  $t = 0.43$ ,  $p = 0.68$ , 95% CI =  $-2.33$ – $3.46$ ; for those who slept 8 h vs 7 h,  $t = 0.35$ ,  $p = 0.73$ , 95% CI =  $-1.45$ – $2.00$ ; and for those who slept 9 h vs 7 h  $t = -0.84$ ,  $p = 0.42$ , 95% CI =  $-3.21$ – $1.47$ ).

## DISCUSSION

Our extensive analysis showed that relative to the group of the people with 7 h daily sleep, all other sleep durations groups ( $\leq 5$  h, 6 h, 8h, and  $\geq 9$  h groups) were accompanied by some higher risk of hypertension. The pooled odds ratio (OR) was still significant, even after adjusted by age and gender. This indicates that excessively longer or shorter periods of sleep may both be risk factors for high blood pressure, especially in female. Further stratified analysis showed that cross-sectional studies depicted an obvious U-shaped change in pooled ORs for hypertension due to the change in the duration of sleep. The existence of this association was also supported in the prospective cohort studies, although it became attenuated to some extent.

In our general analysis of sleep duration and hypertension, all suitable studies showed extreme sleep periods to be associated with a higher risk for hypertension. Sleep duration 5 h or less was found to have the largest OR relative to 7 hours. Although it appears that sleep deprivation causes hypertension, the mechanism(s) underlying this association is not well understood. There are some relevant theories, and nocturnal sympathetic activation is likely to be the key.<sup>47</sup> Under normal sleep conditions, the vagal system is activated and catecholamine biosynthesis is decreased.<sup>48,49</sup> Sleep deprivation, however, seems to act as a stressor on the body and activates the sympathetic system,<sup>50</sup> based on evaluations of serum stress hormones after sleep deprivation. As a result, the rennin-angiotensin-aldosterone system is stimulated, and the synthesis of central catecholamines is increased.<sup>51–53</sup> This leads to blood vessel constriction, which increases blood pressure, potentially leading to hypertension.<sup>54</sup> Another study has shown that after a period of chronic sleep deprivation, flow-mediated dilation of artery and intracellular magnesium concentrations both decreased.<sup>55</sup> Magnesium is considered a physiologic calcium antagonist capable of decreasing vascular tone.<sup>56–58</sup> Magnesium deficiency leads to arterial constriction thus affecting vessel dilation. In this way, conditions of long-term vascular tension after sleep restriction may play a role in the development of hypertension. Maintaining a healthy lifestyle is important to the establishment of normal biological rhythms. The central biological clock or suprachiasmatic nucleus (SCN) requires

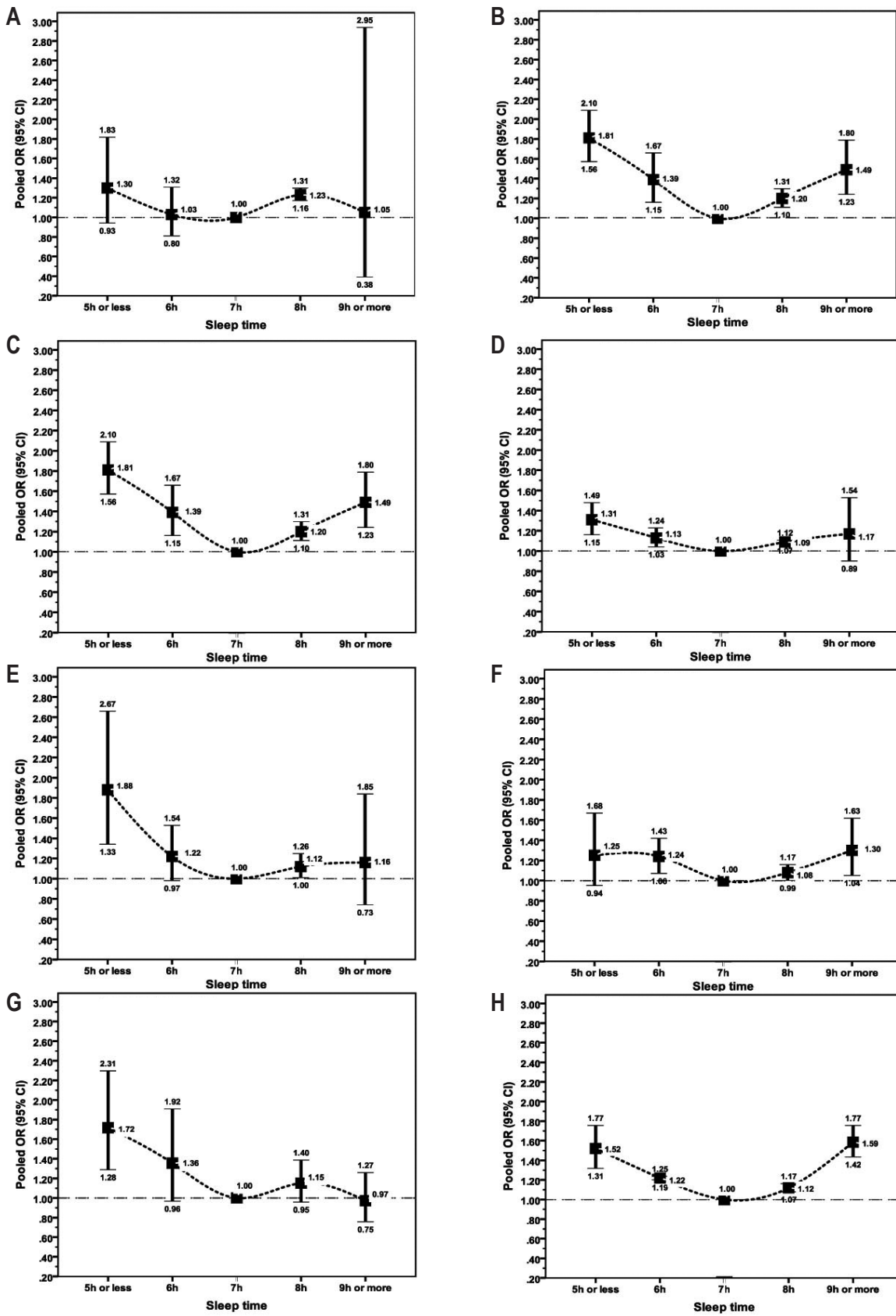
repeated metabolic cues from light exposure, sleep, activity, and feeding to generate and organize autonomic rhythms.<sup>59,60</sup> Dramatic alterations in these parameters due to prolonged wakefulness lead to a disturbance in circadian rhythmicity of blood pressure, and finally results in hypertension.<sup>61</sup>

Excessively long periods of sleep are also associated with increased risk of hypertension. The underlying biologic mechanisms are not well understood, but other risk factors might impact the association, including physical activity. In one study, long periods of sleep were often accompanied by less physical activity, and inactivity was related to increased risk of hypertension.<sup>9</sup> A study from the Netherlands showed that long periods of sleep were related to high total cholesterol concentrations and a high total/HDL cholesterol ratio.<sup>62</sup> There are also studies showing that long periods of sleep are associated with diabetes, obesity, and chronic heart disease.<sup>14,62,63</sup> These diseases are often accompanied by hypertension. Long periods of sleep may be related to sleep-disordered breathing or poor sleep quality.<sup>64–66</sup> These phenomena indicate that long periods of sleep may constitute another marker of poor health.

