

ORIGINAL ARTICLE

Short sleep duration is associated with hypertension risk among adults: a systematic review and meta-analysis

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A number of studies have reported that sleep duration might have an important role in the development of hypertension. However, the results have been inconsistent. In this study, a meta-analysis was performed to clarify the association between sleep duration and hypertension risk. PubMed, Embase and ISI web of science databases updated on 28 October 2011 were searched for eligible publications. Pooled odds ratio (OR) or relative risk (RR) with 95% confidence intervals (CI) was calculated using a random- or fixed-effect model. Six prospective ($N=9959$) and seventeen cross-sectional ($N=105432$) studies were identified for the data analysis on sleep duration. The results indicated that short sleep duration was associated with an increased risk of prevalent hypertension (OR = 1.20, 95% CI: 1.09–1.32, $P<0.001$), especially among subjects younger than 65 years and females. In addition, short sleep duration was also associated with an increased risk of incident hypertension among subjects younger than 65 years (RR = 1.33, 95% CI: 1.11–1.61, $P=0.002$). Overall, there was a significant association between long sleep duration and the risk of prevalent hypertension (OR = 1.11, 95% CI: 1.05–1.17, $P<0.001$). Further subgroup analysis also suggested a significant association between long sleep duration and the risk of prevalent hypertension among subjects younger than 65 years (OR = 1.12, 95% CI: 1.06–1.19, $P<0.001$). The present meta-analysis indicated that short sleep duration was associated with an increased risk of hypertension in the overall population and incident hypertension among subjects younger than 65 years. In addition, long sleep duration might be associated with a risk of prevalent hypertension, especially among subjects younger than 65 years.

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INTRODUCTION

Hypertension, which can cause severe damage to many human organs,¹ contributes greatly to the morbidity and mortality of cardiovascular diseases.² About one-third of adults worldwide are affected by hypertension each year.³ Although the awareness, treatment and control of hypertension have been improved, the success of these measures is still unacceptably low.⁴

Evidence has suggested that the average sleep duration declined by approximately 18 min from 1972 to 2005, especially in working-age men;⁵ and the percentage of short sleepers has increased significantly among full-time workers from 1975 to 2006.⁶ During the past couple of decades, many studies have reported the association of short or long sleep duration with a series of negative health outcomes, including mortality,^{7–9} cardiovascular disease,^{10,11} self-rated health^{12,13} and chronic diseases such as type 2 diabetes, metabolic syndrome, obesity, osteoporosis.^{14–18} Recently, growing evidence has suggested that short or long sleep duration might be associated with hypertension risk.^{19–32} However, the results have been

inconsistent, which could be due to the differences in the studied population, the study design and insufficient statistical power.

Most recently, Dean *et al.*³³ has performed a systematic review to investigate the association between habitual sleep duration and hypertension. However, they did not provide a quantitative risk estimate. Therefore, it is still unclear whether short or long sleep duration is associated with hypertension risk. In this study, we performed a meta-analysis to further clarify the association between sleep duration and the risk of hypertension.

MATERIALS AND METHODS

Literature and search strategy

We searched the literature databases, including PubMed, Embase and ISI Web of Science. The search strategy to identify all possible studies involved the use of the following keywords: ('sleep') and ('blood pressure' or 'hypertension') and ('adult'). The reference lists of retrieved articles were manually searched. The relevant papers were restricted to ones published in the English language. If more than one study was published using the same case series, only the

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study with the largest sample size was included. The literature search was updated on 28 October 2011.

Inclusion criteria and data extraction

Studies were included if they met the following inclusion criteria: (1) using cross-sectional, case-control or cohort design; and (2) evaluating the association between sleep duration and hypertension in adults. The following information was extracted from each study: (1) name of the first author; (2) year of publication; (3) country of origin; (4) ethnicity of study population; (5) study design; (6) gender distribution and mean age of study population; (7) sample size; (8) sleep duration assessment; (9) hypertension assessment; (10) odds ratio (OR) or relative risk (RR) with 95% confidence interval (CI); and (11) covariate adjustment. If one study was prospective, the recruitment year and duration of follow-up were also extracted. Two authors independently assessed the articles for compliance with the inclusion criteria, and disagreement was followed by discussion until consensus was reached.

