Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies

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Background—Effects of extreme sleep duration on risk of mortality and cardiovascular outcomes remain controversial. We aimed to quantify the dose-response relationships of sleep duration with risk of all-cause mortality, total cardiovascular disease, coronary heart disease, and stroke.

Methods and Results—PubMed and Embase were systematically searched for prospective cohort studies published before December 1, 2016, that examined the associations between sleep duration and at least 1 of the 4 outcomes in generally healthy populations. U-shaped associations were indicated between sleep duration and risk of all outcomes, with the lowest risk observed for ≈7-hour sleep duration per day, which was varied little by sex. For all-cause mortality, when sleep duration was <7 hours per day, the pooled relative risk (RR) was 1.06 (95% CI, 1.04–1.07) per 1-hour reduction; when sleep duration was >7 hours per day, the pooled RR was 1.13 (95% CI, 1.11–1.15) per 1-hour increment. For total cardiovascular disease, the pooled RR was 1.06 (95% CI, 1.03–1.08) per 1-hour reduction and 1.12 (95% CI, 1.08–1.16) per 1-hour increment of sleep duration. For coronary heart disease, the pooled RR was 1.07 (95% CI, 1.03–1.12) per 1-hour reduction and 1.05 (95% CI, 1.00–1.10) per 1-hour increment of sleep duration. For stroke, the pooled RR was 1.05 (95% CI, 1.01–1.09) per 1-hour reduction and 1.18 (95% CI, 1.14–1.21) per 1-hour increment of sleep duration.

Conclusions—Our findings indicate that both short and long sleep duration is associated with an increased risk of all-cause mortality and cardiovascular events. **(*J Am Heart Assoc*. 2017;6:e005947. DOI: 10.1161/JAHA.117.005947.)**

Key Words: all-cause death • cardiovascular disease • coronary heart disease • meta-analysis • sleep • stroke

According to the report of World Congress of Cardiology and Cardiovascular Health in 2016, cardiovascular diseases (CVDs) are the leading cause of death globally, with an estimate of >17 million deaths from total CVD. Of these deaths, >7 million were due to coronary heart disease (CHD) and >6 million were due to stroke. In <10 years, the premature deaths from CVDs could rise by a third.[1] To reduce the risk of premature death from noncommunicable diseases by 25% by 2025, as a global target of the World Health Organization,[2] it is imperative to identify modifiable lifestyle factors associated with lower occurrence of CVDs. Sleep is a complex set of brain processes that supports several physiological needs.[3] Increased attention has been paid to understanding the extent of sleep duration problems at the population level and their associated negative effects on various health outcomes, such as metabolic syndrome,

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Accompanying Data S1, Tables S1 through S12 and Figures S1 through S13 are available at http://jaha.ahajournals.org/content/6/9/e005947/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- Uncertainty exists regarding the dose-response relationship between sleep duration and the risk of all-cause mortality and cardiovascular events.
- In our systematic review and meta-analysis, sleep duration that was either too short or too long was associated with higher risk of all-cause mortality and cardiovascular events, with the lowest risk at sleep duration of ≈7 hours per day.

What Are the Clinical Implications?

- The U-shaped associations between sleep duration and adverse outcomes have clinical relevance with respect to recommendations for adequate sleep duration in routine clinical care as well as explicit suggestions for primary prevention in public health settings.

diabetes mellitus, and cancer.[4–6] Previous publications suggest that the prevalence of short sleep duration (defined as <7 hours) may have gradually increased over past decades, whereas the prevalence of long sleep duration (defined as ≥9 hours) shows an opposite trend.[7]

In recent years, increasing evidence has suggested that extreme sleep duration is associated with the risk of mortality and cardiovascular outcomes; however, the results are not entirely consistent. Although several studies found that sleep duration that was either too short or too long was associated with increased risk of all-cause mortality and cardiovascular events,[8–13] reverse associations were observed in other populations.[14,15] In addition, uncertainty exists about the dose-response relationship between sleep duration and risk of the adverse outcomes because different quantitative categories of sleep duration were used in previous studies.[8,16–18] Two meta-analyses reported the association between sleep duration and all-cause mortality with dose-response analysis, but the results were inconsistent.[19,20] A previous meta-analysis published before 2011 reported the association between sleep duration and cardiovascular events[21]; however, without a dose-response analysis, it remains unknown how many hours of habitual sleep are associated with the lowest risk of cardiovascular events. Since 2011, many more studies have been published and the number of prospective studies has nearly tripled, which allows quantitative analysis of the associations. Consequently, we conducted a comprehensive dose-response meta-analysis of prospective studies in generally healthy populations to determine the overall shape of the relationships and quantitative estimates between sleep duration and risk of all-cause mortality, total CVD, CHD, and stroke.

Methods

Search Strategy

This study was conducted in accordance with the MOOSE (Meta-Analysis of Observational Studies in Epidemiology) guidelines.[22] We performed a literature search (up to December 1, 2016) of PubMed and Embase for prospective studies examining the association between sleep duration and risk of all-cause mortality and selected cardiovascular outcomes (Data S1). In addition, we reviewed references from relevant original articles and review articles to identify further pertinent studies. Only articles published in the English language were considered.

Study Selection

Studies were included if they satisfied the following criteria: The study design was a prospective cohort study; the exposure of interest was sleep duration; the outcome was all-cause mortality, CVD, CHD, or stroke; and the investigators reported relative risk (RR), hazard ratio, or odds ratio (OR) with 95% confidence intervals (CIs) for at least 3 quantitative categories of sleep duration. Given that primary prevention of CVD was the main focus of this work (rather than secondary prevention), we excluded studies if participants were not recruited from a generally healthy population (eg, those with diabetes mellitus or under regular dialysis therapy). In addition, we excluded reviews, editorials, nonhuman studies, and letters without sufficient data. Multiple reports from the same cohort study were reviewed, and only articles with the longest follow-up for identical outcomes were included. If insufficient data were presented in the longer follow-up study, we included the shorter follow-up data. Study selection was conducted in 2 stages: an initial screening of titles and abstracts to identify potentially relevant articles, followed by screening of the full-length articles. Two investigators (J.W.Y. and S.Z.L.) independently screened all studies by title or abstract and then by a full-text evaluation. Any discrepancy between the 2 authors was solved by discussion with the senior investigator (X.L.J.).

Data Extraction and Quality Assessment

The extraction of data included authors, year of publication, study name, study location, years of follow-up, sample size (number of participants and incident cases), participant characteristics (age and sex), measurement method of sleep duration (questionnaire and interview), types of sleep duration (24-hour sleep, nighttime sleep), covariates adjusted in the multivariable analysis, and effect size (RR, hazard ratio, OR), with 95% CIs for all categories of sleep duration. When studies had several adjustment models, we extracted those that reflected the maximum extent of adjustment for potentially confounding variables.

Quality assessment was performed according to the Newcastle–Ottawa Quality Assessment Scale (NOS).[23] Scores ranged from 0 to 9 points, with higher scores indicating higher study quality. We considered NOS scores of 0 to 3, 4 to 6, and 7 to 9 as low, medium, and high quality, respectively.

To evaluate potential dose-response relationships, we further extracted numbers of cases, numbers of participants, and median sleep duration in each category. If the numbers of participants and cases were not provided, the corresponding authors were contacted for the data.

Data Synthesis and Analysis

In this meta-analysis, the RR was used as the common measure of association across studies, and the hazard ratio was deemed equivalent to RR.[24] If necessary, the OR was transformed into RR according to this formula: $RR=OR/[(1-P_0)+(P_0\times OR)]$, where P_0 is the incidence of the outcome of interest in the nonexposed group.[25] Any results stratified by sex were treated as 2 separate reports. Those articles reporting >1 outcome (eg, all-cause mortality and total CVD) were also treated as separate reports and included in corresponding analyses. If the number of cases in each category was not available in 1 study and the authors did not give their reply, we used the method by Bekkering et al to provide approximate data.[26]

We recognized that sleeping 7 to 8 hours per night was treated as the reference category in the majority of studies. When the reference category was not 7 to 8 hours, we used the method proposed by Hamling and colleagues to convert risk estimates.[27] We calculated pooled RRs and 95% CIs for the extreme categories of sleep duration versus the reference category of sleep duration. In addition, the reports with at least 3 quantitative categories of short or long sleep duration were included in dose-response analyses. Potential nonlinear dose-response relationships between sleep duration and all-cause mortality and cardiovascular events were examined by using restricted cubic splines model with 4 knots at percentiles 5%, 35%, 65%, and 95% of the distribution.[28,29] We assigned the median or mean sleep duration in each category to the corresponding RR for each study. If the mean or median duration per category was not reported, the midpoint of the upper and lower boundaries in each category was assigned. When the shortest or the longest category was open-ended, we assumed that the open-ended interval length had the same length as the adjacent interval. The dose-response curves are shown in the nonlinear figures. The RR estimates in the tables were based on the nonlinear figures but show RRs for selected sleep-duration values. If a nonlinear shape association was observed, we treated the slope as 2 piecewise and conducted dose-response analyses using the method by Greenland and Longnecker to calculate pooled RR and 95% CIs for 1-hour increment or decrement compared with the reference category in sleep duration.[30] We used a *P* value for curve linearity or nonlinearity to assess the difference between the linear and nonlinear models to test for nonlinearity.[29] All pooled outcome measures were determined using random-effects models, described by DerSimonian and Laird,[31] to provide more conservative results than fixed-effects models.

The heterogeneity among studies was estimated by the Cochran Q test ($P\leq0.1$ to be indicative of statistically significant heterogeneity) and I^2 statistic.[32] We conducted subgroup and metaregression analyses stratified by sex, study location, number of participants, number of cases, duration of follow-up, sleep assessment, sleep duration type, study quality, incidence or mortality (only in total CVD, stroke and CHD), and adjustment for confounders to investigate potential sources of heterogeneity between subgroups. Moreover, stratified analyses were performed to evaluate the influences of selected study and participant characteristics on the results. Publication bias was assessed by inspection of the funnel plots for asymmetry with the Egger test[33] and Begg test.[34] The Duval and Tweedie[35] nonparametric trim-and-fill method was used to further assess the possible effect of publication bias. Additional sensitivity analyses were performed by omitting 1 study at each time to test the robustness of the results and the influence of an individual study on heterogeneity.[36] All statistical analyses were performed with Stata version 12 (StataCorp LP), and all tests were 2-sided with a significance level of 0.05 unless otherwise noted.

Results

Literature Search

Figure 1 shows the results of literature research and selection. We identified 836 articles from PubMed and 837 articles from Embase before December 1, 2016. After exclusion of duplicates and studies that did not fulfill the inclusion criteria, 101 remaining articles seemed to be relevant for this meta-analysis. After evaluating the full texts of these 101 publications and counting 1 study obtained by hand searching, the final meta-analysis included 67 articles with 141 independent reports. Among these 67 articles, 43 articles with 57 reports provided statistical effects relevant to the meta-analyses on all-cause mortality, 26 articles with 37 reports on total CVD, 22 articles with 27 reports on CHD, and 16 articles with 20 reports on stroke (Data S1).

Study Characteristics

A summary of the study characteristics is shown in Tables S1 through S4. The sample sizes ranged from 724 to 1 116 936, with a total of 3 582 016 participants, including 241 107

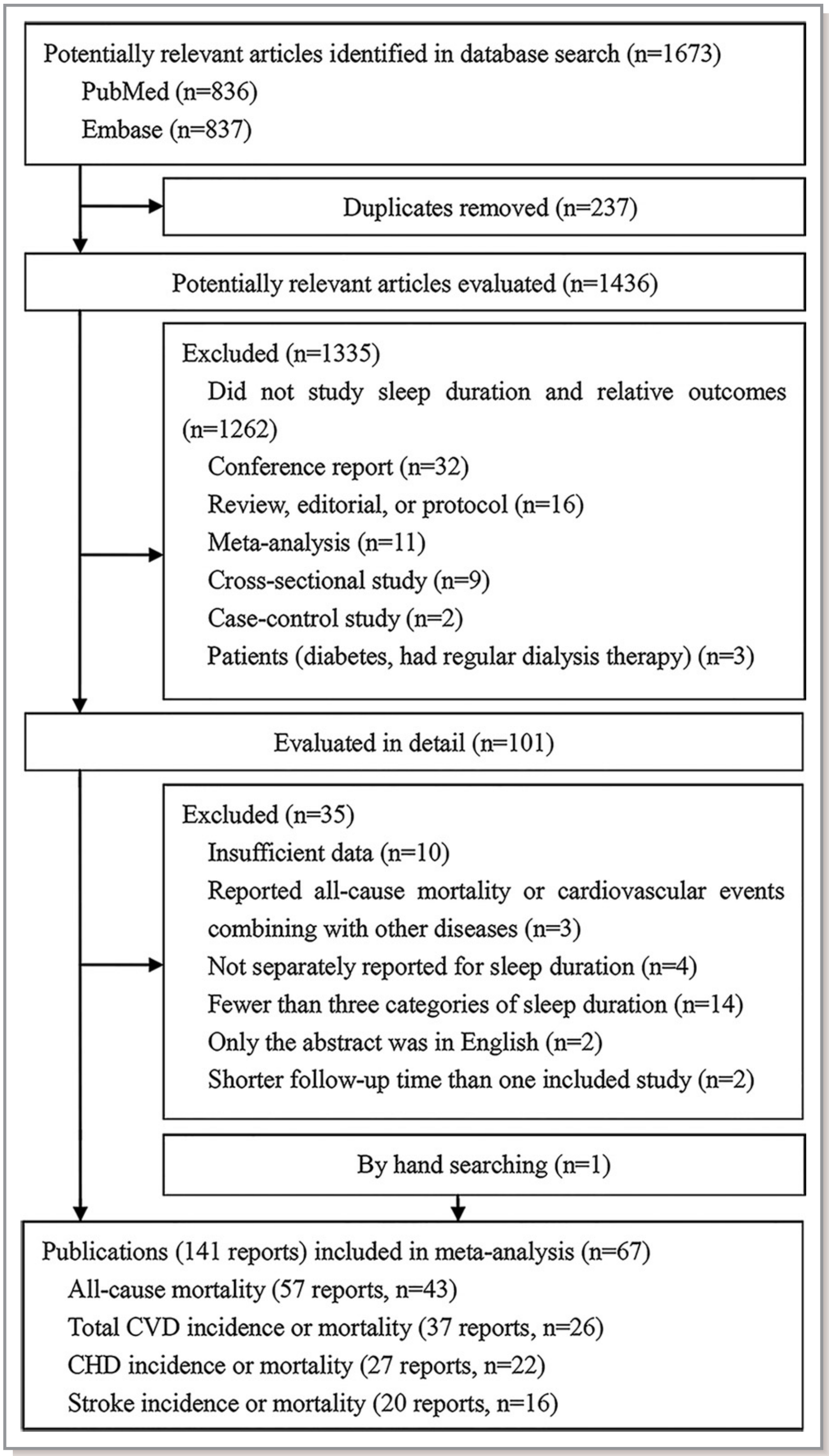

Figure 1. Flowchart of article selection. CHD indicates coronary heart disease; CVD, cardiovascular disease.

cases of all-cause mortality, 58 919 cases of total CVD, 22 511 cases of CHD, and 15 476 cases of stroke. The follow-up periods ranged from 2.3 to 34 years. Among these 67 articles, most were conducted in Europe (n=22), the United States (n=16), and Asia (n=27); the others were done in Australia (n=2). Sleep duration was measured by self-report questionnaires in 48 studies and by interview in 19 studies. The majority of the included studies had high quality, as indicated by the NOS

Table 1. Associations of Sleep Duration With All-Cause Mortality, Total CVD, CHD, and Stroke

		Shortest vs Reference			Longest vs Reference		
	n	RR* (95% CI)	I^2	*P* Value†	RR* (95% CI)	I^2	*P* Value†
All-cause mortality	57	1.13 (1.10–1.17)	37.5	<0.01	1.35 (1.29–1.41)	76.2	<0.01
Total CVD	37	1.14 (1.09–1.20)	31.1	0.04	1.36 (1.26–1.48)	71.2	<0.01
CHD	27	1.22 (1.13–1.31)	39.6	0.02	1.21 (1.12–1.30)	37.4	0.03
Stroke	20	1.09 (0.99–1.19)	40.6	0.03	1.45 (1.30–1.62)	63.5	<0.01

CHD indicates coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; RR, relative risk.
*RR favors the analyses of shortest and longest vs reference sleep duration.
†*P* for heterogeneity.

score, and the mean study quality scores were 6.9 for all-cause mortality, 7.0 for CVD, 7.0 for CHD, and 7.1 for stroke out of a maximum of 9 points (Tables S5 through S8).

Sleep Duration and Risk of All-Cause Mortality

In total, 57 reports were included in the analysis of all-cause mortality and extreme sleep duration. The pooled RR of the shortest and longest sleep duration versus reference sleep duration was 1.13 (95% CI, 1.09–1.17), with low to moderate heterogeneity (I^2=37.5%, *P*<0.01), and 1.35 (95% CI, 1.29–1.41), with high heterogeneity (I^2=76.2%, *P*<0.01), respectively (Table 1, Figure S1).

Reports with at least 3 quantitative categories of short or long sleep duration were included in dose-response analysis. When using a restricted cubic splines model, we observed a U-shape curvilinear association with the lowest risk of all-cause mortality at a sleep duration of about 7 hours per day (*P*<0.01 for nonlinearity; Figure 2A). Both short and long sleep duration was associated with an increased risk of all-cause mortality. Table 2 shows the RR estimates for selected sleep duration values, which were derived from the nonlinear figures. In the linear trend analyses for short sleep, no evidence of nonlinear association between short sleep duration and all-cause mortality was found (*P*=0.12), and the pooled RR for all-cause mortality was 1.06 (95% CI, 1.04–1.07) per 1-hour reduction of sleep duration, with moderate to high heterogeneity (I^2=55.5%, *P*<0.01; Figure 3A).[8–13,18,37–53] The heterogeneity was reduced when we excluded 2 reports[9,38] (I^2=13.0%, *P*=0.26), but the association was not substantially altered (pooled RR: 1.06; 95% CI, 1.05–1.07). For long sleep, nonlinear association between long sleep duration and all-cause mortality was found (*P*=0.02), and the pooled RR for all-cause mortality was 1.13 (95% CI, 1.11–1.15) per 1-hour increment of sleep duration, with high heterogeneity (I^2=76.5%, *P*<0.01) (Figure 3B).* The heterogeneity seemed to be mainly generated by 8 reports,[8,13,40,42,44,45,53,56] and when these were all excluded, the association still remained similar (RR: 1.12; 95% CI, 1.10–1.13) with low heterogeneity (I^2=21.7%, *P*=0.15).

Sleep Duration and Risk of Total CVD

Overall, 37 reports were included in the analysis of total CVD and extreme sleep duration. A U-shaped association was observed with the lowest risk of total CVD at a sleep duration of ≈7 hours per day (*P*<0.01 for nonlinearity; Figure 2B, Table 2). Both short and long sleep duration was associated with an increased risk of total CVD.

For short sleep, the pooled RR of the shortest sleep duration versus the reference sleep duration was 1.14 (95% CI, 1.09–1.20), with low to moderate heterogeneity (I^2=31.1%, *P*=0.04; Table 1, Figure S2). We found no evidence of nonlinear association between short sleep duration and total CVD (*P*=0.19), and the pooled RR was 1.06 (95% CI, 1.03–1.08) per 1-hour reduction of sleep duration, with moderate heterogeneity (I^2=52.0%, *P*<0.01; Figure 4A).† The heterogeneity was reduced when we excluded 1 report[9] (I^2=24.8%, *P*=0.63), and the association remained similar (pooled RR: 1.04; 95% CI, 1.02–1.06).

For long sleep, the pooled RR of the longest sleep duration versus the reference sleep duration was 1.36 (95% CI, 1.26–1.48), with high heterogeneity (I^2=71.2%, *P*<0.01; Table 1, Figure S2). A nonlinear association between long sleep duration and total CVD was found (*P*=0.02), and the pooled RR was 1.12 (95% CI, 1.08–1.16) per 1-hour increment of sleep duration, with high heterogeneity (I^2=75.3%, *P*<0.01; Figure 4B).‡ The heterogeneity seemed to be generated mainly by 4 reports, and when those were all excluded, the association not substantially altered (RR: 1.13; 95% CI, 1.11–1.16) with low heterogeneity (I^2=14.6%, *P*=0.28).

*References 8–13, 18, 37, 39–42, 44–48, 50–59.

†References 8–13, 38, 44, 48–50, 52, 60–63.
‡References 8–13, 15, 44, 48–50, 52, 54–56, 61, 62.

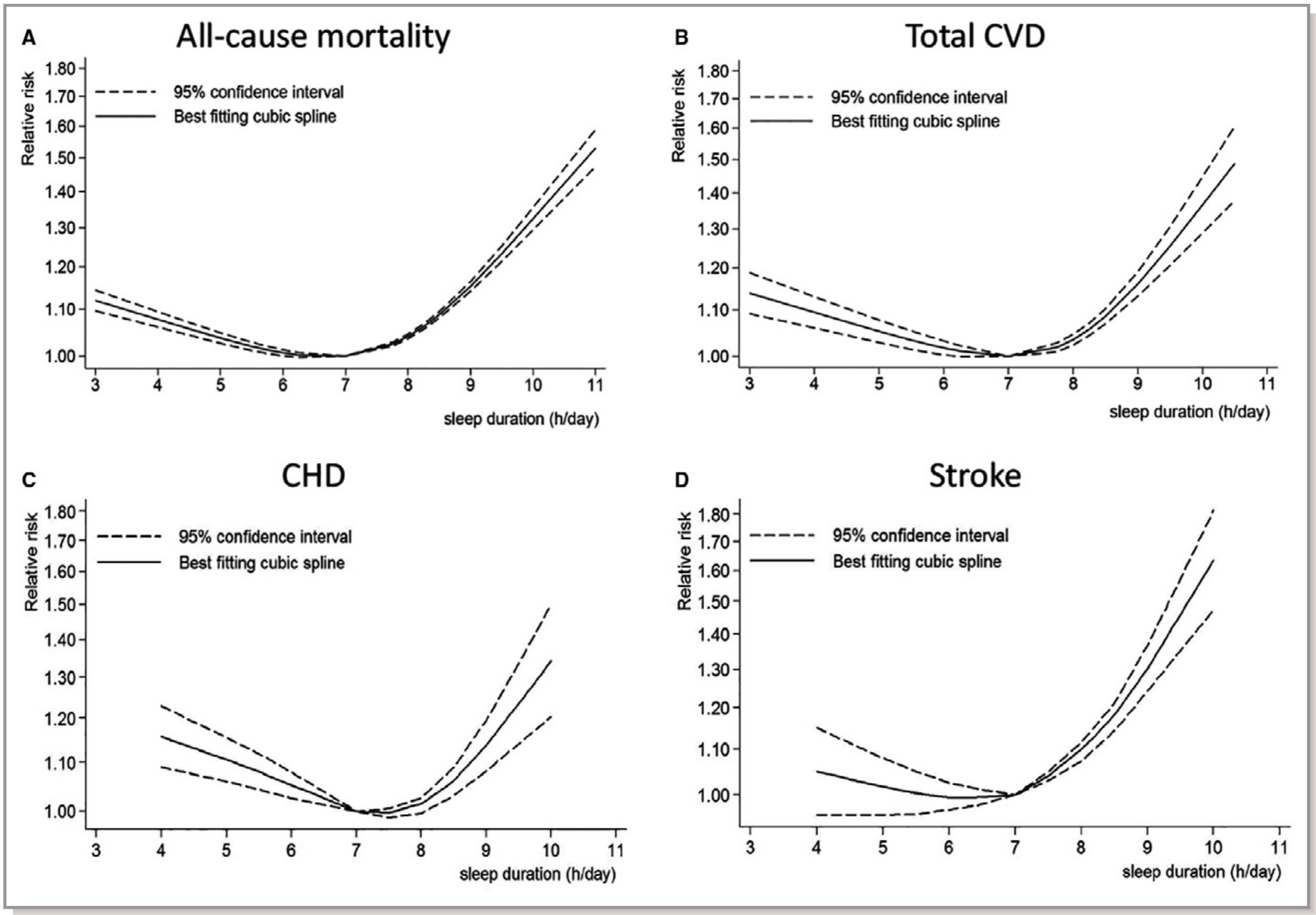

Figure 2. Nonlinear dose-response analyses of sleep duration and risk of all-cause mortality (A), total CVD (B), CHD (C), and stroke (D). CHD indicates coronary heart disease; CVD, cardiovascular disease.

Sleep Duration and Risk of CHD

In total, 27 reports were included in the analysis of CHD and extreme sleep duration. A U-shaped association was observed, with the lowest risk of CHD at a sleep duration of ≈7 hours per day ($P<0.01$ for nonlinearity; Figure 2C, Table 2). Both short and long sleep duration was associated with an increased risk of CHD.

For short sleep, the pooled RR of the shortest sleep duration versus the reference sleep duration was 1.22 (95% CI, 1.13–1.31), with low to moderate heterogeneity (I^2=39.6%, P=0.02; Table 1, Figure S3). In the linear trend analyses for short sleep, a nonlinear association was noted between short sleep duration and CHD (P=0.02), and the pooled RR was 1.07 (95% CI, 1.03–1.12) per 1-hour reduction of sleep duration, with moderate to high heterogeneity (I^2=59.3%, $P<0.01$) (Figure 5A).[§] The heterogeneity was reduced when we excluded 2 reports[13,66] (I^2=23.2%, P=0.19), and the association remained similar (pooled RR: 1.04; 95% CI, 1.01–1.08).

For long sleep, the pooled RR of the longest sleep duration versus the reference sleep duration was 1.21 (95% CI, 1.12–1.30), with low to moderate heterogeneity (I^2=37.4%, P=0.03; Table 1, Figure S3). A nonlinear association was noted between long sleep duration and CHD ($P<0.01$), and the pooled RR was 1.05 (95% CI, 1.00–1.10) per 1-hour increment of sleep duration, with moderate to high heterogeneity (I^2=64.2%, $P<0.01$; Figure 5B).[‖] The heterogeneity was reduced when we excluded 2 reports[15,66] (I^2=4.0%, P=0.41), and the association remained similar (pooled RR: 1.06; 95% CI, 1.03–1.09).

Sleep Duration and Risk of Stroke

Twenty reports were included in the analysis of stroke and extreme sleep duration. An approximate U-shape curvilinear association was observed, with the lowest risk of stroke at a

[§]References 11, 13, 16, 37, 43, 49, 60, 61, 63–68.

[‖]References 11, 13, 15, 37, 49, 54, 61, 64, 66–69.

Table 2. Association Between Sleep Duration and All-Cause Mortality, Total CVD, CHD and Stroke From Non-Linear Dose-Response Analysis

Sleep Duration	All-Cause Mortality (n=40*)	Total CVD (n=26*)	CHD (n=20*)	Stroke (n=17*)
3 h	1.12 (1.10–1.14)	1.14 (1.09–1.19)	...	...
4 h	1.08 (1.06–1.09)	1.09 (1.06–1.13)	1.16 (1.09–1.23)	1.05 (0.96–1.15)
5 h	1.04 (1.03–1.05)	1.05 (1.03–1.08)	1.11 (1.06–1.16)	1.02 (0.96–1.08)
6 h	1.01 (1.00–1.01)	1.02 (1.00–1.03)	1.05 (1.03–1.08)	0.99 (0.96–1.03)
7 h	1.00	1.00	1.00	1.00
8 h	1.04 (1.04–1.05)	1.03 (1.02–1.05)	1.01 (0.99–1.03)	1.08 (1.06–1.11)
9 h	1.15 (1.14–1.16)	1.16 (1.13–1.19)	1.14 (1.08–1.20)	1.30 (1.24–1.37)
10 h	1.32 (1.29–1.35)	1.37 (1.29–1.45)	1.34 (1.20–1.50)	1.64 (1.47–1.82)
11 h	1.53 (1.47–1.59)	...	...	...