In our further stratified analysis, we found that the associations between short sleep duration and hypertension are stronger in women than men. The results from a recent published study might partially explain the mechanisms underlying these sex differences.<sup>67</sup> In their experimental sleep deprivation study, they found sleep deprivation increased blood pressure in both men and women, but the sympathetic baroreflex operating point was shifted rightward and downward only in men, not in women. The baroreflex detected increased in arterial pressure and consequently reduced muscle sympathetic nerve activity (MSNA), which in turn had a protective function on blood pressure. Women, on the other hand, demonstrated a significant increase in arterial blood pressure similar to the men, but the acute hypertensive response was not accompanied by a concurrent decrease of MSNA. In addition, sleep deprivation has also repeatedly been shown to significantly decrease testosterone levels which were correlated to reductions of MSNA in men.<sup>68–70</sup> The self-reported sleep habits between men and women also tends to be different; women were more likely to report feeling unrested, but less likely to have an high Epworth Sleepiness Scale score.<sup>71</sup> This error may be almost impossible to eliminate.

In our analysis stratified by age, extremely short sleep duration ( $\leq 5$  h) is associated with hypertension only in the middle-aged population but not in the elderly group. It is important to pay attention to the phenomenon that the elderly are often retired and therefore have more opportunity to nap. In addition, the prevalence of excessive daytime sleepiness (EDS) increases

**Figure 3**—Subgroup analysis of association between the duration of sleep and hypertension.



Pooled odds ratios (ORs) in each group are presented as squares with 95% confidence intervals (CIs) are represented by extended lines. The horizontal reference line represents an OR value of “one.” The dashed line represents the effects of different sleep durations on hypertension. (A) The male subgroup. (B) The female subgroup. (C) The cross-sectional study subgroup. (D) The cohort study subgroup. (E) The middle-aged subgroup. (F) The older-aged subgroup. (G) The night sleep duration subgroup. (H) The 24 h sleep duration subgroup.



in older populations.<sup>18</sup> So for the elderly group, it is worth investigating the association between nighttime or 24-h sleep duration with hypertension separately; however, we could not analyze this factor because there were only 3 studies involving older population and could not be further subdivided.

The analysis for total populations by different definitions of sleep duration showed that extremely short sleep duration ( $\leq 5$  h) is associated with hypertension in both nighttime and 24-h sleep duration groups. Furthermore, the longer 24-h sleep duration was strongly related to hypertension while the longer nighttime sleep duration was not. This may imply that long daytime naps, instead of nighttime sleep duration, may have an association with hypertension. Some studies have shown that long daytime naps or excessive daytime sleepiness is more common in those people with sleep related breathing disorders (SBD) and obesity, which are both closely related to hypertension.<sup>72,73</sup> Some investigations have found long nap time being associated with high risk of mortality, especially in the elderly. From the two stratified analyses above, daytime naps may be a potential marker of health condition in the aged group, but neither of the above factors could be taken into account in our meta-analysis, as there were widely different study designs within those included studies. But it will be worthwhile to investigate whether this association is independently with SBD or other diseases in the future studies.

There are several points to consider as potential limitations of this study. First, the accuracy and quality of the data in this meta-analysis depends upon that of the individual studies. Second, sleep duration was almost always self-reported. The validity of self-reported sleep duration is limited. It has been reported that self-report sleep duration is usually longer than objective measurements by PSG or actigraphy, but it is hard to apply objective measurements to large scale epidemiological investigations; this matter is likely to remain unresolved for some time. Third, due to the limited nature of the information, various confounders could not be taken into consideration—e.g., insomnia. This is an important confounder. In the short sleep duration group ( $< 6$  h), the hypertension prevalence rate and morbidity of insomnia group was significantly higher than the normal sleep group. So patients who suffered from insomnia would have had an effect on our analysis related to short sleep duration with hypertension. Further, chronic diseases like obesity and cardiovascular system diseases are common in old people and the long sleep duration group, besides antihypertensive medications which could affect sleep.<sup>74</sup> However, not all such studies provided this information, so we likewise did not include it in our analyses.

Our study indicates that excessively longer and shorter periods of sleep may both be risk factors for high blood pressure, and these associations are stronger in women than men. An obvious U-shaped change in pooled ORs for hypertension was depicted due to the change in daily sleep duration with participants, with 7 h sleep duration per day having lowest risk. But regardless of nighttime sleep duration, only people sleeping less than 7 h per night have higher risk of hypertension.