Statistical analysis

Adjusted OR or RR with 95% CI was extracted from the selected papers and used to assess the strength of association between sleep duration and hypertension. The pooled OR (with 95% CI) of prevalent hypertension and the pooled RR (with 95% CI) of incident hypertension were separately calculated according to the types of sleep duration (short or long). Significance was determined by Z test ($P < 0.05$ was considered statistically significant). The heterogeneity among studies was evaluated by the Q-statistic test and the I^2 -statistic of Higgins and Thompson.³⁴ A random- (DerSimonian-Laird method)³⁵ or fixed- (Mantel-Haenszel method)³⁶ effects model was used to calculate the pooled OR or RR in the presence ($P \leq 0.10$) or the absence ($P > 0.10$) of heterogeneity, respectively. Subgroup analysis was performed based on age, gender and ethnicity. Sensitivity analysis, after removing one study at a time, was performed to evaluate the stability of the results. Begg's funnel plot, a scatter plot of effect against a measure of study size, was generated as a visual aid to detect bias or systematic heterogeneity.³⁷ Publication bias was assessed by Egger's test³⁸ ($P < 0.05$ was considered statistically significant). Data analysis was performed using STATA version 11 (StataCorp LP, College Station, TX, USA).

RESULTS

Characteristics of the studies

The detailed steps of our literature search are shown in Figure 1. On the basis of the search strategy and inclusion criteria, 18 papers seemed to be eligible after reading the title or abstract. After the full texts were read, the paper by Bjorvatn *et al.*³⁹ was excluded because it just provided data on the association between sleep duration and systolic hypertension or diastolic hypertension alone. One paper⁴⁰ that duplicated the paper by Gangwisch *et al.*¹⁹ was also excluded. In addition, two comments which did not provide the related data were excluded,^{41,42} with the exception of the one by Lima-Costa *et al.*,²⁵ which reported a new study concerning the association of sleep duration and hypertension. If the results were presented according to gender or age groups in one study, or if different study designs (prospective or cross-sectional) were involved in one paper, these were considered as separate studies in the data analysis. Therefore, 14 papers involving 23 studies were included in the final meta-analysis.^{19–32} Of them, six were prospective studies, including 9959 participants from United Kingdom ($n = 2$), Spain ($n = 1$) and United States ($n = 3$), and 17 were cross-sectional studies, including 105 432 participants from the United Kingdom ($n = 2$), Spain ($n = 1$), Netherlands ($n = 1$), Korea ($n = 2$), Brazil ($n = 1$), Germany ($n = 2$), China ($n = 2$), and the United States ($n = 6$).

In each study the referent category was identified, sleep duration being 7,^{20,21,26,28} 7–8^{19,23–25,30} or 7–9 h per night.³¹ Short sleep was defined as a duration ≤ 5 ,^{19,20,24,26–28} 4–5,²¹ ≤ 6 ,^{23,25,29} or < 7 h per