CHD indicates coronary heart disease; CVD, cardiovascular disease.
*n denotes number of risk estimates.

sleep duration of ≈6 to 7 hours per day ($P<0.01$ for nonlinearity; Figure 2D, Table 2). Both short and long sleep duration was associated with an increased risk of stroke.

For short sleep, the pooled RR of the shortest sleep duration versus the reference sleep duration was 1.09 (95% CI, 0.99–1.19), with low to moderate heterogeneity (I^2=40.6%, P=0.03; Table 1, Figure S4). In the linear trend analyses for short sleep, we found no evidence of nonlinear association between short sleep duration and stroke (P=0.23), and the pooled RR for stroke was 1.05 (95% CI, 1.01–1.09) per 1-hour reduction of sleep duration, with no significant heterogeneity (I^2=0.0%, P=0.55) (Figure 6A).[¶]

For long sleep, the pooled RR of the longest sleep duration versus the reference sleep duration was 1.45 (95% CI, 1.30–1.62), with moderate to high heterogeneity (I^2=63.5%, $P<0.01$; Table 1, Figure S4). No evidence of nonlinear dose-response relationship was detected (P=0.13), and the pooled RR for stroke was 1.18 (95% CI, 1.14–1.21) per 1-hour increment of sleep duration, with low heterogeneity (I^2=4.9%, P=0.40; Figure 6B).[#]

Publication Bias

For the shortest or longest sleep duration versus the reference sleep duration, the publication bias was found between longest sleep duration and total CVD. The Begg rank correlation test indicated no publication bias (P=0.41), but the Egger linear regression test indicated possible publication bias for the association (P=0.01). We used the trim-and-fill method to recalculate our pooled risk estimate, and 13 missing studies were imputed to produce a symmetrical funnel plot (Figure S5). The analysis suggested that the imputed risk estimate was 1.22 (95% CI, 1.12–1.32), which is slightly decreased in risk but still identical to our original risk estimate. No significant publication bias was observed for other outcomes.

For the dose-response analysis, we analyzed the publication bias of short sleep duration and all-cause mortality and found that the Begg rank correlation test indicated no publication bias (P=0.59), but the Egger linear regression test indicated possible publication bias for the association (P=0.01). The trim-and-fill method was used to recalculate our pooled risk estimate, and 10 missing studies were imputed to produce a symmetrical funnel plot (Figure S6). The analysis suggested that the imputed risk estimate was 1.04 (95% CI, 1.03–1.06), which is identical to our original risk estimate. No significant publication bias was observed for other outcomes.

Subgroup, Metaregression, and Sensitivity Analyses

Tables S9 through S12 shows the different subgroup analyses of studies on all-cause mortality, total CVD, CHD, and stroke. To explore potential sources of heterogeneity between subgroups, we carried out metaregression analyses of prespecified moderator variables. In the analyses of all-cause mortality, the association between sleep duration and risk were not substantially changed in most subgroups. There was indication of heterogeneity (P=0.01) when we stratified studies by sleep duration type, and the pooled RRs for 1-hour increment in long sleep duration were 1.16 (95% CI, 1.13–1.18; n=24) and 1.11 (95% CI, 1.10–1.13; n=13) for nighttime and 24-hour sleep duration, respectively. In the nonlinear dose-response analysis, slight variations in the risk

[¶]References 8, 11, 13, 17, 49, 60, 63, 64, 70, 71.
[#]References 8, 11, 13, 17, 49, 54, 64, 70–73.

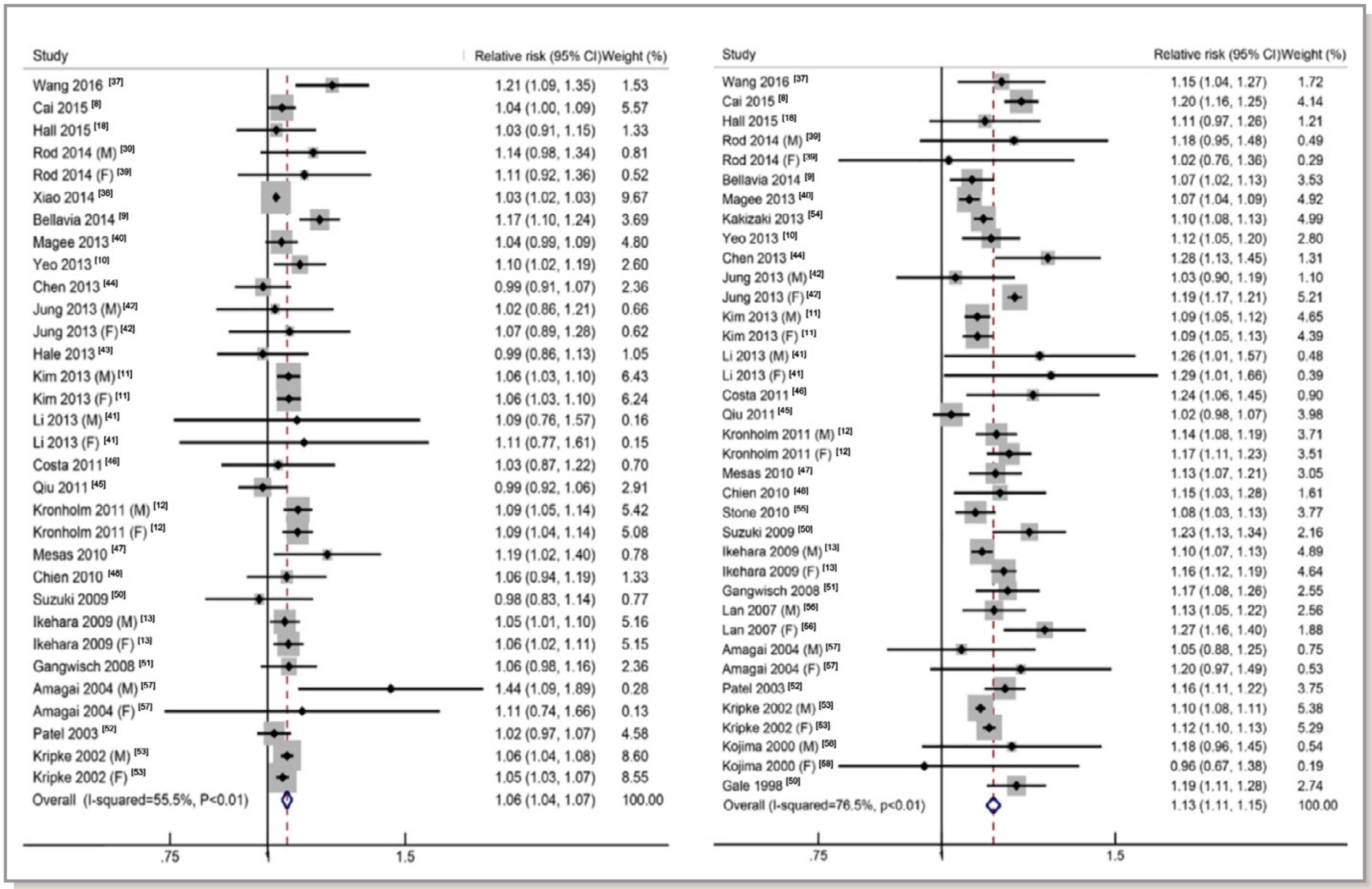

Figure 3. The forest plots between sleep duration (per hour) and risk of all-cause mortality for short sleep (A) and long sleep (B). CI indicates confidence interval.

estimates from the nonlinear dose-response analyses were observed (Figure S7).

In the analyses of total CVD, the associations between sleep duration and risk were not substantially changed in most subgroups. Heterogeneity was indicated (P<0.01) when we stratified studies by incidence or mortality, and the pooled RRs for 1-hour increment in long sleep duration were 1.00 (95% CI, 0.97–1.03; n=6) and 1.15 (95% CI, 1.12–1.16; n=16) for incidence and mortality, respectively. In the nonlinear analysis restricted to studies that reported the incidence of total CVD, there was no significantly increased risk of total CVD at the extreme sleep duration, whereas the U-shaped association was more pronounced among the studies that reported mortality of total CVD (Figure S8). There was evidence of heterogeneity by study location in the linear dose-response analysis of all participants (P=0.01), and the lowest RR was observed at 8-hour sleep duration in Europe (Figure S9).

In the analyses of CHD, the pooled RRs for 1-hour increment in long sleep duration were 0.89 (95% CI, 0.82–0.97; n=4) for Europe with indication of heterogeneity (P=0.02) by study location, which was inconsistent with other results. There was indication of heterogeneity (P=0.02) when we stratified studies by incidence or mortality, and the pooled RRs for 1-hour increment in long sleep duration were 1.01 (95% CI, 0.97–1.07; n=12) and 1.13 (95% CI, 1.06–1.20; n=7) for incidence and mortality, respectively. There was no significantly increased risk of CHD at the extreme sleep duration; the U-shaped association was more pronounced among the studies that reported mortality of CHD (Figure S10).

In the analyses of stroke, the association between sleep duration and risk was not substantially changed in most subgroups. There was indication of heterogeneity (P=0.01) when we stratified studies by duration of follow-up, with a weaker association among studies with increasing durations of follow-up (Figure S11).

To further confirm the robustness of the results, the dose-response analyses were repeated using a fixed-effects model; the pooled estimates were consistent for short and long sleep duration in relation to risk of all-cause mortality and cardiovascular events. Sensitivity analyses omitting 1 study at a time did not substantially alter the pooled results for both short and long sleep duration and all-cause mortality, total

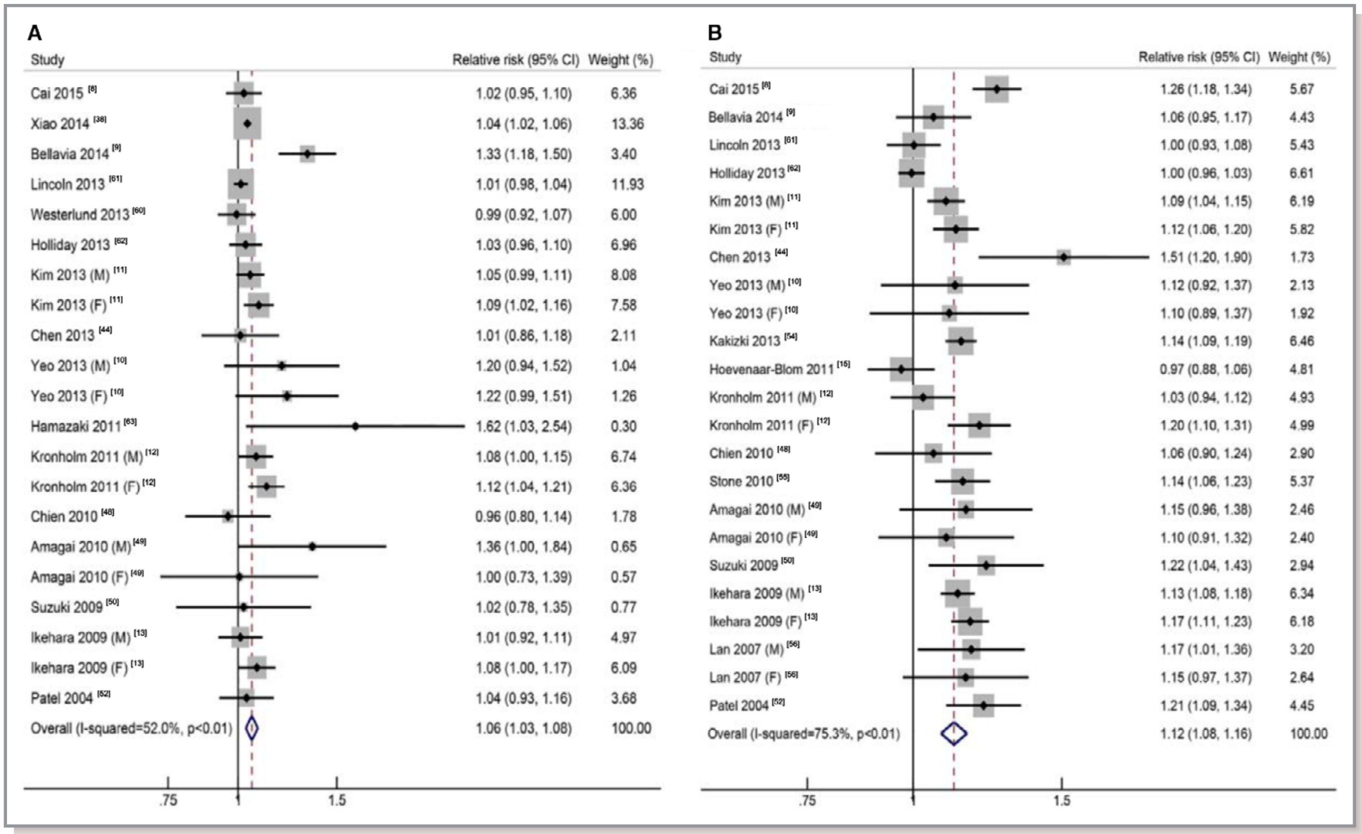

Figure 4. The forest plots between sleep duration (per hour) and risk of total cardiovascular disease for short sleep (A) and long sleep (B). CI indicates confidence interval.

CVD, and CHD. For stroke, when we excluded 1 study,[72] there was a statistically significant association in the analysis of the shortest versus reference sleep duration, and short sleep duration was associated with an increased risk of stroke (Figures S12 and S13).

Discussion

To our knowledge, the present work is the largest and most comprehensive study on the association of sleep duration with all-cause mortality and cardiovascular events. Our study demonstrated U-shaped associations between sleep duration and risk of all-cause mortality, total CVD, CHD, and stroke, with the lowest risk observed with ≈7 hours of sleep duration. Sleep duration that was too short or too long was significantly associated with elevated risks of all-cause mortality, total CVD, CHD, and stroke. Compared with 7 hours per day, a 1-hour decrease was associated with 6%, 6%, 7%, and 5% increased risk of all-cause mortality, total CVD, CHD, and stroke, respectively, and a 1-hour increase in sleep duration was associated with 13%, 12%, 5%, and 18% increased risk, respectively.

To date, association between extreme sleep duration and increased risk of all-cause mortality was reported previously in studies with large sample sizes and high quality,[8–13] which was consistent with our results. Heslop and colleagues,[14] however, analyzed data from a workplace-based study of Scottish men and women who were followed over a 25-year period and found that long sleep was associated with decreased all-cause mortality in men. But this study reported RRs with only 3 quantitative categories of sleep duration; meanwhile, long sleep duration was defined as >8 hours, which may result in inaccurate assessment of extreme long sleep. Recently, 2 systematic reviews,[19,20] both exploring the association between all-cause mortality and sleep duration (separate analysis of 24-hour sleep duration and nighttime sleep duration), observed markedly inconsistent results for short sleep duration. Results from Liu et al[20] showed that short sleep duration was not associated with higher risk of all-cause mortality in nighttime sleep duration. Nevertheless, results from Shen et al[19] showed that for both 24-hour and nighttime sleep duration, U-shaped relationships were found, and the lowest risk of all-cause mortality was observed with 7 hours per day of sleep duration, in line with our results; however, in the study by Shen et al, 1 cohort study[74] was included twice in analysis. Moreover, the linear associations on the 2 sides of 7-hour sleep duration were not detected.

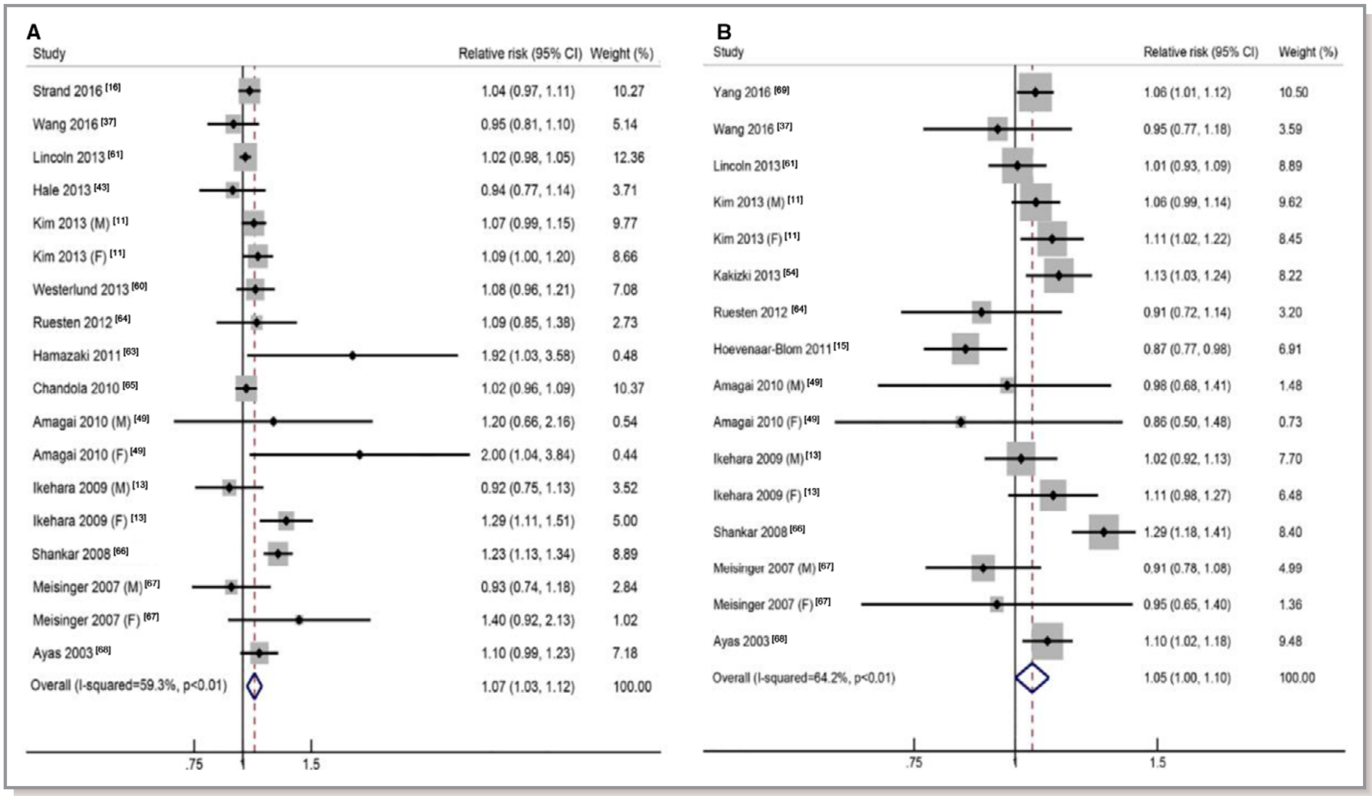

Figure 5. The forest plots between sleep duration (per hour) and risk of coronary heart disease for short sleep (A) and long sleep (B). CI indicates confidence interval.

Some studies have found an adverse association between extreme sleep duration and cardiovascular events. In our study, both short and long sleep duration was indicated to be associated with an increased risk of total CVD, which was inconsistent with a previous systematic review[21] in 2011. In that study, short duration of sleep was not significantly associated with a greater risk of total CVD, possibly because of limited included studies. Nineteen prospective cohort studies (26 reports) have been published since 2011 and were included in our study to describe the dose-response relationship between sleep duration and risk of total CVD. To our surprise, the findings from our subgroup analyses showed a decreased risk of CHD with long sleep duration in Europe, which should be interpreted carefully, given limited included studies. The association disappeared when we omitted the MOGEN study.[15] This research showed that long sleep duration tended to be protective for CHD; however, U-shaped associations were observed in the subgroup analysis of sleep quality in participants with available data. Notably, the proportion of women among long sleepers was significantly higher than that of men in the baseline population, whereas higher mortality rates and risks of CHD were observed in men than in women in published studies.[75] This may lead to the different result. Moreover, our subgroup analyses for total CVD and CHD showed indications of heterogeneity when we stratified studies by incidence and mortality. The U-shaped association was more pronounced among the studies that reported the mortality of total CVD or CHD compared with those that reported the incidence of total CVD or CHD. The association between cardiovascular events and sleep duration might be enhanced in the process through which patients tended to go from the occurrence of disease to death. It may also indicate that appropriate sleep duration is particularly important for delaying death among those people with chronic CVDs, and this needs to be identified further in additional studies. In our study, the adverse effect of short sleep for stroke was not observed in the shortest sleep duration versus reference analysis, whereas short sleep duration was associated with a higher risk of stroke in the dose-response analysis. By sensitivity analysis, we found that 1 study[72] had an obvious influence on the result of the shortest sleep duration versus reference analysis. The research indicated that a decreased risk of mortality from stroke was associated with short duration of sleep. Nonetheless, the small number of participants with short sleep duration limited the ability to separately analyze the effect of ≤5 and 6 hours of sleep, and the study was not included in the dose-response analysis because it had too few categories of short sleep. After omitting the studies with <3 categories of short sleep, the pooled RR of the shortest versus reference sleep duration was

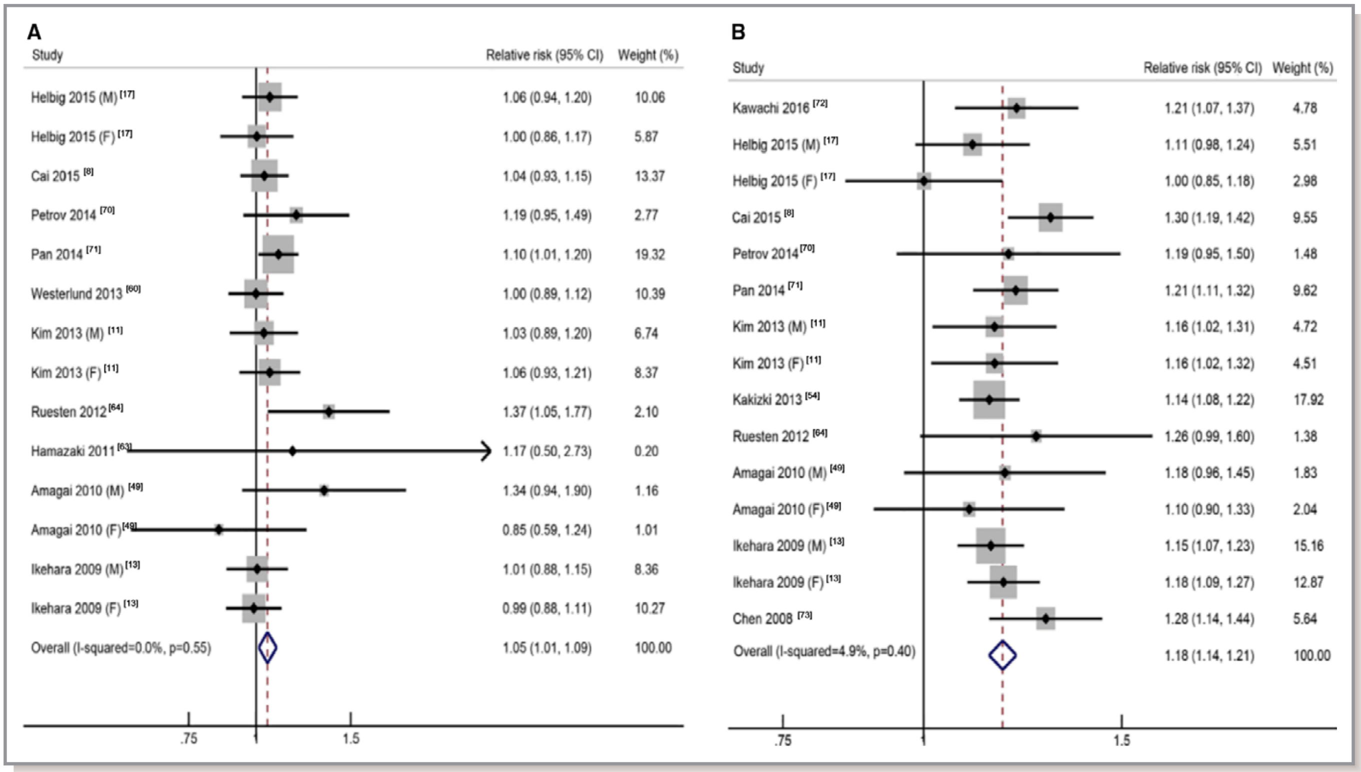

Figure 6. The forest plots between sleep duration (per hour) and risk of stroke for short sleep (A) and long sleep (B). CI indicates confidence interval.

1.16 (95% CI, 1.03–1.31), which was in line with the dose-response analysis.

Sex and age are important variables in risk of death and CVDs; this was generally accepted. In light of previous studies, the association between sleep duration and mortality[8,57,58] and cardiovascular events[16,67] varies by sex; however, in our subgroup analyses, extreme sleep durations were significantly associated with elevated risks of all-cause mortality, total CVD, CHD, and stroke in both men and women. Our metaregression analyses further demonstrated that there was no potential source of heterogeneity from the sex variable; therefore, a sex difference in the association of sleep duration with death and CVDs must be interpreted with caution. In addition, several studies found a stronger U-shaped association between sleep duration and CVDs in older adults compared with younger adults (cutoff at age 65 years).[10,16] Nevertheless, the result in a study including 60 000 Chinese participants (cutoff at age 60 years) was not entirely consistent.[66] Considering that the age range of the study population varied widely and the length of follow-up was different among the included studies, we did not conduct subgroup analyses stratified by age. Further studies concentrated on sleep duration and adverse outcomes among different age groups are warranted in the future.

Short and long sleep duration may share some relevant mechanisms in relation to all-cause mortality and cardiovascular events. As elucidated in published articles, extreme sleep duration on both sides was associated with elevated C-reactive protein.[76] As widely accepted, however, distinctive mechanisms with their own characteristics may operate at either end of the distribution of sleep duration.[77]

Several potential mechanisms may contribute to the relationship between short sleep duration and adverse outcomes. First, sleep restriction during the night has multiple effects on endocrine and metabolic function such as decreases of testosterone[78] and melatonin secretion,[79] which also may be implicated with mortality or cardiovascular events.[80,81] Second, observational studies also found that short duration of sleep was associated with vascular damage, such as coronary artery calcification.[82] Third, short duration of sleep was associated with reduced levels of leptin and elevated levels of ghrelin.[83,84] The serum leptin and ghrelin levels are independent predictors of cardiovascular morbidity and mortality.[85,86] Finally, individuals with sleep deprivation, especially shift workers, have irregular sleep schedules, resulting in circadian misalignment, which may aggravate CVD in humans.[87]

The potential mechanisms underlying the association between long sleep duration and adverse outcomes are considered more speculative. Some insisted that the elevated risk of long sleep duration most likely represented the confounding effects of subhealthy status or uncontrolled chronic illness, such as obstructive sleep apnea, a known cause of increased need for sleep and an identified risk factor for mortality and cardiovascular events.[88] As mentioned, changes in inflammatory markers and vascular health come with long sleep duration, as shown by new evidence in recent years. First, long sleep duration may be associated with an increased risk of atherosclerosis.[82] Second, excessive time in bed has been linked to increased sleep fragmentation,[89] which was considered to be associated with more severe arteriolosclerosis and subcortical macroscopic infarcts. These were independent risk factors of CVD and several medical comorbidities.[90] Third, long sleep duration has been linked with feelings of fatigue and lethargy, which in turn would cause sleep extension. These states may fail to provide sufficient restoration against stress and disease and then lead to increased mortality.[91] Finally, long duration of sleep was associated with depressive symptoms, low socioeconomic status, unemployment, low household income, low level of education, and other risk factors for mortality and cardiovascular events.[92] Further experimental studies are warranted to explore the potential effects of sleep extension on health outcomes.