## REFERENCES

- Kronholm E, Partonen T, Laatikainen T, et al. Trends in self-reported sleep duration and insomnia-related symptoms in Finland from 1972 to 2005: a comparative review and re-analysis of Finnish population samples. *J Sleep Res* 2008;17:54–62.
- Hoffstein V, Chan CK, Slutsky AS. Sleep apnea and systemic hypertension: a causal association review. *Am J Med* 1991;91:190–6.
- National Sleep Foundation. Sleep in America Poll 2005: summary of findings. Washington, DC: National Sleep Foundation, 2005.
- Cao M, Guilleminault C. Acute and chronic sleep loss: implications on age-related neurocognitive impairment. *Sleep* 2012;35:901–2.
- Jackson ML, Gunzelmann G, Whitney P, et al. Deconstructing and reconstructing cognitive performance in sleep deprivation. *Sleep Med Rev* 2013;17:215–25.
- Abedelmalek S, Chtourou H, Aloui A, Aouichaoui C, Souissi N, Tabka Z. Effect of time of day and partial sleep deprivation on plasma concentrations of IL-6 during a short-term maximal performance. *Eur J Appl Physiol* 2013;113:241–8.
- Dixit A, Thawani R, Goyal A, Vaney N. Psychomotor performance of medical students: effect of 24 hours of sleep deprivation. *Indian J Psychol Med* 2012;34:129–32.
- Ayas NT, White DP, Manson JE, et al. A prospective study of sleep duration and coronary heart disease in women. *Arch Intern Med* 2003;163:205–9.
- Ayas NT, White DP, Al-Delaimy WK, et al. A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care* 2003;26:380–4.
- Cappuccio FP, Stranges S, Kandala NB, et al. Gender-specific associations of short sleep duration with prevalent and incident hypertension: the Whitehall II Study. *Hypertension* 2007;50:693–700.
- Gangwisch JE, Heymsfield SB, Boden-Albala B, et al. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. *Hypertension* 2006;47:833–9.
- Robillard R, Lanfranchi PA, Prince F, Filipini D, Carrier J. Sleep deprivation increases blood pressure in healthy normotensive elderly and attenuates the blood pressure response to orthostatic challenge. *Sleep* 2011;34:335–9.
- Lopez-Garcia E, Faubel R, Guallar-Castillon P, Leon-Munoz L, Banegas JR, Rodriguez-Artalejo F. Self-reported sleep duration and hypertension in older Spanish adults. *J Am Geriatr Soc* 2009;57:663–8.
- Magee CA, Kritharides L, Attia J, McElduff P, Banks E. Short and long sleep duration are associated with prevalent cardiovascular disease in Australian adults. *J Sleep Res* 2012;21:441–7.
- Shankar A, Charumathi S, Kalidindi S. Sleep duration and self-rated health: the national health interview survey 2008. *Sleep* 2011;34:1173–7.
- Najafian J, Toghianifar N, Mohammadifard N, Nouri F. Association between sleep duration and metabolic syndrome in a population-based study: Isfahan healthy heart program. *J Res Med Sci* 2011;16:801–6.
- Wang Q, Xi B, Liu M, Zhang Y, Fu M. Short sleep duration is associated with hypertension risk among adults: a systematic review and meta-analysis. *Hypertens Res* 2012;35:1012–8.
- Bixler EO, Vgontzas AN, Lin HM, Calhoun SL, Vela-Bueno A, Kales A. Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes, and depression. *J Clin Endocrinol Metab* 2005;90:4510–5.
- Hoevenaer-Blom MP, Spijkerman AM, Kromhout D, van den Berg JF, Verschuren WM. Sleep duration and sleep quality in relation to 12-year cardiovascular disease incidence: the MORGEN study. *Sleep* 2011;34:1487–92.
- Ferrie JE, Shipley MJ, Cappuccio FP, et al. A prospective study of change in sleep duration: associations with mortality in the Whitehall II cohort. *Sleep* 2007;30:1659–66.
- Guyatt GH, Oxman AD, Vist GE, et al. An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
- Guyatt GH, Oxman AD, Kunz R, et al. What is “quality of evidence” and why is it important to clinicians? *BMJ* 2008;336:995–8.
- Archbold KH, Vasquez MM, Goodwin JL, Quan SF. Effects of sleep patterns and obesity on increases in blood pressure in a 5-year period: report from the Tucson Children's Assessment of Sleep Apnea Study. *J Pediatr* 2012;161:26–30.
- Bayer O, Neuhauser H, Von Kries R. Sleep duration and blood pressure in children: a cross-sectional study. *J Hypertens* 2009;27:1789–93.
- Guo X, Zheng L, Li Y, et al. Association between sleep duration and hypertension among Chinese children and adolescents. *Clin Cardiol* 2011;34:774–81.
- Javaheri S, Storfer-Isser A, Rosen CL, Redline S. Sleep quality and elevated blood pressure in adolescents. *Circulation* 2008;118:1034–40.
- Martikainen S, Pesonen AK, Feldt K, et al. Poor sleep and cardiovascular function in children. *Hypertension* 2011;58:16–21.
- Mezick EJ, Hall M, Matthews KA. Sleep duration and ambulatory blood pressure in black and white adolescents. *Hypertension* 2012;59:747–52.
- Wells JC, Hallal PC, Reichert FF, Menezes AM, Araujo CL, Victora CG. Sleep patterns and television viewing in relation to obesity and blood pressure: evidence from an adolescent Brazilian birth cohort. *Int J Obes (Lond)* 2008;32:1042–9.
- Kim SJ, Lee SK, Kim SH, et al. Genetic association of short sleep duration with hypertension incidence. *Circ J* 2012;76:907–13.