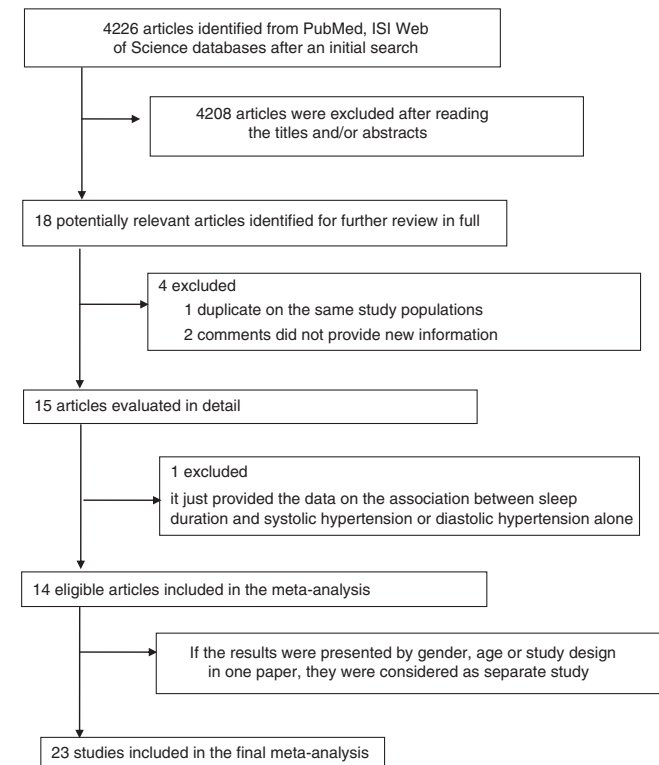


Figure 1 Selection of articles for inclusion in meta-analysis.

night.^{30–32} In most studies, long sleep was defined as a duration ≥ 9 or 10–15 h per night.²¹ However, one study reported the OR value of short sleep duration for incident hypertension without the specific definition of sleep duration.²²

Hypertension was defined as systolic blood pressure/diastolic blood pressure (SBP/DBP) $\geq 140/90$ mm Hg, current use of antihypertensive drugs or self-report of physician's diagnosis in all of the studies except for the one by van den Berg *et al.*²⁴ (which defined hypertension as SBP/DBP $\geq 160/100$ mm Hg or current use of antihypertensive drugs) and the study by Wang *et al.*³¹ (using SBP/DBP $\geq 130/85$ mm Hg or physician diagnosed hypertension as the definition). The characteristics of the included studies are listed in Tables 1 and 2.

Short sleep duration and hypertension

Six prospective studies involving 9959 participants were included in the meta-analysis. The overall result showed that short sleep duration was not associated with the risk of incident hypertension (RR = 1.11, 95% CI: 0.84–1.47, $P = 0.470$), with evidence of heterogeneity between studies ($I^2 = 55.3\%$, $P = 0.048$) and no evidence of publication bias ($P = 0.068$) (Table 3). Further subgroup analysis by age suggested a significant association between short sleep duration and the risk of incident hypertension among subjects younger than 65 years (RR = 1.33, 95% CI: 1.11–1.61, $P = 0.002$) but not among ones older than 65 years (Table 3). In addition, the between-study heterogeneity disappeared within each of the two subgroups.

A total of 17 cross-sectional studies involving 105 432 participants were included in the meta-analysis, and the result indicated that short sleep duration was significantly associated with an increased risk of prevalent hypertension (OR = 1.20, 95% CI: 1.09–1.32, $P < 0.001$), with evidence of heterogeneity between studies ($I^2 = 59.1\%$, $P = 0.001$) and no evidence of publication bias ($P = 0.857$) (Table 3, Figure 2). The sensitivity analysis indicated that the estimates ranged

Table 1 Description of the prospective studies included in the meta-analysis

Author	Year, publication	Country	Year, baseline	Follow-up (years)	Gender	Mean age (age range) (years)	Sleep category (hours)	Sample size	Sleep duration assessment	Hypertension assessment
Gangwisch ¹⁹	2006	USA	1982–1984	8–10	Male Female	32–59 60–86	Referent = '7–8' Short = '≤5' Long = '≥9'	3610 (32–59 years) 1190 (60–86 years)	Questionnaire	Self-report
Cappuccio ²⁰	2007	UK	1997–1999	5	Male Female	55.4 ± 6.0 56.1 ± 6.1	Referent = '7' Short = '≤5' Long = '≥9'	2686 (male) 1005 (female)	Questionnaire	Measurement
Lopez–Garcia ²¹	2009	Spain	2001	2	Male and female	≥65	Referent = '7–8' Short = '4–5' Long = '10–15'	890	Questionnaire	Self-report
Knutson ²²	2009	USA	2000–2001	5	Male and female	40.1 ± 3.6	Not available	578	Objective measurement	Measurement

