Self-reported sleep duration and quality and cardiovascular disease and mortality: a dose-response meta-analysis

Running title: Sleep duration and quality and CVD and mortality

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Abstract

Background: There is growing evidence that sleep duration and quality may be associated with cardiovascular harm and mortality.

Methods and Results: We conducted a systematic review, meta-analysis and spline analysis of prospective cohort studies which evaluate the association between sleep duration and quality, and cardiovascular outcomes. We searched MEDLINE and EMBASE for these studies and extracted data from identified studies. We employed linear and non-linear dose-response meta-analysis models and used DerSimonian-Laird random-effects meta-analysis models of risk ratios, with inverse variance weighting, and the I^2 statistic to quantify heterogeneity. 74 studies including 3,340,684 participants with 164,600 deaths among 1,447,093 participants who reported death events. Findings were broadly similar across both linear and non-linear dose response models in 30 studies with >1,000,000 participants, and we report results from the linear model. Self-reported duration of sleep beyond 8 hours was associated with a moderate increased risk of all-cause mortality, with RR 1.14(1.05-1.25) for 9 hours, RR 1.30(1.19-1.42) for 10 hours and RR 1.47(1.33-1.64) for 11 hours. No significant difference was identified for periods of self-reported sleep below 7 hours, while similar patterns were observed for stroke and cardiovascular disease mortality. Subjective poor sleep quality was associated with coronary heart disease (RR 1.44 95%CI 1.09-1.90) but no difference in mortality and other outcomes.

Conclusions: Divergence from the recommended 7 to 8 hours of sleep is associated with a higher risk of mortality and cardiovascular events. Longer duration of sleep may be more associated with adverse outcomes compared with shorter sleep durations.

Keywords: meta-analysis; coronary artery disease; cardiac risk factors and prevention

Clinical Perspective

What is new?

- In this meta-analysis of 74 studies representing over 3 million participants, we found that a J-shaped relationship between sleep duration and mortality and incident cardiovascular disease.
- Duration of sleep beyond 8 hours of sleep was associated with increased risk of mortality, with RR 1.14 (1.05-1.25) for 9 hours, RR 1.30 (1.19-1.42) for 10 hours and RR 1.47 (1.33-1.64) for 11 hours.
- No significant effect was identified for periods of sleep below 7 hours, while similar patterns were observed for stroke and cardiovascular disease mortality.
- Subjective poor sleep quality was associated with a significant increase in coronary heart disease (RR 1.44 95%CI 1.09-1.90) but not for mortality or any other outcomes.

What are the clinical implications?

- Our study suggests that abnormal sleep is a marker of elevated cardiovascular risk – and greater attention in consultations with patients to ask, and give advice about optimising the duration and quality of sleep may help reduce the burden of cardiovascular disease.

Introduction

Cardiovascular disease causes over 787,000 deaths in the United States.(1) Whilst sleep duration is generally not considered a traditional risk factor for cardiovascular disease, growing evidence supports its association with cardiovascular risk factors(2-7) and disease,(8-11) and quality of sleep appears to contribute to cardiovascular risk.(10,12) Yet, current guidelines for the risk reduction of cardiovascular disease make limited recommendations about the quality or duration of sleep.(13,14)

The National Sleep Foundation recommends 7-9 hours of sleep for people age 26-64 years, 7-8 hours of sleep for people age ≥65 years,(14) and the Center for Disease Control and Prevention has similar recommendations for adults.(15) Whether adults sleep the recommended hours is influenced by cultural, social, psychological, behavioral, pathophysiological and environmental influences.(16,17) Sleep duration may be reduced because of irregular working and shift-work patterns, and round the clock availability of commodities of modern society.(18) However, guidelines makes no specific reference with regards to sleeping beyond the recommended limit. Long sleep duration may be associated with obstructive sleep apnea, heart disease, failing health (19) or may represent a symptom of early 'latent' disease prior to a formal diagnosis.(20)

While previous reviews have evaluated sleep duration and mortality and cardiovascular outcomes, (10,16) these reviews have not quantified the cardiovascular risk associated with each hour deviation below or above the recommended sleep duration. In addition, none of the previous reviews assessed the influence of sleep quality.(10,16) Thus, we conducted a systematic review and meta-analysis of the impact of sleep duration and quality on cardiovascular disease and mortality.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

The full methods including detailed eligibility criteria, search strategy, data selection, extraction and analysis are reported in Appendix 1. The manuscript is prepared according the guidance of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement (Supplementary Material).

Eligibility criteria

We selected prospective cohort studies that reported participants who quantified their duration of sleep or quality of sleep, and their association with subsequent cardiovascular disease and mortality. The primary outcome was all-cause mortality and secondary outcomes were cardiovascular disease and mortality.

Search strategy

We searched Medline and Embase using Ovid SP (from inception to the end of October 2015) using the search terms in Appendix 1.

Study selection and data extraction

Two reviewers (CSK and AM) checked all titles and abstracts for studies that could potentially meet the inclusion criteria. Data extraction and risk of bias assessment was performed independently by at least two reviewers (CSK, GK or MG). Publication bias was assessed using funnel plots.

Data analysis

We used Stata version 14 to perform regression analysis with random-effects dose-response meta-analysis models to estimate the association between hours of sleep and adverse outcomes, using 7 hours of sleep as the reference category. The linear model represents the primary analysis and the cubic model was included as a supplemental analysis.

Conventional random effects meta-analysis was performed as a secondary analysis using RevMan 5.3 (Nordic Cochrane Centre). We decided to use random-effects models since they are more conservative compared to fixed-effect models, in the presence of any heterogeneity. Statistical heterogeneity was assessed using the I^2 statistic. The details of the main and sensitivity analyses are described in Appendix 1. We also performed analysis of sleep quality (Supplementary Table 1) in relation to mortality and cardiovascular outcomes.

Results

Description of included studies

A total of 74 studies met the inclusion criteria; the process of study selection is shown in Figure 1.(8,9,11,12,21-90) The study design and participant characteristics are shown in Table 1. The included studies were dated 1970-2017, which represented 3,340,684 participants. Among studies which reported crude events there were 242,240 all-cause deaths in 2,564,029 participants from 44 studies (9.4%), 5,435 coronary heart disease deaths in 741,695 participants from 7 studies (0.7%), 6,380 stroke deaths in 374,728 participants from 5 studies (1.7%), 32,988 cardiovascular deaths in 759,939 participants from 14 studies (4.3%), 32,084 coronary heart disease events in 540,538 participants from 14 studies (5.9%), 14,946 stroke events in 525,620 participants from 11 studies (2.8%) and 4,160 cardiovascular disease events in 97,832 participants from 6 studies (4.3%). Supplementary Table 2 shows the prevalence of cardiovascular disease and cardiovascular risk factor profiles for each cohort.

Quality assessment of included studies

The quality assessment is shown in Supplementary Table 3. The studies used questionnaires or direct questioning to ascertain information about sleep quality or sleep duration. Methods used to estimate outcomes included population registries, death certification, questionnaires, review of medical records or patient through interview or telephone call. Most studies adjusted for potential confounders, but the factors adjusted for varied across studies. Loss to follow up was unclear in 30 studies and 12 studies had 10% or more loss to follow up or missing data. The study reference group and studies included for each analysis is shown in Supplementary Table 4.

Sleep duration and all-cause mortality

The numeric results of the analyses are shown in Table 2 and Table 3. For the spline analysis a total of 30 studies (11,21,23,25,26,29,32,33,36,41,44,47-49,52,55-57,60,64,66,68,70,71,79,80,84,86-88) reported data that could be used for the all-cause mortality analysis. When spline analysis was applied using linear model, incremental deviation below 7 hours of self-reported sleep was not associated with increased risk of all-cause mortality but sleep durations longer than 8 hours were associated with increased risk of all-cause mortality (Figure 2). The cubic spline analysis model is shown in Supplementary Figure 1.

The pooled risk of all-cause mortality for the entire cohort (Figure 2, Supplementary Figure 2) and the subgroup of men and women only are shown in Supplementary Table 4. There were a total of 39 studies included in the analysis (11,21,23,25-27,29,32-34,36,39-41,44,46-49,51-54,56,57,61,64,66,68,70-72,77,79,80,84,86-88). The funnel plot for sleep duration and mortality did not suggest there was publication bias. Deviation from self-reported sleep duration of 7 or 8 hours appeared to be associated with all-cause mortality, where longer sleep durations are associated with greater mortality compared to small increases for shorter durations. The similar J-shaped relationship was observed for the subgroup of men and women.

Sleep duration and coronary heart disease mortality and coronary heart disease

A total of 5(37,47,49,75,78) and 12(8,12,22,24,38,42,58,63,69,74,83,84) studies were included in spline analysis for coronary heart disease mortality and coronary heart disease respectively. Linear spline analysis failed to demonstrate any significant difference for both outcomes for self-reported shorter and longer sleep durations (Figure 3, cubic model in Supplementary Figure 1).

For the meta-analysis there were 7 studies (37,47,49,51,61,75,78) (Supplementary Figure 3) and 15 studies (8,12,22,24,38,40,42,58,59,63,69,74,81,83,84) (Supplementary Figure 4) for coronary heart disease mortality and coronary heart disease respectively. While there were fewer studies, a similar J-shaped pattern was observed where there was greater risk of coronary heart disease mortality and events with incremental deviation from the reference 7 to 8 hours of self-reported sleep (a modest increase for 6 hours and greater increase for ≤5 hours) (Supplementary Table 5). The funnel plot for self-reported sleep duration and coronary heart disease mortality suggested possible publication bias while for coronary heart disease the plot did not suggest there was publication bias.