31. Bansil P, Kuklina EV, Merritt RK, Yoon PW. Associations between sleep disorders, sleep duration, quality of sleep, and hypertension: results from the National Health and Nutrition Examination Survey, 2005 to 2008. *J Clin Hypertens* 2011;13:739–43.
32. Stranges S, Dorn JM, Cappuccio FP, et al. A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women. *J Hypertens* 2010;28:896–902.
33. Stranges S, Dorn JM, Shipley MJ, et al. Correlates of short and long sleep duration: a cross-cultural comparison between the United Kingdom and the United States: the Whitehall II Study and the Western New York Health Study. *Am J Epidemiol* 2008;168:1353–64.
34. Van den Berg JF, Tulen JHM, Neven AK, et al. Sleep duration and hypertension are not associated in the elderly. *Hypertension* 2007;50:585–9.
35. Wang H, Zee P, Reid K, et al. Gender-specific association of sleep duration with blood pressure in rural Chinese adults. *Sleep Med* 2011;12:693–9.
36. Gottlieb DJ, Redline S, Nieto FJ, et al. Association of usual sleep duration with hypertension: the Sleep Heart Health Study. *Sleep* 2006;29:1009–14.
37. Knutson KL. Association between sleep and blood pressure in midlife: the CARDIA sleep study. *Arch Intern Med* 2009;169:1055–61.
38. Gangwisch JE, Heymsfield SB, Boden-Albala B, et al. Sleep duration as a risk factor for diabetes incidence in a large U.S. sample. *Sleep* 2007;30:1667–73.
39. Fang J, Wheaton AG, Keenan NL, Greenlund KJ, Perry GS, Croft JB. Association of sleep duration and hypertension among US adults varies by age and sex. *Am J Hypertens* 2012;25:335–41.
40. Vgontzas AN, Liao D, Bixler EO, Chrousos GP, Vela-Bueno A. Insomnia with objective short sleep duration is associated with a high risk for hypertension. *Sleep* 2009;32:491–7.
41. Lima-Costa MF, Peixoto SV, Rocha FL. Usual sleep duration is not associated with hypertension in Brazilian elderly: the Bambui Health Aging Study (BHAS). *Sleep Med* 2008;9:806–7.
42. Faraut B, Touchette É, Gamble H, et al. Short sleep duration and increased risk of hypertension: a primary care medicine investigation. *J Hypertens* 2012;30:1354–63.
43. Stang A, Moebus S, Mohlenkamp S, Erbel R, Jockel KH, Heinz Nixdorf Recall Study Investigative. Gender-specific associations of short sleep duration with prevalent hypertension. *Hypertension* 2008;51:e15–6; author reply e17.
44. Kim J, Jo I. Age-dependent association between sleep duration and hypertension in the adult Korean population. *Am J Hypertens* 2010;23:1286–91.
45. Yu Q, Xu YJ, SL W. Association between sleep duration and hypertension in mine workers. *Chinese Journal of Coal Industry Medicine* 2009;12:873–5.
46. Chien KL, Chen PC, Hsu HC, et al. Habitual sleep duration and insomnia and the risk of cardiovascular events and all-cause death: report from a community-based cohort. *Sleep* 2010;33:177–84.
47. Levy P, Tamisier R, Arnaud C, et al. Sleep deprivation, sleep apnea and cardiovascular diseases. *Front Biosci (Elite Ed)* 2012;4:2007–21.
48. Somers VK, Dyken ME, Mark AL, Abboud FM. Sympathetic-nerve activity during sleep in normal subjects. *N Engl J Med* 1993;328:303–7.
49. Aston-Jones G, Chen S, Zhu Y, Oshinsky ML. A neural circuit for circadian regulation of arousal. *Nat Neurosci* 2001;4:732–8.
50. Joo EY, Yoon CW, Koo DL, Kim D, Hong SB. Adverse effects of 24 hours of sleep deprivation on cognition and stress hormones. *J Clin Neurol* 2012;8:146–50.
51. Lusardi P, Zoppi A, Preti P, Pesce RM, Piazza E, Fogari R. Effects of insufficient sleep on blood pressure in hypertensive patients: a 24-h study. *Am J Hypertens* 1999;12:63–8.
52. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet* 1999;354:1435–9.
53. Tochikubo O, Ikeda A, Miyajima E, Ishii M. Effects of insufficient sleep on blood pressure monitored by a new multi-biomedical recorder. *Hypertension* 1996;27:1318–24.
54. Staessen J, Bulpitt CJ, O'Brien E, et al. The diurnal blood pressure profile. A population study. *Am J Hypertens* 1992;5:386–92.
55. Takase B, Akima T, Uehata A, Ohsuzu F, Kurita A. Effect of chronic stress and sleep deprivation on both flow-mediated dilation in the brachial artery and the intracellular magnesium level in humans. *Clin Cardiol* 2004;27:223–7.
56. Yang ZW, Gebrewold A, Nowakowski M, Altura BT, Altura BM. Mg(2+)-induced endothelium-dependent relaxation of blood vessels and blood pressure lowering: role of NO. *Am J Physiol Regul Integr Comp Physiol* 2000;278:R628–39.
57. Pearson PJ, Evora PR, Seccombe JF, Schaff HV. Hypomagnesemia inhibits nitric oxide release from coronary endothelium: protective role of magnesium infusion after cardiac operations. *Ann Thorac Surg* 1998;65:967–72.
58. Dickens BF, Weglicki WB, Li YS, Mak IT. Magnesium deficiency in vitro enhances free radical-induced intracellular oxidation and cytotoxicity in endothelial cells. *FEBS Lett* 1992;311:187–91.
59. Asher G, Schibler U. Crosstalk between components of circadian and metabolic cycles in mammals. *Cell Metab* 2011;13:125–37.
60. Kohsaka A, Laposky AD, Ramsey KM, et al. High-fat diet disrupts behavioral and molecular circadian rhythms in mice. *Cell Metab* 2007;6:414–21.
61. Kreier F, Yilmaz A, Kalsbeek A, et al. Hypothesis: shifting the equilibrium from activity to food leads to autonomic unbalance and the metabolic syndrome. *Diabetes* 2003;52:2652–6.
62. Van den Berg JF, Miedema HM, Tulen JH, et al. Long sleep duration is associated with serum cholesterol in the elderly: the Rotterdam Study. *Psychosom Med* 2008;70:1005–11.
63. Nagai M, Tomata Y, Watanabe T, Kakizaki M, Tsuji I. Association between sleep duration, weight gain, and obesity for long period. *Sleep Med* 2013;14:206–10.
64. Hale L, Parente V, Dowd JB, et al. Fibrinogen may mediate the association between long sleep duration and coronary heart disease. *J Sleep Res* 2013;22:305–14.
65. Patel SR, Ayas NT, Malhotra MR, et al. A prospective study of sleep duration and mortality risk in women. *Sleep* 2004;27:440–4.
66. Suzuki E, Yorifuji T, Ueshima K, et al. Sleep duration, sleep quality and cardiovascular disease mortality among the elderly: a population-based cohort study. *Prev Med* 2009;49:135–41.
67. Parry BL, Newton RP. Chronobiological basis of female-specific mood disorders. *Neuropsychopharmacol* 2001;25:S102–8.
68. Carter JR, Durocher JJ, Larson RA, DellaValla JP, Yang H. Sympathetic neural responses to 24-hour sleep deprivation in humans: sex differences. *Am J Physiol Heart Circ Physiol* 2012;302:H1991–7.
69. Baumgartner A, Graf KJ, Kurten I, Meinhold H, Scholz P. Neuroendocrinological investigations during sleep deprivation in depression. I. Early morning levels of thyrotropin, TH, cortisol, prolactin, LH, FSH, estradiol, and testosterone. *Biol Psychiatry* 1990;28:556–68.
70. Gonzalez-Santos MR, Gaja-Rodriguez OV, Alonso-Uriarte R, Sojo-Aranda I, Cortes-Gallegos V. Sleep deprivation and adaptive hormonal responses of healthy men. *Arch Androl* 1989;22:203–7.
71. Baldwin CM, Kapur VK, Holberg CJ, Rosen C, Nieto FJ, Sleep Heart Health Study G. Associations between gender and measures of daytime somnolence in the Sleep Heart Health Study. *Sleep* 2004;27:305–11.
72. Slater G, Steier J. Excessive daytime sleepiness in sleep disorders. *J Thorac Dis* 2012;4:608–16.
73. Slater G, Pengo MF, Kosky C, Steier J. Obesity as an independent predictor of subjective excessive daytime sleepiness. *Respir Med* 2013;107:305–9.
74. Paran E, Anson O, Neumann L. The effects of replacing beta-blockers with an angiotensin converting enzyme inhibitor on the quality of life of hypertensive patients. *Am J Hypertens* 1996;9:1206–13.

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## SUBMISSION & CORRESPONDENCE INFORMATION

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Address correspondence to: Fan Jiang, Department of Developmental and Behavioral Pediatrics, Institute of Pediatric Translational Medicine, Shanghai Children's Medical Center affiliated Shanghai Jiaotong University School of Medicine, Ministry of Education Shanghai Key Laboratory of Children's Environmental Health, Shanghai, China; Tel.: 86-21-58750573; Fax: 86-21-58706129; Email: fanjiang@shsmu.edu.cn and Shi-jian Liu, Department of Bioinformatics and Clinical Epidemiology, Institute of Pediatric Translational Medicine, Shanghai Children's Medical Center affiliated Shanghai Jiaotong University School of Medicine, Shanghai, China; Email: arrow64@163.com

## DISCLOSURE STATEMENT

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## SUPPLEMENTAL MATERIAL

Table S1—Description of the 10 studies excluded from the meta-analyses.