Table 2 Description of the cross-sectional studies included in the meta-analysis

Author	Year, publication	Country	Gender	Mean age (age range) (years)	Sleep category (hours)	Sample size	Sleep duration assessment	Hypertension assessment
Gottlieb ²³	2006	USA	Male and female	63.1 ± 10.7	Referent = '7–8' Short = '≤6' Long = '≥9'	5910	Questionnaire	Measurement
Cappuccio ²⁰	2007	UK	Male Female	55.4 ± 6.0 56.1 ± 6.1	Referent = '7' Short = '≤5' Long = '≥9'	4199 (male) 1567 (female)	Questionnaire	Measurement
van den Berg ²⁴	2007	Netherlands	Male and female	72.1 ± 7.5	Referent = '7–8' Short = '≤5' Long = '≥9'	5058	Questionnaire	Measurement ^a
Lima-Costa ²⁵	2008	Brazil	Male and female	68.9	Referent = '7–8' Short = '≤6' Long = '≥9'	1423	Questionnaire	Measurement
Stang ²⁶	2008	German	Male and female	<65	Referent = '7' Short = '≤5' Long = '≥9'	2374 (male) 2423 (female)	–	–
Lopez–Garcia ²¹	2009	Spain	Male and female	≥65	Referent = '7–8' Short = '4–5' Long = '10–15'	3686	Questionnaire	Self-report
Vgontzas ²⁷	2009	USA	Male and female	48.7 ± 13.5	Referent = '>6' Short = '<5'	1741	Objective measurement	Measurement
Kim and Jo ²⁸	2010	Korea	Male Female	<65 ≥65	Referent = '7' Short = '≤5' Long = '≥9'	4515 (<65 years) 878 (≥65 years)	Questionnaire	Measurement
Stranges ²⁹	2010	USA	Male and female	<60	Referent = '≥6' Short = '<6'	1317 (male) 1710 (female)	Questionnaire	Measurement
Buxton and Marcelli ³⁰	2010	USA	Male and female	45 ± 17	Referent = '7–8' Short = '<7' Long = '>8'	56 507	Questionnaire	Measurement
Wang ³¹	2011	China	Male and female	18–65	Referent = '7–9' Short = '<7' Long = '≥9'	1033 (male) 783 (female)	Questionnaire	Measurement ^b
Bansil ³²	2011	USA	Male and female	<60	Referent = '≥7' Short = '<7'	10 308	Questionnaire	Measurement

^aHypertension was defined as SBP/DBP ≥ 160/100 mm Hg, or current use of antihypertensive medication.^bHypertension was defined as SBP/DBP ≥ 130/85 mm Hg, or physician-diagnosed hypertension.

Table 3 Pooled ORs and 95% CIs of the association between sleep duration and hypertension risk