This meta-analysis has several strengths. All studies included in our meta-analysis used a prospective design, thus the differential misclassification of sleep duration attributable to recall bias was minimized. The majority of the included studies had relatively high quality. Moreover, we investigated a dose-response relationship between sleep duration and the outcomes, allowing us to examine the shape of this possible association. Linear and nonlinear relationships were also tested to assess the dose-response relationship.

Several limitations of our study should also be acknowledged. First, nearly all studies relied on sleep duration that was self-reported by questionnaire or interview; 1 study[93] provided the RRs between all-cause mortality and both subjective and objective sleep duration, but no substantial difference was observed. Meanwhile, in the big data era, the widespread availability and acceptance of electronic wearable devices, such as consumer-level activity monitors, may allow accurate, reliable, and scalable objective sleep-duration assessment in large epidemiological studies.[94] Second, sleep duration is a dynamic biological process. A single measure of exposure may not fully capture the sustained effects of sleep duration over time when related to long-term disease incidence. One included study[95] addressed this issue by measuring changes in sleep duration twice, several years apart, and found that stable short and stable long sleep was associated with a significantly increased risk of mortality; moreover, moving to either shorter of longer sleep from average sleep was also associated with increased mortality. This finding was in line with our result that appropriate sleep duration was important for the delay or prevention of premature mortality. Third, we cannot rule out the possibility of residual or unmeasured confounding, even though we have taken into consideration major confounding factors by using adjusted risk estimates from multivariate models from each contributing study. Finally, sleep quality affected by factors like sleep apnea is an independent predictor of risk of adverse outcomes[96] but was not assessed in our study. Despite the limitations, at this stage, results from prospective cohort studies are still the best evidence available to assess the longitudinal effect of sleep duration on all-cause mortality and cardiovascular events.

Conclusions

In summary, our dose-response meta-analysis of prospective studies provides further evidence that sleep duration that is either too short or too long is associated with higher risk of all-cause mortality and cardiovascular events, with the lowest risk with ≈7 hours per day of sleep duration. Longer term randomized controlled trials are needed to establish causality and to elucidate the underlying mechanisms.

Author Contributions

Yin, Shan, Chen, and Liu conceived the study. Yin searched the databases, checked them according to the eligible criteria and exclusion criteria, extracted and analyzed the data, and wrote the draft of the article. S.Z. Li and Jin helped extract quantitative data from some articles and contributed to writing, reviewing, or revising the article. Huang, P.Y. Li, Shan, Bao, Yang, X.B. Peng, Z. Peng and Yu critically reviewed and revised for important intellectual content. Shan and Bao provided advice on meta-analysis methodology and contributed to reviewing, or revising the article. Liu is the guarantor and had full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Data S1.

Literature Search strategy：

PubMed：

((sleep duration) OR sleep length) AND (((cardiovascular disease) OR myocardial infarction) OR coronary OR stroke OR death OR mortality OR mortalities OR fatal) AND (cohort OR prospective OR (follow-up))

Embase：

'sleep'/exp OR sleep AND duration OR (sleep AND length) AND (cardiovascular AND disease OR (myocardial AND infarction) OR coronary OR stroke OR death OR mortality OR mortalities OR fatal) AND (cohort OR prospective OR 'follow-up')

Literature Search result:

After exclusion of duplicates and studies that did not fulfill the inclusion criteria, 101 remaining articles seemed to be relevant for this meta-analysis. After evaluating the full texts of these 101 publications, we excluded 35 articles as follows:

Ten articles [68-77] were excluded owing to lack of sufficient data for estimation of RRs. Three articles [78-80] were excluded because they reported all-cause mortality or cardiovascular events combining with other diseases, and another four articles were excluded because they did not separately report sleep duration [81-84]. Fourteen studies were excluded for providing less than three categories of sleep duration [85-98]. We also excluded two reports because only their abstracts were written in English [99, 100].Two studies [101, 102] were excluded because they respectively reported the intermediate follow-up results of the JACC Study and the Whitehall II cohort. After counting one study obtained by hand searching[40], the final meta-analysis included 67 articles with 141 independent reports. Among these 67 articles, 43 articles with 57 reports provided statistical effects relevant to the meta-analyses on all-cause mortality [1-43], 26 articles with 37 reports on total CVD[4, 7-9, 12-14, 17, 18, 23, 25-28, 31, 33, 34, 38, 44-51], 22 articles with 27 reports on CHD[3, 11, 12, 16, 17, 28, 36, 44, 46, 47, 49-60], and 16 articles with 20 reports on stroke[4, 12, 17, 28, 47, 50, 51, 55, 60-67].

Table S1. Sleep duration and all-cause mortality

Author, publication year, country	Study name	Age at baseline (years)	Follow-up (years)	Exposure	Exposure assessment	Sex, Sample size(cases)	Sleep categories	corresponding relative risk (95% CI)	Covariates in fully adjusted model
Nisha Aurora et al, 2016, US[1]	Sleep Heart Health Study	≥40	10.8	Nighttime sleep	Interview	Both: 5784 (1509)	<7 7-8 ≥9	0.98 (0.87 to 1.10) 1 1.25 (1.05 to 1.47)	Age, sex, race, BMI, smoking status, and prevalent hypertension, cardiovascular disease, diabetes, AHI, and antidepressant medications
Wei-Ju Lee et al, 2016, Taiwan[2]	The Social Environment and Biomarkers of Aging Study	≥53	4.7	Nighttime sleep	Interview	Both: 937 (72)	<6 6-7 ≥8	1.18 (0.66 to 2.12) 1 2.37 (1.35 to 4.19)	Age, sex, body mass index, education years, smoking, drinking, and number of chronic diseases, frailty states, use of hypnotics
Xizhu Wang et al, 2016, China[3]	Kailuan study	18-98	3.98	Nighttime sleep	Questionnaire	Both: 95903 (1793)	≤5 6 7 8 ≥9	1.23 (1.03 to 1.8) 1.95 (0.81 to 1.12) 1 1.06 (0.92 to 1.2) 1.65 (1.22 to 2.22)	Age, sex, family per member monthly income, education level, marital status, smoking status, drinking status, physical activity, history of hypertension, diabetes mellitus, and hyperlipidemia
Hui Cai et al, 2015, China[4]	Shanghai Women's and Men's Health Studies	Male: 40-75 Female: 44-79	Male: 6.07 Female: 7.12	24-hour sleep	Interview	Both: 113138 (4277) Male: 44590 (1921) Female: 68548 (2356)	Both: 4-5 6 7 8 9 ≥10 Male: 4-5 6 7 8 9 ≥10 Female: 4-5 6 7 8 9 ≥10	Both: 1.11 (1.00 to 1.23) 1.06 (0.97 to 1.16) 1 1.15 (1.05 to 1.26) 1.34 (1.17 to 1.54) 1.81 (1.59 to 2.06) Male: 1.06 (0.90 to 1.25) 1.07 (0.94 to 1.23) 1 1.13 (1.00 to 1.28) 1.34 (1.10 to 1.62) 1.55 (1.29 to 1.86) Female: 1.15 (1.01 to 1.32) 1.06 (0.94 to 1.20) 1 1.17 (1.04 to 1.32) 1.36 (1.13 to 1.64) 2.11 (1.77 to 2.52)	Age, education, income, smoking, alcohol consumption, tea consumption, comorbidity score, history of night-shift work, participation in regular exercise, body mass index, and waist-to-hip ratio, cardiovascular disease, upper gastrointestinal tract

Lisette A. Zuurbier et al, 2015, Netherlands[5]	Rotterdam Study	45–98	7.3	Nighttime sleep	Questionnaire	Both: 1734 (154)	<6 6-7.5 >7.5	1.41(0.93 to 2.13) 1 1.10(0.74 to 1.64)	Age, sex, activities of daily living score, current smoking, diabetes, myocardial infarction, stroke, cognitive functioning, depressive symptoms, body mass index, use of sleep medication, possible sleep apnea, and napping
Martica H. Hall et al, 2015, US[6]	Health, Aging and Body Composition (Health ABC) Study	70-79	8.2	Nighttime sleep	Interview	Both: 3013 (953)	<6 6 7 8 >8	1.06 (0.83 to 1.34) 1.00 (0.82 to 1.22) 1 1.10 (0.91 to 1.33) 1.23 (0.93 to 1.63)	Age, sex, race, education, BMI, smoking status, alcohol consumption, physical activity, consumption per week, site, chronic conditions, medication use
Naja Hulvej Rod et al, 2014, British[7]	British Whitehall II prospective cohort study	35-55	22	Nighttime sleep	Questionnaire	Male: 6114 (538) Female: 2984 (266)	Male: ≤5 6 7 8 >9 Female: ≤5 6 7 8 >9	Male: 1.11 (0.73 to 1.68) 1.23 (1.01 to 1.50) 1 1.18 (0.92 to 1.50) 1.44 (0.59 to 3.50) Female: 1.21 (0.76 to 1.91) 1.14 (0.86 to 1.52) 1 0.91 (0.63 to 1.30) 1.48 (0.60 to 3.65)	Age, employment grade, ethnicity, and marital status
Qian Xiao et al, 2014, US[8]	National Institutes of Health-AARP Diet and Health Study	51-72	14	Nighttime sleep	Questionnaire	Both: 239896 (44100)	<5 5-6 7-8 ≥9	1.16(1.10 to 1.23) 1.04(1.02 to 1.06) 1 1.11(1.06 to 1.19)	Sex , age, race/ethnicity , marital status, education, self-reported health, smoking, smoking dose, years since quitting smoking, alcohol drinking, moderate-to-vigorous physical activity, TV viewing, and baseline BMI
Andrea Bellavia et al, 2014, Sweden[9]	Cohort of Swedish Men and the Swedish Mammography Cohort	45-83	15	24-hour sleep	Questionnaire	Both: 70973 (14575)	<6 6–6.5 6.6–7.4 7.5–8 >8	1.25(1.13 to 1.37) 1.10(1.04 to 1.17) 1 1.03(0.98 to 1.08) 1.14(1.05 to 1.24)	Sex, age , body mass index , smoking status and pack-years of smoking , alcohol consumption, total physical activity, and educational level, total physical activity

Christopher A. Magee et al, 2013, Australia[10]	45 and Up Study	≥45	2.8	24-hour sleep	Questionnaire	Both: 227815 (8782)	<6 6 7 8 9 ≥10	1.13(1.01 to 1.25) 0.99(0.91 to 1.06) 1 1.02(0.96 to 1.08) 1.04(0.96 to 1.12) 1.26(1.16 to 1.36)	Age, sex, marital status, private health insurance, smoking status, alcohol consumption, body mass index, sufficient physical activity, and baseline health status
Garde AH et al, 2013, Denmark[11]	Copenhagen Male Study	40-59	30	24-hour sleep	Questionnaire	Both: 4943 (2663)	<6 6-7 ≥8	1.06(0.90 to 1.25) 1 0.99(0.84 to 1.09)	Age, BMI, systolic BP, diastolic BP, diabetes , hypertension , physical fitness , alcohol use, smoking, leisure-time physical activity, and social class
Masako Kakizaki et al, 2013, Japan[12]	Ohsaki Cohort Study	40-79	10.8	24-hour sleep	Questionnaire	Both: 49256 (8447)	≤6 7 8 9 ≥10	1.01 (0.93 to 1.09) 1 1.07 (1.01 to 1.14) 1.14 (1.06 to 1.24) 1.37 (1.27 to 1.47)	Age, sex, total caloric intake, body mass index, marital status, level of education, job status, history of myocardial infarction, history of cancer, history of stroke, history of hypertension, history of diabetes mellitus, smoking status, alcohol drinking, time spent walking, perceived mental stress, self-rated health, physical function
Yohwan Yeo et al, 2013, Korea[13]	Korean Multi-center Cancer Cohort study	>20	9.44	24-hour sleep	Interview	Both: 13164 (1580) Male: 5447 (923) Female: 7717 (657)	Both: ≤5 6 7 8 9 ≥10 Male: ≤5 6 7 8 9 ≥10 Female: ≤5 6 7 8 9 ≥10	Both: 1.21 (1.03 to 1.41) 1.10 (0.95 to 1.27) 1 1.03 (0.89 to 1.19) 1.36 (1.11 to 1.67) 1.36 (1.07 to 1.72) Male: 1.10 (0.89 to 1.36) 1.09 (0.90 to 1.30) 1 1.02 (0.85 to 1.23) 1.28 (0.97 to 1.69) 1.15 (0.85 to 1.56) Female: 1.41 (1.12 to 1.79) 1.16 (0.92 to 1.46) 1 1.03 (0.81 to 1.30) 1.50 (1.11 to 2.02) 1.87 (1.28 to 2.73)	Age, sex, educational attainment, body mass index, cigarette smoking, alcohol consumption, past history of hypertension, type 2 diabetes, CVD and metabolic syndrome

Hsi-Chung Chen et al, 2013, Taiwan[14]	Shih-Pai Sleep Study	>65	9	Nighttime sleep	Interview	Both: 4064 (1004)	≤4 5 6 7 8 9	1.00 (0.75 to 1.33) 0.92 (0.74 to 1.15) 0.88 (0.73 to 1.06) 1 1.26 (1.04 to 1.53) 1.66 (1.28 to 2.17)	Sex, age, education, marital status, living status, depression, body mass index, insomnia, hypnotics use, total sleep time, excessive daytime sleepiness, pain, smoking, alcohol drinking, snorers, diabetes mellitus, hypertension, cardiovascular disease, stroke, and gouty arthritis
Kyu-In Jung et al, 2013, US[15]	Rancho Bernardo Study	60-96	19	Nighttime sleep	Questionnaire	Male: 889 (632) Female: 1112 (592)	Male: <6 6.0-6.9 7.0-7.9 8.0-8.9 ≥9 Female: <6 6.0-6.9 7.0-7.9 8.0-8.9 ≥9	Male: 0.98 (0.67 to 1.43) 1.12 (0.85 to 1.48) 1 0.98 (0.79 to 1.22) 1.09 (0.82 to 1.45) Female: 1.11 (0.77 to 1.60) 1.17 (0.85 to 1.61) 1 1.19 (0.90 to 1.57) 1.51 (1.05 to 2.18)	Age, nap duration, Beck Depression Inventory (only in men), education (only in men), exercise (only in men), smoking (only in women), alcohol consumption, and medical history of hypertension, diabetes, coronary heart disease, stroke, and cancer, sleep-related medications (sedating antidepressants, antianxiety drugs, and hypnotics) and postmenopausal estrogen (only in women)
Lauren Hale et al, 2013, US[16]	Women's Health Initiative (WHI) clinical trial (CT) and observational study (OS)	50-79	12–15	Nighttime sleep	Questionnaire	Female: 3942 (335)	≤5 6 7–8 ≥9	1.01 (0.68 to 1.51) 0.94 (0.71 to 1.24) 1 1.55 (0.92 to 2.60)	Age, ethnicity, education, income, fibrinogen, body mass index, low physical exercise, high alcohol intake, ever smoke, elevated blood pressure, diabetes, depression, general health, life satisfaction scale
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	45-75	12.9	24-hour sleep	Questionnaire	Male: 61936 (10738) Female: 73749 (8597)	Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9	Male: 1.15 (1.06 to 1.23) 1.04 (0.99 to 1.10) 1 1.07 (1.01 to 1.12) 1.19 (1.12 to 1.27) Female: 1.15 (1.06 to 1.23) 1.05 (0.99 to 1.12) 1 1.02 (0.96 to 1.08) 1.22 (1.13 to 1.31)	5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity, hours spent daily watching television, and smoking history

Ying Li et al, 2013, Japan[18]	SAKU cohort	20-79	7	Nighttime sleep	Questionnaire	Both: 9455 (male: 181; female: 131)	Male: ≤5 6 7 8 9 Female: ≤5 6 7 8 9	Male: 1.44 (0.65 to 3.19) 0.86 (0.50 to 1.48) 1 1.05 (0.72 to 1.53) 1.70 (1.07 to 2.70) Female: 1.01 (0.42 to 2.39) 1.01 (0.42 to 2.39) 1 1.01 (0.63 to 1.60) 1.85 (1.09 to 3.13)	Age, body mass index, systolic blood pressure, diastolic blood press, smoking status, drinking habits and physical activity
Jiska Cohen-Mansfield et al, 2012, Israel[19]	Cross-Sectional and Longitudinal Aging Study	75-94	20	Nighttime sleep	Interview	Both: 1166 (1108)	<7 7-9 >9	0.98(0.84 to 1.13) 1 1.32(1.09 to 1.58)	Age, sex, country of origin, education, financial status, having children, demographics, health and function variables
Chul Woo Rhee et al, 2012, Korea[20]	Seoul Male Cohort Study	40-59	15	24-hour sleep	Questionnaire	Male: 14095 (935)	≤5 6-7 ≥8	1.53 (1.11 to 2.12) 1.04 (0.88 to 1.22) 1	Age, smoking, alcohol drinking, BMI, regular exercise, education level, hypertension, diabetes mellitus
Castro-Costa et al, 2011, Brasil[21]	Bambui Health and Ageing Study (BHAS)	≥60	7.5	Nighttime sleep	Interview	Both: 1512 (440)	<6 6-7 7-8 8-9 ≥9	1.09 (0.78 to 1.53) 0.84 (0.60 to 1.17) 1 1.31 (0.97 to 1.78) 1.53 (1.12 to 2.09)	Age, schooling marital status, working status, education, alcohol consumption, coffee consumption, smoking, physical exercises, depressive symptoms, cognitive functioning, psychoactive medications, physical functioning, arthritis ascertainment, systolic blood pressure, high-density lipoprotein cholesterol ratio, diabetes mellitus and body mass index

Li Qiu et al, 2011, China[22]	Chinese Longitudinal Healthy Longevity Survey	>65	3	24-hour sleep	Interview	Both: 20143 (8254) Male: 8774 (3343) Female: 11369 (4911)	Both: ≤5 6 7 8 9 ≥10 Male: ≤5 6 7 8 9 ≥10 Female: ≤5 6 7 8 9 ≥10	Both: 0.97 (0.88 to 1.08) 1.05 (0.95 to 1.16) 1.00 (0.90 to 1.11) 1 0.95 (0.83 to 1.07) 1.09 (1.00 to 1.18) Male: 1.17 (1.01 to 1.38) 1.06 (0.91 to 1.25) 1.17 (0.99 to 1.37) 1 1.08 (0.89 to 1.31) 1.22 (1.08 to 1.38) Female: 0.85 (0.75 to 0.98) 1.02 (0.90 to 1.15) 0.88 (0.76 to 1.01) 1 0.86 (0.72 to 1.02) 1.00 (0.90 to 1.11)	Age, ethnicity, urban–rural residence, and geographic region, SES, family/social support, and health practices, health condition
Erkki Kronholm et al, 2011, Finland[23]		25-59,30-64	29–34	Nighttime sleep	Questionnaire	Male: 11373 (5241) Female: 11917 (3747)	Male: <5 6 7-8 9 >10 Female: <5 6 7-8 9 >10	Male: 1.32(1.15 to 1.50) 1.09(0.99 to 1.20) 1 1.1 (0.99 to 1.21) 1.61(1.36 to 1.89) Female: 1.25 (1.08 to 1.44) 1.14 (1.03 to 1.26) 1 1.18(1.05 to 1.32) 1.62(1.37 to 1.91)	Age, smoking, BMI, systolic blood pressure and total cholesterol

Arthur Eumann Mesas et al, 2010, Spain[24]		≥60	6.8	24-hour sleep	Interview	Both: 3820 (897)	Both: ≤5 6 7 8 9 10 ≥11	Both: 1.42 (1.04 to 1.96) 1.23 (0.90 to 1.69) 1 1.34 (1.02 to 1.76) 1.48 (1.12 to 1.96) 1.73 (1.30 to 2.29) 1.66 (1.23 to 2.24)	Age, BMI, educational level, municipality of residence, physical activity, smoking, alcohol consumption, coffee consumption, social links, perceived health, MEC score, depression, SF-36 PCS and MCS scores, IADL limitations, hypertension, ischemic heart disease, stroke, diabetes mellitus, cancer at any site, chronic obstructive pulmonary disease, Parkinson's disease, arousal from sleep at night, and use of anxiolytic medication
Kuo-Liong Chien et al, 2010, Taiwan[25]	Chin-shan Community Cardiovascular Cohort Study	35	15.9	Nighttime sleep	Interview	Both: 3430 (901)	≤5 6 7 8 ≥9	1.15 (0.90 to 1.46) 0.97 (0.79 to 1.21) 1 1.04 (0.86 to 1.27) 1.34 (1.08 to 1.67)	Age, sex, BMI, smoking, current alcohol drinking, marital status, education level, occupation, regular exercise, family history of coronary heart disease, hypertension, diabetes, cholesterol, HDL, triglyceride, glucose, and uric acid level
Katie L. Stone et al, 2009, US[26]	Study of Osteoporotic Fractures prospective cohort study	≥69	7	Nighttime sleep and 24-hour sleep	Questionnaire	Female: 8101 (1922)	nighttime sleep: <6 6-8 >8 24h sleep: <6 6-8 8-9 9-10 ≥10	nighttime sleep: 1.02 (0.87 to 1.19) 1 1.16 (0.97 to 1.39) 24h sleep: 0.95 (0.76 to 1.18) 1.07 (0.94 to 1.22) 1 1.28 (1.08 to 1.52) 1.58 (1.27 to 1.95)	Age, body mass index, history of at least one medical condition including diabetes mellitus, Parkinson's disease, dementia, chronic obstructive pulmonary disease, non-skin cancer, and osteoarthritis, history of cardiovascular disease, history of hypertension, walks for exercise, alcohol use, smoking status, depression, cognitive impairment, estrogen use, and benzodiazepine use

Etsuji Suzuki et al, 2009, Japan[27]	Shizuoka Study	65-85	5.3	Nighttime sleep	Questionnaire	Both: 11395 (1004) Male: 5825 (689) Female: 5570 (315)	Both: ≤5 6 7 8 9 ≥10 Male: ≤5 6 7 8 9 ≥10 Female: ≤5 6 7 8 9 ≥10	Both: 0.92 (0.66 to 1.28) 1.06 (0.80 to 1.39) 1 1.36 (1.09 to 1.70) 1.41 (1.05 to 1.90) 1.96 (1.49 to 2.57) Male: 1.08 (0.72 to 1.61) 1.05 (0.75 to 1.47) 1 1.36 (1.04 to 1.78) 1.52 (1.08 to 2.15) 1.86 (1.34 to 2.56) Female: 0.71 (0.39 to 1.29) 1.08 (0.67 to 1.74) 1 1.39 (0.92 to 2.09) 1.15 (0.64 to 2.09) 2.27 (1.37 to 3.76)	Age, sex (only in the models for all participants), body mass index, smoking status, alcohol consumption, the frequency of physical activity, socioeconomic status, and mental health, hypertension and diabetes mellitus
Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	40-79	14.3	24-hour sleep	Questionnaire	Male: 41489 (8548) Female: 57145 (5992)	Male: <4 5 6 7 8 9 ≥10 Female: <4 5 6 7 8 9 ≥10	Male: 1.29 (1.02 to 1.64) 1.02 (0.90 to 1.16) 1.08 (1.00 to 1.16) 1 1.06 (1.00 to 1.12) 1.13 (1.05 to 1.22) 1.41 (1.29 to 1.54) Female: 1.28 (1.03 to 1.60) 1.11 (0.98 to 1.25) 1.05 (0.97 to 1.14) 1 1.16 (1.08 to 1.24) 1.32 (1.20 to 1.45) 1.56 (1.40 to 1.75)	Age, body mass index (quintiles), history of hypertension, history of diabetes, alcohol consumption, smoking, education level, hours of exercise, hours of walking, regular employment, perceived mental stress, depressive symptoms and frequency of fresh fish intake

James E. Gangwisch et al, 2008, US[29]	NHANES I Epidemiologic Follow-up Study	32-86	8–10	Nighttime sleep	Interview	Both: 9789 (1877)	≤5 6 7 8 ≥9	1.17 (0.99 to 1.39) 0.95 (0.81 to 1.11) 1 1.23 (1.08 to 1.39) 1.34 (1.15 to 1.56)	Age, physical activity, smoking, depression, sex, education, living alone, low income, daytime sleepiness, nighttime awakening, ethnicity, and sleeping pill use, body weight, diabetes, and hypertension, general health and cancer
Christer Hublin et al, 2007, Finland[30]	Finnish Twin Cohort	≥18	22	24-hour sleep	Questionnaire	Male: 10140 (2023) Female: 11128 (1672)	Men: <7 7-8 >8 Women: <7 7-8 >8	Men: 1.26 (1.11 to 1.43) 1 1.24 (1.09 to 1.41) Women: 1.21 (1.05 to 1.40) 1 1.17 (1.03 to 1.34)	Age, education, marital status, working status, social class, BMI, smoking status, binge drinking, grams of alcohol consumed daily, conditioning physical activity, and life satisfaction
Tzuo-Yun Lan et al, 2007, Taiwan[31]	Survey of Health and Living Status of the Elderly in Taiwan	≥64	8.4	Nighttime sleep	Interview	Male: 1748 (816) Female: 1331 (522)	Male: <7 7-7.9 8-8.9 9-9.9 ≥10 Female: <7 7-7.9 8-8.9 9-9.9 ≥10	Male: 0.98 (0.76 to 1.25) 1 1.09 (0.89 to 1.33) 1.14 (0.91 to 1.42) 1.51 (1.19 to 1.92) Female: 1.14 (0.77 to 1.67) 1 1.36 (1.01 to 1.84) 1.86 (1.36 to 2.53) 2.06 (1.50 to 2.83)	Age at 1993, marital status, monthly income, cigarettes smoking, alcohol consumption, body mass index, exercise, disease history, depression, afternoon nap duration
Yoko Amagai et al, 2004, Japan[32]	Jichi Medical School Cohort Study	19-93	8.2	Nighttime sleep	Interview	Male: 4419 (289) Female: 6906 (206)	Male: <5.9 6.0-6.9 7.0-7.9 8.0-8.9 9.0- Female: -5.9 6.0-6.9 7.0-7.9 8.0-8.9 >9.0	Male: 2.4 (1.3 to 4.2) 1.1 (0.7 to 1.8) 1 0.9 (0.6 to 1.2) 1.1 (0.8 to 1.6) Female: 0.7 (0.2 to 2.3) 1.3 (0.8 to 2.1) 1 1.1 (0.8 to 1.6) 1.5 (1.0 to 2.4)	Age, systolic blood pressure, total cholesterol, body mass index, smoking habits, alcohol drinking habits, education, and marital status