Study	Study Design	Study Population	Sample Size (n)	Age (y)	Data Collection Type	Hypertension Criteria	Categories of Sleep Duration	Summary of Findings	Reason for Exclusion
Bansil et al. 2011	CSS	The National Health and Nutrition Examination Survey	10,308	≥ 18	Self-reported	≥ 140/90 mm Hg, Drug	< 7, ≥ 7 h; ≥ 7 h is for reference	Short sleep duration people were more likely to have hypertension.	Sleep duration categories are not meticulous.
Gangwisch et al. 2007	PCS	Participants in the epidemiologic follow-up studies of the NHANES I 1982–1992	8,992	32–86	Self-reported	≥ 140/90 mm Hg, Drug	≤ 5, 6, 7, 8, ≥ 9 h	Short (≤ 5) and long (≥ 9) sleep duration had the largest incidence to have hypertension, 66.6% and 65.2%, respectively.	There is another including article which published in 2006 year also by Gangwisch used the same database, and main topic is about diabetes.
Gottlieb et al. 2006	CSS	The Sleep Heart Health Study	5,910	40–100	Self-reported	≥ 140/90 mm Hg, Drug	< 6, 6–7, 7–8, 8–9, ≥ 9; 7–8 is for reference	< or > 7h per night was more likely to have hypertension, particularly < 6 h per night.	The hypertension morbidity and number of people with high blood pressure is absent.
Kim et al. 2012	PCS	The Korean Genome and Epidemiology Study (KoGES)	4,965	40–69	Self-reported	≥ 140/90 mm Hg, Drug	< 5, 5 to 7, > 7 h; 5–7 h is for reference	Women with short sleep duration had an increased risk of incident hypertension.	The sleep duration categories are not meticulous.
Kristen et al. 2009	PCS	The Coronary Artery Risk Development in Young Adults study	578	33–45	Wrist actigraphy	≥ 140/90 mm Hg, Drug	≤ 4, 4–5, 5–6, 6–7, ≥ 7 or as continuous variables	Reduced sleep duration predicted higher blood pressure.	The hypertension morbidity and number of people with high blood pressure is absent.
Najafian et al. 2011	CSS	The Isfahan Healthy Heart Program	12,514	≥ 19	Self-reported	≥ 130/85 mm Hg, Drug	≤ 5, 6, 7–8, ≥ 9; 7–8 h is for reference	Sleep duration of less than 5 h was associated with a higher odds ratio for metabolic syndrome.	The hypertension criterion is different from the guideline.
Stranges et al. 2010	CSS	The Western New York Health Study	3,027	56	Self-reported	> 140/90 mm Hg, Drug	< 6, ≥ 6; ≥ 6 is for reference	< 6 h sleep was significantly increased risk of hypertension only among women, no significant association was found among men.	The sleep duration categories are not meticulous.
Stranges et al. 2008	CSS	The Whitehall II Study (W II) and the Western New York Health Study (WNYHS)	9,499	W II: 58.8 ± 6.1 WNYHS: 56.4 ± 11.5	Self-reported	≥ 140/90 mm Hg, Drug	< 6, 6 to 8, > 8h	The shortest sleep duration group had the largest hypertension incidence.	The sleep duration categories are not meticulous.
van den Berg et al. 2007	CSS	The Rotterdam Study	5,058	72.1 ± 7.5	Self-reported and actigraphy	≥ 160/100 mm Hg, Drug	< 5, 5–6, 6–7, 7–8, 8–9, ≥ 9; 7–8 h is for reference	Whether measured by self-report or actigraphy, sleep duration was not associated with hypertension in the elderly.	The hypertension criterion is different from the guideline.
Wang, Hongjian et al. 2011	CSS	Community-based prospective twin cohort enrolled in the rural area of the Anqing region in Anhui province	1,816	18–65	Self-reported	≥ 130/85 mm Hg or physician diagnosed hypertension	< 7, 7 to 9, ≥ 9 h; 7–9 h is for reference	HBp is associated with short sleep duration in women and long sleep duration in men.	The hypertension criterion is different from the others. Sleep duration categories are not meticulous.

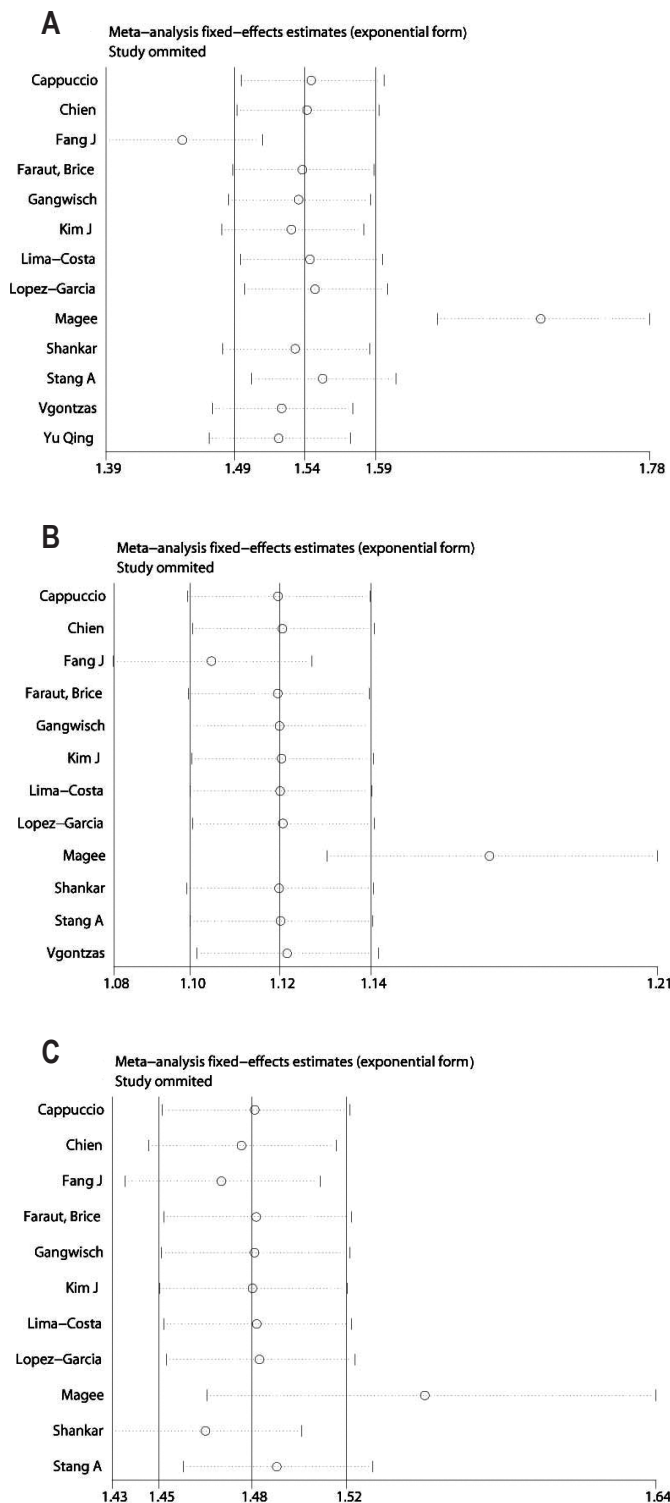
CSS, cross-sectional survey; PCS, prospective cohort study.