Sleep duration and stroke mortality and stroke

Linear spline analysis for stroke mortality and stroke included 3 (47,49,65) and 9 (8,22,31,42,43,50,69,76,83) studies, respectively. There was no difference in stroke events associated with self-reported sleep duration shorter or longer than 7 hours but a moderate increase in stroke mortality if sleep duration was greater than 7 hours (Figure 3, cubic model in Supplementary Figure 1).

Meta-analysis of 5 studies (27,47,49,51,65) were included in the analysis of stroke mortality (Supplementary Figure 5). For stroke events, there were 13 studies (8,9,22,31,42,43,59,69,73,76,81,83) The funnel plot for sleep duration and stroke mortality did not suggest publication bias. For stroke mortality, there appeared to be no difference in events with self-reported sleep duration below 7 hours but significant and moderate increase in events with longer sleep duration beyond 8 hours (Supplementary Figure 5). However, for stroke events the increase in event rates are preserved for both sleep duration shorter than 7 hours (modest for 6 hours and a greater increase for ≤5 hours) and a moderate increase for

longer than 8 hours (Supplementary Figure 6). The funnel plot for sleep duration and stroke did not suggest publication bias.

Sleep duration and cardiovascular mortality and cardiovascular disease

Spline analysis using linear models did not shown any difference in events with shorter duration than 7 hours for both cardiovascular mortality (8 studies) (11,25,44,47,49,71,87,88) and cardiovascular disease (7 studies) (8,12,22,33,38,42,74). However, longer self-reported sleep duration beyond 7 hours appeared to be associated with a moderate increase in greater stroke mortality (Cubic model shown in Supplementary Figure 1).

There were 16 studies (8,11,25-27,32,44,47,49,51,54,57,66,71,87,88) (Supplementary Figure 7), which evaluated cardiovascular disease mortality and 8 studies (8,12,22,28,33,38,42,74) (Supplementary Figure 8) which evaluated cardiovascular disease events. The J-shaped pattern was observed for self-reported sleep duration and cardiovascular disease mortality but this was not the case for cardiovascular disease events but there were fewer studies in the event analysis. The funnel plot for sleep duration and cardiovascular disease mortality and cardiovascular disease did not suggest publication bias. Incremental decrease in hours of sleep was associated with significant increase in mortality (Supplementary Table 5).

Sleep quality and mortality and adverse cardiovascular outcomes

A total of 17 studies (8,11,12,30,32,35,38,43,45,46,52,61-63,68,71,78,82) were included in the analysis of subjective sleep quality and adverse outcomes (Supplementary Figure 9, Supplementary Table 4). For all-cause mortality there were 12,652 deaths among 73,702 participants from 10 studies and the pooled results suggest that poor subjective quality

of sleep was not associated with significant increase in mortality (RR 1.03 95%CI 0.93-1.14). Poor sleep quality was associated with a significant and moderate increase in coronary heart disease (RR 1.44 95% CI 1.09-1.90) but not for any other outcomes. The funnel plot for sleep quality did not suggest publication bias.

Sensitivity analysis excluding studies which did not exclude baseline cardiovascular disease, adjust for cardiac risk factors and adjusted for snoring or obstructive sleep apnea

Sensitivity analysis was performed on the meta-analysis data (Supplementary Table 6). After exclusion of studies that included participants with baseline cardiovascular disease, there was significant increase in all-cause mortality with longer and shorter self-reported hours of sleep (small for 6 hours, modest for 5 and 9 hours and moderate for 4 and 10 hours) and moderate increase in cardiovascular disease mortality and stroke mortality with longer hours of sleep. Similar observations were found for studies that adjusted for cardiovascular risk factors. For the analysis of coronary heart disease and stroke, there were significant and moderate increases in events when baseline cardiovascular disease was excluded with 5 hours duration of sleep. For the adjustments for obstructive sleep apnea analysis some of the results were no longer statistically significant because there were fewer studies.

Discussion

In this meta-analysis of 60 studies representing over 3 million participants, we observed that divergence from the recommended 7 to 8 hours of sleep was significantly associated with a moderate increase in mortality and incident cardiovascular disease. We observed a J-shaped relationship between sleep duration and mortality and incident adverse cardiovascular events was observed. When spline analysis was applied to evaluate the incremental association of sleep duration and adverse events our results suggest that longer than the recommended duration of 7-8 hours of sleep may be associated with a moderate degree of harm, compared with those who slept for durations shorter than that recommended.

Our study provides evidence that may contribute to important clinical and public health messages. Firstly, we observed through spline analysis a more precise estimation of the risk gradient of cardiovascular disease and mortality on the greater side of the recommended 7 to 8 hours of sleep compared to existing studies. Secondly, deviations in sleep duration and quality may be a non-specific marker for increased cardiovascular risk that might warrant determination of cardiovascular risk. In particular, clinicians may need to be aware that the risk gradient appears to be steeper for long sleep duration compared to short duration so individuals with excessive sleeping patterns may warrant further clinical assessment. Thirdly, we provide updated evidence that supports the J-shaped relationship where longer sleep is associated with significant higher mortality and cardiovascular disease and further the knowledge by highlighting that excess sleep is possibly associated with a greater likelihood of harm than less sleep with spline analysis. In addition, we found that sleep *quality* emerged as an important risk factor for coronary heart disease, so clinicians should consider non-restorative sleep (or ‘waking up unrefreshed`) during patient assessment. Finally, our study highlights current evidence that sleep may be an important factor for individuals who wish to adopt a healthier lifestyle – our findings support public health

campaigns promoting good sleep practices and behaviors, and the importance of the clinician discussing sleep in primary care consultations.

St-Onge et al, recently published a scientific statement on behalf of the American Heart Association.(91) There review surveyed the literature and found that sleep duration, mostly short sleep and sleep disorders are related to adverse cardiometabolic risk such as obesity, hypertension, type 2 diabetes and cardiovascular disease. Unlike their review, we focused on mortality and cardiovascular disease and quantitatively pooled the impact of individual hours of sleep duration and these events. We were able to show with meta-regression that the association of short sleep duration and adverse events was lost but the association of long sleep duration and adverse events still persists. It is possible that the adverse outcomes associated with short sleep duration may be manifested through the risk factors described by St-Onge's review. Our findings support the clinical recommendations of the American Heart Association in which sleep behaviors should be addressed to promote cardiac health, and public health campaigns addressing sleep behavior should include explicit guidelines for adequate sleep.

Our meta-analysis results show a possible increase in mortality with both long and short duration of sleep relative to 7 or 8 hours but after spline analysis there is no difference in mortality for patients with shorter sleep duration. The spline regression is the gold standard for meta-regression for non-linear relationships to model exposures and outcomes. We further used this method to perform analysis on the subgroups studies that had more complete reporting that includes crude event rates.

The exact mechanisms that underlie the association between sleep and cardiovascular disease and mortality are not fully understood. Short sleep duration has been shown to increase levels of leptin and ghrelin (92,93) which leads to increased appetite, caloric intake, reduce energy expenditure and facilitates the development of obesity(80) and impaired

glycemic control.(94) Cortisol also increases with reduced sleep and altered growth hormone metabolism may increase cardiovascular risk.(95) Low grade inflammation occurs with reduced sleep which may be associated with cardiovascular disease and cancer. Long sleep duration may be associated with an increased risk of cardiovascular disease because of an adverse cardiometabolic risk factor profile or prevalent comorbidities that lead to fatigue such as chronic inflammatory disorders and anemia. Depressive symptoms, low socioeconomic status, unemployment, low physical activity are also associated with long sleep duration which may confound the association of long sleep with morbidity and mortality.(96)

An important consideration in the temporal relationship between sleep and adverse outcomes is the potential influence of cardiovascular risk factors. For example, a Japanese study observed that sleep disturbances was associated with a higher risk of later onset of type 2 diabetes.(97) In addition, it is unclear whether abnormal sleep is a marker of undiagnosed prevalent cardiovascular diseases or of early/latent disease that subsequently manifests in adverse cardiovascular outcomes and death. Some studies have attempted to reduce the effect of baseline prevalent cardiovascular disease by excluding patients with these conditions while other studies adjusted for these factors. Despite our sensitivity analysis considering exclusion and adjustments, there may still be residual confounding as there may be undiagnosed or latent disease or risk factors as some of these population-based studies do investigate patients at baseline for these variables and rely on self reporting. The other important consideration is whether the increased incident cardiovascular risk is causally related to sleep directly or whether abnormal sleep patterns may contribute to adverse health behaviors that increase cardiovascular risk thereby contributing to the increase in cardiovascular events.

Several studies have evaluated the mismatch between self-reported sleep and more objective measures. An analysis of 669 participants in the CARDIA Sleep Study suggests a moderate correlation between self-reported and objectively measured sleep duration with

evidence of systematic errors in the mean and calibration.(98) Another study of 2,086 Hispanic Americans suggests a moderate correlation between self-reported sleep and actigraphy results.(99) A smaller study compared self-reported sleep and actigraphy in 56 participants reported a poor agreement between sleep duration and quality as assessed by a questionnaire and objectively measure sleep.(100) In addition, a different analysis of 63 patients overweight and obese individuals who underwent actigraphy also reported a weak correlation between usual sleep time and actigraph estimates.(101) With respect to cardiovascular risk, studies suggest that self-reported sleep duration are different from objectively assess sleep duration.(102,103) While the exact reasons for discrepancies between subjective and objective measures is not clear, it appears that self-reported sleep is only at best moderately correlated with objective measures of sleep and perhaps multiple measure of sleep duration should be recommended for future studies.

In the current analysis, the study by Kripke et al(53) represented more than a third of the entire cohort and this large study has implications to the interpretation of the results. This cohort was a diverse group of adults who were friends or relatives of American of Cancer Society volunteers who were aged between 30 and 102 years. The mean age in this study was 57 years and 43% of participants were female which were both slightly lower than the average of 60 years of age and 52% female in all the included studies. In addition, the study took place in the 1980s which may affect the applicability of its findings to the current population. Collectively, these findings may limit the generalizability of the current study.