Sanjay R. Patel et al, 2003, US[33]	Nurses' Health Study (NHS) Cohort	30-55	14	24-hour sleep	Questionnaire	Female: 82969 (5409)	Female: ≤5 6 7 8 ≥9	Female: 1.08 (0.96 to 1.22) 0.99 (0.92 to 1.06) 1 1.11 (1.03 to 1.19) 1.40 (1.25 to 1.55)	Age, smoking status, alcohol consumption, physical activity, depression, history of snoring, body mass index, history of cancer, cardiovascular disease, hypertension, or diabetes, and shift-working history
Genc Burazeri et al, 2003, Israel[34]	Kiryat Yovel Community Health Study	≥50	10	Nighttime sleep and 24-hour sleep	Questionnaire	Male: 841 (198) Female:1001 (205)	nighttime sleep: Male: <6 6-8 >8 Female: <6 6-8 >8 24h sleep : Male : <6 6-8 >8 Female: <6 6-8 >8	nighttime sleep: Male: 1 1.25(0.83 to 1.87) 1.91(1.16 to 3.13) Female: 1 0.80(0.54 to 1.17) 1.08(0.70 to 1.66) 24h sleep : Male : 1 1.41 (0.83 to 2.39) 2.13 (1.23 to 3.71) Female: 1 0.64 (0.42 to 0.97) 0.80 (0.51 to 1.24)	Men: age, self-appraised health, activities of daily living, CHD, alcohol consumption, systolic blood pressure, homocysteine and glucose, siesta and its duration women: age, diabetes, congestive heart failure, BMI, systolic blood pressure, and albumin, siesta and its duration
Aya Goto et al, 2003, Japan[35]		≥65	12	Nighttime sleep	Questionnaire	Male: 251 (139) Female: 473 (166)	Male: <6 6-7 >7 Female: <6 6-7 >7	Male: 1.29(0.50 to 3.34) 1 1.54(0.92 to 2.58) Female: 2.62(1.36 to 5.07) 1 1.40(0.91 to 2.15)	Women: exercise, smoking, drinking, and social role, age, presence of spouse, education, and working status, activities of daily living, hearing, vision, and basic activities of daily living, body mass index, hemoglobin, serum albumin, total cholesterol, creatinine, blood pressure, and electrocardiograph abnormality Men: exercise, smoking, drinking, and social role, age, presence of spouse, education, and working status, cerebrovascular disease, hypertension, activities of daily living, hearing, vision, and basic activities of daily living, body mass index, hemoglobin, serum albumin, total cholesterol, creatinine, blood pressure, and electrocardiograph abnormality

L. MALLON et al, 2002, Sweden[36]		45-65	12	Nighttime sleep	Questionnaire	Male: 906 (165) Female: 964 (101)	Male: <6 6-8 >8 Female: <6 6-8 >8	Male: 1.1 (0.6 to 7.0) 1 2.0 (1.2 to 3.2) Female: 1.0 (0.6 to 1.8) 1 1.3 (0.6 to 2.6)	Age
Daniel F. Kripke et al, 2002, US[37]	Cancer Prevention Study II	30-102	6	Nighttime sleep	Questionnaire	Male: 480841 (45199) Female: 636095 (32440)	Male: 3 4 5 6 7 8 9 ≥10 Female: 3 4 5 6 7 8 9 ≥10	Male: 1.19(0.96 to 1.47) 1.17(1.06 to 1.28) 1.11(1.05 to 1.18) 1.08(1.04 to 1.11) 1 1.12(1.09 to 1.15) 1.17(1.13 to 1.21) 1.34(1.28 to 1.40) Female: 1.33(1.08 to 1.64) 1.11(1.01 to 1.22) 1.07(1.01 to 1.13) 1.07(1.03 to 1.11) 1 1.13(1.09 to 1.16) 1.23(1.17 to 1.28) 1.41(1.34 to 1.50)	Age, race education, occupation, marital status, exercise level, smoking at intake, years of smoking, churchgoing, fat in diet, fiber in diet, insomnia frequency, health, body mass index, leg pain, history of heart disease, history of hypertension, history of cancer, history of diabetes, history of stroke, history of bronchitis, history of emphysema, history of kidney disease, medications
Pauline Heslop et al, 2002, British[38]		65	25	24-hour sleep	Questionnaire	Male: 5819 (2303) Female: 978(262)	Male: <7 7-8 >8 Female: <7 7-8 >8	Male: 1.00(0.89 to 1.12) 1 0.81(0.67 to 0.97) Female: 0.98(0.70 to 1.37) 1 1.20(0.71 to 2.04)	Age, marital status, social class, known risk factors for disease and self-perceived stress

Masayo Kojima et al, 2000, Japan[39]		20-67	11.9	Nighttime sleep	Questionnaire	Male: 2438 (149) Female: 2884(109)	Male: -6.9 7.0-8.9 9.0-9.9 10.0- Female: -6.9 7.0-8.9 9.0-9.9 10.0-	Male: 1.93(1.12 to 3.35) 1 1.15(0.74 to 1.77) 1.77(0.88 to 3.54) Female: 0.90(0.50 to 1.61) 1 1.07(0.58 to 1.95) 0.40(0.06 to 2.92)	Baseline age, present and past history of hypertension, cerebrovascular, heart and renal diseases and diabetes, and use of sleeping pills (smoking and drinking habits only in males)
Catharine Gale et al, 1998, British[40]		≥65	23	Nighttime sleep	Interview	Both: 1229 (1158)	≤7 8 9 10 11 ≥12	1.0 (0.7 to 1.4) 0.8 (0.7 to 1.0) 1 1.2 (1.0 to 1.4) 1.3 (1.0 to 1.7) 1.7 (1.2 to 2.5)	Age, sex, geriatrician's diagnoses of illness, social class, systolic blood pressure, and body mass index
Ana Ruigomez et al, 1995, Spain[41]	Health Interview Survey of Barcelona	65	4.6	24-hour sleep	Interview	Both: 1219 (224) Male: 470 (115) Female: 749(109)	Both: <7 7-9 >9 Male: <7 7-9 >9 Female: <7 7-9 >9	Both: 0.83(0.56 to 1.23) 1 1.37(0.89 to 2.11) Male: 1.06(0.61 to 1.83) 1 1.30(0.71 to 2.38) Female: 0.66(0.37 to 1.16) 1 1.46(0.79 to 2.70)	Age, sex, education level and self perceived health status
Yoshitaka Tsubono et al, 1993, Japan[42]	National Collaborative Cohort Study	≥40	4	Nighttime sleep	Questionnaire	Both: 4318 (207)	≤6 7-8 ≥9	1.26(0.81 to 1.97) 1 1.58(1.16 to 2.15)	Age, sex
Roger Rumble et al, 1992, England[43]	Nottingham Longitudinal Study of Activity	≥65	5	24-hour sleep	Interview	Both: 1042 (352)	<4 4.0-9.9 ≥10	1.12(0.47 to 2.69) 1 1.60(0.74 to 3.47)	Sex, sleep pills, health

AHI; apnea hypopnea index, BMI; body mass index, BP; blood pressure, CVD; cardiovascular disease, CHD; coronary heart disease, HDL; high density lipoprotein, MEC; mini ex-amen cognoscitivo, MCS; mental component summary, PCS; physical component summary, SES; socioeconomic status, SF-36; 36-item short form surve

Table S2. Sleep duration and total cardiovascular disease

Author, publication year, country	Study name	Age at baseline (years)	Follow-up (years)	Exposure	Exposure assessment	CVD incidence or mortality	Sex, Sample size(cases)	Sleep categories	corresponding relative risk (95% CI)	Covariates in fully adjusted model
Francesco Gianfagna et al, 2016, Italy[44]	MONICA Brianza and PAMELA	35-74	17	Nighttime sleep	Questionnaire	Incidence	Male: 2277 (293)	≤6 7-8 ≥9	1.14 (0.84 to 1.53) 1 1.55 (1.08 to 2.21)	Age, systolic BP, total cholesterol, HDL cholesterol, diabetes, smoking habits, and educational level, sleep disturbances, LTPA and depression
Hui Cai et al, 2015, China[4]	Shanghai Women's and Men's Health Studies	Male: 40-75 Female: 44-79	male: 6.07 Female: 7.12	24-hour sleep	Interviews	Mortality	Both: 113138 (1389)	Both: 4-5 6 7 8 9 ≥10 Male: 4-5 6 7 8 9 ≥10 Female: 4-5 6 7 8 9 ≥10	Both: 1.05 (0.87–1.26) 1.10 (0.94–1.29) 1 1.22 (1.05 to 1.43) 1.47 (1.17 to 1.85) 2.04 (1.65 to 2.53) Male: 1.09 (0.82 to 1.46) 1.06 (0.83 to 1.34) 1 1.25 (1.00 to 1.56) 1.68 (1.23 to 2.30) 1.58 (1.14 to 2.18) Female: 1.02 (0.80 to 1.30) 1.12 (0.91 to 1.39) 1 1.20 (0.96 to 1.50) 1.28 (0.91 to 1.82) 2.64 (1.99 to 3.52)	Age, education, income, smoking, alcohol consumption, tea consumption, comorbidity score, history of night-shift work, participation in regular exercise, body mass index, and waist-to-hip ratio, cardiovascular disease, upper gastrointestinal tract
Catarina Canivet et al, 2014, Sweden[45]	Malmö Diet and Cancer Study	45-64	12	Nighttime sleep	Questionnaire	Incidence	Male: 5875 (952) Female: 7742 (650)	Male: ≤6 7-8 ≥9 Female: ≤6 7-8 ≥9	Male: 1.1 (0.96 to 1.3) 1 1.3 (1.01 to 1.7) Female: 1.3 (1.1 to 1.5) 1 1.5 (1.1 to 2.1)	Age

Qian Xiao et al, 2014, US[8]	National Institutes of Health-AARP Diet and Health Study	51-72	14	Nighttime sleep	Questionnaire	Mortality	Both: 239896 (11635)	<5 5-6 7-8 ≥9	1.25(1.13 to 1.38) 1.06(1.02 to 1.10) 1 1.07(0.97 to 1.17)	Sex , age, race/ethnicity, marital status, education, self-reported health, smoking, smoking dose, years since quitting smoking, alcohol drinking, moderate-to-vigorous physical activity, TV viewing, and baseline BMI
Naja Hulvej Rod et al, 2014, British[7]	British Whitehall II prospective cohort study	35-55	22	Nighttime sleep	Questionnaire	Mortality	Male: 6114 (167) Female: 2984 (54)	Male: ≤6 7-8 >9 Female: ≤6 7-8 >9	Male: 1.18 (0.87 to 1.63) 1 1.61 (0.40 to 6.59) Female: 1.81 (1.05 to 3.10) 1 NA(n=0)	Age, employment grade, ethnicity, and marital status
Andrea Bellavia et al, 2014, Sweden[9]	Cohort of Swedish Men and the Swedish Mammography Cohort	45-83	15	24-hour sleep	Questionnaire	Mortality	Both: 70973 (3981)	<6 6–6.5 6.6–7.4 7.5–8 >8	1.44(1.20 to 1.73) 1.23(1.09 to 1.38) 1 1.02(0.92 to 1.12) 1.11(0.95 to 1.31)	Sex, age, body mass index ,smoking status and pack-years of smoking, alcohol consumption, total physical activity, and educational level, total physical activity
Megan Sands-Lincoln et al, 2013, US[46]	Women's Health Initiative Observational Study	50-79	10.3	Nighttime sleep	Questionnaire	Incidence	Female: 86329 (7257)	≤5 6 7-8 9 ≥10	1.06(0.96 to 1.16) 1.00(0.95 to 1.06) 1 0.95(0.83 to 1.08) 1.23(0.89 to 1.70)	Age, race, education, income, smoking, BMI, physical activity, alcohol intake, depression, diabetes, high blood pressure, hyperlipidemia, comorbid conditions
Anna Westerlund et al, 2013, Sweden[47]	National March Cohort Study	≥18	13.2	24-hour sleep	Questionnaire	Incidence and mortality	CVD incidence, Both: 41192 (4031) CVD mortality, Both: 41192 (857)	≤5 6 7 ≥8 5 6 7 ≥8	1.05 (0.88 to 1.26) 0.97 (0.86 to 1.09) 1 1.00 (0.89 to 1.13) 1.11 (0.76 to 1.64) 1.17 (0.88 to 1.55) 1 1.12 (0.85 to 1.47)	Age, sex, education, employment status, smoking, alcohol, snoring, work schedule, depressive symptoms, self-rated health, physical activity, BMI, diabetes, lipid disturbance, and hypertension

Elizabeth G. Holliday et al, 2013, Australia[48]	45 and Up Study	≥45	2.3	Nighttime sleep	Questionnaire	Incidence	Both: 156902 (4852)	<6 6 7 8 9 ≥10	1.03 (0.88 to 1.21) 1.06 (0.96 to 1.17) 1 0.98 (0.91 to 1.05) 0.98 (0.89 to 1.09) 1.00 (0.88 to 1.14)	Age, sex, education, marital status, residential remoteness, alcohol consumption, smoking status, health insurance status, income, body mass index, physical activity and baseline health status
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	45-75	12.9	24-hour sleep	Questionnaire	Mortality	Male: 61936 (3772) Female: 73749 (2838)	Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9	Male: 1.13 (1.00 to 1.28) 1.01 (0.92 to 1.11) 1 1.05 (0.96 to 1.14) 1.22 (1.09 to 1.35) Female: 1.20 (1.05 to 1.36) 1.06 (0.96 to 1.18) 1 1.08 (0.98 to 1.20) 1.29 (1.13 to 1.47)	5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity, hours spent daily watching television, and smoking history
Hsi-Chung Chen et al, 2013, Taiwan[14]	Shih-Pai Sleep Study	>65	7	Nighttime sleep	Interviews	Mortality	Both: 4064 (259)	≤4 5 6 7 8 9	1.05 (0.61 to 1.79) 0.95 (0.62 to 1.48) 0.79 (0.54 to 1.16) 1 1.36 (0.92 to 2.01) 2.36 (1.46 to 3.80)	Sex, age, education, marital status, living status, depression, body mass index, insomnia, hypnotics use, total sleep time, excessive daytime sleepiness, pain, smoking, alcohol drinking, snorers, diabetes mellitus, hypertension, cardiovascular disease, stroke, and gouty arthritis

Yohwan Yeo et al , 2013, Korea[13]	Korean Multi-center Cancer Cohort study	>20	9.44	24-hour sleep	Interviews	Mortality	Both: 13164 (363) Male: 5447 (169) Female: 7717 (194)	Both: ≤5 6 7 8 9 ≥10 Male: ≤5 6 7 8 9 ≥10 Female: ≤5 6 7 8 9 ≥10	Both: 1.40 (1.02 to 1.93) 1.25 (0.92 to 1.69) 1 1.04 (0.76 to 1.42) 1.26 (0.81 to 1.96) 1.37 (0.82 to 2.29) Male: 1.43 (0.89 to 2.30) 1.21 (0.77 to 1.91) 1 1.06 (0.68 to 1.67) 1.05 (0.51 to 2.19) 1.53 (0.79 to 2.95) Female: 1.48 (0.97 to 2.28) 1.32 (0.87 to 2.00) 1 1.00 (0.64 to 1.55) 1.40 (0.80 to 2.46) 1.13 (0.48 to 2.67)	Age, sex, educational attainment, body mass index, cigarette smoking, alcohol consumption, past history of hypertension, type 2 diabetes, CVD and metabolic syndrome
Masako Kakizki et al, 2013, Japan[12]	Ohsaki Cohort Study	40-79	10.8	24-hour sleep	Questionnaire	Mortality	Both: 49256 (2549)	≤6 7 8 9 ≥10	1.10 (0.96 to 1.28) 1 1.21 (1.08 to 1.36) 1.32 (1.15 to 1.52) 1.49 (1.30 to 1.71)	Age, sex, total caloric intake, body mass index in, marital status, level of education, job status , history of myocardial infarction, history of cancer, history of stroke, history of hypertension, history of diabetes mellitus, smoking status, alcohol drinking, time spent walking, perceived mental stress, self-rated health, physical function

Ying Li et al, 2013, Japan[18]	SAKU cohort	20-79	7	Nighttime sleep	Questionnaire	Mortality	Both: 9455 (NA)	Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9	Male: 1.57 (0.35 to 7.15) 0.60 (0.17 to 2.15) 1 1.04 (0.49 to 2.21) 2.73 (1.22 to 6.11) Female: 0.80 (0.18 to 3.47) 0.91 (0.38 to 2.23) 1 1.13 (0.57 to 2.23) 1.72 (0.76 to 3.89)	Age, body mass index, systolic blood pressure, diastolic blood press, smoking status, drinking habits and physical activity
Marieke P. Hoevenaar-Blom et al, 2011, Netherlands[49]	MORGEN Study	20-65	11.9	24-hour sleep	Questionnaire	Incidence	Both: 20432 (1486)	≤6 7 8 ≥9	1.11 (0.97 to 1.27) 1 0.95 (0.84 to 1.08) 0.96 (0.77 to 1.18)	Age, sex, smoking, alcohol, coffee, subjective health, educational level, BMI, total-/HDL cholesterol ratio, systolic blood pressure, CVD risk factor medication, and prevalence of type 2 diabetes
Yuko Hamazaki et al, 2011, Japan[50]		35-54	14	24-hour sleep	Questionnaire	Incidence	Male: 2282 (64)	<6 6-6.9 7-7.9 ≥8	3.49(1.30 to 9.40) 1.11(0.55 to 2.25) 1 1.71(0.90 to 3.24)	Age, type of job, working hours, mental workload, body mass index, mean blood pressure, HbA1c, total cholesterol, current smoking habit, drinking habit, leisure–time physical activity , medication for hypertension, diabetes, and hypercholesterolemia
Erkki Kronholm et al, 2011, Finland[23]		25-59,30-64	29-34	Nighttime sleep	Questionnaire	Mortality	Male: 10851 (1830) Female: 11633 (1344)	Male: < 5 6 7-8 9 > 10 Female: < 5 6 7-8 9 > 10	Male: 1.20 (0.96 to 1.50) 1.12 (0.96 to 1.31) 1 0.95 (0.80 to 1.14) 1.27 (0.94 to 1.75) Female: 1.33 (1.06 to 1.67) 1.20 (1.01 to 1.42) 1 1.20 (1.00 to 1.45) 1.76 (1.34 to 2.32)	Age, smoking, BMI, systolic blood pressure and total cholesterol

Kuo-Liong Chien et al, 2010, Taiwan[25]	Chin-shan Community Cardiovascular Cohort study	>35	15.9	Nighttime sleep	Interview	Incidence	Both: 3430 (420)	≤5 6 7 8 ≥9	0.94 (0.65 to 1.35) 0.91 (0.67 to 1.24) 1 1.05 (0.80 to 1.39) 1.12 (0.81 to 1.55)	Age, sex, BMI, smoking, current alcohol drinking, marital status, education level, occupation, regular exercise, family history of coronary heart disease, baseline hypertension, diabetes, cholesterol, HDL, triglyceride, glucose, and uric acid level
Yoko Amagai et al, 2010, Japan[51]	Jichi Medical School Cohort Study	18-90	10.7	Nighttime sleep	Interview	Incidence	Male: 4413 (255) Female: 6954 (226)	Male: <5.9 6.0–6.9 7.0–7.9 8.0–8.9 9.0 Female: <5.9 6.0–6.9 7.0–7.9 8.0–8.9 9.0	Male: 2.14 (1.11 to 4.13) 1.04 (0.61 to 1.76) 1 0.98 (0.69 to 1.40) 1.33 (0.93 to 1.92) Female: 1.46 (0.70 to 3.04) 0.64 (0.38 to 1.10) 1 0.85 (0.60 to 1.20) 1.28 (0.88 to 1.87)	Age, systolic blood pressure, total cholesterol, body mass index, smoking habits, and alcohol drinking habits
Katie L. Stone et al, 2009, US[26]	Study of Osteoporotic Fractures Prospective Cohort study	≥69	7	Nighttime sleep and 24-hour sleep	Questionnaire	Mortality	Female: 8101 (723)	<6 6-8 >8	1.03 (0.80 to 1.31) 1 1.21 (0.92 to 1.61)	Age, body mass index, history of at least one medical condition including diabetes mellitus, Parkinson's disease, dementia, chronic obstructive pulmonary disease, non-skin cancer, and osteoarthritis, history of cardiovascular disease, history of hypertension, walks for exercise, alcohol use, smoking status, depression, cognitive impairment, estrogen use, and benzodiazepine use

Etsuji Suzuki et al, 2009, Japan[27]	Shizuoka Study	65-85	5.3	Nighttime sleep	Questionnaire	Mortality	Both: 11395 (310) Male: 5825 (184) Female: 5570 (126)	Both: ≤5 6 7 8 9 ≥10 Male: ≤5 6 7 8 9 ≥10 Female: ≤5 6 7 8 9 ≥10	Both: 1.10 (0.62 to 1.93) 0.85 (0.50 to 1.45) 1 1.52 (1.01 to 2.29) 1.55 (0.91 to 2.63) 1.95 (1.18 to 3.21) Male: 0.97 (0.46 to 2.05) 0.75 (0.38 to 1.48) 1 1.05 (0.63 to 1.75) 1.26 (0.65 to 2.45) 1.71 (0.94 to 3.11) Female: 1.48 (0.59 to 3.67) 1.08 (0.44 to 2.66) 1 2.83 (1.39 to 5.76) 2.32 (0.93 to 5.77) 2.31 (0.91 to 5.82)	Age, sex (only in the models for all participants), body mass index, smoking status, alcohol consumption, the frequency of physical activity, socioeconomic status, and mental health, hypertension and diabetes mellitus
Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	40-79	14.3	24-hour sleep	Questionnaire	Mortality	Male :41489 (2297) Female: 57145 (1990)	Male: <4 5 6 7 8 9 ≥10 Female: <4 5 6 7 8 9 ≥10	Male: 1.11 (0.67 to 1.83) 0.99 (0.77 to 1.27) 1.01 (0.87 to 1.18) 1 1.11 (1.00 to 1.24) 1.14 (0.99 to 1.32) 1.56 (1.33 to 1.83) Female: 1.28 (0.88 to 1.86) 1.22 (1.00 to 1.50) 1.00 (0.86 to 1.16) 1 1.28 (1.14 to 1.44) 1.37 (1.17 to 1.62) 1.54 (1.28 to 1.86)	Age, body mass index (quintiles), history of hypertension, history of diabetes, alcohol consumption, smoking, education level, hours of exercise, hours of walking, regular employment, perceived mental stress, depressive symptoms and frequency of fresh fish intake

Tzuo-Yun Lan et al, 2007, Taiwan[31]	Survey of Health and Living Status of the Elderly in Taiwan	≥64	8.4	Nighttime sleep	Interviews	Mortality	Male: 1748 (209) Female: 1331 (170)	Male: <7 7-7.9 8-8.9 9-9.9 ≥10 Female: <7 7-7.9 8-8.9 9-9.9 ≥10	Male: 0.91 (0.53 to 1.57) 1 1.40 (0.93 to 2.10) 1.26 (0.80 to 1.98) 1.81 (1.13 to 2.89) Female: 1.07 (0.54 to 2.15) 1 1.77 (1.05 to 2.98) 1.75 (1.00 to 3.07) 1.85 (1.04 to 3.27)	Age at 1993, marital status, monthly income, cigarettes smoking, alcohol consumption, body mass index, exercise, disease history (heart disease, stroke, and cancer), depression, afternoon nap duration
Sanjay R. Patel et al, 2004, US[33]	Nurses' Health Study (NHS) Cohort	30-55	14	24-hour sleep	Questionnaire	Mortality	Female: 82969 (1084)	≤5 6 7 8 ≥9	1.04 (0.79 to 1.35) 1.06 (0.91 to 1.25) 1 1.12 (0.95 to 1.31) 1.56 (1.25 to 1.96)	Age, smoking status, alcohol consumption, physical activity, depression, history of snoring, body mass index, history of cancer, cardiovascular disease, hypertension, or diabetes, and shift-working history
Genc Burazeri et al, 2003, Israel[34]	Kiryat Yovel Community Health Study	≥50	10	Nighttime sleep and 24-hour sleep	Questionnaire	Mortality	Male: 750 (77) Female: 910 (93)	Male: <6 6-8 >8 Female: <6 6-8 >8	Male: 1 1.35 (0.71 to 2.58) 1.91 (0.86 to 4.23) Female: 1 0.83 (0.47 to 1.45) 1.02 (0.54 to 1.93)	Men included: age, self-appraised health, activities of daily living, CHD, alcohol consumption, systolic blood pressure, homocysteine, glucose, siesta and its duration Women included: age, diabetes, congestive heart failure, BMI , systolic blood pressure, albumin, siesta and its duration
Pauline Heslop et al, 2002, British[38]		Male: 65 Female: 60	25	24-hour sleep	Questionnaire	Mortality	Male: 5819 (1182) Female: 978 (117)	Male: <7 7-8 >8 Female: <7 7-8 >8	Male: 1.00 (0.85 to 1.17) 1 0.82 (0.64 to 1.07) Female: 0.80 (0.47 to 1.37) 1 1.35 (0.62 to 2.95)	Age, marital status, social class, known risk factors for disease and self-perceived stress

BMI; body mass index, BP; blood pressure, CVD; cardiovascular disease, CHD; coronary heart disease, HDL; high density lipoprotein, LTPA; leisure time physical activity, NA; not available

Table S3. Sleep duration and coronary heart disease

Author, publication year, country	Study name	Age at baseline (years)	Follow-up (years)	Exposure	Exposure assessment	Outcome	Sex, Sample size(cases)	Sleep categories	Corresponding relative risk (95% CI)	Covariates in fully adjusted model
Francesco Gianfagna et al, 2016, Italy[44]	MONICA Brianza and PAMELA Population-based Cohorts	35-74	17	Nighttime sleep	Questionnaire	CHD incidence	Male: 2277 (213)	≤6 7-8 ≥9	1.14 (0.80 to 1.61) 1 1.32 (0.85 to 2.07)	Age, systolic BP, total cholesterol, HDL cholesterol, diabetes, smoking habits, and educational level, sleep disturbances, LTPA and depression
Liangle Yang et al, 2016, China[52]	Dongfeng-Tongji Cohort Study	62.8	3-5	Nighttime sleep	Questionnaire	CHD incidence	Both: 19370 (2058)	<7 7-<8 8-<9 9-<10 ≥10	1.08 (0.90 to 1.29) 1 1.04 (0.93 to 1.16) 1.03 (0.90 to 1.18) 1.33 (1.10 to 1.62)	Age, sex, BMI, education, smoking status, drinking status, physical activity, hypertension, hyperlipidemia, diabetes, family history of CHD, and midday napping
Xizhu Wang et al, 2016, China[3]	Kailuan Study	18-98	3.98	Nighttime sleep	Questionnaire	MI mortality	Both: 95903 (423)	≤5 6 7 8 ≥9	0.89 (0.60 to 1.30) 0.84 (0.61 to 1.16) 1 0.86 (0.66 to 1.13) 1.12 (0.58 to 2.16)	Age, sex, family per member monthly income, education level, marital status, smoking status, drinking status, physical activity, history of hypertension, diabetes mellitus, and hyperlipidemia
Linn B. Strand et al, 2016, Taiwan[53]		≥20	9.7	Nighttime sleep	Questionnaire	CHD mortality	Both: 392164 (711) Male: 191656 (489) Female: 200508 (222)	Both: 0-4 4-6 6-8 >8 Male: 0-4 4-6 6-8 >8 Female: 0-4 4-6 6-8 >8	Both: 1.36 (0.88 to 2.10) 1.03 (0.85 to 1.24) 1 1.28 (1.05 to 1.56) Male: 1.03 (0.53 to 2.00) 1.06 (0.85 to 1.32) 1 1.11 (0.88 to 1.41) Female: 1.84 (1.03 to 3.29) 0.99 (0.72 to 1.37) 1 1.81 (1.28 to 2.56)	Age, sex, education, marital status, smoking, alcohol consumption, physical activity, history of hypertension, history of diabetes, history of heart disease, body mass index, systolic blood pressure, fasting glucose, total cholesterol, HDL cholesterol, triglycerides and use of hypnotics/sedatives
J. Liu et al, 2014, US[54]	Framingham Offspring Study	≥30	20	24-hour sleep	Questionnaire	CHD incidence	Both: 3086 (491)	<6 7-8 >9	1.29 (1.03 to 1.61) 1 1.13 (0.81 to 1.58)	Age, sex, current cigarette smoking, weekly alcohol drinking, systolic blood pressure, total cholesterol level, BMI, diabetes, treatment of hypertension, C-reactive protein