Contrasts	No of studies	OR	95% CI	P _Z	Statistical model	I ² (%)	P _H
<i>Prospective studies</i>							
<i>Short sleep</i>							
All	6	1.11	0.84–1.47	0.470	Random	55.3	0.048
Age (years)							
<65	4	1.33	1.11–1.61	0.002	Fixed	29.6	0.234
≥65	2	0.74	0.47–1.14	0.169	Fixed	0.0	0.345
<i>Long sleep</i>							
All	5	0.83	0.52–1.33	0.606	Random	57.7	0.051
Age (years)							
<65	3	0.86	0.58–1.28	0.457	Fixed	47.7	0.148
≥65	2	0.87	0.36–2.06	0.748	Random	81.3	0.021
<i>Cross-sectional studies</i>							
<i>Short sleep</i>							
All	17	1.20	1.09–1.32	<0.001	Random	59.1	0.001
Age (years)							
<65	13	1.26	1.13–1.39	<0.001	Random	63.1	0.001
≥65	4	0.99	0.84–1.16	0.910	Fixed	0.0	0.848
Gender							
Male	4	1.03	0.91–1.18	0.611	Fixed	0.0	0.400
Female	4	1.35	1.18–1.55	0.000	Fixed	7.8	0.354
Ethnicity							
Caucasian	10	1.15	0.99–1.34	0.063	Random	67.1	0.001
East	4	1.34	1.13–1.59	0.001	Fixed	0.0	0.811
Asian							
Mixed	3	1.21	1.01–1.44	0.034	Random	77.3	0.012
<i>Long sleep</i>							
All	13	1.11	1.05–1.17	<0.001	Fixed	33.6	0.114
Age (years)							
<65	9	1.12	1.06–1.19	<0.001	Fixed	23.0	0.239
≥65	4	1.00	0.85–1.17	0.978	Fixed	48.8	0.119
Gender							
Male	3	1.23	0.78–1.96	0.373	Random	55.5	0.106
Female	3	1.13	0.92–1.40	0.243	Fixed	25.1	0.263
Ethnicity							
Caucasian	8	1.08	0.99–1.19	0.088	Fixed	24.5	0.233
East	4	1.39	0.95–2.05	0.094	Random	51.5	0.103
Asian							
Mixed	1	1.10	1.03–1.19	0.555	–	–	–

Abbreviations: CI, confidence interval; OR, odds ratio.
P_H, P value based on Q test for between-study heterogeneity.
P_Z, P value for Z test.

from 1.17 (1.10–1.24) to 1.23 (1.16–1.29) by excluding one study at a time, which further confirmed the positive association. Subsequent subgroup analysis by age suggested a significant association between short sleep duration and prevalent hypertension risk among subjects younger than 65 years (OR = 1.26, 95% CI: 1.13–1.39, P < 0.001) but no association among subjects older than 65 years (Table 3). In the stratified analysis by gender, the statistically significant association was observed among the female population (OR = 1.35, 95% CI: 1.18–1.55, P = 0.000) but not among the male population (Table 3). Meanwhile, the between-study heterogeneity disappeared within both subgroups. Moreover, subgroup analysis based on ethnicity also showed a significant association between short sleep and the risk of prevalent hypertension among the East Asian

population (OR = 1.34, 95% CI: 1.13–1.59, P = 0.001) but not among Caucasians (Table 3).

Long sleep duration and hypertension

Five prospective studies involving 9381 participants were included in the meta-analysis. The overall result showed that long sleep duration was not associated with the risk of incident hypertension (RR = 0.83, 95% CI: 0.52–1.33, P = 0.606), with evidence of heterogeneity between studies (I² = 57.7%, P = 0.051) and no evidence of publication bias (P = 0.249). Further subgroup analysis showed that there was no statistically significant association among either subjects younger than 65 years or older than 65 years (Table 3).

A total of 13 cross-sectional studies involving 90 356 participants were included in the meta-analysis, and the result showed that there was a significant association between long sleep duration and an increased risk of prevalent hypertension (OR = 1.11, 95% CI: 1.05–1.17, P < 0.001), with moderate heterogeneity between studies (I² = 33.6%, P = 0.114) and no evidence of publication bias (P = 0.555). The sensitivity analysis indicated that the estimates ranged from 1.09 (1.03–1.16) to 1.12 (1.06–1.19) by excluding one study at a time. Further subgroup analysis by age suggested a significant association between long sleep duration and the risk of prevalent hypertension among subjects younger than 65 years (OR = 1.12, 95% CI: 1.06–1.19, P < 0.001) but no association among ones older than 65 years. However, there was no statistically significant association among each subgroup according to gender or ethnicity (Table 3).