Our study has a number of limitations. While we used adjusted estimates where available, there is likely to be residual or unmeasured confounding and bias. For example, an underlying physical or mental health condition may be the driver behind extreme sleep patterns. A key limitation was that sleep duration was assessed by self-reported questionnaires. It is unclear if this is truly reflective of actual sleep patterns as there are

studies which clearly show that with respect to cardiovascular risk, self-reported sleep duration and objectively assessed sleep duration are significantly different. (102,103) Another limitation was the absence of individual patient level data, so we could not make assumptions about the cardiovascular risk factor profiles of patients based on their sleep duration or quality. Some studies did report baseline risk factors for patients, but every study reported different risk factors, and the combinations of the risk factors profiles reported was too heterogeneous to make general assumptions. While we demonstrated an association between sleep quality, duration and outcomes, these relationships cannot infer causality and it is unclear whether sleep duration or quality is a marker of prevalent cardiovascular risk, an adverse cardiovascular risk factor profile or adverse health behaviors that contribute to the adverse outcomes reported.

Conclusion

In conclusion, we found a significant association between deviations in sleep duration and both mortality and adverse cardiovascular outcomes. National guidelines should consider advocating this as the recommended sleep duration. We also found evidence that sleep duration above the recommended level of 7-8 hours was associated with a moderate degree of harm compared to sleeping less than the suggested duration. Furthermore, the greater the divergence from the recommended durations of sleep, the greater the association for cardiovascular harm and mortality. Our study suggests that abnormal sleep is a marker of elevated cardiovascular risk – and greater consideration should be given in exploring during patient consultations both the duration and quality of sleep.

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Disclosures

None.

List of Tables and Figures

Supplementary Figure 9: Sleep quality and adverse outcomes and funnel plot

Appendix 1: Search strategy

Table 1: Study design and demographics table

Study ID	Design; Country; Year	No. of participants	Mean age	% Male	Participant inclusion criteria
Akersted 2017 (21)	Prospective cohort study; Sweden; 1997-2010.	43,868	51	36	Participants were >18 years in the Swedish National March study.
Amagai 2010 (22)	Prospective cohort study; Japan; April 1992-July 1995.	11,367	55	39	Participants were adults of varying ages in 12 rural areas of Japan from the Jichi Medical School Cohort Study.
Aurora 2016 (23)	Prospective cohort study; USA; 1995-2011.	5,784	64	46	Participants were age 40 years and not treated for sleep-disordered breathing in the Sleep Heart Health Study.
Ayas 2003 (24)	Prospective cohort study; USA; 1986-1996.	71,617	Unclear	0	Participants were US female health professionals aged 45-65 years who were enrolled in the Nurses' Health Study.
Bellavia 2014 (25)	Prospective cohort study; Sweden; 1998-2012.	70,973	Unclear	53	Participants were Swedish males and aged 45-79 years females aged 39-76 years from the population based Cohort of Swedish Men and the Swedish Mammography Cohort.
Burazeri 2003 (26)	Prospective cohort study; Israel; 1985 with up to 11 years follow up.	1,842	Unclear	46	Participants were age >50 years in West Jerusalem in the Kiryat Yovel Community Health Study.
Cai 2015 (27)	Prospective cohort study; China; 1996-2010.	113,138	54	41	Participants were Chinese men and women in Shanghai, China in the Shanghai Women's Health Study and the Shanghai Men's Health Study.
Canivet 2014 (28)	Prospective cohort study; Sweden; 1991-2005.	13,617	Unclear	43	Participants were all people between the ages of 45 and 65 residing in Malmo, Sweden from the Malmo Diet and Cancer Study 1991.
Castro-Costa 2011 (29)	Prospective cohort study; Brazil; 1997-2005.	1,512	Median 69	38	Participants were all residents of Bambui city, Brazil aged 60 years and over on 1st January 1997 and part of the Bambui Cohort Study.
Chandola 2010 (30)	Prospective cohort study; England; 1985-1988	10,308	Unclear	67	Participants were adults aged 35-55 years from 20 London based civil service departments in the Whitehall II Cohort.
Chen 2008 (31)	Prospective cohort study; USA; 1994-1998.	93,175	Unclear	0	Participants were postmenopausal women aged 50-79 years from all over the United States in the Women's Health Initiative Observational study cohort.
Chen 2013 (32)	Prospective cohort study; Taiwan; 1999-2002.	4,064	73.8	56	Participants were residents of the Shih-Pai area of Taipei, Taiwan who were over 65 years of age and part of the Shih-Pai Sleep Study.
Chien 2010 (33)	Prospective cohort study; Taiwan; 1990-1991.	3,430	54.8	50	Participants were adults aged over 35 in the Chin-Shan Community Cardiovascular Cohort study and of Chinese ethnicity living in Chin-Shan township, Taiwan.
Cohen-Mansfeld 2012 (34)	Prospective cohort study; Israel; 1989-1992.	1,166	83	55	Participants were older Jewish adults age >75 years in the Cross-Sectional and Longitudinal Aging Study.
Ensrud 2012 (35)	Prospective cohort study; USA; 2003-2005.	2,505	76	100	Participants were non-frail males aged 65 or over, recruited via the prospective Osteoporotic Fractures in Men study.
Gangwisch 2008 (36)	Prospective cohort study; USA; 1982-1992.	9,789	Unclear	37	Participants were men and women age 25-74 years in the NHANES I epidemiologic follow-up study.
Garde 2013 (37)	Prospective cohort study; Denmark; 1970-2001.	5,249	49	100	Participants were in the Copenhagen Male Study who were all men aged 40-59 at 14 companies were invited.
Gianfagna 2016 (38)	Prospective cohort study; Italy; 1986-2008.	2,277	51	100	Participants were men aged 35-74 years and CVD free in the MONICA-Brianza and PAMELA population based cohorts.
Goto 2013 (39)	Prospective cohort study; Japan; 1987-1999.	724	Unclear	65	Participants were age 65 or over in Okinawa Japan.
Hale 2013 (40)	Prospective cohort study; USA; 1993-2009.	3,942	62	0	Participants were in the Women's Health Initiative clinical trial and observational study who were postmenopausal women aged 50-79 and did not have history of coronary heart disease.
Hall 2015 (41)	Prospective cohort study: USA; 1997 start follow up of 9 years.	3,013	73.6	48.6	Participants were adults in the Health, Aging and Body Composition Study.
Hamazaki 2011 (42)	Prospective cohort study; Japan; 1994-2008.	2,282	44	100	Participants were men aged 35-54 years old at a light metal factory (Japan) who did not have previous cardiovascular event or missing information at baseline survey.

Helbig 2015 (43)	Prospective cohort study; Germany; 1984-2001.	17,604	48	50	Participants were age 25-74 years in the Monitoring Trends and Determinants in Cardiovascular Disease/Cooperative Health Research in the Region of Augsburg study.
Heslop 2002 (44)	Prospective cohort study; Scotland; 1970-1995.	3,030	Unclear	85	Participants were working Scottish men and women recruited between 1970 and 1973.
Hoevenaar-Blom 2011 (12)	Prospective cohort study; Netherlands; 1993-2012.	20,432	42	45	Participants were age 20-65 years in the MORGEN study.
Huang 2013 (45)	Prospective cohort study; Taiwan; 1999-2010.	1901	Unclear	51	Participants were aged ≥65 years in the Elderly Nutrition and Health Survey in Taiwan.
Hublin 2007 (46)	Prospective cohort study; Finland; 1975-2003.	21,268	41	48	Participants were in Finnish Twin Cohort who were all Finnish twin pairs of same sex born before 1958 with both co-twins alive in 1975.
Ikehara 2009 (47)	Prospective cohort study; Japan; 1988-2003.	98,634	Unclear	42	Participants were in the Japan Collaborative Cohort Study for Evaluation of Cancer Risk where were aged 40-79 years and living in Japan.
Jung 2013 (48)	Prospective cohort study; USA; 1984-2001.	2,001	74	44	Participants were in the community-dwelling adults age 60-96 years in The Rancho Bernardo Study.
Kakizaki 2013 (49)	Prospective cohort study; Japan; 1994-2008.	49,256	60	48	Participants were aged 40-79 years in the Ohsaki Cohort Study.
Kawachi 2016 (50)	Prospective cohort study; Japan; 1992-2008.	27,896	54	54	Participants were men and women aged 35 years or older in the Takayama Cohort Study.
Kim 2013 (51)	Prospective cohort study; USA; 1993-2007.	135,685	Unclear	46	Participants were age 45-75 years in the Multiethnic Cohort Study from Hawaii and Los Angeles.
Kojima 2000 (52)	Prospective cohort study; Japan; 1982-1996.	5,322	47	46	Participants were aged 20-76 years from Shirakawa town, Japan.
Kripke 2002 (53)	Prospective cohort study; USA; 1982-1988.	1,116,936	57	43	Participants were age 30-102 years in the Cancer Prevention Study II mainly friends/relatives of American Cancer Society volunteers.
Lan 2007 (54)	Prospective cohort study; Taiwan; 1993-2003.	3,079	71	55	Participants were ≥64 years or greater in the Survey of Health and Living Status of the Elderly in Taiwan.
Lee 2014 (55)	Prospective cohort study; Hong Kong; 2001-2010.	3,427	74	51	Participants were men and women in Hong Kong age ≥65 years.
Lee 2017 (56)	Prospective cohort study; Taiwan; 2006-2010.	937	65	55	Participants were Taiwanese aged 53 years or older in the Social Environment and Biomarkers of Aging Study.
Leng 2015 (9)	Prospective cohort study; United Kingdom; 1998-2009.	9,692	62	46	Participants were adults age 42-81 years in the European Prospective Investigation into Cancer-Norfolk cohort.
Li 2013 (57)	Prospective cohort study; Japan; 1983-1990.	12,489	Unclear	38	Participants were residents age 20-79 years in the Minami Saku area of Japan who were a part of the SAKUCESS project.
Liu 2014 (58)	Prospective cohort study; USA; 1971-2007.	3,381	45	48	Participants were age >30 and were free from coronary heart disease in the Framingham Offspring Study.
Magee 2011 (59)	Prospective cohort study; Australia; 2006-2009.	218,155	63	47	Participants were Australian adults aged ≥45 years, residing in the state of New South Wales and part of the 45 and Up study.
Magee 2013 (60)	Prospective cohort study; Australia; 2006-2009.	227,815	Unclear	46.3	Participants were Australian adults aged ≥45 years, residing in the state of New South Wales and part of the 45 and Up study.
Mallon 2002 (61)	Prospective cohort study; Sweden; 1983-1995.	1,870	56	48	Participants were a random adults aged 45-65 years in the population register of the County of Dalarna in Sweden.
Martin 2011 (62)	Prospective cohort study; USA; Unclear.	245	81	62	Participants were adults aged ≥65 years admitted to post-acute rehabilitation sites in the Los Angeles area in USA.
Meisinger 2007 (63)	Prospective cohort study; Germany; 1984-1995.	6,896	58	50.9	Participants were German adults aged 45-74 years which were part of the MONICA Augsburg project.
Mesas 2010 (64)	Prospective cohort study; Spain; 2001-2008.	3,820	71.8	44	Participants were noninstitutionalized adults aged ≥60 year living in Spain.
Pan 2014 (65)	Prospective cohort study; Singapore; 1993-1998.	63,257	57	44	Participants were Chinese adults in Singapore aged 45-74, recruited from Hokkiens and Cantonese dialect groups residing in government housing estates.
Patel 2004 (66)	Prospective cohort study; USA; 1986-2000.	82,969	53	0	Participants were women aged 30-55 years and residing in 11 US states that were part of the Nurses' Health Study.