Megan Sands-Lincoln et al, 2013, US[46]	Women's Health Initiative Observational Study	50-79	10.3	Nighttime sleep	Questionnaire	CHD incidence	Female: 86329 (5359)	≤5 6 7-8 9 ≥10	1.08 (0.96 to 1.20) 1.00 (0.94 to 1.07) 1 0.93 (0.80 to 1.08) 1.33 (0.94 to 1.88)	Age, race, education, income, smoking, BMI, physical activity, alcohol intake, depression, diabetes, high blood pressure, hyperlipidemia, comorbid conditions
Lauren Hale et al, 2013, US[16]	Women's Health Initiative (WHI) clinical trial (CT) and observational study (OS)	50-79	11-16	Nighttime sleep	Questionnaire	CHD incidence	Female:3942 (132)	≤5 6 7–8 ≥9	1.09 (0.63 to 1.89) 0.66 (0.42 to 1.04) 1 1.88 (0.92 to 3.83)	Age, ethnicity, education, income, fibrinogen, body mass index, low physical exercise, high alcohol intake, ever smoke, elevated blood pressure, diabetes, depression, general health, life satisfaction scale
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	45-75	12.9	24-hour sleep	Questionnaire	CHD mortality, IHD mortality and MI mortality	CHD mortality, Male: 61936 (2096) Female: 73749 (1380) IHD mortality, Male: 61936 (1429) Female: 73749 (859) MI mortality, Male: 61936 (667) Female: 73749 (521)	Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9 Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9 Male: ≤5 6 7 8	Male: 1.20 (0.99 to 1.45) 0.98 (0.84 to 1.13) 1 1.01 (0.88 to 1.16) 1.16 (0.98 to 1.39) Female: 1.18 (0.94 to 1.49) 1.06 (0.88 to 1.29) 1 1.13 (0.94 to 1.36) 1.20 (0.95 to 1.53) Male: 1.24 (0.94 to 1.64) 0.92 (0.74 to 1.15) 1 0.98 (0.80 to 1.20) 1.16 (0.89 to 1.50) Female: 1.18 (0.87 to 1.59) 1.23 (0.96 to 1.56) 1 1.10 (0.86 to 1.40) 1.29 (0.94 to 1.75) 1.21 (1.04 to 1.42) 0.96 (0.85 to 1.08) 1 1.00 (0.89 to 1.12) 1.16 (1.00 to 1.34)	5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity, hours spent daily watching television, and smoking history

								≥9 Female: ≤5 6 7 8 ≥9	Female: 1.18 (0.98 to 1.42) 1.13 (0.97 to 1.31) 1 1.12 (0.96 to 1.29) 1.23 (1.02 to 1.49)	
Masako Kakizki et al, 2013, Japan[12]	Ohsaki Cohort Study	40-79	10.8	24-hour sleep	Questionnaire	IHD mortality	Both:49256 (561)	≤6 7 8 9 ≥10	1.38 (1.02 to 1.86) 1 1.36 (1.06 to 1.73) 1.49 (1.10 to 2.02) 1.41 (1.04 to 1.92)	Age, sex, total caloric intake, body mass index, marital status, level of education, job status, history of myocardial infarction, history of cancer, history of stroke, history of hypertension, history of diabetes mellitus, smoking status , alcohol drinking , time spent walking, perceived mental stress, self-rated health, physical function
Garde AH et al, 2013, Denmark[11]	Copenhagen Male Study	40-59	30	24-hour sleep	Questionnaire	IHD mortality	Male: 4943 (587)	Male: <6 6-7 ≥8	Male: 1.46 (1.07 to 2.00) 1 1.20 (0.97 to 1.49)	Age, BMI, systolic BP, diastolic BP, diabetes, hypertension, physical fitness, alcohol use, smoking, leisure-time physical activity, and social class.
Anna Westerlund et al, 2013, Sweden[47]	National March Cohort Study	≥18	13.2	24-hour sleep	Questionnaire	MI incidence	Both: 41192 (1908)	5 6 7 ≥8	1.19 (0.92 to 1.55) 1.05 (0.88 to 1.25) 1 1.19 (1.00 to 1.41)	Age, sex, education, employment status, smoking, alcohol, snoring, work schedule, depressive symptoms, self-rated health, physical activity, BMI, diabetes, lipid disturbance, and hypertension
Anne von Ruesten et al, 2012, Germany[55]	European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study	Male: 65 Female: 60	7.8	24-hour sleep	Interview	MI incidence	Both: 23620 (197)	<6 6-7 7-8 8-9 ≥9	1.44 (0.85 to 2.43) 0.80 (0.53 to 1.20) 1 0.82 (0.56 to 1.19) 0.89 (0.54 to 1.49)	Age, sex, sleeping disorders, sleep duration at night, alcohol intake from beverages, smoking status, walking, cycling, sports, employment status, and education, BMI, waist-to-hip ratio, history of high blood lipid levels at baseline.
Marieke P. Hoevenaar-Blom et al, 2011, Netherlands[49]	MORGEN Study	20-65	11.9	24-hour sleep	Questionnaire	CHD incidence	Both: 20432 (1148)	≤6 7 8 ≥9	1.19 (1.00 to 1.40) 1 0.85 (0.73 to 1.00) 0.78 (0.58 to 1.04)	Age, sex, smoking, alcohol, coffee, subjective health, educational level, BMI, total-/HDL cholesterol ratio, systolic blood pressure, CVD risk factor medication, and prevalence of type 2 diabetes

Yuko Hamazaki et al, 2011, Japan[50]		35-54	14	24-hour sleep	Questionnaire	CHD incidence	Male: 2282 (27)	<6 6-6.9 7-7.9 ≥8	4.95 (1.31 to 18.73) 1.12 (0.40 to 3.13) 1 1.78 (0.67 to 4.76)	Age, type of job, working hours, and mental workload, body mass index, mean blood pressure, HbA1c, total cholesterol, current smoking habit, drinking habit, leisure–time physical activity , and medication for hypertension, diabetes, and hypercholesterolemia
Tarani Chandola et al, 2010, British[56]	British Whitehall II Prospective Cohort Study	35-55	15	Nighttime sleep	Questionnaire	CHD incidence	Both: 8998 (1025)	≤5 6 7 ≥8	1.05 (0.92 to 1.20) 0.98 (0.83 to 1.16) 1 0.99 (0.77 to 1.27)	Sleep variables, age, sex, ethnicity, employment grade, car access, and housing tenure, self-rated health status, total cholesterol concentration, hypertension, body mass index, diabetes, smoking, alcohol consumption, vigorous and moderate exercise, and fruit and vegetable consumption
Yoko Amagai et al, 2010, Japan[51]	Jichi Medical School Cohort Study	18-90	10.7	Nighttime sleep	Interview	MI incidence	Male: 4413 (55) Female: 6954 (25)	Male: <5.9 6.0–6.9 7.0–7.9 8.0–8.9 9.0 Female: <5.9 6.0–6.9 7.0–7.9 8.0–8.9 9.0	Male: 1.78 (0.50 to 6.28) 0.77 (0.25 to 2.33) 1 0.69 (0.34 to 1.41) 0.99 (0.47 to 2.06) Female: 4.93 (1.31 to 18.61) 0.59 (0.13 to 2.73) 1 0.59 (0.21 to 1.66) 0.84 (0.27 to 2.62)	Age, systolic blood pressure, total cholesterol, body mass index, smoking habits, and alcohol drinking habits.
Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	40-79	14.3	24-hour sleep	Questionnaire	CHD mortality	Male: 41489 (508) Female: 57145 (373)	Male: <4 5 6 7 8 9 ≥10 Female: <4 5 6 7 8	Male: 0.29 (0.04 to 2.05) 1.02 (0.62 to 1.70) 0.86 (0.63 to 1.19) 1 1.02 (0.82 to 1.27) 0.96 (0.70 to 1.31) 1.12 (0.77 to 1.63) Female: 2.32 (1.19 to 4.50) 1.64 (1.07 to 2.53) 1.23 (0.88 to 1.72) 1 1.24 (0.94 to 1.64)	Age, body mass index , history of hypertension, history of diabetes, alcohol consumption, smoking, education level, hours of exercise, hours of walking, regular employment, perceived mental stress, depressive symptoms and frequency of fresh fish intake

								9 ≥10	1.52 (1.05 to 2.19) 1.04 (0.63 to 1.72)	
Anoop Shankar et al, 2008, Singapore[57]	Singapore Chinese Health Study	≥45	13	Nighttime sleep	Interview	CHD mortality	Both: 58044 (1416) Male: 25552 (846) Female: 32492 (570)	Both: ≤5 6 7 8 ≥9 Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9	Both: 1.57 (1.32 to 1.88) 1.13 (0.98 to 1.31) 1 1.12 (0.97 to 1.29) 1.79 (1.48 to 2.17) Male: 1.70 (1.35 to 2.15) 1.20 (0.99 to 1.45) 1 1.10 (0.92 to 1.32) 1.88 (1.48 to 2.40) Female: 1.43 (1.09 to 1.88) 1.04 (0.82 to 1.31) 1 1.15 (0.92 to 1.44) 1.67 (1.24 to 2.27)	Age, sex, dialect group, education, year of recruitment, body mass index, smoking , alcohol intake, moderate physical activity , dietary intakes of total calories , fruits, vegetables , fiber, total fat and cholesterol , weekly use of vitamin/mineral supplements (among women, menopausal statusand ever use of postmenopausal hormone replacement therapy)
Christa Meisinger et al, 2007, Germany[58]	MONICA/KORA Augsburg Cohort Study	45-74	10.1	Nighttime sleep	Interview	MI incidence	Male: 3508 (295) Female: 3388 (85)	Male: 5 6 7 8 ≥9 Female: 5 6 7 8 ≥9	Male: 1.13 (0.66 to 1.92) 1.05 (0.71 to 1.55) 1.22 (0.92 to 1.61) 1 1.07 (0.75 to 1.53) Female: 2.98 (1.48 to 6.03) 1.05 (0.49 to 2.27) 1.34 (0.75 to 2.40) 1 1.40 (0.74 to 2.64)	Age, survey, BMI, education, dyslipidemia, alcohol intake, parental history of MI, physical activity, regular smoking, hypertension, diabetes, and menopause status (only women)
Najib T.Ayas et al, 2003, US[59]	Nurse's Health Study	35-55	10	Nighttime sleep	Questionnaire	CHD incidence , CHD mortality and MI incidence	CHD incidence, Female: 71617 (934) CHD mortality, Female: 71617 (271)	≤5 6 7 8 ≥9 5 6 7 8	1.39 (1.05 to 1.84) 1.18 (0.98 to 1.43) 1.10 (0.92 to 1.31) 1 1.37 (1.02 to 1.85) 1.12 (0.68 to 1.84) 0.91 (0.65 to 1.28) 0.83 (0.60 to 1.14) 1	Age, shift work, hypercholesterolemia, body mass index, smoking, snoring, exercise level, alcohol consumption, depression, aspirin use, postmenopausal hormone use, family history of MI, diabetes mellitus and hypertension

							MI incidence, Female: 71617 (663)	≥9 ≤5 6 7 8 ≥9	1.45 (0.89 to 2.36) 1.52 (1.08 to 2.14) 1.32 (1.05 to 1.65) 1.23 (0.99 to 1.52) 1 1.35 (0.93 to 1.95)	
L. MALLON et al, 2002, Sweden[36]		45-65	12	Nighttime sleep	Questionnaire	CHD incidence	Male: 906 (71) Female: 964 (20)	Male: <6 6-8 >8 Female: <6 6-8 >8 Female: <6 6-8 >8	Male: 0.7 (0.3 to 1.7) 1 2.2 (1.0 to 4.4) Female: 1.2 (0.4 to 4.2) 1 0.7 (0.1 to 5.2) Female: 1.2 (0.4 to 4.2) 1 0.7 (0.1 to 5.2)	Age
Adnan I. Qureshi et al, 1997, US[60]	First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study	32-74	10	Nighttime sleep	Questionnaire	CHD incidence	Both: 7844 (413)	<6 6-8 >8	1.3 (1.0 to 1.8) 1 1.1 (0.8 to 1.5)	Age, sex, race, education, cigarette smoking, systolic blood pressure, serum cholesterol level, diabetes, and body mass index

BMI; body mass index, BP; blood pressure, CVD; cardiovascular disease, CHD; coronary heart disease, HDL; high density lipoprotein, IHD; ischemic heart disease, LTPA; leisure time physical activity, MI; myocardial infarction

Table S4. Sleep duration and stroke

Author, publication year, country	Study name	Age at baseline (years)	Follow-up (years)	Exposure	Exposure assessment	Stroke incidence or mortality	Sex, Sample size(cases)	Sleep categories	corresponding relative risk (95% CI)	Covariates in fully adjusted model
Qiaofeng Song et al, 2016, China[61]	The Kailuan Study	18-98	7.9	Nighttime sleep	Questionnaire	Incidence	Both: 95023 (3135)	<6 6-8 >8	0.92 (0.80 to 1.05) 1 1.29 (1.01 to 1.65)	Age, sex, marital status, family per member monthly income, education level, smoking status, drinking status, physical activity, family history of stroke, body mass index, systolic blood pressure, diastolic blood pressure, fasting blood glucose, total cholesterol, hypotensive drug use, lipid-lowering drug use, hypoglycemic drug use, history of myocardial infarction, and snoring status, sensitive C-reactive protein, and atrial fibrillation
Toshiaki Kawachi et al, 2016, Japan[62]	Takayama Cohort Study	≥35	16	Nighttime sleep	Questionnaire	Mortality	Both: 27896 (611) Male: 12875 (296) Female: 15021 (315)	Both: ≤6 7 8 ≥9 Male: ≤6 7 8 ≥9 Female: ≤6 7 8 ≥9	Both: 0.77 (0.59 to 1.01) 1 1.13 (0.91 to 1.40) 1.51 (1.16 to 1.97) Male: 0.51 (0.34 to 0.77) 1 0.88 (0.66 to 1.17) 1.23 (0.90 to 1.69) Female: 1.06 (0.75 to 1.50) 1 1.50 (1.10 to 2.04) 1.93 (1.38 to 2.70)	Sex, age, education years, marital status, histories of hypertension and diabetes, body mass index, physical activity score, smoking status, and alcohol consumption

A. Katharina Helbig et al, 2015, Germany[63]	MONICA/KORA Augsburg Cohort Study	25-74	14	24-hour sleep	Interview	Incidence and mortality	Stroke incidence, Male: 6157 (508) Female: 5974 (318) Stroke mortality, Male: 6157 (109) Female: 5974 (89)	Male: ≤5 6 7-8 9 ≥10 Female: ≤5 6 7-8 9 ≥10 Male: ≤5 6 7-8 9 ≥10 Female: ≤5 6 7-8 9 ≥10	Male: 1.36 (0.95 to 1.94) 0.92 (0.70 to 1.22) 1 1.05 (0.78 to 1.43) 1.38 (0.98 to 1.94) Female: 0.68 (0.40 to 1.18) 1.25 (0.91 to 1.70) 1 1.09 (0.76 to 1.57) 0.91 (0.55 to 1.51) Male: 1.36 (0.95 to 1.94) 0.92 (0.70 to 1.22) 1 1.05 (0.78 to 1.43) 1.38 (0.98 to 1.94) Female: 0.68 (0.40 to 1.18) 1.25 (0.91 to 1.70) 1 1.09 (0.76 to 1.57) 0.91 (0.55 to 1.51)	Age, survey, education, physical activity, alcohol consumption, current smoking, dyslipidemia activity, BMI, hypertension, diabetes
Yue Leng et al, 2015, British[64]	European Prospective Investigation of Cancer–Norfolk Cohort Study	42-81	9.5	24-hour sleep	Questionnaire	Incidence	Both: 9692 (346) Male: 4444 (198) Female: 5248 (148)	Both: <6 6-8 >8 Male: <6 6-8 >8 Female: <6 6-8 >8	Both: 1.18 (0.91 to 1.53) 1 1.46 (1.08 to 1.98) Male: 1.08 (0.75 to 1.57) 1 1.21 (0.80 to 1.82) Female: 1.25 (0.86 to 1.83) 1 1.80 (1.13 to 2.85)	Age, sex, social class, education, marital status, smoking, alcohol intake, hypnotic drug use, family history of stroke, body mass index, physical activity, depression, hypnotic drug use, systolic blood pressure, diastolic blood pressure, preexisting diabetes and myocardial infarction, cholesterol level, and hypertension drug use

Hui Cai et al, 2015, China[4]	Shanghai Women's and Men's Health Studies	Male: 40-75 Female: 44-79	male: 6.07 Female: 7.12	24-hour sleep	Interview	Mortality	Both: 113138 (746)	Both: 4-5 6 7 8 9 ≥10 Male: 4-5 6 7 8 9 ≥10 Female: 4-5 6 7 8 9 ≥10	Both: 0.91 (0.70 to 1.18) 0.99 (0.79 to 1.23) 1 1.28 (1.04 to 1.58) 1.31 (0.94 to 1.82) 2.35 (1.78 to 3.09) Male: 0.93 (0.62 to 1.40) 0.78 (0.55 to 1.10) 1 1.20 (0.89 to 1.62) 1.62 (1.06 to 2.48) 1.73 (1.14 to 2.64) Female: 0.92 (0.65 to 1.29) 1.14 (0.85 to 1.52) 1 1.36 (1.01 to 1.82) 0.98 (0.58 to 1.66) 3.09 (2.14 to 4.47)	Age, education, income, smoking, alcohol consumption, tea consumption, comorbidity score, history of night-shift work, participation in regular exercise, body mass index, and waist-to-hip ratio, cardiovascular disease, upper gastrointestinal tract
Megan E. Ruiter Petrov et al, 2014, US[65]	Reasons for Geographic And Racial Differences in Stroke (REGARDS) Study	≥45	3	Nighttime sleep	Questionnaire	Incidence	Both: 5666 (224)	< 6 6-6.9 7-7.9 8-8.9 ≥ 9	1.43 (0.88 to 2.32) 1.16 (0.79 to 1.69) 1 1.17 (0.84 to 1.62) 1.44 (0.86 to 2.42)	Age, race, sex, income, education, region

An Pan et al, 2014, Singapore[66]	Singapore Chinese Health Study	45-74	14.7	24-hour sleep	Questionnaire	Mortality	Both: 63257 (1381) Male: 27954 (693) Female: 35303 (688)	Both: ≤5 6 7 8 ≥9 Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9	Both: 1.25 (1.05 to 1.50) 1.01 (0.87 to 1.18) 1 1.09 (0.95 to 1.26) 1.54 (1.28 to 1.85) Male: 1.13 (0.86 to 1.47) 0.93 (0.75 to 1.16) 1 0.98 (0.80 to 1.20) 1.49 (1.16 to 1.92) Female: 1.37 (1.08 to 1.75) 1.10 (0.88 to 1.37) 1 1.23 (1.00 to 1.51) 1.62 (1.24 to 2.13)	Age, year of recruitment, sex, dialect, education, body mass index, alcohol drinking , years of smoking, dose of smoking, moderate activity, energy intake, dietary intakes of vegetables, fruits, fiber, polyunsaturated fatty acids, self-reported history of physician-diagnosed hypertension, diabetes, stroke and coronary heart disease, and history of cancer reported by the nationwide cancer registry
Anna Westerlund et al, 2013, Sweden[47]	National March Cohort Study	≥18	13.2	24-hour sleep	Questionnaire	Incidence	Both: 41192 (1685)	5 6 7 ≥8	1.05 (0.80 to 1.37) 0.95 (0.79 to 1.14) 1 0.87 (0.72 to 1.04)	Age, sex, education, employment status, smoking, alcohol, snoring, work schedule, depressive symptoms, self-rated health, physical activity, BMI, diabetes, lipid disturbance, and hypertension
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	45-75	12.9	24-hour sleep	Questionnaire	Mortality	Male: 61936 (627) Female: 73749 (632)	Male: ≤5 6 7 8 ≥9 Female: ≤5 6 7 8 ≥9	Male: 1.14 (1.06 to 1.23) 1.10 (0.88 to 1.37) 1 1.13 (0.91 to 1.39) 1.35 (1.03 to 1.75) Female: 1.16 (0.88 to 1.52) 0.99 (0.79 to 1.23) 1 1.07 (0.87 to 1.33) 1.39 (1.06 to 1.83)	5-year age groups at cohort entry, sex, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, body mass index, physical activity, hours spent daily watching television, and smoking history

Masako Kakizki et al, 2013, Japan[12]	Ohsaki Cohort Study	40-79	10.8	24-hour sleep	Questionnaire	Mortality	Both: 49256 (1165)	≤6 7 8 9 ≥10	1.05 (0.84 to 1.30) 1 1.17 (0.99 to 1.39) 1.30 (1.06 to 1.60) 1.51 (1.24 to 1.85)	Age, sex, total caloric intake, body mass index, marital status, level of education, job status, history of myocardial infarction, history of cancer, history of stroke, history of hypertension, history of diabetes mellitus, smoking status, alcohol drinking, time spent walking, perceived mental stress, self-rated health, physical function
Anne von Ruesten et al, 2012, Germany[55]	European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study	35-65	7.8	24-hour sleep	Interview	Incidence	Both: 23620 (169)	<6 6-7 7-8 8-9 ≥9	2.06 (1.18 to 3.59) 1.13 (0.72 to 1.77) 1 1.16 (0.77 to 1.73) 1.65 (1.00 to 2.73)	Sex, age, education, marital status, living status, depression, body mass index, insomnia, hypnotics use, total sleep time, excessive daytime sleepiness, pain, smoking, alcohol drinking, snorers, diabetes mellitus, hypertension, cardiovascular disease, stroke, and gouty arthritis
Yuko Hamazaki et al, 2011, Japan[50]		35-54	14	24-hour sleep	Questionnaire	Incidence	Male: 2282 (30)	<6 6-6.9 7-7.9 ≥8	1.84 (0.23 to 14.90) 0.96 (0.30 to 3.10) 1 2.25 (0.91 to 5.57)	Age, sex, education, employment status, smoking, alcohol, snoring, work schedule, depressive symptoms, self-rated health, physical activity, BMI, diabetes, lipid disturbance, and hypertension
Yoko Amagai et al, 2010, Japan[51]	Jichi Medical School Cohort Study	18-90	10.7	Nighttime sleep	Interview	Incidence	Male: 4413 (207) Female: 6954 (204)	Male: <5.9 6.0–6.9 7.0–7.9 8.0–8.9 9.0 Female: <5.9 6.0–6.9 7.0–7.9 8.0–8.9 9.0	Male: 2.00 (0.93 to 4.31) 1.13 (0.63 to 2.03) 1 1.03 (0.69 to 1.53) 1.39 (0.92 to 2.10) Female: 0.97 (0.39 to 2.41) 0.68 (0.39 to 1.18) 1 0.86 (0.60 to 1.23) 1.29 (0.86 to 1.91)	Age, sex, educational attainment, body mass index, cigarette smoking, alcohol consumption, past history of hypertension, type 2 diabetes, CVD and metabolic syndrome

Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	40-79	14.3	24-hour sleep	Questionnaire	Mortality	Male: 41489 (1038) Female: 57145 (926)	Male: <4 5 6 7 8 9 ≥10 Female: <4 5 6 7 8 9 ≥10	Male: 1.56 (0.82 to 2.94) 0.85 (0.58 to 1.26) 0.95 (0.76 to 1.20) 1 1.11 (0.95 to 1.30) 1.14 (0.92 to 1.42) 1.66 (1.31 to 2.08) Female: 1.07 (0.59 to 1.91) 0.99 (0.72 to 1.37) 0.93 (0.75 to 1.16) 1 1.24 (1.05 to 1.47) 1.29 (1.01 to 1.64) 1.69 (1.29 to 2.20)	Age, body mass index (quintiles), history of hypertension, history of diabetes, alcohol consumption, smoking, education level, hours of exercise, hours of walking, regular employment, perceived mental stress, depressive symptoms and frequency of fresh fish intake
Jiu-Chiuan Chen et al, 2008, US[67]	Women's Health Initiative Observational Study Cohort	50-79	7.5	Nighttime sleep	Questionnaire	Incidence	Female: 93175 (1166)	≤6 7 8 ≥9	1.14 (0.97 to 1.33) 1 1.24 (1.04 to 1.47) 1.70 (1.32 to 2.21)	Age, sex, total caloric intake, body mass index in, marital status, level of education, job status, history of myocardial infarction, history of cancer, history of stroke, history of hypertension, history of diabetes mellitus, smoking status, alcohol drinking, time spent walking, perceived mental stress, self-rated health, physical function
Yoko Amagai et al, 2004, Japan[32]	Jichi Medical School Cohort Study	19-93	8.2	Nighttime sleep	Interview	Mortality	Male: 4419 (34) Female: 6906 (29)	Male: -5.9 6.0-6.9 7.0-7.9 8.0-8.9 9.0- Female: -5.9 6.0-6.9 7.0-7.9 8.0-8.9 9.0-	Male: 1.3 (0.2 to 11.0) 0.8 (0.2 to 3.9) 1 0.2 (0.1 to 0.8) 1.2 (0.5 to 3.0) Female: NA(n=0) 3.2 (1.0 to 10.5) 1 1.4 (0.4 to 4.3) 2.5 (0.8 to 8.2)	Age, systolic blood pressure, total cholesterol, body mass index, smoking habits, alcohol drinking habits, education, and marital status

Adnan I. Qureshi et al, 1997, US[60]	First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study	32-74	10	Nighttime sleep	Questionnaire	Incidence	Both: 7844 (285)	<6 6-8 >8	1.0 (0.7 to 1.5) 1 1.5 (1.1 to 2.0)	Age, body mass index, systolic blood pressure, diastolic blood press, smoking status, drinking habits and physical activity

BMI; body mass index, CVD; cardiovascular disease

Table S5. Study quality of studies included in the analysis of sleep duration and all-cause mortality

