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. National surveys in the U.S. have shown a 1.5- to 2-hour trend of reduced sleep, which leads to a growing sleep debt. 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 (≤ 5 h, 6 h, 7 h, 8 h, ≥ 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 ≤ 5 h vs 7 h was 1.61, 95% CI = 1.28–2.02; those who slept ≥ 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 ≤ 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

regular naps.\textsuperscript{16} 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 ≤ 5 h, 6 h, 7 h, 8 h, and ≥ 9 h. Seven hours was treated as a baseline.\textsuperscript{19,20} Objective methods in large population mainly included polysomnography. Assessment criteria for hypertension were as follows: individuals who had systolic blood pressure readings ≥ 140 mm Hg or diastolic readings ≥ 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).\textsuperscript{21,22} 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$^2$ ≤ 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
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.23–29 The remaining 23 studies were carefully analyzed, and 4 studies were excluded because of a lack of suitable sleep time categorization.30–33 Three studies were excluded because the diagnostic criteria for hypertension did not meet the WHO guideline criteria.6,34,35 Two studies were excluded because of a lack of suitable hypertension population data.36,37 One study was excluded as an approximate duplicate (the same author published 2 related papers on the same population).38 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,10,11,13–15,39–46 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 ≤ 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 ≥ 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 investigations.10,13

### 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 ≤ 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, I² > 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 (≤ 5 h, 6 h, 7 h, 8 h, ≥ 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 ≤ 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 ≥ 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 ≤ 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 ≤ 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 ≥ 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 ≤ 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 ≤ 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 ≥ 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,13,40,41,43 The summary odds ratio simultaneously adjusted by age and gender for ≤ 5 h vs 7 h was 1.23, 95% CI = 1.01–1.49; for 6–7 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 ≥ 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 ≤ 5 h
### Table 1—Summary of the 13 studies included in the meta-analysis.

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

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.
Although it appears that sleep deprivation causes hypertension, which increases blood pressure, potentially leading to hypertension.54  Another study has shown that after the period of chronic sleep deprivation, flow-mediated 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.59,60  Dramatic alterations in these parameters due to prolonged wakefulness lead to a disturbance in circadian rhythmicity of blood pressure, and finally results in hypertension.61

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.9  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.62  There are also studies showing that long periods of sleep are associated with diabetes, obesity, and chronic heart disease.14,62,63  These diseases are often accompanied by hypertension. Long periods of sleep may be related to sleep-disordered breathing or poor sleep quality.54–66  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.60  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.68–70  The self-reported sleep habits between men and women also tends to be different; women were more likely to report sleeping more than the recommended hours. However, women are more likely to report feeling unrested, but less likely to have an high Epworth Sleepiness Scale score.71  This error may be almost impossible to eliminate.

In our analysis stratified by age, extremely short sleep duration (<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

Table 2—Meta-regression analysis.

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

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 (<5 h, 6 h, 8h, and ≥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.67  Under normal sleep conditions, the vagal system is activated and catecholamine biosynthesis is decreased.48–49  Sleep deprivation, however, seems to act as a stressor on the body and activates the sympathetic system,50  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.51–53  This leads to blood vessel constriction, which increases blood pressure, potentially leading to hypertension.54  Another study has shown that after a period of chronic sleep deprivation, flow-mediated dilation of artery and intracellular magnesium concentrations both decreased.55  Magnesium is considered a physiologic calcium antagonist capable of decreasing vascular tone.56–58  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

1053  Journal of Clinical Sleep Medicine, Vol. 11, No. 9, 2015
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. 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 (< 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. 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 independent 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 measured 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 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


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DISCLOSURE STATEMENT

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

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

CSS, cross-sectional survey; PCS, prospective cohort study.
### Table S2—Heterogeneity of subgroup analysis.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>5 h vs 7 h</th>
<th>6 h vs 7 h</th>
<th>8 h vs 7 h</th>
<th>9 h vs 7 h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p*</td>
<td>I² (%)</td>
<td>p</td>
<td>I² (%)</td>
</tr>
<tr>
<td>Study design subgroup</td>
<td>&lt; 0.00001</td>
<td>89</td>
<td>&lt; 0.00001</td>
<td>89</td>
</tr>
<tr>
<td>Cross-sectional survey</td>
<td>&lt; 0.00001</td>
<td>83</td>
<td>&lt; 0.00001</td>
<td>93</td>
</tr>
<tr>
<td>Cohort study</td>
<td>0.04</td>
<td>58</td>
<td>0.07</td>
<td>51</td>
</tr>
<tr>
<td>Sex subgroup</td>
<td>0.0003</td>
<td>79</td>
<td>&lt; 0.00001</td>
<td>83</td>
</tr>
<tr>
<td>Male</td>
<td>0.0008</td>
<td>86</td>
<td>&lt; 0.00001</td>
<td>89</td>
</tr>
<tr>
<td>Female</td>
<td>0.12</td>
<td>52</td>
<td>0.005</td>
<td>81</td>
</tr>
<tr>
<td>Sleep duration subgroup</td>
<td>&lt; 0.00001</td>
<td>90</td>
<td>&lt; 0.00001</td>
<td>90</td>
</tr>
<tr>
<td>Night</td>
<td>&lt; 0.00001</td>
<td>89</td>
<td>&lt; 0.00001</td>
<td>95</td>
</tr>
<tr>
<td>24-h sleep</td>
<td>&lt; 0.00001</td>
<td>92</td>
<td>0.75</td>
<td>0</td>
</tr>
<tr>
<td>Age subgroup</td>
<td>&lt; 0.00001</td>
<td>84</td>
<td>0.0004</td>
<td>74</td>
</tr>
<tr>
<td>Middle-aged</td>
<td>&lt; 0.00001</td>
<td>87</td>
<td>0.0003</td>
<td>81</td>
</tr>
<tr>
<td>The old</td>
<td>0.05</td>
<td>66</td>
<td>0.28</td>
<td>21</td>
</tr>
</tbody>
</table>

*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 ≥ 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.

A  Funnel plot with pseudo 95% confidence limits

B  Funnel plot with pseudo 95% confidence limits

C  Funnel plot with pseudo 95% confidence limits

D  Funnel plot with pseudo 95% confidence limits
Duration of Sleep and Hypertension in Adults

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

<table>
<thead>
<tr>
<th>Quality</th>
<th>No. of studies</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>1</td>
<td>None</td>
<td>Good</td>
<td>Low</td>
</tr>
<tr>
<td>Average</td>
<td>1</td>
<td>None</td>
<td>Average</td>
<td>Low</td>
</tr>
<tr>
<td>Poor</td>
<td>1</td>
<td>None</td>
<td>Poor</td>
<td>Low</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Quality</th>
<th>No. of studies</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>1</td>
<td>None</td>
<td>Good</td>
<td>Low</td>
</tr>
<tr>
<td>Average</td>
<td>1</td>
<td>None</td>
<td>Average</td>
<td>Low</td>
</tr>
<tr>
<td>Poor</td>
<td>1</td>
<td>None</td>
<td>Poor</td>
<td>Low</td>
</tr>
</tbody>
</table>

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