Pollak 1990 (67)	Prospective cohort study; USA; 1984-1985.	1,855	75	Unclear	Participants were elderly residents of an urban community age 65-98 years.
Qiu 2011 (68)	Prospective cohort study; China; 2005-2008.	12,671	86	57	Participants were elderly Chinese adults from 22 provinces in China in the Chinese Longitudinal Healthy Longevity Survey.
Qureshi 1997 (69)	Prospective cohort study; USA; 1982-1992.	7,844	Unclear	36	Participants were US civilian noninstitutionalized adults aged >31 years and in the NHANES I Epidemiologic Follow-up Study (NHEFS).
Rhee 2012 (70)	Prospective cohort study; Korea; 1992-2008.	14,533	51	100	Participants were male subjects age 40-59 years in the Seoul Male Cohort Study.
Rod 2014 (71)	Prospective cohort study; UK; 1985-2010.	9,098	45	67	Participants were in the Whitehall II Cohort Study who were London-based office staff aged 35 to 55 years working in 20 civil service departments in 1985.
Ruigomez 1995 (72)	Prospective cohort study; Spain; 1986-1991.	1219	Unclear	39	Participants were elderly population in the 1986 Health Interview Survey of Barcelona.
Ruiter Petrov 2014 (73)	Prospective cohort study; USA; 2003-2010.	5,666	61	44	Participants were aged ≥45 years in the Reasons for Geographic And Racial Differences in Stroke study.
Sands-Lincoln 2013 (74)	Prospective cohort study; USA; 1993-2009.	86,329	63	0	Participants were in the Women's Health Initiative clinical trial and observational study who were postmenopausal women aged 50-79 and did not have history of coronary heart disease.
Shankar 2008 (75)	Prospective cohort study; Singapore; 1993-2006.	58,044	56	44	Participants were Chinese adults age 45-75 years in the Singapore Chinese Health Study.
Song 2016 (76)	Prospective cohort study; China; 2006-2010.	95,203	51	79	Participants were age 18-98 years in the Kailuan study.
Stone 2009 (77)	Prospective cohort study; USA; Unclear.	6,107	80	50	Participants were community-dwelling older adults participating in the Study of Osteoporotic Fractures and the Outcomes of Sleep Disorders in Older Men Study.
Strand 2016 (78)	Prospective cohort study; Taiwan; 1998-2011.	392,164	40	49	Participants were Taiwanese adults age 20 years who participants in health check-up program run by MJ Health Management Institution.
Suzuki 2009 (11)	Prospective cohort study; Japan; 1999-2006.	12,601	74	51	Participants are elderly residence age 65-85 years in the Shizuoka Study.
Tamakoshi 2004 (79)	Prospective cohort study; Japan; 1988-1999.	104,010	58	42	Participants were age 40-79 years in the Japan Collaborative Cohort Study on Evaluation of Cancer Risk study.
Tsubono 1993 (80)	Prospective cohort study; Japan; 1988-1992.	4,318	Unclear	40	Participants were ≥40 years in Japan who participated in the annual health examination program implemented by the Town Council.
Tu 2012 (81)	Prospective cohort study; China; 1997-2006.	68,832	60	0	Participants were women age 40-70 years in the Shanghai Women's Health Study.
Twig 2016 (82)	Prospective cohort study; Israel; Unclear.	23,690	30	100	Participants were men older than 25 years in the Israeli Defense Forces who were in the MELANY cohort study.
Von Ruesten 2012 (83)	Prospective cohort study; Germany; 1994-2007.	23,620	49	39	Participants were in the European Prospective Investigation into Cancer and Nutrition (EPIC) study in Potsdam.
Wang 2016 (84)	Prospective cohort study; China; 2006-2010.	95,903	51	80	Participants were age 18-98 years in the Kailuan study.
Werle 2011 (85)	Prospective cohort study; Brazil; 1994-2009.	187	84	36	Participants were >80 years in the city of Veranopolis, Brazil.
Westerlund 2013 (8)	Prospective cohort study; Sweden; 1997-2010.	41,192	Unclear	35	Participants were ≥18 years in the Swedish National March Cohort Study.
Wingard 1983 (86)	Prospective cohort study; USA; 1965-1974.	6928	Unclear	47	Participants were 30-69 years of age in 1965 in California, USA.
Xiao 2014 (87)	Prospective cohort study; USA; 1995-2011	239,896	63	56	Participants were 51-72 years in the NIH AARP Diet and Health Study.
Yeo 2013 (88)	Prospective cohort study; Korea; 1993-2010.	13,164	55	41	Participants were ≥20 years in the Korean Multi-center Cancer Cohort study.
Zawisza 2015 (89)	Prospective cohort study; Poland; 1986-2008.	2,449	72	35	Participants were ≥65 years from Krakow city centre in Poland.
Zuubier 2015	Prospective cohort study; Netherlands;	1,734	62	47	Participants were ≥45 years in the Rotterdam Study.

(90)	2004-2013.				

Table 2: Study cohort, follow up and results for studies with authors A-L.