Author, publication year, country	Study	Selection	Comparability	Outcome	Total Score
Nisha Aurora et al, 2016, US[1]	Sleep Heart Health Study	***	**	***	8
Wei-Ju Lee et al, 2016, Taiwan[2]	The Social Environment and Biomarkers of Aging Study	***	**	*	6
Xizhu Wang et al, 2016, China[3]	Kailuan study	***	**	*	6
Hui Cai et al, 2015, China[4]	Shanghai Women's and Men's Health Studies	***	**	***	8
Lisette A. Zuurbier et al, 2015, Netherlands[5]	Rotterdam Study	***	**	***	8
Martica H. Hall et al, 2015, US[6]	Health, Aging and Body Composition (Health ABC) Study	****	**	***	9
Naja Hulvej Rod et al, 2014, British[7]	British Whitehall II Prospective Cohort Study	***	**	***	8
Qian Xiao et al, 2014, US[8]	National Institutes of Health-AARP Diet and Health Study	**	**	**	6
Andrea Bellavia et al, 2014, Sweden[9]	Cohort of Swedish Men and the Swedish Mammography Cohort	***	**	***	8
Christopher A. Magee et al, 2013, Australia[10]	45 and Up Study	**	**	**	6
Garde AH et al, 2013, Denmark[11]	Copenhagen Male Study	**	**	***	7
Masako Kakizaki et al, 2013, Japan[12]	Ohsaki Cohort Study	**	**	***	7
Yohwan Yeo et al, 2013, Korea[13]	Korean Multi-center Cancer Cohort study	***	**	**	7
Hsi-Chung Chen et al, 2013, Taiwan[14]	Shih-Pai Sleep Study	***	**	**	7
Kyu-In Jung et al, 2013, US[15]	Rancho Bernardo Study	**	**	***	7
Lauren Hale et al, 2013, US[16]	Women's Health Initiative (WHI) clinical trial (CT) and observational study (OS)	**	*	**	5
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	***	**	**	7
Ying Li et al, 2013, Japan[18]	SAKU Cohort	**	**	**	6
Jiska Cohen-Mansfield et al, 2012, Israel[19]	Cross-Sectional and Longitudinal Aging Study	***	**	***	8
Chul Woo Rhee et al, 2012, Korea[20]	Seoul Male Cohort Study	**	**	**	6
Castro-Costa et al, 2011, Brasil[21]	Bambui Health and Ageing Study (BHAS)	***	**	***	8
Li Qiu et al, 2011, China[22]	Chinese Longitudinal Healthy Longevity Survey	***	**	**	7
Erkki Kronholm et al, 2011, Finland[23]		**	**	***	7
Arthur Eumann Mesas et al, 2010, Spain[24]		***	**	***	8
Kuo-Liong Chien et al, 2010, Taiwan[25]	Chin-shan Community Cardiovascular Cohort Study	***	**	***	8
Katie L. Stone et al, 2009, US[26]	Study of Osteoporotic Fractures Prospective Cohort Study	**	**	**	6
Etsuji Suzuki et al, 2009, Japan[27]	Shizuoka Study	**	**	***	7
Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	***	**	**	7
James E. Gangwisch et al, 2008, US[29]	NHANES I Epidemiologic Follow-up Study	***	**	**	7
Christer Hublin et al, 2007, Finland[30]	Finnish Twin Cohort	*	**	**	5
Tzuo-Yun Lan et al, 2007, Taiwan[31]	Survey of Health and Living Status of the Elderly in Taiwan	***	**	***	8
Yoko Amagai et al, 2004, Japan[32]	Jichi Medical School Cohort Study	****	**	**	8
Sanjay R. Patel et al, 2003, US[33]	Nurses' Health Study (NHS) Cohort	*	**	**	5
Genc Burazeri et al, 2003, Israel[34]	Kiryat Yovel Community Health Study	***	**	**	7
Aya Goto et al, 2003, Japan[35]		**	**	***	7
L. MALLON et al, 2002, Sweden[36]		**	**	**	6

Daniel F. Kripke et al, 2002, US[37]	Cancer Prevention Study II	**	**	***	7
Pauline Heslop et al, 2002, British[38]		*	**	**	5
Masayo Kojima et al, 2000, Japan[39]		**	**	**	6
Catharine Gale et al, 1998, British[40]		***	**	***	8
Ana Ruigomez et al, 1995, Spain[41]	Health Interview Survey of Barcelona	***	**	*	6
Yoshitaka Tsubono et al, 1993, Japan[42]	National Collaborative Cohort Study	**	**	**	6
Roger Rumble et al, 1992, England[43]	Nottingham Longitudinal Study of Activity	**	*	***	6

Selection: 1) Representativeness of the exposed cohort; 2) Selection of the non-exposed cohort; 3) Ascertainment of exposure; 4) Demonstration that outcome of interest was not present at start of study (cardiovascular events);

Comparability: 1a) study controls for age (the most important factor); 1b) study controls for any additional factor;

Outcome: 1) Assessment of outcome; 2) Was follow-up long enough (≥5 years) for outcomes to occur; 3) Adequacy of follow up of cohorts (≥80%)

Table S6. Study quality of studies included in the analysis of sleep duration and total CVD

Author, publication year, country	Study	Selection	Comparability	Outcome	Total Score
Francesco Gianfagna et al, 2016, Italy[44]	MONICA Brianza and PAMELA	***	**	***	8
Hui Cai et al, 2015, China[4]	Shanghai Women's and Men's Health Studies	***	**	***	8
Catarina Canivet et al, 2014, Sweden[45]	Malmö Diet and Cancer Study	***	**	**	7
Qian Xiao et al, 2014, US[8]	National Institutes of Health-AARP Diet and Health Study	**	**	**	6
Naja Hulvej Rod et al, 2014, British[7]	British Whitehall II Prospective Cohort Study	***	**	***	8
Andrea Bellavia et al, 2014, Sweden[9]	Cohort of Swedish Men and the Swedish Mammography Cohort	***	**	***	8
Megan Sands-Lincoln et al, 2013, US[46]	Women's Health Initiative Observational Study	***	**	**	7
Anna Westerlund et al, 2013, Sweden[47]	National March Cohort Study	***	**	**	7
Elizabeth G. Holliday et al, 2013, Australia[48]	45 and Up Study	***	**	**	7
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	***	**	**	7
Hsi-Chung Chen et al, 2013, Taiwan[14]	Shih-Pai Sleep Study	***	**	**	7
Yohwan Yeo et al , 2013, Korea[13]	Korean Multi-center Cancer Cohort study	***	**	**	7
Masako Kakizki et al, 2013, Japan[12]	Ohsaki Cohort Study	**	**	***	7
Ying Li et al, 2013, Japan[18]	SAKU Cohort	**	**	**	6
Marieke P. Hoevenaar-Blom et al, 2011, Netherlands[49]	MORGEN Study	***	**	**	7
Yuko Hamazaki et al, 2011, Japan[50]		**	**	***	7
Erkki Kronholm et al, 2011, Finland[23]		**	**	***	7
Kuo-Liong Chien et al, 2010, Taiwan[25]	Chin-shan Community Cardiovascular Cohort study	***	**	***	8
Yoko Amagai et al, 2010, Japan[51]	Jichi Medical School Cohort Study	****	**	**	8
Katie L. Stone et al, 2009, US[26]	Study of Osteoporotic Fractures Prospective Cohort Study	**	**	**	6
Etsuji Suzuki et al, 2009, Japan[27]	Shizuoka Study	**	**	***	7
Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	***	**	**	7
Tzuo-Yun Lan et al, 2007, Taiwan[31]	Survey of Health and Living Status of the Elderly in Taiwan	***	**	***	8
Sanjay R. Patel et al, 2004, US[33]	Nurses' Health Study (NHS) Cohort	*	**	**	5
Genc Burazeri et al, 2003, Israel[34]	Kiryat Yovel Community Health Study	***	**	**	7
Pauline Heslop et al, 2002, British[38]		*	**	**	5

Selection: 1) Representativeness of the exposed cohort; 2) Selection of the non-exposed cohort; 3) Ascertainment of exposure; 4) Demonstration that outcome of interest was not present at start of study;

Comparability: 1a) study controls for age (the most important factor); 1b) study controls for any additional factor;

Outcome: 1) Assessment of outcome; 2) Was follow-up long enough (≥5 years) for outcomes to occur; 3) Adequacy of follow up of cohorts (≥80%)

Table S7. Study quality of studies included in the analysis of sleep duration and CHD

Author, publication year, country	Study	Selection	Comparability	Outcome	Total Score
Francesco Gianfagna et al, 2016, Italy[44]	MONICA Brianza and PAMELA Population-based Cohorts	***	**	***	8
Liangle Yang et al, 2016, China[52]	Dongfeng-Tongji Cohort Study	**	**	**	6
Xizhu Wang et al, 2016, China[3]	Kailuan Study	***	**	*	6
Linn B. Strand et al, 2016, Taiwan[53]		**	**	**	6
J. Liu et al, 2014, US[54]	Framingham Offspring Study	***	**	**	7
Megan Sands-Lincoln et al, 2013, US[46]	Women's Health Initiative Observational Study	***	**	**	7
Lauren Hale et al, 2013, US[16]	Women's Health Initiative (WHI) clinical trial (CT) and observational study (OS)	**	*	**	5
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	***	**	**	7
Masako Kakizki et al, 2013, Japan[12]	Ohsaki Cohort Study	**	**	***	7
Garde AH et al, 2013, Denmark[11]	Copenhagen Male Study	**	**	***	7
Anna Westerlund et al, 2013, Sweden[47]	National March Cohort Study	***	**	**	7
Anne von Ruesten et al, 2012, Germany[55]	European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study	****	**	***	9
Marieke P. Hoevenaar-Blom et al, 2011, Netherlands[49]	MORGEN Study	***	**	**	7
Yuko Hamazaki et al, 2011, Japan[50]		**	**	***	7
Tarani Chandola et al, 2010, British[56]	British Whitehall II Prospective Cohort Study	***	**	**	7
Yoko Amagai et al, 2010, Japan[51]	Jichi Medical School Cohort Study	****	**	**	8
Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	***	**	**	7
Anoop Shankar et al, 2008, Singapore[57]	Singapore Chinese Health Study	****	**	***	9
Christa Meisinger et al, 2007, Germany[58]	MONICA/KORA Augsburg Cohort Study	****	**	**	8
Najib T.Ayas et al, 2003, US[59]	Nurse's Health Study	**	**	**	6
L. MALLON et al, 2002, Sweden[36]		**	**	**	6
Adnan I. Qureshi et al, 1997, US[60]	First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study	***	**	**	7

Selection: 1) Representativeness of the exposed cohort; 2) Selection of the non-exposed cohort; 3) Ascertainment of exposure; 4) Demonstration that outcome of interest was not present at start of study;

Comparability: 1a) study controls for age (the most important factor); 1b) study controls for any additional factor;

Outcome: 1) Assessment of outcome; 2) Was follow-up long enough (≥5 years) for outcomes to occur; 3) Adequacy of follow up of cohorts (≥80%)

Table S8. Study quality of studies included in the analysis of sleep duration and stroke

Author, publication year, country	Study	Selection	Comparability	Outcome	Total Score
Qiaofeng Song et al, 2016, China[61]	The Kailuan Study	**	**	**	6
Toshiaki Kawachi et al, 2016, Japan[62]	Takayama Cohort Study	***	**	***	8
A. Katharina Helbig et al, 2015, Germany[63]	MONICA/KORA Augsburg Cohort Study	****	**	**	8
Yue Leng et al, 2015, British[64]	European Prospective Investigation of Cancer–Norfolk Cohort Study	***	**	**	7
Hui Cai et al, 2015, China[4]	Shanghai Women's and Men's Health Studies	***	**	***	8
Megan E. Ruiter Petrov et al, 2014, US[65]	Reasons for Geographic And Racial Differences in Stroke (REGARDS) Study	***	*		4
An Pan et al, 2014, Singapore[66]	Singapore Chinese Health Study	**	**	***	7
Anna Westerlund et al, 2013, Sweden[47]	National March Cohort Study	***	**	**	7
Yeonju Kim et al, 2013, US[17]	Multiethnic Cohort Study	***	**	**	7
Masako Kakizki et al, 2013, Japan[12]	Ohsaki Cohort Study	**	**	***	7
Anne von Ruesten et al, 2012, Germany[55]	European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study	****	**	***	9
Yuko Hamazaki et al, 2011, Japan[50]		**	**	***	7
Yoko Amagai et al, 2010, Japan[51]	Jichi Medical School Cohort Study	****	**	**	8
Satoyo Ikehara et al, 2009, Japan[28]	JACC Study	***	**	**	7
Jiu-Chiuan Chen et al, 2008, US[67]	Women's Health Initiative Observational Study Cohort	***	**	**	7
Adnan I. Qureshi et al, 1997, US[60]	First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study	***	**	**	7

Selection: 1) Representativeness of the exposed cohort; 2) Selection of the non-exposed cohort; 3) Ascertainment of exposure; 4) Demonstration that outcome of interest was not present at start of study;

Comparability: 1a) study controls for age (the most important factor); 1b) study controls for any additional factor;

Outcome: 1) Assessment of outcome; 2) Was follow-up long enough (≥5 years) for outcomes to occur; 3) Adequacy of follow up of cohorts (≥80%)

Table S9. Subgroup analyses of sleep duration and all-cause mortality, per hour per day

		Short sleep					Long sleep				
		No	RR (95% CI)	P_{het}^{*}	I²	$P_{het}^{\dagger}$	No	RR (95% CI)	P_{het}^{*}	I²	$P_{het}^{\dagger}$
Total		32	1.06 (1.04 to 1.07)	0.00	58.0%	NC	37	1.13 (1.11 to 1.15)	0.00	76.5%	NC
Sex											
Men		11	1.06 (1.05 to 1.08)	0.57	0.0%	0.57/0.97	13	1.10 (1.09 to 1.11)	0.54	0.0%	0.21/0.49
Women		13	1.05 (1.04 to 1.07)	0.30	14.9%		14	1.15 (1.11 to 1.18)	0.00	81.5%	
Mix		14	1.06 (1.03 to 1.09)	0.00	64.2%		16	1.13 (1.10 to 1.16)	0.00	75.8%	
Location											
Asia		13	1.05 (1.02 to 1.09)	0.02	52.1%	0.05	18	1.15 (1.11 to 1.18)	0.00	70.9%	0.41
Europe		6	1.12 (1.09 to 1.15)	0.38	6.5%		7	1.14 (1.10 to 1.17)	0.22	27.9%	
USA		11	1.04 (1.03 to 1.06)	0.05	45.2%		10	1.12 (1.09 to 1.15)	0.00	87.0%	
Others		2	1.04 (0.99 to 1.09)	0.92	0.0%		2	1.13 (0.98 to 1.30)	0.00	70.7%	
Duration of follow-up											
<10 years		17	1.05 (1.03 to 1.07)	0.02	45.9%	0.40	20	1.13 (1.10 to 1.16)	0.00	73.9%	0.78
≥10 years		15	1.07 (1.04 to 1.09)	0.00	66.6%		17	1.13 (1.10 to 1.15)	0.00	75.1%	
No of participants											
<10000		15	1.05 (1.02 to 1.09)	0.55	0.0%	1.00	20	1.16 (1.13 to 1.19)	0.06	34.9%	0.05
≥10000		17	1.06 (1.04 to 1.07)	0.00	73.6%		17	1.13 (1.11 to 1.15)	0.00	77.5%	
No of cases											
<1000		13	1.07 (1.02 to 1.13)	0.65	0.0%	0.51	17	1.15 (1.11 to 1.19)	0.04	40.3%	0.31
≥1000		19	1.06 (1.04 to 1.07)	0.00	71.2%		20	1.12 (1.10 to 1.14)	0.00	75.5%	
Sleep assessment											
Self-report questionnaire		21	1.06 (1.04 to 1.08)	0.00	63.7%	0.29	23	1.12 (1.10 to 1.14)	0.00	78.7%	0.16
Interview		11	1.06 (1.02 to 1.11)	0.17	44.0%		14	1.16 (1.11 to 1.20)	0.00	71.0%	
Sleep duration type											
Nighttime sleep		21	1.06 (1.04 to 1.08)	0.00	53.3%	0.93	24	1.16 (1.13 to 1.18)	0.00	73.0%	0.01
24-hour sleep		11	1.06 (1.03 to 1.08)	0.00	64.4%		13	1.11 (1.10 to 1.13)	0.00	78.4%	
Study quality score											
<7		8	1.04 (1.01 to 1.07)	0.05	35.1%	0.30	8	1.14 (1.08 to 1.20)	0.01	60.5%	0.85
≥7		24	1.06 (1.05 to 1.08)	0.01	46.2%		29	1.13 (1.11 to 1.15)	0.00	78.8%	
Adjustment for confounders											
Age	Yes	32	1.06 (1.04 to 1.07)	0.00	58.0%	NC	37	1.13 (1.11 to 1.15)	0.00	76.5%	NC
	No	0					0				
Education	Yes	21	1.06 (1.04 to 1.08)	0.00	63.0%	0.81	20	1.12 (1.10 to 1.14)	0.00	59.4%	0.43
	No	11	1.06 (1.03 to 1.09)	0.23	22.3%		17	1.14 (1.10 to 1.19)	0.00	82.6%	
Hypertension, blood pressure	Yes	24	1.06 (1.05 to 1.07)	0.24	16.0%	0.37	28	1.13 (1.11 to 1.15)	0.00	72.7%	0.32
	No	8	1.05 (1.02 to 1.10)	0.00	67.8%		9	1.12 (1.06 to 1.18)	0.00	83.1%	
	Yes	7	1.10 (1.06 to 1.15)	0.25	23.3%	0.02	7	1.15 (1.12 to 1.19)	0.83	0.0%	0.36

Hypercholesterolemia, serum cholesterol	No	25	1.05 (1.04 to 1.07)	0.00	47.9%		30	1.13 (1.11 to 1.15)	0.00	80.2%	
Diabetes	Yes	18	1.06 (1.04 to 1.07)	0.41	3.9%	0.66	21	1.13 (1.11 to 1.15)	0.00	77.6%	0.96
	No	14	1.07 (1.04 to 1.10)	0.00	68.9%		16	1.14 (1.10 to 1.18)	0.00	76.2%	
Smoke	Yes	28	1.06 (1.05 to 1.08)	0.00	60.0%	0.15	31	1.13 (1.11 to 1.15)	0.00	77.3%	0.30
	No	4	1.03 (0.97 to 1.03)	0.27	23.5%		6	1.10 (1.00 to 1.21)	0.00	67.7%	
Alcohol	Yes	24	1.06 (1.04 to 1.08)	0.00	55.5%	0.93	26	1.13 (1.11 to 1.16)	0.00	77.5%	0.57
	No	8	1.06 (1.03 to 1.08)	0.00	62.7%		11	1.12 (1.09 to 1.15)	0.00	67.8%	
Physical activity	Yes	20	1.06 (1.04 to 1.08)	0.00	55.5%	0.97	23	1.13 (1.11 to 1.16)	0.00	79.4%	0.67
	No	12	1.05 (1.03 to 1.07)	0.00	59.9%		14	1.12 (1.09 to 1.15)	0.00	63.6%	
BMI	Yes	26	1.06 (1.04 to 1.08)	0.00	59.8%	0.84	28	1.13 (1.11 to 1.14)	0.00	67.4%	0.63
	No	6	1.08 (1.01 to 1.15)	0.02	60.7%		9	1.13 (1.11 to 1.15)	0.00	81.8%	
Sleep disorder	Yes	5	1.05 (1.03 to 1.07)	0.22	29.7%	0.52	5	1.12 (1.09 to 1.15)	0.01	68.4%	0.83
	No	27	1.06 (1.04 to 1.08)	0.00	57.0%		32	1.13 (1.11 to 1.15)	0.00	76.7%	
Depression	Yes	9	1.04 (1.02 to 1.06)	0.77	0.0%	0.11	11	1.15 (1.12 to 1.19)	0.00	64.6%	0.15
	No	23	1.07 (1.05 to 1.09)	0.00	66.0%		26	1.12 (1.10 to 1.14)	0.00	79.4%	
Sleeping pills	Yes	6	1.04 (0.99 to 1.09)	0.44	0.0%	0.64	8	1.18 (1.14 to 1.21)	0.26	20.9%	0.10
	No	26	1.06 (1.04 to 1.08)	0.00	61.4%		29	1.20 (1.10 to 1.14)	0.00	68.8%	

No denotes the number of studies.

P_{het}^{*} for heterogeneity within each subgroup,

$P_{het}^{\dagger}$ for heterogeneity between subgroups with meta-regression analysis,

NC = not calculable

Table S10. Subgroup analyses of sleep duration and total cardiovascular disease, per hour per day

		Short sleep					Long sleep				
		No	RR (95% CI)	P_{het}*	I²	P_{het}†	No	RR (95% CI)	P_{het}*	I²	P_{het}†
Total		21	1.06 (1.03 to 1.09)	0.00	52.0%	NC	23	1.12 (1.08 to 1.16)	0.00	75.3%	NC
Sex											
Men		7	1.07 (1.01 to 1.13)	0.19	31.0%	0.57/0.63	7	1.11 (1.08 to 1.14)	0.53	0.0%	0.66/0.99
Women		8	1.07 (1.02 to 1.12)	0.06	48.7%		9	1.14 (1.08 to 1.19)	0.04	51.0%	
Mix		8	1.05 (1.03 to 1.08)	0.00	63.2%		9	1.12 (1.04 to 1.20)	0.00	87.4%	
Location											
Asia		11	1.06 (1.01 to 1.11)	0.25	20.0%	0.34	13	1.16 (1.13 to 1.20)	0.24	19.7%	0.01
Europe		4	1.12 (1.01 to 1.23)	0.00	82.3%		4	1.06 (0.97 to 1.16)	0.01	75.2%	
USA		5	1.04 (1.02 to 1.06)	0.24	27.6%		5	1.11 (1.05 to 1.17)	0.02	64.3%	
Others		1	1.03 (0.96 to 1.10)				1	1.00 (0.96 to 1.03)			
Duration of follow-up											
<10 years		6	1.04 (0.99 to 1.09)	0.56	0.0%	0.75	9	1.17 (1.07 to 1.28)	0.00	85.1%	0.24
≥10 years		15	1.06 (1.03 to 1.09)	0.00	62.9%		14	1.10 (1.07 to 1.14)	0.00	60.1%	
No of participants											
<10000		7	1.12 (1.00 to 1.26)	0.13	39.1%	0.47	10	1.18 (1.12 to 1.24)	0.24	21.9%	0.08
≥10000		14	1.05 (1.03 to 1.08)	0.00	57.4%		13	1.10 (1.05 to 1.14)	0.00	80.8%	
No of cases											
<1000		8	1.11 (1.00 to 1.22)	0.19	30.5%	0.53	10	1.15 (1.10 to 1.21)	0.60	0.0%	0.22
≥1000		13	1.05 (1.03 to 1.08)	0.00	60.7%		13	1.10 (1.06 to 1.15)	0.00	84.5%	
Sleep assessment											
Self-report questionnaire		14	1.06 (1.03 to 1.09)	0.00	61.8%	0.95	15	1.11 (1.01 to 1.16)	0.00	82.6%	0.40
Interview		7	1.06 (0.98 to 1.14)	0.27	21.4%		8	1.15 (1.08 to 1.23)	0.45	0.0%	
Sleep duration type											
Nighttime sleep		10	1.04 (1.02 to 1.07)	0.18	28.7%	0.43	11	1.11 (1.04 to 1.18)	0.00	72.4%	0.71
24-hour sleep		11	1.08 (1.03 to 1.13)	0.00	61.4%		12	1.13 (1.09 to 1.17)	0.00	60.2%	
Study quality score											
<7		2	1.04 (1.02 to 1.06)	0.95	0.0%	0.58	1	1.21 (1.09 to 1.34)			0.33
≥7		19	1.07 (1.03 to 1.10)	0.00	56.1%		22	1.11 (1.07 to 1.15)	0.00	75.3%	
Incidence or mortality											
Incidence		7	1.02 (0.98 to 1.07)	0.20	30.0%	0.10	6	1.00 (0.97 to 1.03)	0.50	0.0%	0.00
Mortality		16	1.08 (1.04 to 1.11)	0.00	53.8%		19	1.15 (1.12 to 1.18)	0.01	46.3%	
Adjustment for confounders											
Age	Yes	21	1.06 (1.03 to 1.09)	0.00	52.0%	NC	23	1.12 (1.08 to 1.16)	0.00	75.3%	NC
	No	0					0				
Education	Yes	16	1.05 (1.02 to 1.08)	0.00	54.2%	0.36	16	1.10 (1.06 to 1.15)	0.00	80.1%	0.26
	No	5	1.09 (1.03 to 1.15)	0.31	16.1%		7	1.15 (1.10 to 1.21)	0.18	32.0%	

Hypertension, blood pressure	Yes	17	1.06 (1.03 to 1.09)	0.07	36.0%	0.77	18	1.12 (1.08 to 1.15)	0.00	57.1%	0.88
	No	4	1.08 (1.00 to 1.16)	0.00	82.0%		5	1.12 (0.99 to 1.26)	0.00	89.8%	
Hypercholesterolemia, serum cholesterol	Yes	8	1.05 (1.00 to 1.11)	0.02	58.8%	0.69	7	1.06 (0.99 to 0.13)	0.02	60.4%	0.06
	No	13	1.06 (1.03 to 1.10)	0.03	48.7%		16	1.14 (1.10 to 1.19)	0.00	77.6%	
Diabetes	Yes	13	1.04 (1.01 to 1.07)	0.18	25.9%	0.29	14	1.12 (1.08 to 1.16)	0.00	61.1%	0.86
	No	8	1.09 (1.03 to 1.14)	0.00	70.9%		9	1.20 (1.03 to 1.21)	0.00	83.3%	
Smoke	Yes	21	1.06 (1.03 to 1.09)	0.00	52.0%	NC	23	1.12 (1.08 to 1.16)	0.00	75.3%	NC
	No	0					0				
Alcohol	Yes	19	1.06 (1.03 to 1.08)	0.00	53.2%	0.38	21	1.12 (1.08 to 1.16)	0.00	75.9%	0.90
	No	2	1.10 (1.05 to 1.16)	0.10	0.0%		2	1.11 (0.96 to 1.29)	0.01	83.3%	
Physical activity	Yes	14	1.05 (1.02 to 1.08)	0.00	58.6%	0.17	15	1.12 (1.08 to 1.17)	0.00	79.4%	0.76
	No	7	1.10 (1.01 to 1.15)	0.50	0.0%		8	1.12 (1.03 to 1.22)	0.00	66.5%	
BMI	Yes	21	1.06 (1.03 to 1.09)	0.00	52.0%	NC	23	1.12 (1.08 to 1.16)	0.00	75.3%	NC
	No	0					0				
Sleep disorder	Yes	1	1.01 (0.86 to 1.18)			0.64	1	1.51 (1.20 to 1.90)			0.03
	No	20	1.06 (1.03 to 1.09)	0.00	54.2%		22	1.11 (1.07 to 1.15)	0.00	74.4%	
Depression	Yes	7	1.02 (0.99 to 1.04)	0.81	0.0%	0.09	9	1.15 (1.10 to 1.21)	0.00	61.3%	0.16
	No	14	1.08 (1.04 to 1.12)	0.00	60.9%		14	1.10 (1.05 to 1.15)	0.00	78.4%	
Sleeping pills	Yes	1	1.01 (0.86 to 1.18)			0.64	1	1.51 (1.20 to 1.90)			0.03
	No	20	1.06 (1.03 to 1.09)	0.00	54.2%		22	1.12 (1.07 to 1.15)	0.00	74.4%	

No denotes the number of studies.