**Table S2**—Heterogeneity of subgroup analysis.

Risk Factors	5 h vs 7 h		6 h vs 7 h		8 h vs 7 h		9 h vs 7 h	
	p*	I <sup>2</sup> (%)	p	I <sup>2</sup> (%)	p	I <sup>2</sup> (%)	p	I <sup>2</sup> (%)
Study design subgroup	< 0.00001	89	< 0.00001	89	0.0004	67	< 0.00001	93
Cross-sectional survey	< 0.00001	83	< 0.00001	93	0.004	68	< 0.0001	83
Cohort study	0.04	58	0.07	51	0.91	0	< 0.00001	90
Sex subgroup	0.0003	79	< 0.00001	83	0.17	36	< 0.00001	93
Male	0.0008	86	< 0.0001	89	0.94	0	< 0.00001	96
Female	0.12	52	0.005	81	0.14	50	0.002	84
Sleep duration subgroup	< 0.00001	90	< 0.00001	90	< 0.0001	73	< 0.00001	86
Night	< 0.00001	89	< 0.00001	95	0.0002	80	0.03	62
24-h sleep	< 0.00001	92	0.75	0	0.04	58	< 0.0001	83
Age subgroup	< 0.00001	84	0.0004	74	0.81	0	0.002	72
Middle-aged	< 0.00001	87	0.0003	81	0.62	0	0.002	79
The old	0.05	66	0.28	21	0.57	0	0.05	68

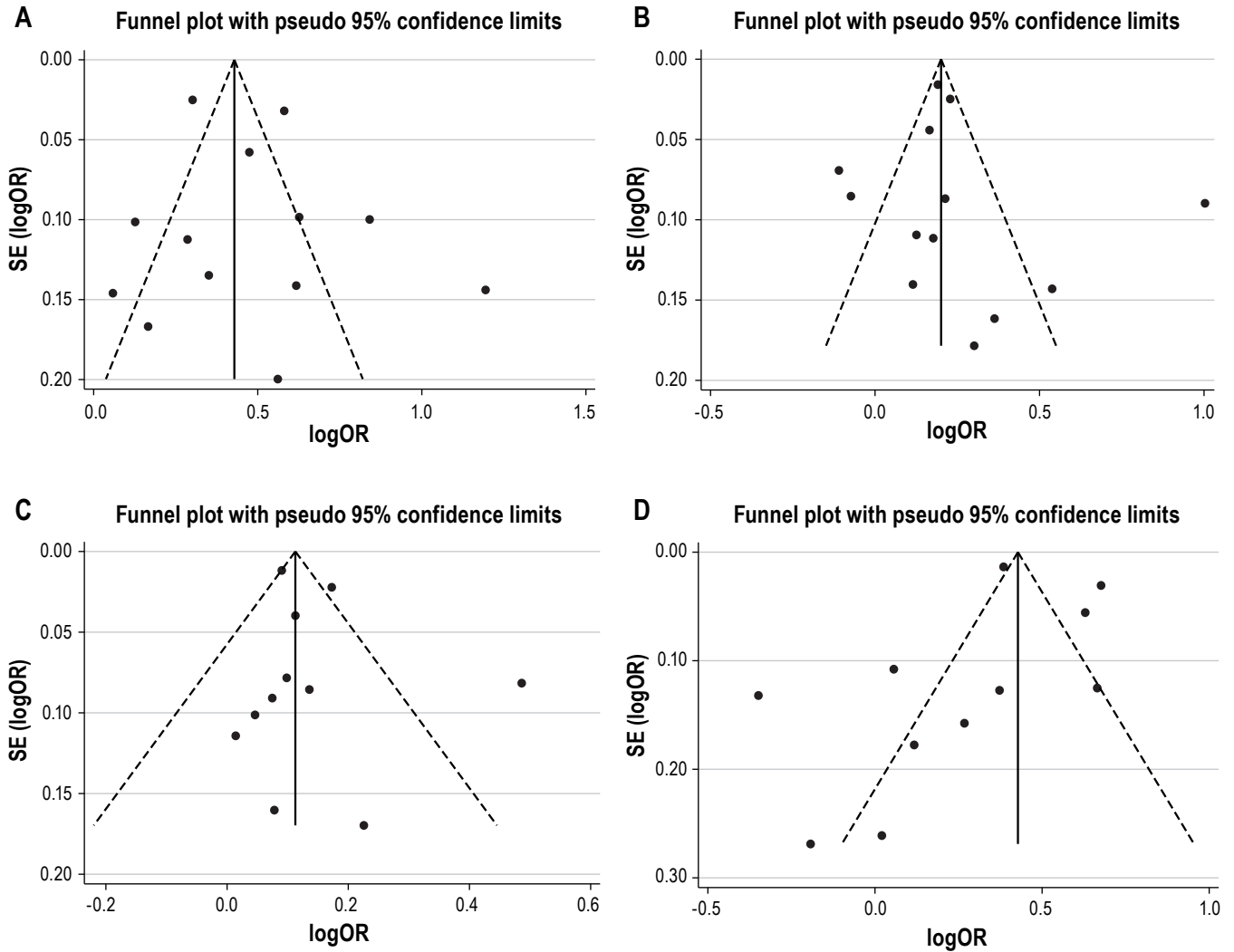
\*p value of Q statistic.

Figure S1—Meta-analysis fixed-effects estimates.



(A) Sensitivity analysis of those who slept 5 h or less versus those who slept 7 h. Two studies were omitted and the remaining pooled effects were found to be significantly influenced. (B) Sensitivity analysis of those who slept 8 h versus those who slept 7 h. One study was omitted and the remaining pooled effects were found to be significantly influenced. (C) Sensitivity analysis of those who slept  $\geq 9$  h versus those who slept 7 h. One study was omitted and the remaining pooled effects were found to be significantly influenced.

Figure S2—Funnel plot of the included literatures.



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Figure S3A–S3B—Quality of literature in each subgroup.