Study ID	Follow up duration	Outcomes and crude rate of outcomes	Results
Akersted 2017 (21)	13 years.	All-cause mortality: 3,548/39,191.	Sleep duration and mortality: ≤5h: aHR 1.12 (0.99-1.27), 6h: aHR 0.98 (0.88-1.09), 7h: aHR 1.00, ≥8h: aHR 1.10 (1.00-1.20).
Amagai 2010 (22)	10.7 years.	CVD events: 481/11,367. MI: 80/11,367. Stroke: 411/11,367.	Sleep duration and CVD in males: <5.9h: aHR 2.14 (1.11-4.13), 6.0-6.9h: aHR 1.04 (0.61-1.76), 7.0-7.9h: aHR 1.00, 8.0-8.9h: aHR 0.98 (0.69-1.40), ≥9.0h: aHR 1.33 (0.93-1.92). Sleep duration and CVD in females: <5.9h: aHR 1.46 (0.70-3.04), 6.0-6.9h: aHR 0.64 (0.38-1.10), 7.0-7.9h: aHR 1.00, 8.0-8.9h: aHR 0.85 (0.60-1.20), ≥9.0h: aHR 1.28 (0.88-1.87). Sleep duration and MI in men: <5.9h: aHR 1.78 (0.50-6.28), 6.0-6.9h: aHR 0.77 (0.25-2.33), 7.0-7.9h: aHR 1.00, 8.0-8.9h: aHR 0.69 (0.34-1.41), ≥9.0h: aHR 0.99 (0.47-2.06). Sleep duration and MI in women: <5.9h: aHR 4.93 (1.31-18.61), 6.0-6.9h: aHR 0.59 (0.13-2.73), 7.0-7.9h: aHR 1.00, 8.0-8.9h: aHR 0.59 (0.21-1.66), ≥9.0h: aHR 0.84 (0.27-2.62). Sleep duration and stroke in men: <5.9h: aHR 2.00 (0.93-4.31), 6.0-6.9h: aHR 1.13 (0.63-2.03), 7.0-7.9h: aHR 1.00, 8.0-8.9h: aHR 1.03 (0.69-1.53), ≥9.0h: aHR 1.39 (0.92-2.10). Sleep duration and stroke in women: <5.9h: aHR 0.97 (0.39-2.41), 6.0-6.9h: aHR 0.68 (0.39-1.18), 7.0-7.9h: aHR 1.00, 8.0-8.9h: aHR 0.86 (0.60-1.23), ≥9.0h: aHR 1.29 (0.86-1.91).
Aurora 2016 (23)	10.8 years.	All-cause mortality: 1,509/5,784.	Sleep duration and mortality: <7h: aHR 0.98 (0.87-1.10), 7-8h: aHR 1.00, ≥9h: aHR 1.25 (1.05-1.47).
Ayas 2003 (24)	10 years.	CHD: 934/71,617.	Sleep duration and CHD: ≤5h: aOR 1.39 (1.05-1.84), 6h: aOR 1.18 (0.98-1.43), 7h: aOR 1.10 (0.92-1.31), 8h: aOR 1.00, >9h: aOR 1.37 (1.02-1.85).
Bellavia 2014 (25)	15 years.	All-cause mortality 13,450/70,973. CVD mortality: 3,981/70,973.	Sleep duration and all-cause mortality: <6h: aHR 1.25 (1.13-1.37), 6-6.5h: aHR 1.10 (1.04-1.17), 6.6-7.4h: aHR 1.00 (reference), 7.5-8h: aHR 1.03 (0.98-1.08), >8h: aHR 1.14 (1.05-1.24). Sleep duration and CVD mortality: <6h: aHR 1.44 (1.20-1.73), 6-6.5h: aHR 1.23 (1.09-1.38), 6.6-7.4h: aHR 1.00, 7.5-8h: aHR 1.02 (0.92-1.12), >8h: aHR 1.11 (0.95-1.31).
Burazeri 2003 (26)	10 years.	All-cause mortality: 403/1,842.	Total sleep duration and all-cause mortality in men: <6h: aHR 1.00, 6-8h: aHR 1.41 (0.83-2.39), >8h: aHR 2.13 (1.23-3.71). Total sleep duration and all-cause mortality in women: <6h: aHR 1.00, 6-8h: aHR 0.63 (0.42-0.97), >8h: aHR 0.80 (0.51-1.24). Total sleep duration and CVD mortality in men: <6h: aHR 1.00, 6-8h: aHR 1.54 (0.75-3.15), >8h: aHR 2.02 (1.01-4.03). Total sleep duration and CVD mortality in women: <6h: aHR 1.00, 6-8h: aHR 0.69 (0.37-1.29), >8h: aHR 0.79 (0.42-1.48).
Cai 2015 (27)	Median 6-7 years.	All-cause mortality: 4,277/113,138.	Sleep duration and all-cause mortality: 4-5h: aHR 1.11 (1.00-1.23), 6h: aHR 1.06 (0.97-1.16), 7h: aHR 1.00, 8h: aHR 1.15 (1.05-1.26), 9h: aHR 1.34 (1.17-1.54), ≥10h: 1.81 (1.59-2.06). Sleep duration and all-cause mortality in men: 4-5h: aHR 1.06 (0.90-1.25), 6h: aHR 1.07 (0.94-1.23), 7h: aHR 1.00, 8h: aHR 1.13 (1.00-1.28), 9h: aHR 1.34 (1.10-1.62), ≥10h: aHR 1.55 (1.29-1.86). Sleep duration and all-cause mortality in women: 4-5h: aHR 1.15 (1.01-1.32), 6h: aHR 1.06 (0.94-1.20), 7h: aHR 1.00, 8h: aHR 1.17 (1.04-1.32), 9h: aHR 1.36 (1.13-1.64), ≥10h: aHR 2.11 (1.77-2.52). Sleep duration and cardiovascular mortality: 4-5h: aHR 1.05 (0.87-1.26), 6h:aHR 1.10 (0.94-1.29), 7h: aHR 1.00, 8h: aHR 1.22 (1.05-1.43), 9h: aHR 1.47 (1.17-1.85), ≥10h: aHR 2.04 (1.65-2.53). Sleep duration and cardiovascular mortality in men: 4-5h: aHR 1.09 (0.82-1.46), 6h: aHR 1.06 (0.83-1.34), 7h: aHR 1.00, 8h: aHR 1.25 (1.00-1.56), 9h: aHR 1.68 (1.23-2.30), ≥10h: aHR 1.58 (1.14-2.18). Sleep duration and cardiovascular mortality in women: 4-5h: aHR 1.02 (0.80-1.30), 6h: aHR 1.12 (0.91-1.39), 7h: aHR 1.00, 8h: aHR 1.20 (0.96-1.50), 9h: aHR 1.28 (0.91-1.82), ≥10h: aHR 2.64 (1.99-3.52). Sleep duration and stroke mortality: 4-5h: aHR 0.91 (0.70-1.18), 6h: aHR 0.99 (0.79-1.23), 7h: aHR 1.00, 8h: aHR 1.28 (1.04-1.58), 9h: aHR 1.31 (0.94-1.82), ≥10h: aHR 2.35 (1.78-3.09). Sleep duration and stroke mortality in men: 4-5h: aHR 0.93 (0.62-1.40), 6h: aHR 0.78 (0.55-1.10), 7h: aHR 1.00, 8h: 1.20 (0.89-1.62), 9h: aHR 1.62 (1.06-2.48), ≥10h: aHR 1.73 (1.14-2.64). Sleep duration and stroke mortality in women: 4-5h: aHR 0.92 (0.65-1.29), 6h: aHR 1.14 (0.85-1.52), 7h: aHR 1.00, 8h: aHR 1.36 (1.01-1.82), 9h: aHR 0.98 (0.58-1.66), ≥10h: aHR 3.09 (2.14-4.47).
Canivet 2014 (28)	14 years.	Unclear.	Sleep duration and CV events in men: ≤6h: aHR 1.1 (0.96-1.3), 7-8h: aHR 1.0, ≥9h:aHR 1.3 (1.01-1.7). Sleep duration and CV events in women: ≤6h: aHR 1.3 (1.1-1.5), 7-8h: aHR 1.0, ≥9h: aHR 1.5 (1.1-2.1).
Castro-Costa 2011 (29)	Unclear.	All-cause mortality: 440/1,512.	Night-time sleep duration and all-cause mortality: <6h: aHR 1.09 (0.78-1.53), 6-7h: aHR 0.84 (0.60-1.17), 7-8h: aHR 1.00 (reference), 8-9h: aHR 1.31 (0.97-1.78), ≥9h: aHR 1.53 (1.12-2.09).
Chandola 2010 (30)	15 years.	CHD mortality, MI, angina: 1,205/8,998.	Sleep duration and CHD mortality, MI and angina: <5h: aRR 1.05 (0.92-1.20), 6h: aRR 0.98 (0.83-1.16), 7h: aRR 1.00, >8h: aRR 0.99 (0.77-1.27). Poor sleep quality (more than usual restless, disturbed nights) and CHD mortality, MI and angina: aRR 1.36 (1.10-1.68).
Chen 2008 (31)	7.5 years.	Ischaemic stroke: 1,166/93,175.	Sleep duration and ischemic stroke: <6h: aHR 1.14 (0.97-1.33), 7h: aHR 1.00, 8h: aHR 1.24 (1.04-1.47), >9h: aHR 1.70 (1.32-2.21).
Chen 2013 (32)	9 years.	All-cause mortality: 1,004/4,064. CVD mortality: 259/4,064.	Sleep duration and all-cause mortality: <4h: aHR 1.00 (0.75-1.33), 5h: aHR 0.92 (0.74-1.15), 6h: aHR 0.88 (0.73-1.06), 7h: aHR 1.00, 8h: aHR 1.26 (1.04-1.53), >9h: aHR 1.66 (1.28-2.17). Sleep duration and CVD mortality: <4h: aHR 1.05 (0.61-1.79), 5h:aHR 0.95 (0.62-1.48), 6h:aHR 0.79 (0.54-1.16), 7h: aHR 1.00, 8h: aHR 1.36 (0.92-2.01), >9h: aHR 2.36 (1.46-3.80). Poor sleep quality (subjective) and all-cause mortality: aHR 0.81 (0.47-1.38). Poor sleep quality (subjective) and CVD mortality: aHR 0.60 (0.19-1.93).
Chien 2010 (33)	Median 15.9 years.	All-cause mortality: 901/3,430. CVD events: 420/3,430.	Sleep duration and all-cause mortality: <5h: aRR 1.15 (0.9-1.46), 6h: aRR 0.97 (0.79-1.21), 7h: aRR 1, 8h: aRR 1.04 (0.86-1.27), ≥9h: aRR 1.34 (1.08-1.67). Sleep duration and CVD event: <5h: aRR 0.94 (0.65-1.35), 6h: aRR 0.91 (0.67-1.24), 7h: aRR 1, 8h: aRR 1.05 (0.80-1.39), >9h: aRR 1.12 (0.81-1.55).
Cohen-Mansfeld 2012 (34)	20 years.	All-cause mortality: 1,108/1,166.	Sleep duration and mortality: <7h: aHR 0.98 (0.84-1.13), 7-9h: 1.00, >9h: aHR 1.32 (1.09-1.58).
Ensrud 2012 (35)	3.4 years.	All-cause mortality: 180/2,505.	Poor sleep quality (PSQI score >5) and all-cause mortality: >5 81/1,018 vs ≤5 99/1,487, aOR 1.02 (0.73-1.42). Sleep duration and all-cause mortality: ≤5h: 21/269 vs 159/2236, aOR 1.08 (0.65-1.80).
Gangwisch 2008 (36)	Up to 10 years.	All-cause mortality: 1,877/9,789.	Sleep duration and all-cause mortality: ≤5h: aHR 1.17 (0.99-1.39), 6h: aHR 0.95 (0.81-1.11), 7h: aHR 1.00, 8h: aHR 1.23 (1.08-1.39), ≥9h: aHR 1.34 (1.15-1.56).
Garde 2013 (37)	30 years.	All-cause mortality: 2,643/5,249. Ischaemic heart disease mortality: 587/5,249.	Sleep duration on all-cause mortality in men: <6h: aHR 1.06 (0.90-1.25). 6-7h: aHR 1.00. ≥8h: aHR 0.99 (0.84-1.09). Sleep duration and ischemic heart disease mortality in men: <6h: aHR 1.46 (1.07-2.00). 6-7h: aHR 1.00. ≥8h: aHR 1.20 (0.97-1.49).
Gianfagna 2016 (38)	Median 17 years.	CVD event: 293/2,277. CHD event: 214/2,277.	Sleep duration and CVD event: ≤6h: aHR 1.14 (0.84-1.53), 7-8h: aHR 1.00, ≥9h: aHR 1.55 (1.08-2.21). Sleep duration and CHD event: ≤6h: aHR 1.14 (0.80-1.61), 7-8h: aHR 1.00, ≥9h: aHR 1.32 (0.85-2.07). Sleep disturbance on CVD event vs none/some: moderate aHR 1.14 (0.74-1.77), severe aHR 1.80 (1.07-3.03). Sleep disturbance on CHD event vs none/some: moderate aHR 1.35 (0.83-2.21), severe aHR 1.83 (0.98-3.41).
Goto 2013 (39)	12 years.	All-cause mortality: 305/724.	Sleep duration and all-cause mortality in men: aHR <6h: aHR 1.29 (0.50-3.34), 6-7h: aHR 1.00, >7h: aHR 1.54 (092-2.58). Sleep duration and all-cause mortality in women: aHR <6h: aHR 2.62 (1.36-5.07), 6-7h: aHR 1.00, >7 h: aHR 1.40 (0.91-2.15).
Hale 2013 (40)	Up to 16 years.	All-cause mortality: 335/3,942.	Sleep duration and all-cause mortality: ≤5h: aOR 1.01 (0.68-1.51), 6h: aOR 0.94 (0.71-1.24), 7-8h: aOR 1.00, ≥9h: aOR 1.55 (0.92-2.60).