P_{het}^{*} for heterogeneity within each subgroup,

$P_{het}^{\dagger}$ for heterogeneity between subgroups with meta-regression analysis,

NC = not calculable

Table S11. Subgroup analyses of sleep duration and coronary heart disease, per hour per day

		Short sleep					Long sleep				
		No	RR (95% CI)	P_{het}^{*}	I²	$P_{het}^{\dagger}$	No	RR (95% CI)	P_{het}^{*}	I²	$P_{het}^{\dagger}$
Total		18	1.07 (1.03 to 1.12)	0.00	59.3%	NC	16	1.05 (1.00 to 1.10)	0.00	64.2%	NC
Sex											
Men		7	1.08 (0.98 to 1.19)	0.01	66.1%	0.23/0.60	5	1.07 (0.95 to 1.20)	0.00	75.8%	0.23/0.58
Women		9	1.10 (1.03 to 1.18)	0.01	63.6%		7	1.09 (1.03 to 1.16)	0.17	33.8%	
Mix		6	1.07 (0.99 to 1.15)	0.01	68.1%		6	1.04 (0.93 to 1.17)	0.00	84.6%	
Location											
Asia		8	1.13 (1.00 to 1.27)	0.00	73.6%	0.36	8	1.09 (1.02 to 1.18)	0.01	63.3%	0.02
Europe		5	1.04 (0.98 to 1.09)	0.48	0.0%		4	0.89 (0.82 to 0.97)	0.94	0.0%	
USA		5	1.05 (1.00 to 1.09)	0.23	28.1%		4	1.07 (1.03 to 1.11)	0.35	9.0%	
Duration of follow-up											
<10 years		3	1.03 (0.97 to 1.09)	0.48	0.0%	0.38	3	1.03 (0.95 to 1.11)	0.30	18.0%	0.48
≥10 years		15	1.09 (1.03 to 1.14)	0.00	64.8%		13	1.06 (1.00 to 1.12)	0.00	69.0%	
No of participants											
<10000		7	1.08 (0.94 to 1.25)	0.07	48.1%	0.65	4	0.92 (0.81 to 1.06)	0.98	0.0%	0.15
≥10000		11	1.08 (1.03 to 1.13)	0.00	66.1%		12	1.06 (1.01 to 1.12)	0.00	70.4%	
No of cases											
<500		9	1.12 (0.97 to 1.30)	0.01	59.2%	0.74	7	1.00 (0.92 to 1.08)	0.52	0.0%	0.18
≥500		9	1.07 (1.02 to 1.11)	0.01	62.9%		9	1.07 (1.01 to 1.13)	0.00	76.2%	
Sleep assessment											
Self-report questionnaire		12	1.05 (1.01 to 1.09)	0.04	45.9%	0.05	10	1.05 (1.01 to 1.09)	0.03	50.9%	0.98
Interview		6	1.17 (1.02 to 1.35)	0.14	39.9%		6	1.00 (0.83 to 1.21)	0.00	75.3%	
Sleep duration type											
Nighttime sleep		11	1.06 (1.00 to 1.12)	0.00	63.9%	0.48	9	1.06 (0.98 to 1.14)	0.00	67.5%	0.82
24-hour sleep		7	1.10 (1.02 to 1.18)	0.10	43.9%		7	1.04 (0.97 to 1.11)	0.01	64.0%	
Study quality score											
<7		4	1.03 (0.97 to 1.10)	0.32	14.4%	0.29	4	1.08 (1.04 to 1.12)	0.39	1.4%	0.54
≥7		14	1.09 (1.03 to 1.16)	0.00	65.7%		12	1.03 (0.96 to 1.11)	0.00	71.2%	
Incidence or mortality											
Incidence		11	1.04 (1.00 to 1.10)	0.15	30.8%	0.42	9	1.00 (0.94 to 1.06)	0.04	50.5%	0.03
Mortality		8	1.10 (1.02 to 1.17)	0.00	66.3%		8	1.12 (1.05 to 1.19)	0.01	62.4%	
Adjustment for confounders											
Age	Yes	18	1.07 (1.03 to 1.12)	0.00	59.3%	NC	16	1.05 (1.00 to 1.10)	0.00	64.2%	NC
	No	0					0				
Education	Yes	12	1.07 (1.01 to 1.12)	0.00	66.4%	0.69	12	1.05 (1.00 to 1.11)	0.00	71.5%	0.69
	No	6	1.04 (0.99 to 1.24)	0.11	44.6%		4	1.06 (0.97 to 1.15)	0.35	8.2%	
	Yes	16	1.05 (1.01 to 1.10)	0.03	44.7%	0.03	14	1.04 (1.00 to 1.08)	0.05	41.6%	0.13

Hypertension, blood pressure	No	2	1.22 (1.12 to 1.32)	0.33	0.0%		2	1.10 (0.78 to 1.54)	0.00	87.0%	
Hypercholesterolemia, serum cholesterol	Yes	12	1.04 (1.00 to 1.08)	0.18	26.5%	0.17	10	1.00 (0.94 to 1.06)	0.05	46.0%	0.02
	No	6	1.10 (1.01 to 1.20)	0.00	69.7%		6	1.12 (1.05 to 1.19)	0.01	66.1%	
Diabetes	Yes	14	1.05 (1.01 to 1.09)	0.04	43.6%	0.01	12	1.04 (1.00 to 1.09)	0.03	49.0%	0.29
	No	4	1.22 (1.11 to 1.34)	0.37	5.2%		4	1.04 (0.82 to 1.33)	0.01	71.7%	
Smoke	Yes	18	1.07 (1.03 to 1.12)	0.00	59.3%	NC	16	1.05 (1.00 to 1.10)	0.00	64.2%	NC
	No	0					0				
Alcohol	Yes	18	1.07 (1.03 to 1.12)	0.00	59.3%	NC	16	1.05 (1.00 to 1.10)	0.00	64.2%	NC
	No	0					0				
Physical activity	Yes	16	1.07 (1.02 to 1.12)	0.00	60.3%	0.19	13	1.07 (1.02 to 1.12)	0.00	58.6%	0.03
	No	2	1.52 (0.92 to 2.50)	0.25	23.0%		3	0.88 (0.79 to 0.98)	0.83	0.0%	
BMI	Yes	17	1.08 (1.03 to 1.13)	0.00	59.9%	0.27	15	1.05 (1.00 to 1.11)	0.00	70.0%	0.49
	No	1	0.95 (0.81 to 1.10)				1	0.95 (0.77 to 1.18)			
Sleep disorder	Yes	1	1.09 (0.86 to 1.38)			0.94	1	0.91 (0.72 to 1.14)			0.33
	No	17	1.07 (1.02 to 1.12)	0.00	61.6%		15	1.06 (1.01 to 1.11)	0.00	65.0%	
Depression	Yes	6	1.06 (0.98 to 1.14)	0.03	61.0%	0.71	4	1.06 (1.00 to 1.11)	0.31	15.6%	0.80
	No	12	1.08 (1.02 to 1.15)	0.00	57.4%		12	1.04 (0.97 to 1.11)	0.00	71.1%	
Sleeping pills	Yes	1	1.04 (0.97 to 1.11)			0.72	0				NC
	No	17	1.08 (1.02 to 1.13)	0.00	61.6%		16	1.05 (1.00 to 1.10)	0.00	64.2%	

No denotes the number of studies.

P_{het}^{*} for heterogeneity within each subgroup,

$P_{het}^{\dagger}$ for heterogeneity between subgroups with meta-regression analysis,

NC = not calculable

Table S12. Subgroup analyses of sleep duration and stroke, per hour per day

		Short sleep					Long sleep				
		No	RR (95% CI)	P_{het}^{*}	I^2	$P_{het}^{\dagger}$	No	RR (95% CI)	P_{het}^{*}	I^2	$P_{het}^{\dagger}$
Total		14	1.05 (1.01 to 1.09)	0.55	0.0%	NC	15	1.18 (1.14 to 1.21)	0.40	4.9%	NC
Sex											
Men		6	1.05 (0.98 to 1.11)	0.79	0.0%	0.53/0.63	6	1.14 (1.09 to 1.19)	0.94	0.0%	0.14/0.88
Women		5	1.05 (0.97 to 1.13)	0.26	24.6%		7	1.20 (1.12 to 1.28)	0.07	48.7%	
Mix		5	1.08 (1.00 to 1.13)	0.18	35.5%		6	1.20 (1.15 to 1.26)	0.36	9.4%	
Location											
Asia		7	1.05 (0.99 to 1.10)	0.47	0.0%	0.71	8	1.18 (1.14 to 1.22)	0.43	0.5%	0.13
Europe		4	1.06 (0.96 to 1.16)	0.18	38.7%		3	1.09 (0.99 to 1.21)	0.28	21.6%	
USA		3	1.07 (0.98 to 1.17)	0.60	0.0%		4	1.20 (1.20 to 1.29)	0.58	0.0%	
Duration of follow-up											
<10 years		3	1.15 (0.98 to 1.35)	0.12	53.8%	0.36	4	1.28 (1.20 to 1.37)	0.92	0.0%	0.01
≥10 years		11	1.04 (1.00 to 1.09)	1.09	0.0%		11	1.15 (1.12 to 1.19)	0.83	0.0%	
No of participants											
<10000		6	1.06 (0.98 to 1.16)	0.49	0.0%	0.75	5	1.10 (1.02 to 1.18)	0.69	0.0%	0.08
≥10000		8	1.05 (1.00 to 1.09)	0.41	2.4%		10	1.19 (1.15 to 1.22)	0.45	0.0%	
No of cases											
<500		6	1.13 (0.98 to 1.30)	0.20	32.0%	0.30	4	1.09 (1.00 to 1.20)	0.53	0.0%	0.16
≥500		8	1.04 (1.00 to 1.09)	0.87	0.0%		11	1.18 (1.15 to 1.22)	0.42	2.1%	
Sleep assessment											
Self-report questionnaire		9	1.05 (1.00 to 1.09)	0.82	0.0%	0.57	10	1.19 (1.15 to 1.22)	0.47	0.0%	0.11
Interview		5	1.09 (0.96 to 1.24)	0.14	42.6%		5	1.10 (1.03 to 1.19)	0.55	0.0%	
Sleep duration type											
Nighttime sleep		3	1.13 (0.90 to 1.42)	0.20	37.8%	0.35	5	1.22 (1.13 to 1.30)	0.73	0.0%	0.35
24-hour sleep		11	1.05 (1.01 to 1.09)	1.09	0.0%		10	1.17 (1.13 to 1.21)	0.24	22.6%	
Study quality score											
<7		1	1.19 (0.95 to 1.49)			0.30	1	1.19 (0.95 to 1.50)			0.92
≥7		13	1.05 (1.01 to 1.09)	0.56	0.0%		14	1.18 (1.14 to 1.21)	0.33	11.6%	
Incidence or mortality											
Incidence		8	1.07 (0.99 to 1.16)	0.25	22.6%	0.86	7	1.15 (1.08 to 1.24)	0.26	22.0%	0.60
Mortality		10	1.05 (1.01 to 1.10)	0.66	0.0%		12	1.18 (1.14 to 1.21)	0.50	0.0%	
Adjustment for confounders											
Age	Yes	14	1.05 (1.01 to 1.09)	0.55	0.0%	NC	15	1.18 (1.14 to 1.21)	0.40	4.9%	NC
	No	0					0				
Education	Yes	11	1.05 (1.01 to 1.09)	0.56	0.0%	0.76	12	1.17 (1.14 to 1.21)	0.37	7.8%	0.41
	No	3	1.09 (0.79 to 1.50)	0.23	32.7%		3	1.22 (1.12 to 1.34)	0.37	0.0%	
	Yes	11	1.04 (1.00 to 1.09)	0.77	0.0%	0.36	12	1.16 (1.13 to 1.20)	0.63	0.0%	0.04

Hypertension, blood pressure	No	3	1.15 (0.98 to 1.35)	0.16	53.8%		3	1.28 (1.19 to 1.38)	0.78	0.0%	
Hypercholesterolemia, serum cholesterol	Yes	7	1.06 (0.97 to 1.16)	0.34	24.9%	0.96	6	1.15 (1.06 to 1.25)	0.18	34.5%	0.52
	No	7	1.05 (1.00 to 1.10)	0.71	0.0%		9	1.18 (1.15 to 1.22)	0.57	0.0%	
Diabetes	Yes	9	1.04 (1.00 to 1.09)	0.90	0.0%	0.34	10	1.16 (1.13 to 1.20)	0.48	0.0%	0.09
	No	5	1.32 (0.98 to 1.31)	1.22	45.0%		5	1.25 (1.16 to 1.33)	0.58	0.0%	
Smoke	Yes	13	1.05 (1.01 to 1.09)	0.56	0.0%	0.30	14	1.18 (1.14 to 1.21)	0.33	11.6%	0.92
	No	1	1.19 (0.95 to 1.49)				1	1.19 (0.95 to 1.49)			
Alcohol	Yes	13	1.05 (1.01 to 1.09)	0.56	0.0%	0.30	13	1.17 (1.14 to 1.20)	0.42	2.6%	0.18
	No	1	1.19 (0.95 to 1.49)				2	1.26 (1.14 to 1.40)	0.52	0.0%	
Physical activity	Yes	8	1.05 (0.99 to 1.10)	0.65	0.0%	0.74	9	1.18 (1.12 to 1.24)	0.10	40.1%	0.80
	No	6	1.06 (0.98 to 1.14)	0.25	24.0%		6	1.17 (1.12 to 1.22)	0.94	0.0%	
BMI	Yes	13	1.05 (1.01 to 1.09)	0.56	0.0%	0.30	14	1.18 (1.14 to 1.21)	0.33	11.6%	0.92
	No	1	1.19 (0.95 to 1.49)				1	1.19 (0.95 to 1.47)			
Sleep disorder	Yes	1	1.37 (1.05 to 1.77)			0.07	1	1.26 (0.99 to 1.60)			0.58
	No	13	1.05 (1.00 to 1.09)	0.80	0.0%		14	1.18 (1.14 to 1.21)	0.35	9.7%	
Depression	Yes	3	1.00 (0.93 to 1.07)	0.99	0.0%	0.11	3	1.18 (1.12 to 1.25)	0.30	25.9%	0.77
	No	11	1.07 (1.03 to 1.12)	0.55	0.0%		12	1.17 (1.13 to 1.22)	0.37	8.2%	
Sleeping pills	Yes	1	1.00 (0.89 to 1.12)			0.40	1	1.26 (0.99 to 1.60)			0.58
	No	13	1.06 (1.02 to 1.10)	0.53	0.0%		14	1.18 (1.14 to 1.21)	0.35	9.7%	

No denotes the number of studies.

P_{het}^{*} for heterogeneity within each subgroup,

$P_{het}^{\dagger}$ for heterogeneity between subgroups with meta-regression analysis,

NC = not calculable

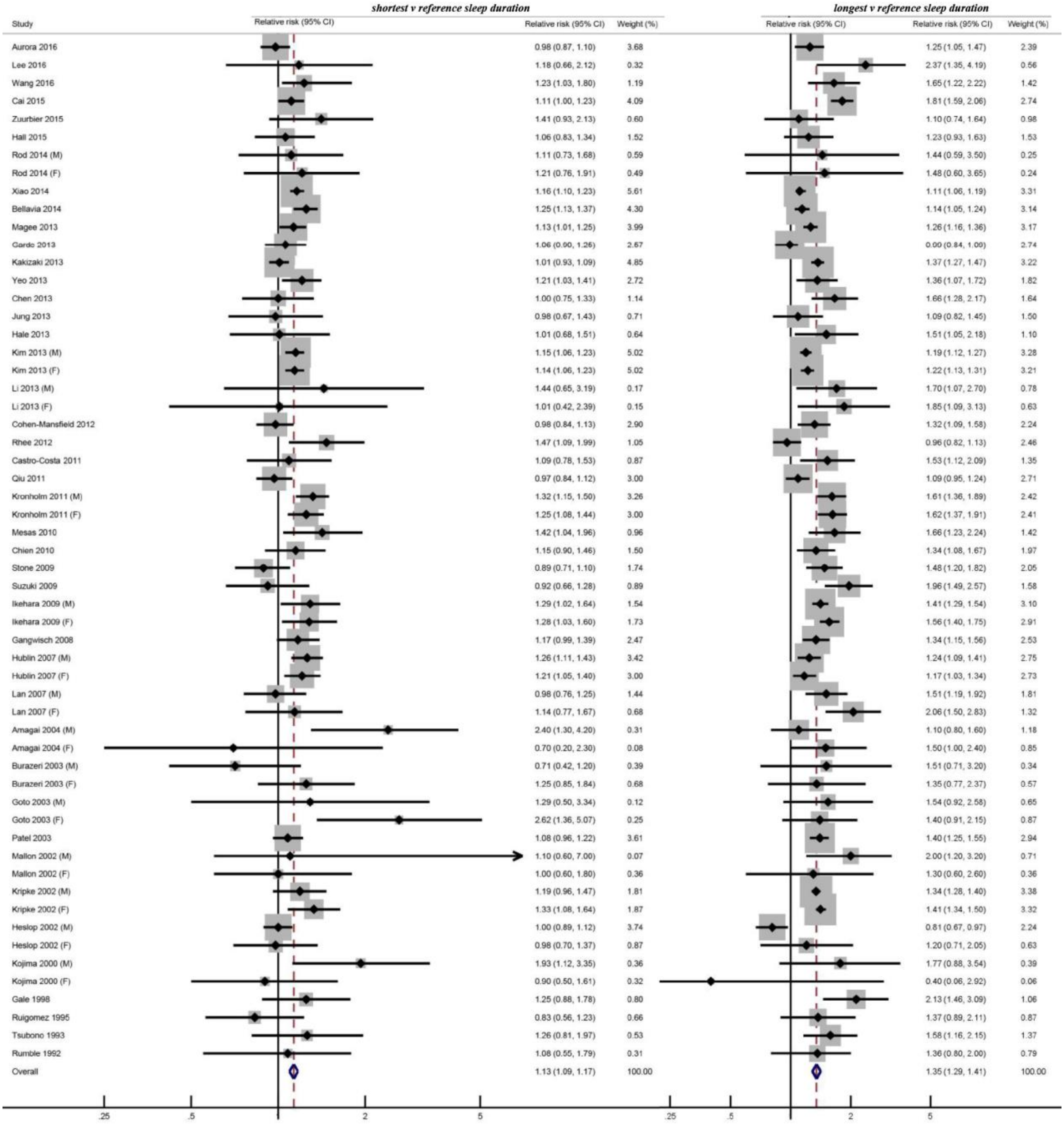

Figure S1. Sleep duration and all-cause mortality, shortest and longest vs. reference analysis

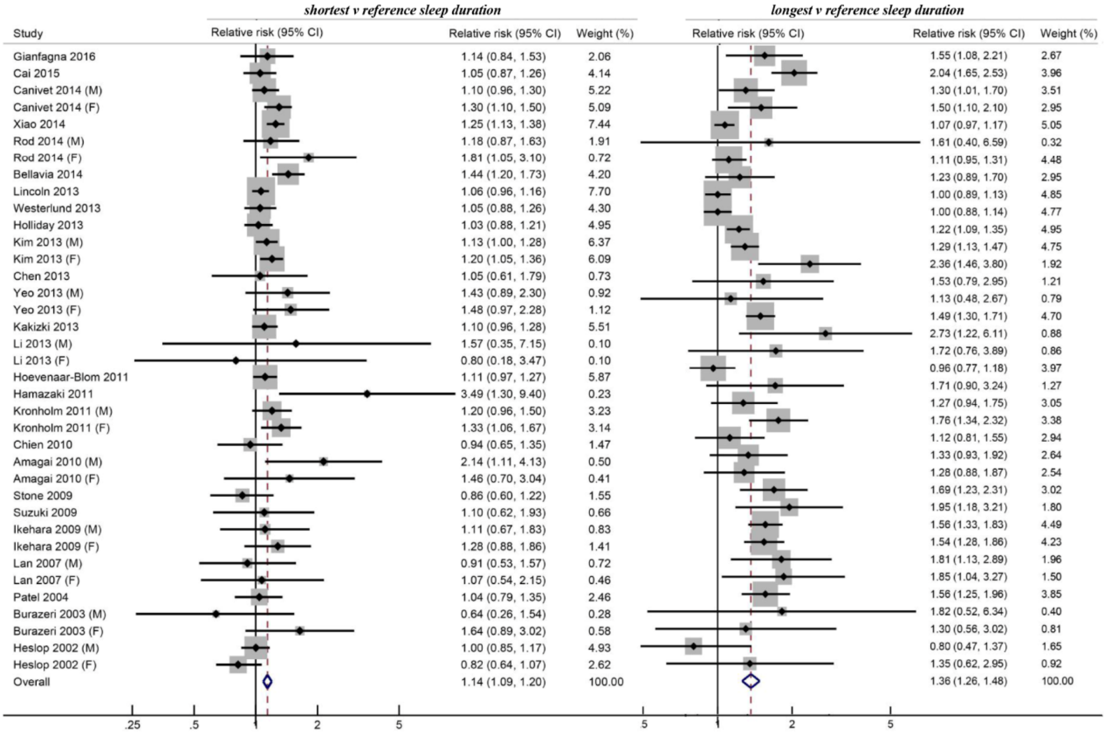

Figure S2. Sleep duration and total cardiovascular disease, shortest and longest vs. reference analysis

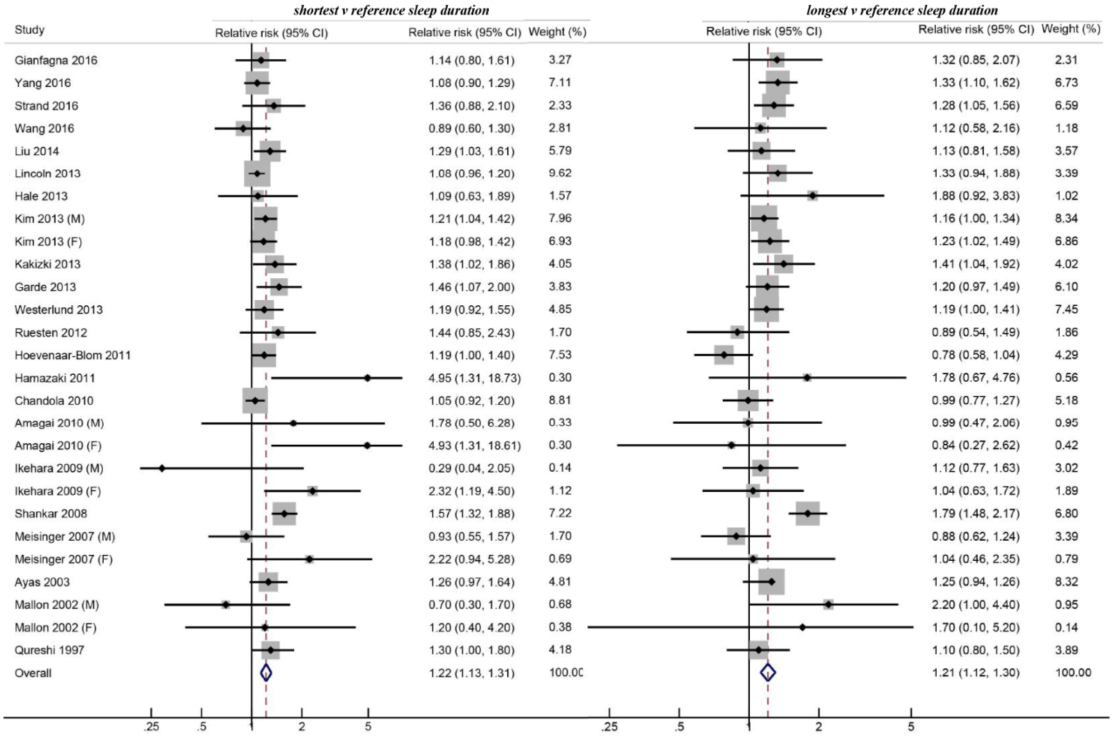

Figure S3. Sleep duration and coronary heart disease, shortest and longest vs. reference analysis

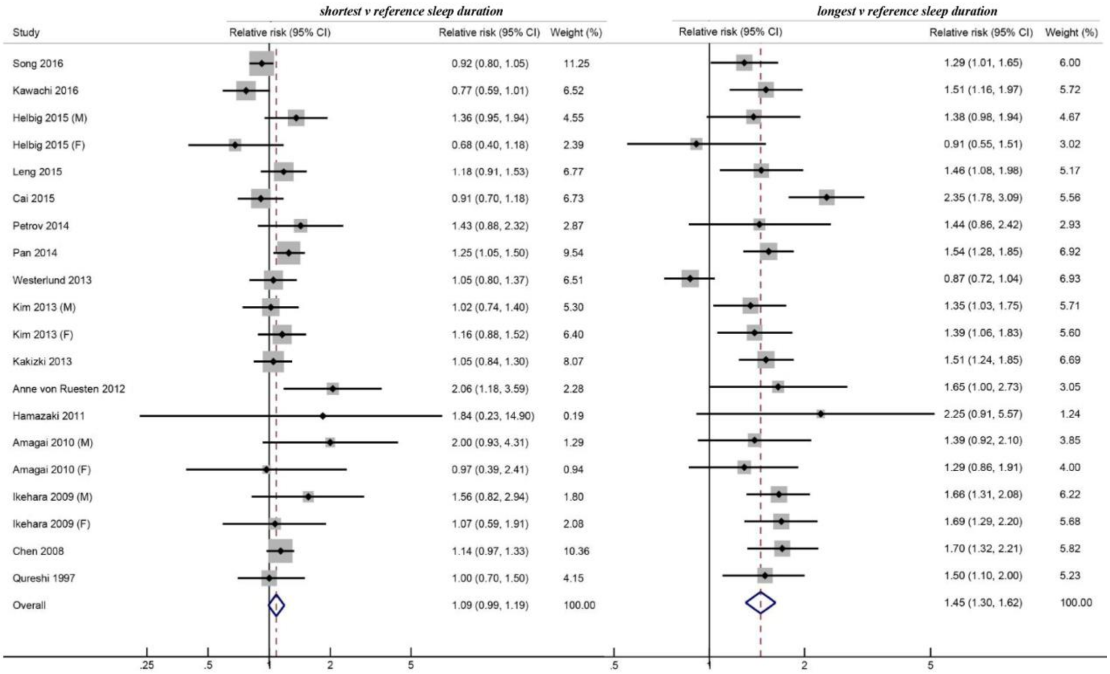

Figure S4. Sleep duration and stroke, shortest and longest vs. reference analysis

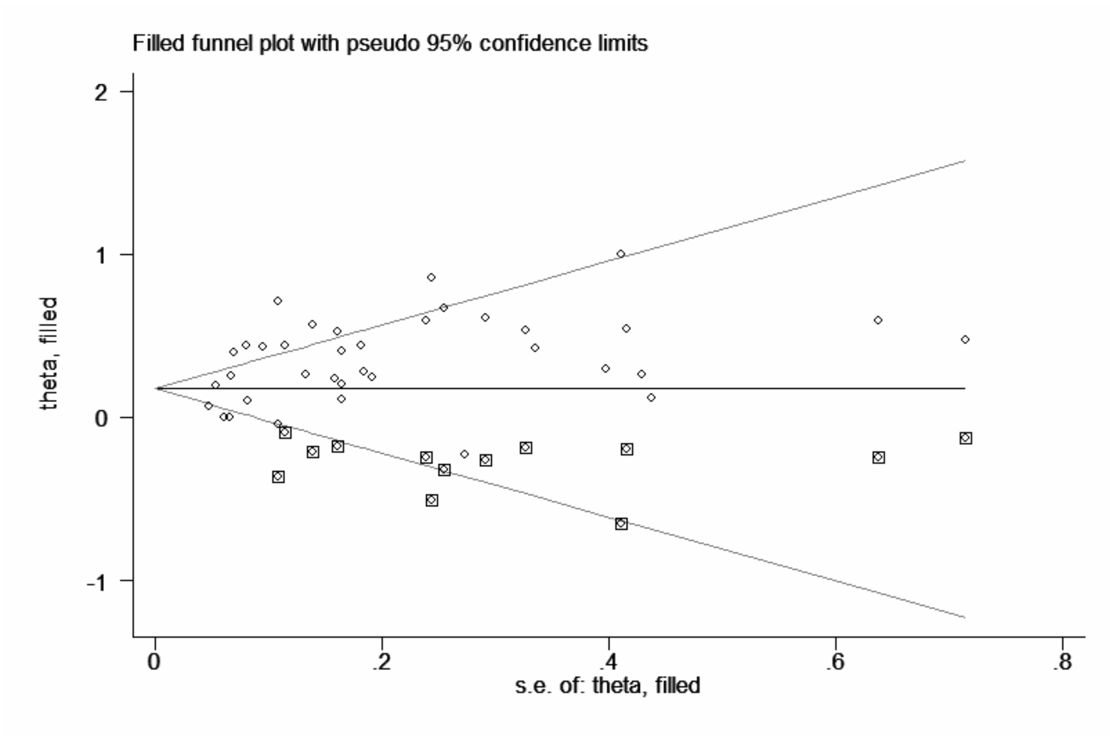

Figure S5. Trim-and-Fill correction for publication bias for total cardiovascular disease, longest vs. reference analysis