**A** Author(s):  
Date: 2015-01-19  
Question: T<5h vs T 7h group for hypertension  
Settings:  
Bibliography: Sleep Deprivation for hypertension. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

No of studies	Design	Risk of bias	Quality assessment				No of patients		Relative (95% CI)	Effect		Quality	Importance
			Inconsistency	Indirectness	Imprecision	Other considerations	T<5h	T 7h group		Absolute			
<b>Total T&lt;5h VS T 7h group</b>													
13	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	7452/19695 (37.8%)	26449/92895 (28.7%)	OR 1.61 (1.41 to 1.83)	106 more per 1000 (from 75 more to 137 more)	8500	LOW	
										104 more per 1000 (from 74 more to 135 more)			
										27.6%			
<b>Study design subgroup - Cross-sectional survey subgroup</b>													
9	observational studies	no serious risk of bias	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	3772/10313 (36.6%)	8315/24546 (24.1%)	OR 1.81 (1.58 to 2.1)	124 more per 1000 (from 92 more to 159 more)	8500	LOW	
										131 more per 1000 (from 96 more to 167 more)			
										26.8%			
<b>Study design subgroup - Cohort Study subgroup</b>													
6	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none <sup>1</sup>	3729/9617 (38.8%)	18640/59667 (31.1%)	OR 1.31 (1.15 to 1.49)	61 more per 1000 (from 31 more to 91 more)	8500	LOW	
										59 more per 1000 (from 30 more to 89 more)			
										29.2%			
<b>Sex subgroup - Male subgroup</b>													
3	observational studies	no serious risk of bias	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	960/2937 (32.7%)	3021/12642 (23.9%)	OR 1.3 (0.93 to 1.83)	51 more per 1000 (from 13 fewer to 126 more)	8500	LOW	
										56 more per 1000 (from 14 fewer to 138 more)			
										28.3%			
<b>Sex subgroup - Female subgroup</b>													
3	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1406/3922 (35.8%)	3106/13097 (23.7%)	OR 1.88 (1.39 to 2.63)	106 more per 1000 (from 65 more to 150 more)	8500	LOW	
										110 more per 1000 (from 67 more to 155 more)			
										25.5%			
<b>Age subgroup - Middle-aged subgroup</b>													
5	observational studies	no serious risk of bias	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	600/1533 (39.1%)	1594/7457 (21.4%)	OR 1.88 (1.33 to 2.67)	124 more per 1000 (from 72 more to 207 more)	8500	LOW	
										141 more per 1000 (from 60 more to 228 more)			
										27.8%			
<b>Age subgroup - Old Subgroup</b>													
3	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	884/1458 (60.8%)	2262/4647 (48.7%)	OR 1.25 (0.94 to 1.68)	58 more per 1000 (from 15 fewer to 128 more)	8500	LOW	
										55 more per 1000 (from 15 fewer to 124 more)			
										53.2%			
<b>Sleep duration subgroup - Night sleep</b>													
7	observational studies	no serious risk of bias	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	1174/2891 (40.8%)	2397/9765 (24.5%)	OR 1.72 (1.28 to 2.31)	113 more per 1000 (from 52 more to 184 more)	8500	LOW	
										120 more per 1000 (from 52 more to 193 more)			
										27.8%			
<b>Sleep duration subgroup - 24h sleep</b>													
6	observational studies	no serious risk of bias	serious <sup>2</sup>	no serious indirectness	no serious imprecision	none	6278/16804 (37.4%)	2425/18313 (29.2%)	OR 1.52 (1.31 to 1.77)	93 more per 1000 (from 59 more to 130 more)	8500	LOW	
										88 more per 1000 (from 55 more to 124 more)			
										26.2%			

<sup>1</sup> The p value for heterogeneity is less than 0.05, and I<sup>2</sup> is 90%.  
<sup>2</sup> The p value for heterogeneity is less than 0.05, and I<sup>2</sup> is more than 80%.

**B** Author(s):  
Date: 2015-01-19  
Question: T6h vs T7h group for hypertension  
Settings:  
Bibliography: Sleep Deprivation for hypertension. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

No of studies	Design	Risk of bias	Quality assessment				No of patients		Relative (95% CI)	Effect		Quality	Importance
			Inconsistency	Indirectness	Imprecision	Other considerations	T6h	T7h group		Absolute			
<b>Total T6h VS T 7h group</b>													
13	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	17524/53603 (32.7%)	26649/92895 (28.7%)	OR 1.26 (1.14 to 1.4)	49 more per 1000 (from 28 more to 73 more)	8500	LOW	
										48 more per 1000 (from 27 more to 72 more)			
										27.6%			
<b>Study design subgroup - Cross-sectional survey subgroup</b>													
9	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	6942/24196 (28.7%)	8315/24546 (24.1%)	OR 1.39 (1.15 to 1.67)	65 more per 1000 (from 28 more to 105 more)	8500	LOW	
										69 more per 1000 (from 28 more to 111 more)			
										28.3%			
<b>Study design subgroup - Cohort Study subgroup</b>													
6	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1038/30637 (33.4%)	18640/59667 (31.1%)	OR 1.13 (1.03 to 1.24)	27 more per 1000 (from 6 more to 48 more)	8500	LOW	
										26 more per 1000 (from 6 more to 46 more)			
										29.2%			
<b>Sex subgroup - Male subgroup</b>													
3	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	2244/8459 (26.5%)	3021/12642 (23.9%)	OR 1.03 (0.8 to 1.32)	5 more per 1000 (from 38 fewer to 54 more)	8500	LOW	
										6 more per 1000 (from 43 fewer to 60 more)			
										28.3%			
<b>Sex subgroup - Female subgroup</b>													
3	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	2470/8990 (27.5%)	3106/13097 (23.7%)	OR 1.04 (0.8 to 1.36)	7 more per 1000 (from 38 fewer to 60 more)	8500	LOW	
										8 more per 1000 (from 40 fewer to 63 more)			
										25.5%			
<b>Age subgroup - Middle-aged subgroup</b>													
5	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	1037/3908 (26.5%)	1403/6735 (20.9%)	OR 1.22 (0.97 to 1.54)	36 more per 1000 (from 5 fewer to 83 more)	8500	LOW	
										41 more per 1000 (from 8 fewer to 94 more)			
										27.6%			
<b>Age subgroup - Old Subgroup</b>													
3	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1598/2340 (68.1%)	2115/4474 (47.3%)	OR 1.24 (1.06 to 1.43)	54 more per 1000 (from 15 more to 89 more)	8500	LOW	
										53 more per 1000 (from 14 more to 87 more)			
										53.2%			
<b>Sleep duration subgroup - Night sleep duration</b>													
7	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	1802/5696 (31.1%)	2397/9765 (24.5%)	OR 1.36 (0.96 to 1.92)	61 more per 1000 (from 7 fewer to 139 more)	8500	LOW	
										66 more per 1000 (from 8 fewer to 147 more)			
										27.8%			
<b>Sleep duration subgroup - 24h sleep duration</b>													
6	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	15632/47717 (32.8%)	2425/18313 (29.2%)	OR 1.22 (1.19 to 1.25)	43 more per 1000 (from 37 more to 49 more)	8500	LOW	
										40 more per 1000 (from 35 more to 45 more)			
										26.2%			

<sup>1</sup> The p value for heterogeneity is less than 0.05, and I<sup>2</sup> is more than 80%.