		CHD: 132/3,942.	Sleep duration and CHD: ≤5h: aOR 1.09 (0.63-1.89), 6h: aOR 0.66 (0.42-1.04), 7-8h: aOR 1.00, ≥9h: aOR 1.88 (0.92-3.83).
Hall 2015 (41)	9 years.	All-cause mortality: 953/3,075.	Sleep duration and all-cause mortality: <6h: aHR 1.06 (0.83-1.34), 6h: aHR 1.00 (0.82-1.22), 7h: aHR 1.00, 8h: aHR 1.10 (0.91-1.33), >8h: aHR 1.23 (0.93-1.63).
Hamazaki 2011 (42)	14 years.	CVD events: 64/2,282. Stroke: 30/2,282. Coronary events: 27/2,282.	Sleep duration and CVD events: <6h: aHR 3.49 (1.30-9.40), 6-6.9h: aHR 1.11 (0.55-2.25), 7-7.9h: aHR 1.00, ≥8h: aHR 1.71 (0.90-3.24). Sleep duration and stroke: <6h: aHR 1.84 (0.23-14.90), 6-6.9h: aHR 0.96 (0.30-3.10), 7-7.9h: aHR 1.00, ≥8h: aHR 2.25 (0.91-5.57). Sleep duration and coronary events: <6h: aHR 4.95 (1.31-18.73), 6-6.9h: aHR 1.12 (0.40-3.13), 7-7.9h: aHR 1.00 (reference), ≥8h: aHR 1.78 (0.67-4.76).
Helbig 2015 (43)	14 years.	Stroke: 917/17,604.	Sleep duration and strokes in men: ≤5h: aHR 1.36 (0.95-1.94), 6h: aHR 0.92 (0.70-1.22), 7-8h: aHR 1.00, 9h: aHR 1.05 (0.78-1.43), ≥10h: aHR 1.38 (0.98-1.94). Sleep duration and strokes in women: ≤5h: aHR 0.68 (0.40-1.18), 6h: aHR 1.25 (0.91-1.70), 7-8h: aHR 1.00, 9h: aHR 1.09 (0.76-1.57), ≥10h: aHR 0.91 (0.55-1.51). Poor sleep quality (difficulty staying asleep) and stroke in men: aHR 1.06 (0.87-1.30). Poor sleep quality (difficulty staying asleep) and stroke in women: aHR 0.87 (0.68-1.10).
Heslop 2002 (44)	25 years.	All-cause mortality: 1,062/7,028. CVD mortality: 557/7,028.	Sleep duration and all-cause mortality in men: <7h: aHR 1.15 (0.93-1.42), 7-8h: aHR 1.00, >8h: aHR 0.91 (0.57-1.46). Sleep duration and all-cause mortality in women: <7h: aHR 1.73 (0.99-3.03), 7-8h: 1.00, >8h: aHR 0.58 (0.08-4.22). Sleep duration and CVD mortality in men: <7h: aHR 1.19 (0.90-1.58), 7-8h: aHR 1, >8h: aHR 0.63 (0.30-1.34). Sleep duration and CVD mortality in women: <7h: aHR 2.30 (0.94-5.60), 7-8h: aHR 1, >8h: aHR 1.53 (0.20-11.8).
Hoevenaar-Blom 2011 (12)	11.9 years.	CVD events: 1,486/20,432. CHD: 1,148/20,432.	Sleep duration on incident CVD: ≤6h: aHR 1.11 (0.97-1.27), 7h: aHR 1.00, 8h: aHR 0.95 (0.84-1.08), ≥9h: aHR 0.96 (0.77-1.18). Sleep duration and incident CHD: ≤6h: aHR 1.19 (1.00-1.40), 7h: aHR 1.00, 8h: aHR 0.85 (0.73-1.00), ≥9h: aHR 0.78 (0.58-1.04). Poor sleep quality and incident CVD: aHR 1.04 (0.87-1.26). Poor sleep quality and incident CHD: aHR 1.19 (0.96-1.50).
Huang 2013 (45)	10 years.	All-cause mortality: 182/1,865.	Poor sleep quality (good vs poor) and all-cause mortality in men: aHR 0.60 (0.42-0.87). Poor sleep quality (good vs poor) and all-cause mortality in women: aHR 0.99 (0.68-1.45).
Hublin 2007 (46)	22 years.	All-cause mortality: 3,700/21,268.	Sleep duration and all-cause mortality in men: <7h: aHR 1.26 (1.11-1.43), 7-8h: aHR 1.00, >8h: aHR 1.24 (1.09-1.41). Sleep duration and all-cause mortality in women: <7h: aHR 1.21 (1.05-1.40), 7-8h: aHR 1.00, >8h: aHR 1.17 (1.03-1.34). Poor sleep quality and all-cause mortality in men: aHR 1.10 (0.87-1.39). Poor sleep quality and all-cause mortality in women: aHR 0.99 (0.77-1.27).
Ikehara 2009 (47)	Median 14.3 years.	All-cause mortality 14,540/98,634. CVD mortality 4,287/98,634. Stroke mortality: 1,964/98,634. CHD mortality 881/98,634.	Sleep duration and all-cause mortality in men: ≤4h: aHR 1.29 (1.02-1.64), 5h: aHR 1.02 (0.90-1.16), 6h: aHR 1.08 (1.00-1.16), 7h: aHR 1.00, 8h: aHR 1.06 (1.00-1.12), 9h: aHR 1.13 (1.05-1.22), ≥10h: aHR 1.41 (1.29-1.54). Sleep duration and all-cause mortality in women: ≤4h: aHR 1.28 (1.03-1.60), 5h: aHR 1.11 (0.98-1.25), 6h: aHR 1.05 (0.97-1.14), 7h: aHR 1.00, 8h: aHR 1.16 (1.08-1.24), 9h: aHR 1.32 (1.20-1.45), ≥10h: aHR 1.56 (1.40-1.75). Sleep duration and CVD mortality in men: ≤4h: aHR 1.11 (0.67-1.83), 5h: aHR 0.99 (0.77-1.27), 6h: aHR 1.01 (0.87-1.18), 7h: aHR 1.00, 8h: aHR 1.11 (1.00-1.24), 9h: aHR 1.14 (0.99-1.32), ≥10h: aHR 1.56 (1.33-1.83). Sleep duration and CVD mortality in women: ≤4h: aHR 1.28 (0.88-1.86), 5h: aHR 1.22 (1.00-1.50), 6h: aHR 1.00 (0.86-1.16), 7h: aHR 1.00, 8h: aHR 1.28 (1.14-1.44), 9h: aHR 1.37 (1.17-1.62), ≥10h: aHR 1.54 (1.28-1.86). Sleep duration and stroke mortality in men: ≤4h: aHR 1.56 (0.82-2.94), 5h: aHR 0.85 (0.58-1.26), 6h: aHR 0.95 (0.76-1.20), 7h: aHR 1.00, 8h: aHR 1.11 (0.95-1.30), 9h: aHR 1.14 (0.92-1.42), ≥10h: aHR 1.66 (1.31-2.08). Sleep duration and stroke mortality in women: ≤4h: aHR 1.07 (0.59-1.91), 5h: aHR 0.99 (0.72-1.37), 6h: aHR 0.93 (0.75-1.16), 7h: aHR 1.00, 8h: aHR 1.24 (1.05-1.47), 9h: aHR 1.29 (1.01-1.64), ≥10h: aHR 1.69 (1.29-2.20). Sleep duration and CHD mortality in men: ≤4h: aHR 0.29 (0.04-2.05), 5h: aHR 1.02 (0.62-1.70), 6h: aHR 0.86 (0.63-1.19), 7h: aHR 1.00, 8h: aHR 1.02 (0.82-1.27), 9h: aHR 0.96 (0.70-1.31), ≥10h: aHR 1.12 (0.77-1.63). Sleep duration and CHD mortality in women: ≤4h: aHR 2.32 (1.19-4.50), 5h: aHR 1.64 (1.07-2.53), 6h: aHR 1.23 (0.88-1.72), 7h: aHR 1.00, 8h: aHR 1.24 (0.94-1.64), 9h: aHR 1.52 (1.05-2.19), ≥10h: aHR 1.04 (0.63-1.72).
Jung 2013 (48)	Up to 19 years.	All-cause mortality: 1,224/2,001.	Night-time sleep duration and all-cause mortality in men: <6h: aHR 0.98 (0.673-1.43), 6.0-6.9h: aHR 1.12 (0.85-1.48) 7.0-7.9h: aHR 1.0, 8.0-8.9h: aHR 0.98 (0.79-1.22), ≥9h: aHR 1.09 (0.82-1.45). Night-time sleep duration and all-cause mortality in women: <6h: aHR 1.11 (0.77-1.60), 6.0-6.9h: aHR 1.17 (0.85-1.61) 7.0-7.9h: aHR 1.0, 8.0-8.9h: aHR 1.19 (0.90-1.57), ≥9h: aHR 1.51 (1.05-2.18).
Kakizaki 2013 (49)	13 years.	All-cause mortality 8,447/49,256. CVD mortality 2,549/49,256. Stroke mortality 1,165/49,256. IHD mortality 561/49,256.	Sleep duration and all-cause mortality: ≤6h: aHR 1.01 (0.93-1.09), 7h: aHR 1.00, 8h: aHR 1.07 (1.01-1.14), 9h: aHR 1.14 (1.06-1.24), ≥10h: aHR 1.37 (1.27-1.47). Sleep duration on CVD mortality: ≤6h: aHR 1.10 (0.96-1.28), 7h: aHR 1.00, 8h: aHR 1.21 (1.08-1.36), 9h: aHR 1.32 (1.15-1.52), ≥10h: aHR 1.49 (1.30-1.71). Sleep duration and stroke mortality: ≤6h: aHR 1.05 (0.84-1.30), 7h: aHR 1.00, 8h: aHR 1.17 (0.99-1.39), 9h: aHR 1.30 (1.06-1.60), ≥10h: aHR 1.51 (1.24-1.85). Sleep duration and IHD mortality: ≤6h: aHR 1.38 (1.02-1.86), 7h: aHR 1.00, 8h: aHR 1.36 (1.06-1.73), 9h: aHR 1.49 (1.10-2.02), ≥10h: aHR 1.41 (1.04-1.92).
Kawachi 2016 (50)	Up to 16 years.	Stroke mortality: 611/27,896	Sleep duration and stroke mortality: ≤6h: aHR 0.77 (0.59-1.01), 7h: aHR 1.00, 8h: aHR 1.13 (0.91-1.40), ≥9h: aHR 1.51 (1.16-1.97). Sleep duration and stroke mortality in men: ≤6h: aHR 0.51 (0.34-0.77), 7h: aHR 1.00, 8h: aHR 0.88 (0.66-1.17), ≥9h: aHR 1.23 (0.90-1.69). Sleep duration and stroke mortality in women: ≤6h: aHR 1.06 (0.75-1.50), 7h: aHR 1.00, 8h: aHR 1.50 (1.10-2.04), ≥9h: aHR 1.93 (1.38-2.70).
Kim 2013 (51)	13 years.	All-cause mortality: 19,335/135,685. CVD mortality 6,610/135,685. Stroke mortality: 1,259/135,685. MI mortality: 1,188/135,685.	Sleep duration and all-cause mortality in men: aHR ≤5h: 1.15 (1.06-1.23), 6h: aHR 1.04 (0.99-1.10), 7h: aHR 1.00, 8h: 1.07 (1.01-1.12), ≥9h: 1.19 (1.12-1.27). Sleep duration and all-cause mortality in women: aHR ≤5h: 1.14 (1.06-1.23), 6h: aHR 1.05 (0.99-1.12), 7h: aHR 1.00, 8h: 1.02 (0.96-1.08), ≥9h: 1.22 (1.13-1.31). Sleep duration and CVD mortality in men: aHR ≤5h: 1.13 (1.00-1.28), 6h: aHR 1.01 (0.92-1.11), 7h: aHR 1.00, 8h: 1.05 (0.96-1.14), ≥9h: 1.22 (1.09-1.35). Sleep duration and CVD mortality in women: aHR ≤5h: 1.20 (1.05-1.36), 6h: aHR 1.06 (0.96-1.18), 7h: aHR 1.00, 8h: 1.08 (0.98-1.20), ≥9h: 1.29 (1.13-1.47). Sleep duration and stroke mortality in men: aHR ≤5h: 1.02 (0.74-1.40), 6h: aHR 1.10 (0.88-1.37), 7h: aHR 1.00, 8h: 1.13 (0.91-1.39), ≥9h: 1.35 (1.03-1.75). Sleep duration and stroke mortality in women: aHR ≤5h: 1.16 (0.88-1.52), 6h: aHR 0.99 (0.79-1.23), 7h: aHR 1.00, 8h: 1.07 (0.87-1.33), ≥9h: 1.39 (1.06-1.83). Sleep duration and MI mortality in men: aHR ≤5h: 1.24 (0.94-1.64), 6h: aHR 0.92 (0.74-1.15), 7h: aHR 1.00, 8h: 0.98 (0.80-1.20), ≥9h: 1.16 (0.89-1.50). Sleep duration and MI mortality in women: aHR ≤5h: 1.18 (0.87-1.59), 6h: aHR 1.23 (0.96-1.56), 7h: aHR 1.00, 8h: 1.10 (0.86-1.40), ≥9h: 1.29 (0.95-1.75).
Kojima 2000 (52)	12 years.	All-cause mortality: 256/5,322.	Sleep duration and all-cause mortality in men: <7h: aRR 1.93 (1.12-3.35), 7.0-8.9h: aRR 1.00, 9.0-9.9h: aRR 1.15 (0.74-1.77), ≥10.0h: aRR 1.77 (0.88-3.54). Sleep duration and all-cause mortality in women: <7h: aRR 0.90 (0.50-1.61), 7.0-8.9h: aRR 1.00, 9.0-9.9h: aRR 1.07 (0.58-1.95), ≥10.0h: aRR 0.40 (0.06-2.92). Poor sleep quality (waking up feeling bad) on all-cause mortality (Male): aRR 1.13 (0.60-2.12). Poor sleep quality (waking up feeling bad) on all-cause mortality (Female): aRR 2.03 (1.10-3.74).
Kripke 2002 (53)	Up for 6 years.	All-cause mortality: 77,640/1,116,936.	Sleep duration and all-cause mortality in men: 3h: aHR 1.19 (0.96-1.47), 4h: aHR 1.17 (1.06-1.28), 5h: aHR 1.11 (1.05-1.18), 6h: aHR 1.08 (1.04-1.11), 7h: aHR 1.00 (ref), 8h: aHR 1.12 (1.09-1.15), 9h: aHR 1.34 (1.28-1.40), ≥10h: 1.08 (1.01-1.16). Sleep duration and all-cause mortality in women: 3h: aHR 1.33 (1.08-1.64), 4h: aHR 1.11 (1.01-1.22), 5h: aHR 1.07 (1.01-1.13), 6h: 1.07 (1.03-1.11), 7h: aHR 1.00 (ref), 8h: aHR 1.13 (1.09-1.16), 9h: 1.23 (1.17-1.28), ≥10 aHR 1.41 (1.34-1.50).
Lan 2007 (54)	8 years.	All-cause mortality: 1,338/3,079. CVD mortality: 379/3,079.	Sleep duration and all-cause mortality in men: <7h: aHR 0.98 (0.76-1.25), 7h: aHR 1.00, 8h: aHR 1.09 (0.89-1.33), 9h: aHR 1.14 (0.91-1.42), ≥10h: aHR 1.51 (1.19-1.92). Sleep duration and all-cause mortality in women: <7h: aHR 1.14 (0.77-1.67), 7h: aHR 1.00, 8h: aHR 1.36 (1.01-1.84), 9h: aHR 1.86 (1.36-2.53), ≥10h: aHR 2.06 (1.50-2.83).