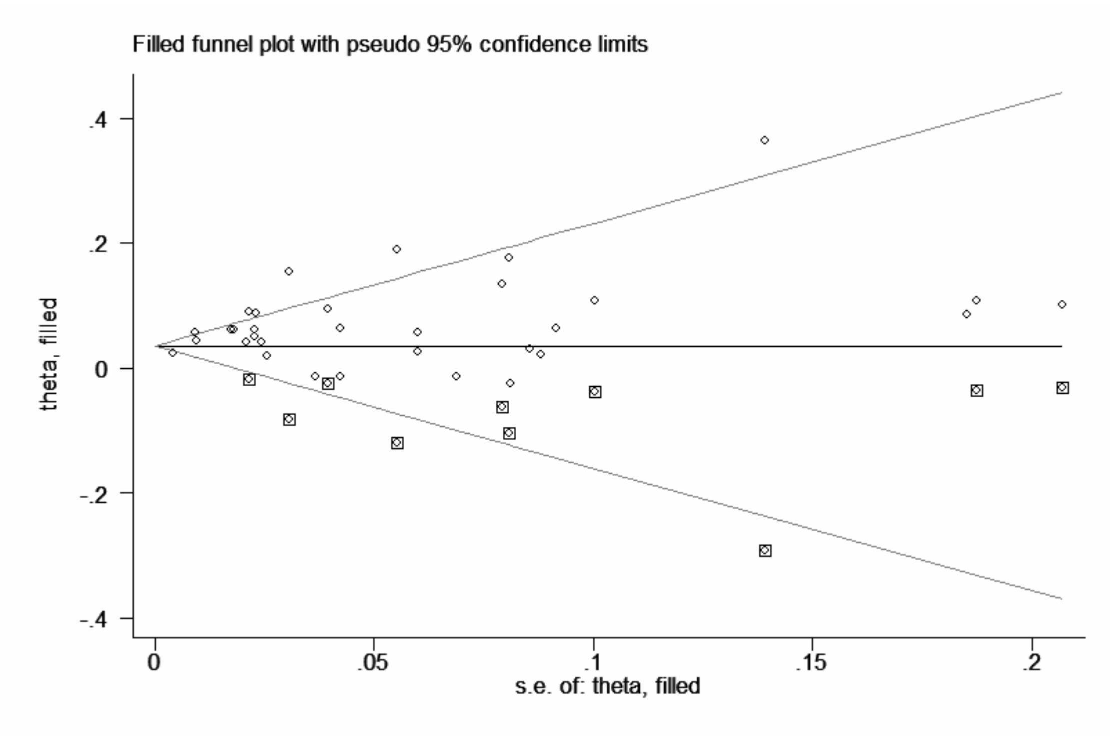

Figure S6. Trim-and-Fill correction for publication bias for all-cause mortality, dose-response analysis for short sleep

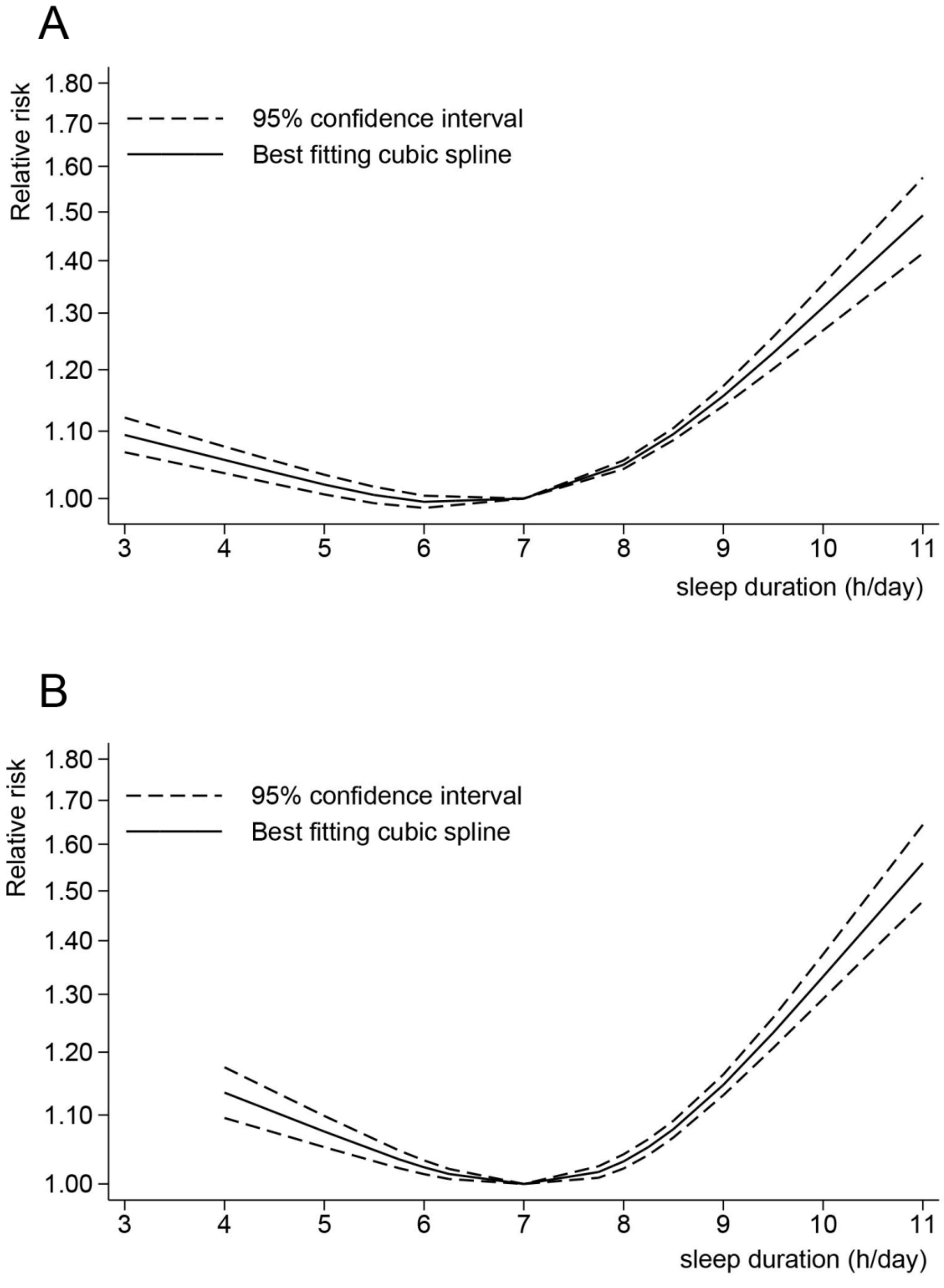

Figure S7. Non-linear dose-response analysis of sleep duration and all-cause mortality by nighttime sleep duration (A) and 24-hour sleep duration (B)

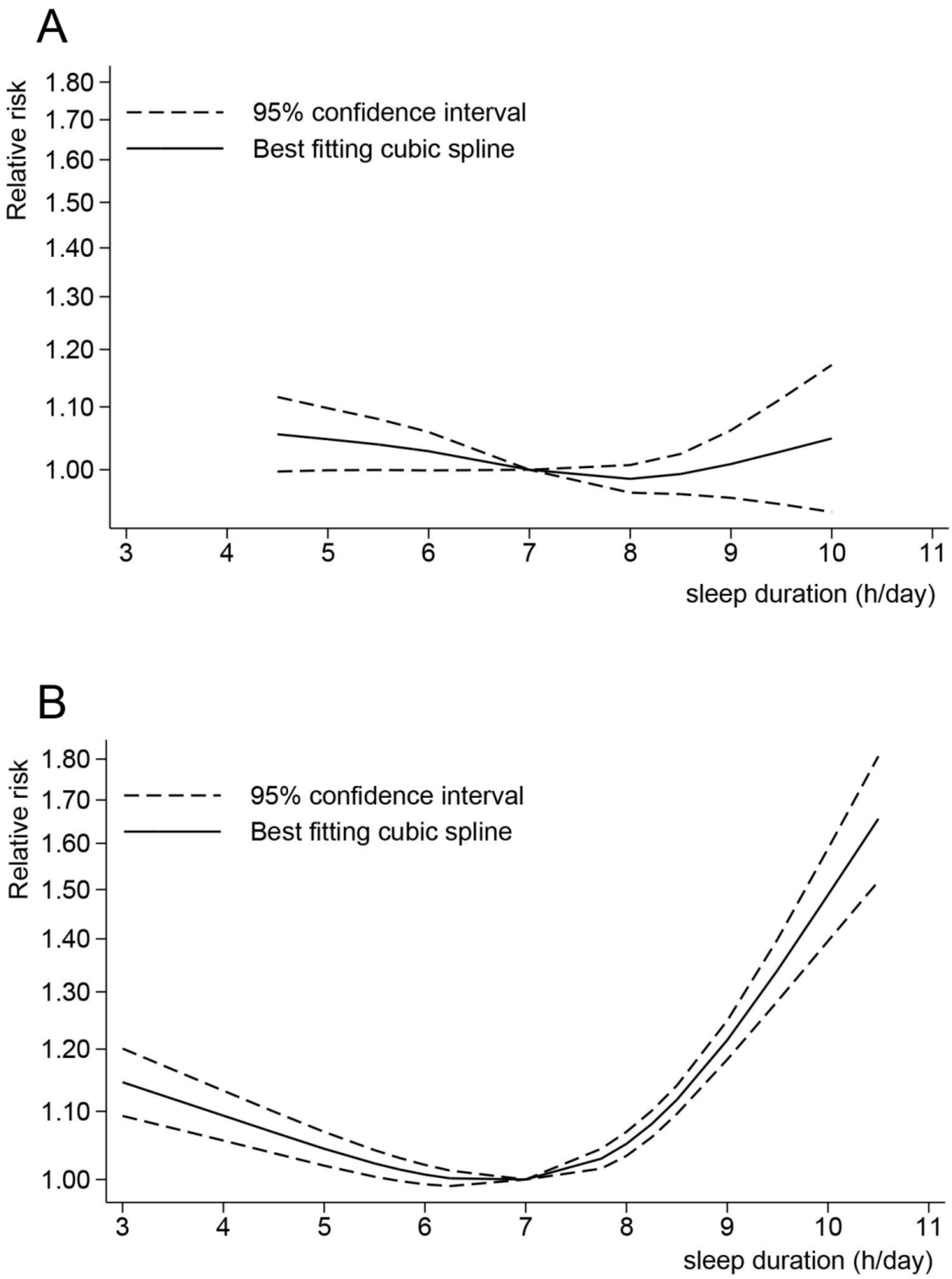

Figure S8. Non-linear dose-response analysis of sleep duration and total cardiovascular disease by incidence (A) and mortality (B)

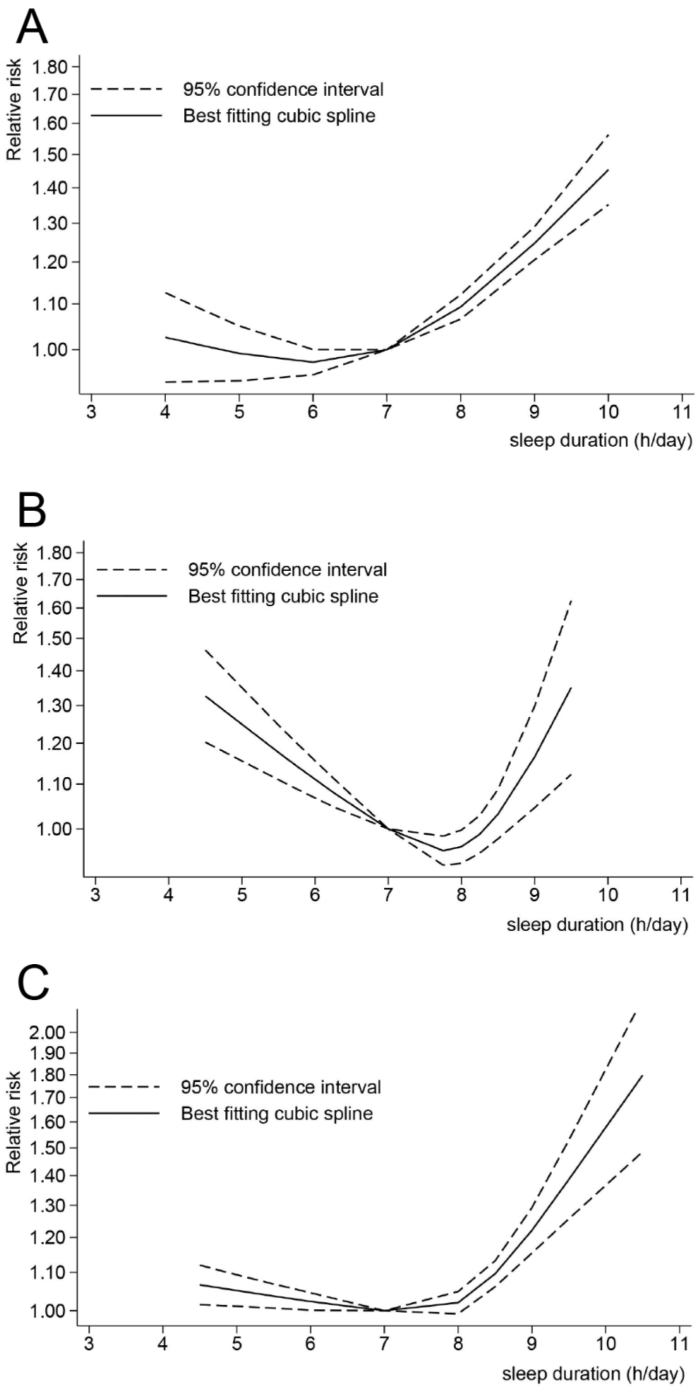

Figure S9. Non-linear dose-response analysis of sleep duration and total cardiovascular disease by Asia (A), Europe (B) and US (C).

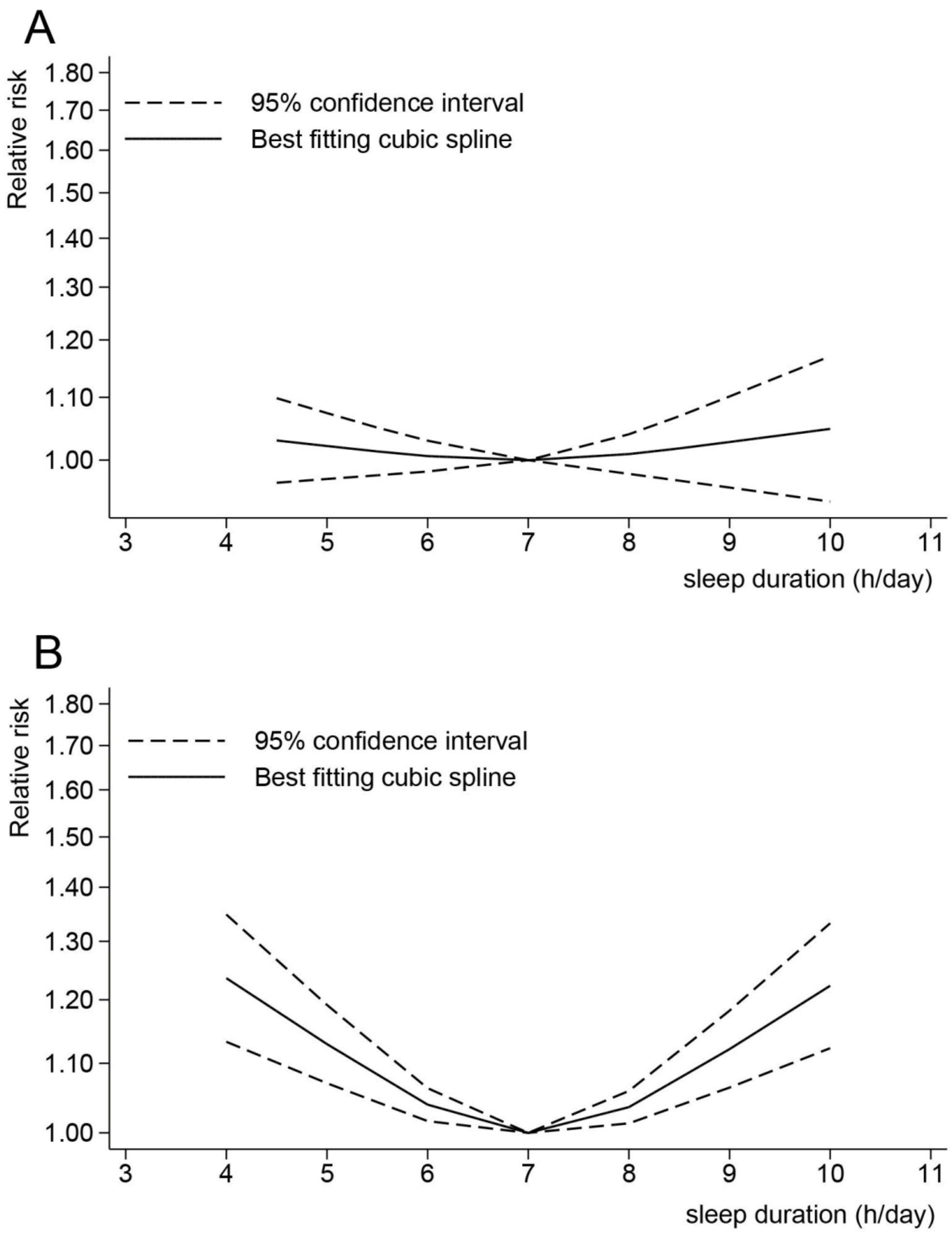

Figure S10. Non-linear dose-response analysis of sleep duration and coronary heart disease by incidence (A) and mortality (B)

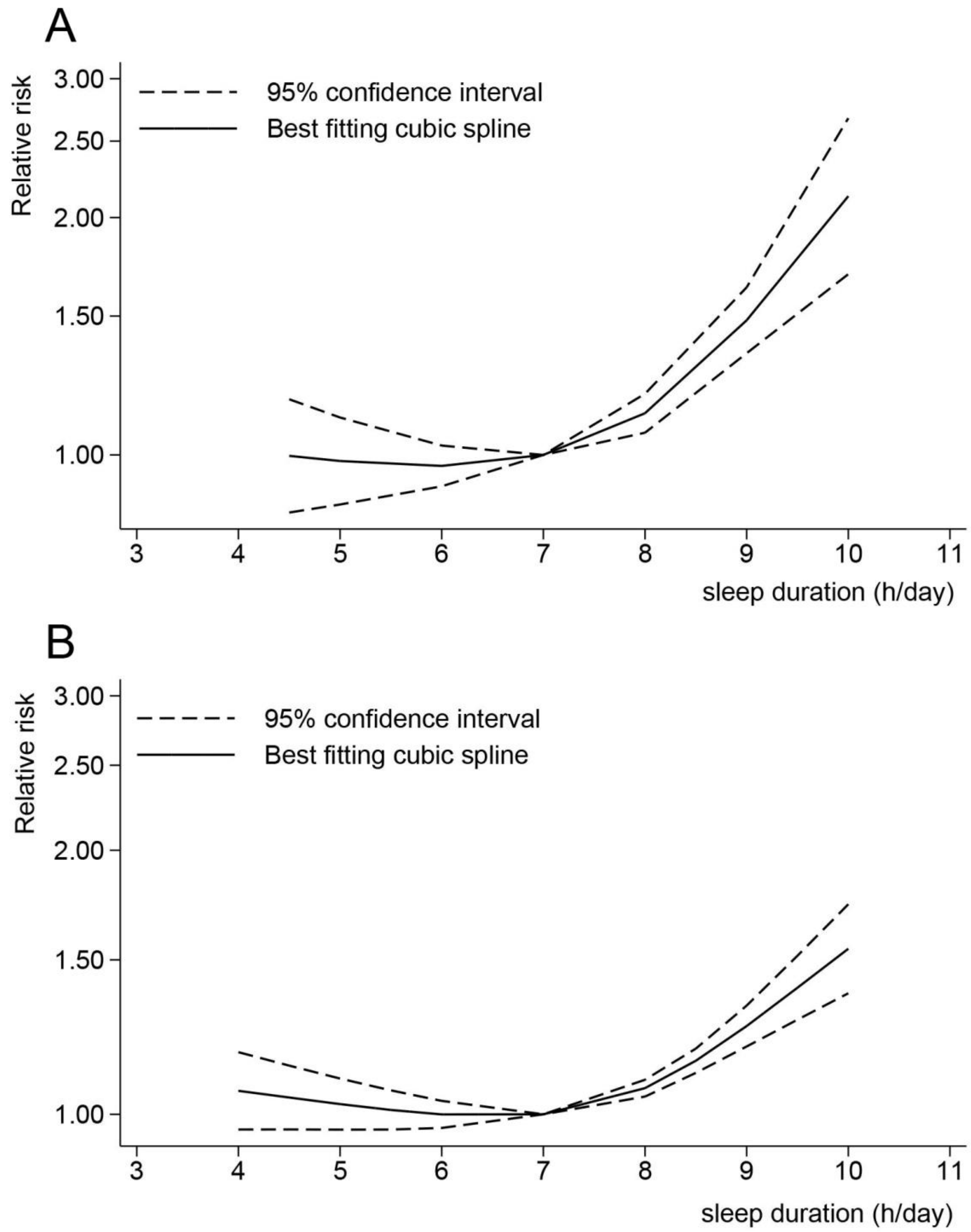

Figure S11. Non-linear dose-response analysis of sleep duration and stroke by follow-up duration <10 years (A), follow-up duration ≥10 years (B)

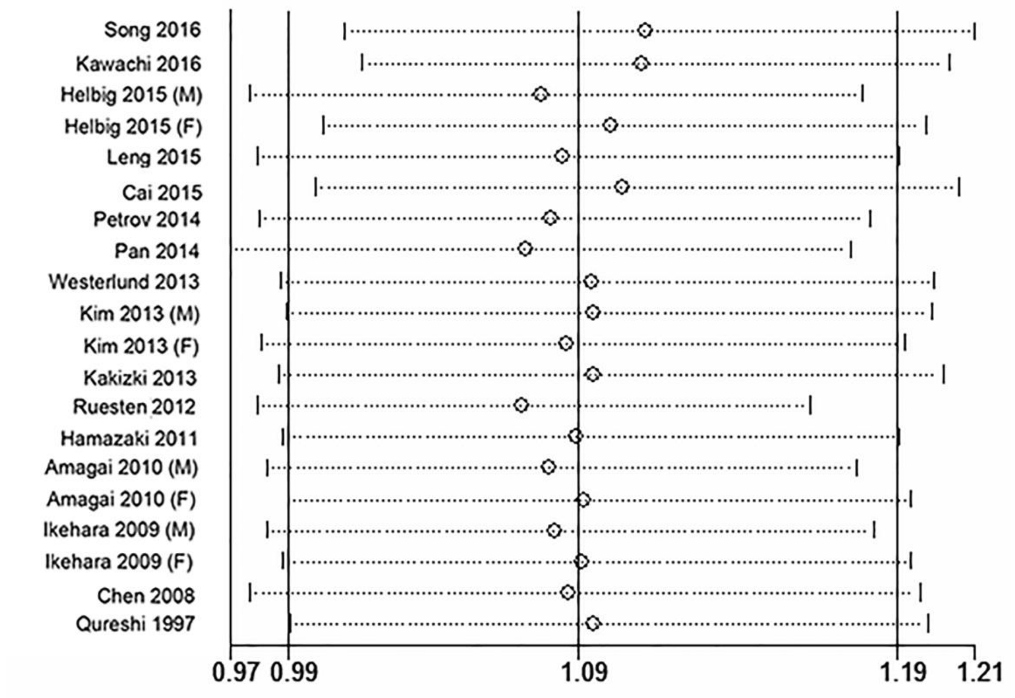

Figure S12. Sensitive analysis of stroke and sleep duration, shortest vs. reference analysis

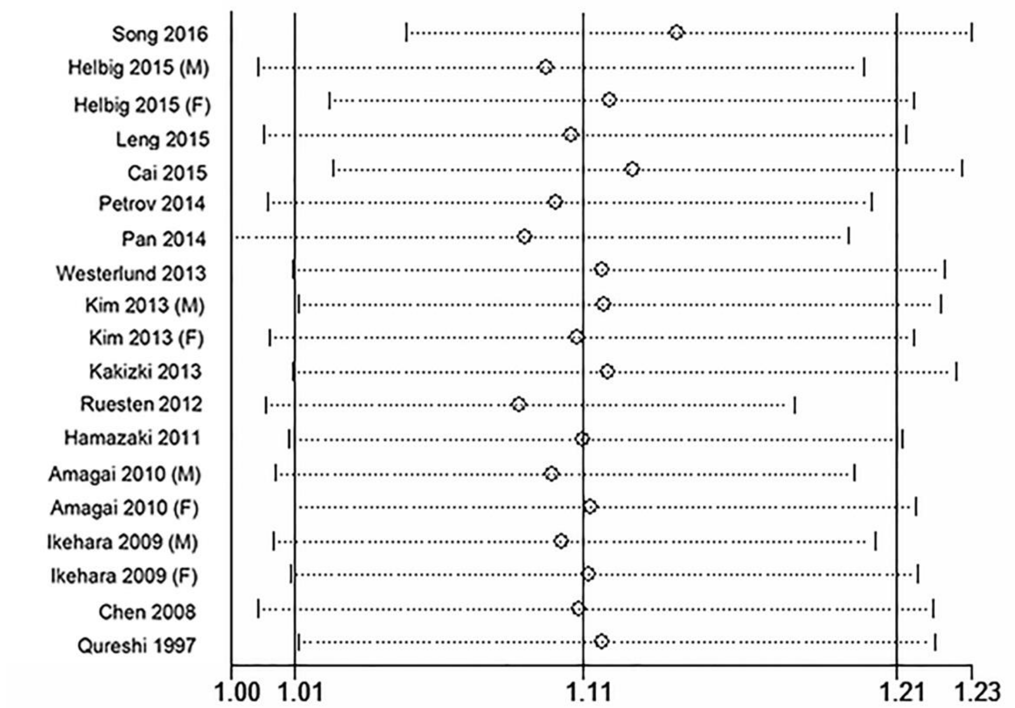

Figure S13. Sensitive analysis of stroke and sleep duration after excluding the study of Kawachi (2016), shortest vs. reference analysis

Supplemental References:

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