(A) Literature quality of those who slept ≤ 5 h versus those who slept 7 h. All quality was low. (B) Literature quality of those who slept 6 h versus those who slept 7 h. All quality was low.

Figure S3C–S3D—Quality of literature in each subgroup.

**C** Author(s):  
Date: 2015-01-19  
Question: T 8h vs T 7h group for hypertension  
Settings:  
Bibliography: Sleep Deprivation for hypertension. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

No of studies	Design	Risk of bias	Quality assessment				No of patients		Relative (95% CI)	Effect		Quality	Importance
			Inconsistency	Indirectness	Imprecision	Other considerations	T 8h	T 7h group		Absolute			
<b>Total T8h VS T7h group</b>													
11	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	41073/26544 (32.5%)	26116/95214 (29.3%)	OR 1.15 (1.05 to 1.22)	30 more per 1000 (from 16 more to 43 more)	8900	LOW	
<b>Study design subgroup - Cross-sectional survey subgroup</b>													
7	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	9272/4391 (27%)	6174/34038 (24%)	OR 1.2 (1.1 to 1.31)	35 more per 1000 (from 18 more to 53 more)	8900	LOW	
<b>Study design subgroup - Cohort Study subgroup</b>													
5	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	31923/92884 (34.4%)	18249/56794 (32.1%)	OR 1.09 (1.07 to 1.12)	19 more per 1000 (from 15 more to 25 more)	8900	LOW	
<b>Sex subgroup - Female subgroup</b>													
3	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	3637/1364 (26%)	3106/13097 (23.7%)	OR 1.14 (1.05 to 1.2)	25 more per 1000 (from 14 more to 35 more)	8900	LOW	
<b>Sex subgroup - Male subgroup</b>													
3	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	3013/11170 (27%)	3021/12042 (25.2%)	OR 1.23 (1.16 to 1.31)	40 more per 1000 (from 28 more to 52 more)	8900	LOW	
<b>Age subgroup - Middle-aged subgroup</b>													
3	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	662/2186 (29.3%)	1062/3776 (28.1%)	OR 1.12 (1 to 1.26)	23 more per 1000 (from 0 more to 49 more)	8900	LOW	
<b>Age subgroup - Old Subgroup</b>													
2	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	343/6058 (5.2%)	2161/13925 (15.5%)	OR 1.08 (0.99 to 1.17)	19 more per 1000 (from 2 fewer to 38 more)	8900	LOW	
<b>Sleep duration subgroup - Night sleep duration</b>													
6	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	1813/3367 (33.8%)	2006/5592 (35.4%)	OR 1.15 (0.95 to 1.4)	30 more per 1000 (from 11 fewer to 75 more)	8900	LOW	
<b>Sleep duration subgroup - 24h sleep duration</b>													
6	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	3536/121646 (32.4%)	24251/83130 (29.2%)	OR 1.12 (1.07 to 1.17)	24 more per 1000 (from 13 more to 33 more)	8900	LOW	

<sup>1</sup>The p value for heterogeneity is less than 0.05, and I<sup>2</sup> is more than 80%.

**D** Author(s):  
Date: 2015-01-19  
Question: T>9h vs T 7h group for hypertension  
Settings:  
Bibliography: Sleep Deprivation for hypertension. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

No of studies	Design	Risk of bias	Quality assessment				No of patients		Relative (95% CI)	Effect		Quality	Importance
			Inconsistency	Indirectness	Imprecision	Other considerations	T>9h	T 7h group		Absolute			
<b>Total T&gt;9h VS T 7h group</b>													
11	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	22310/54534 (40.3%)	26225/91054 (28.9%)	OR 1.35 (1.16 to 1.57)	65 more per 1000 (from 31 more to 100 more)	8900	LOW	
<b>Study design subgroup - Cross-sectional survey subgroup</b>													
6	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	3342/8978 (37.2%)	7892/32726 (24.1%)	OR 1.49 (1.23 to 1.8)	80 more per 1000 (from 40 more to 123 more)	8900	LOW	
<b>Study design subgroup - Cohort Study subgroup</b>													
6	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	18974/85008 (41.6%)	18402/59667 (31.1%)	OR 1.17 (0.89 to 1.54)	35 more per 1000 (from 24 fewer to 99 more)	8900	LOW	
<b>Sex subgroup - Male subgroup</b>													
3	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	1615/2866 (35.4%)	3021/12042 (25.2%)	OR 1.05 (0.38 to 2.95)	9 more per 1000 (from 132 fewer to 242 more)	8900	LOW	
<b>Sex subgroup - Female subgroup</b>													
3	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	1427/9841 (36.2%)	3106/13057 (23.7%)	OR 1.32 (0.79 to 2.22)	54 more per 1000 (from 40 fewer to 171 more)	8900	LOW	
<b>Age subgroup - Middle-aged subgroup</b>													
4	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	234/752 (31.1%)	1352/6227 (21.7%)	OR 1.16 (0.73 to 1.85)	26 more per 1000 (from 49 fewer to 122 more)	8900	LOW	
<b>Age subgroup - Old Subgroup</b>													
3	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	2399/3848 (62.3%)	2262/8647 (48.7%)	OR 1.3 (1.04 to 1.63)	65 more per 1000 (from 10 more to 120 more)	8900	LOW	
<b>Sleep duration subgroup - Night sleep duration</b>													
5	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	321/1048 (30.6%)	1974/7954 (24.6%)	OR 0.97 (0.75 to 1.27)	6 fewer per 1000 (from 50 fewer to 47 more)	8900	LOW	
<b>Sleep duration subgroup - 24h sleep duration</b>													
6	observational studies	no serious risk of bias	serious <sup>1</sup>	no serious indirectness	no serious imprecision	none	20201/86848 (40.7%)	24251/83130 (29.2%)	OR 1.59 (1.42 to 1.77)	104 more per 1000 (from 77 more to 130 more)	8900	LOW	

<sup>1</sup>The p value for heterogeneity is less than 0.05, and I<sup>2</sup> is more than 80%.

(C) Literature quality of those who slept 8 h versus those who slept 7 h. All quality was low. (D) Literature quality of those who slept ≥ 9 h versus those who slept 7 h. All quality was low.