			Sleep duration and CVD mortality in men: <7h: aHR 0.91 (0.53-1.57), 7h: aHR 1.00, 8h: aHR 1.40 (0.93-2.10) 9h: aHR 1.26 (0.80-1.98), ≥10h: aHR 1.81 (1.13-2.89). Sleep duration and CVD mortality in women: <7h: aHR 1.07 (0.54-2.15), 7h: aHR 1.00, 8h: aHR 1.77 (1.05-2.98), 9h: aHR 1.75 (1.00-3.07), ≥10h: aHR 1.85 (1.04-3.27).
Lee 2014 (55)	61.7 months.	All-cause mortality: 297/3,427.	Night time sleep duration ≥10h and mortality in men: aHR 1.75 (1.09-2.81). Night time sleep duration ≥10h and mortality in women: aHR 2.88 (1.01-8.18).
Lee 2017 (56)	4.7 years.	All-cause mortality: 72/937.	Sleep duration and all-cause mortality: <6h: aHR 1.21 (0.67-2.17), 6-7h: aHR 1.00, ≥8h: aHR 2.11 (1.19-3.76).
Leng 2015 (9)	9.5 years.	Stroke 346/9,692.	Sleep duration and stroke: <6h: aHR 1.18 (0.91-1.53), 6-8h: aHR 1.00, >8h: aHR 1.46 (1.08-1.98). Sleep duration and stroke in men: <6h: aHR 1.08 (0.75-1.57), 6-8h: aHR 1.00, >8h: aHR: 1.21 (0.80-1.82). Sleep duration and stroke in women: <6h: aHR 1.25 (10.86-1.83), 6-8h: aHR 1.00, >8h: aHR: 1.80 (1.13-2.85).
Li 2013 (57)	7 years.	All-cause mortality: 312/12,489.	Sleep duration and all-cause mortality in men: <5h: aHR 1.44 (0.65-3.19), 6h: aHR 0.86 (0.50-1.48), 7h: aHR1.00, 8h: aHR 1.05 (0.72-1.53), >9h: aHR 1.70 (1.07-2.70). Sleep duration and all-cause mortality in women: <5h: aHR 1.01 (0.42-2.39), 6h: aHR 1.31 (0.78-2.21), 7h: aHR 1.00, 8h: aHR 1.01 (0.63-1.60), >9h: aHR 1.85 (1.09-3.13). Sleep duration and CVD mortality in men: <5h: aHR 1.57 (0.35-7.15), 6h: aHR 0.60 (0.17-2.15), 7h: aHR 1.00, 8h: aHR 1.04 (0.49-2.21), >9h: aHR 2.73 (1.22-6.11). Sleep duration and CVD mortality in women: <5h: aHR 0.80 (0.18-3.47), 6h: aHR 0.91 (0.38-2.23), 7h: aHR 1.00, 8h: aHR 1.13 (0.57-2.23), >9h: aHR 1.72 (0.76-3.89).
Liu 2014 (58)	Over 20 years.	CHD: 491/3,381.	Sleep duration and CHD: ≤6h: aHR 1.29 (1.03-1.61), 7-8h: aHR 1.00, ≥9h: aHR 1.13 (0.81-1.58).