DISCUSSION

To our knowledge, our present study was the first meta-analysis investigating the association between sleep duration and risk of hypertension. The results from cross-sectional studies suggested statistically significant associations between short and long sleep duration and the risk of prevalent hypertension, confirming the presence of a U-shape association. The stability of sensitivity analyses and absence of publication biases further confirmed the positive associations. Moreover, subgroup analyses indicated that short sleep duration was significantly associated with prevalent hypertension among subjects younger than 65 years, females, East Asians, and long sleep duration was significantly associated with prevalent hypertension only among subjects younger than 65 years. However, for either end of the distribution of sleep duration, the meta-analyses from prospective studies did not provide consistent results. Nevertheless, for the short sleep duration–hypertension relationship, the age-specific effect of prospective studies was in agreement with the conclusion from cross-sectional studies: that is, the significant association of short sleep duration with the risk of incident hypertension was found among subjects younger than 65 years but not among those older than 65 years.

The biological mechanism underlying the association of short sleep duration with hypertension risk remains unclear. It has been suggested that short sleep duration could increase the average 24-h blood pressure and heart rate, elevate the sympathetic nervous system activity and stimulate physical and psychosocial stressors,^{19,23,43} and these forces in turn could lead to sustained hypertension. In addition, altered activity of the hypothalamic pituitary adrenal axis as a result of the elevated cortisol levels, renal impairment, endothelial dysfunction and proinflammatory responses could also contribute to hypertension.^{44–46} In addition, some evidence points to the disruption of circadian rhythmicity and autonomic balance by chronic short sleep duration being one potential contributing

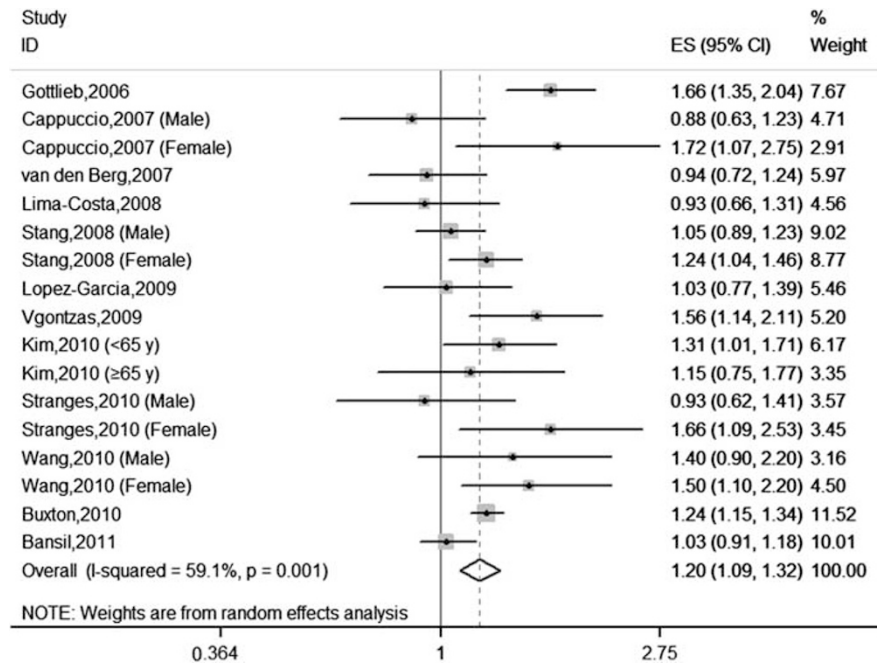


Figure 2 Meta-analysis of the association between short sleep duration and the risk of prevalent hypertension. A full color version of this figure is available at the *Hypertension Research* journal online.

mechanism.^{19,47} Finally, short sleep duration is likely to be associated with emotional changes such as irritability, impatience, pessimism and feeling tired and stressed,⁴⁸ which would make it more difficult to maintain a healthy lifestyle to protect against hypertension.¹⁹

There is evidence that the full-time workers are more likely to be short sleepers compared with part-time workers and the retired.⁶ With regards to potential mechanisms of the age-specific effect on the association, it should be noted that younger people, who are often full-time workers, tend to experience more work-family strains, which may directly increase their blood pressure levels, as well as reduce their sleep duration or influence behaviors such as physical activity, diet and tobacco consumption to elevate their blood pressure levels.⁴⁹ Another possibility is that older people, who are often retired, have a decreased demand for sleep and can also compensate for their nightly short sleep duration by daytime napping.^{19,23,24} People in poor physical condition, such as those with hypertension, diabetes and obesity, are less likely to survive into their later years, which could also partly explain the lack of association between short sleep duration and hypertension in older people.¹⁹ For the gender-specific association, the potential mechanisms are unknown. However, it is possible that the gender differences in psychosocial factors⁵⁰ and in stress and responses to stress⁵¹ may have a role in the association. Another explanation may be that women in menopause tend to be more vulnerable because of fluctuations in sex hormones.²⁰

Moreover, it should be noted that short sleep duration may lead to increased mortality, as a result of negative health outcomes such as hypertension, cardiovascular disease, diabetes, metabolic syndrome and obesity. This is one of the possible pathways to explain the relationship between short sleep duration and mortality. However, the specific mechanism remains unknown and deserves further investigation.⁵² Thus, more in-depth research is required to clarify the underlying mechanisms of the short sleep duration–hypertension–mortality relationship.

Regarding the association between long sleep duration and hypertension risk, this was consistent with other relationships

between long sleep duration and cardiovascular disease and mortality.^{8–11} However, there has hitherto been little speculation on the potential mechanisms underlying the associations of long sleep duration with morbidity and mortality. Rather, one vigorous argument has focused on sleep apnea, which could confound the associations because individuals with this disorder spend more time or an excessive amount of time asleep to compensate for the fragmented nature of their sleep.⁵³ However, there is not sufficient evidence that people with sleep apnea sleep more than the average.⁵⁴ In addition, the associations may be explained by some other residual confounding factors associated with long sleep duration such as depressive symptoms, low socio-economic status, unemployment status, being single and low education levels.^{55,56} And therefore long sleep duration might be a marker, rather than a causative risk factor, of morbidity and mortality.⁵⁵ However, further prospective studies are required to confirm the positive association of long sleep duration with hypertension.

Several limitations of our analysis should be noted. First, the information on sleep duration was self-reported by questionnaire for most studies, with the exception of two studies (by Knutson *et al.*²² and Vgontzas *et al.*²⁷ where the data were obtained by objective measurement with actigraphy). Nevertheless, self-reported sleep duration assessment has been validated against quantitative sleep assessments.^{22,55} Second, there were also a few small differences in the measurement of blood pressure or the definition of hypertension between the studies; however, in most of the included studies, hypertension was defined as SBP/DBP \geq 140/90 mm Hg. Third, as is known, cross-sectional studies do not allow for establishing the causality of an observed association, although a positive association was found based on these studies. In addition, the sample size of the included prospective studies in our meta-analysis was so small that the result was not consistent with that of the cross-sectional studies. However, the present meta-analysis does have some strengths. For instance, the pooled results were based on adjusted estimates from multivariate regression models, including a number of confounding

factors, although the covariates that were controlled for were somewhat different for each study.

In conclusion, our meta-analysis indicated that short sleep duration was associated with an increased risk of prevalent hypertension in the overall population, especially among subjects younger than 65 years and females, and short sleep duration was associated with an increased risk of incident hypertension only among subjects younger than 65 years. In addition, a long sleep duration might be associated with the risk of prevalent hypertension among subjects younger than 65 years. Large-scale prospective studies are needed to further investigate the causal association between sleep duration and hypertension.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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