Table 3: Study cohort, follow up and results for studies with authors M-Z.

Study ID	Follow up duration	Outcomes and crude rate of outcomes	Results
Magee 2011 (59)	Unclear.	Stroke 6,541/218,155. Heart disease 25,669/218,155.	Sleep duration and stroke: <6h: aOR 1.54 (1.36-1.75), 6h: aOR 1.25 (1.14-1.38), 7h: aOR 1.00, 8h: aOR 1.08 (1.01-1.17), ≥9h: 1.50 (1.38-1.62). Sleep duration and heart disease: <6h: aOR 1.23 (1.15-1.33), 6h: aOR 1.11 (1.06-1.17), 7h: aOR 1.00, 8h: aOR 1.01 (0.97-1.05), ≥9h: aOR 1.14 (1.09-1.19).
Magee 2013 (60)	2.8 years.	All-cause mortality 8,782/227,815.	Sleep duration and all-cause mortality: <6h: aHR 1.13 (1.01-1.25), 6h: aHR 0.99 (0.91-1.06), 7h: aHR 1.00, 8h: aHR 1.02 (0.96-1.08), 9h: aHR 1.04 (0.96-1.12), >10h: aHR 1.26 (1.16-1.36).
Mallon 2002 (61)	12 years.	All-cause mortality 266/2,663. Coronary artery disease mortality: 91/2,663.	Sleep duration and all-cause mortality in men: <6h: aRR 1.1 (0.6-7.0), 7-8h: aRR 1.00, >8h: aRR 2.0 (1.2-3.2). Sleep duration and all-cause mortality in women: <6h: aRR 1.0 (0.6-1.8), 7-8h: aRR 1.00, >8h: aRR 1.3 (0.6-2.6). Sleep duration and coronary artery disease mortality in men: <6h: aRR 0.7 (0.3-1.7), 7-8h: aRR 1.00, >8h: aRR 2.2 (1.0-4.4). Sleep duration and coronary artery disease mortality in women: <6h: aRR 1.2 (0.4-4.2), 7-8h: aRR 1.00, >8h: aRR 0.7 (0.1-5.2). Poor sleep quality (difficulty maintaining sleep) and all-cause mortality in men: aRR 1.4 (1.1-1.9). Poor sleep quality (difficulty maintaining sleep) and coronary artery disease mortality in men: aRR 1.2 (0.7-1.9). Poor sleep quality (difficulty maintaining sleep) and all-cause mortality in women: aRR 1.1 (0.7-1.7). Poor sleep quality (difficulty maintaining sleep) and coronary artery disease mortality in women: aRR 1.1 (0.5-2.9).
Martin 2011 (62)	1 year.	All-cause mortality: 57/245.	Sleep quality (high PQSI-7 day score) and all-cause mortality: aHR 1.12 (1.04-1.21).
Meisinger 2007 (63)	Unclear.	Acute coronary event: 295/6,896.	Sleep duration and acute coronary event in men: ≤5h: aHR 1.13 (0.66-1.92), 6h: aHR 1.05 (0.71-1.55), 7h: aHR 1.22 (0.92-1.61), 8h: aHR 1.00 (reference), ≥9h: aHR 1.07 (0.75-1.53). Sleep duration and acute coronary event in women: ≤5h: aHR 2.98 (1.48-6.03), 6h: aHR 1.05 (0.49-2.27), 7h: aHR 1.34 (0.75-2.40), 8h: aHR 1.00 (reference), ≥9h: aHR 1.40 (0.74-2.64). Poor sleep quality (difficulty maintaining sleep) and acute coronary events in men: aHR 1.12 (0.84-1.48). Poor sleep qualtiy (difficulty maintaining sleep) and acute coronary events in women: aHR 1.53 (0.99-2.37).
Mesas 2010 (64)	6.8 years.	All-cause mortality: 897/3,820.	Sleep duration and all-cause mortality: <5h: aOR 1.42 (1.04-1.96), 6h: aOR 1.23 (0.90-1.69), 7h: aOR 1.00, 8h: aOR 1.34 (1.02-1.76), 9h: aOR 1.48 (1.12-1.96), 10h: aOR 1.73 (1.30-2.29), >11h: aOR 1.66 (1.23-2.24).
Pan 2014 (65)	Up to 8 years.	Stroke mortality: 1,381/63,257.	Sleep duration and stroke deaths: <5h: aHR 1.25 (1.05-1.50), 6h: aHR 1.01 (0.87-1.18), 7h: aHR 1.00, 8h: aHR 1.09 (0.95-1.26), >9h: aHR 1.54 (1.28-1.85). Sleep duration and ischaemic or unspecified stroke deaths: <5h: aHR 1.37 (1.12-1.68), 6h: aHR 1.04 (0.87-1.24), 7h: aHR 1.00, 8h: aHR 1.14 (0.96-1.34), >9h: aHR 1.68 (1.36-2.06). Sleep duration and haemorrhagic stroke death: <5h: aHR 0.92 (0.62-1.36), 6h: aHR 0.91 (0.67-1.24), 7h: aHR 1.00, 8h: aHR 0.97 (0.73-1.29), >9h: aHR 1.14 (0.76-1.72).
Patel 2004 (66)	14 years.	All-cause mortality: 5409/82,969. CVD mortality: 1084/82,969.	Sleep duration and all-cause mortality: <5h: aRR 1.08 (0.96-1.22), 6h: aRR 0.99 (0.92-1.06), 7h: aRR 1.00, 8h: aRR 1.11 (1.03-1.19), >9h: aRR 1.40 (1.25-1.55). Sleep duration and cardiovascular mortality: <5h: aRR 1.04 (0.79-1.35), 6h: aRR 1.06 (0.91-1.25), 7h: aRR 1.00, 8h: aRR 1.12 (0.95-1.31), >9h: aRR 1.56 (1.25-1.96).
Pollak 1990 (67)	3.5 years.	All-cause mortality: 309/1,855.	Incremental increase in hours of sleep and all-cause mortality in men: HR 0.96 (0.66-1.39). Incremental increase in hours of sleep and all-cause mortality in women: HR 1.11 (0.80-1.54).
Qiu 2011 (68)	3 years.	All-cause mortality: 5,199/12,671.	Sleep duration and all-cause mortality: <5h: aHR 0.97 (0.88-1.08), 6h: aHR 1.05 (0.95-1.16), 7h: aHR 1.00 (0.90-1.11), 9h: aHR 0.95 (0.83-1.07), >10h: aHR 1.09 (1.00-1.18). Sleep duration and all-cause mortality and men: <5h: aHR 1.17 (1.01-1.38), 6h: aHR 1.06 (0.91-1.25), 7h: aHR 1.17 (0.99-1.37), 9h: aHR 1.08 (0.89-1.31), >10h: aHR 1.22 (1.08-1.38). Sleep duration and all-cause mortality and women: <5h: aHR 0.85 (0.75-0.98), 6h: aHR 1.02 (0.90-1.15), 7h: aHR 0.88 (0.76-1.01), 9h: aHR 0.86 (0.72-1.02), >10h: aHR 1.00 (0.90-1.11). Sleep quality (poor vs. good) and all-cause mortality: aHR 0.91 (0.83-1.00). Sleep quality (poor vs. good) and all-cause mortality in men: aHR 1.11 (0.95-1.30). Sleep quality (poor vs. good) and all-cause mortality in women: aHR 0.81 (0.71-0.91).
Qureshi 1997 (69)	10 years.	Stroke 322/7,844. CHD: 474/7,844.	Sleep duration and risk for stroke: <6h: aOR 1.0 (0.7-1.5), 6-8h: aOR 1.0, >8h: aOR 1.5 (1.1-2.0). Sleep duration and CHD: <6h: aOR 1.3 (1.0-1.8), 6-8h: aOR 1.0, >8h: aOR 1.1 (0.8-1.5).
Rhee 2012 (70)	Up to 15 years.	All-cause mortality: 990/14,533.	Sleep duration and all-cause mortality: ≤5h: aHR 1.53 (1.11-2.12), 6-7h: aHR 1.04 (0.88-1.22), ≥8h: aHR 1.00.
Rod 2014 (71)	22 years.	All-cause mortality: 804/9,098. CVD mortality: 221/9,098.	Sleep duration and all-cause mortality in men: ≤5h: aHR 1.11 (0.73-1.68), 6h: aHR 1.23 (1.01-1.50), 7h: aHR 1.00, 8h: aHR 1.18 (0.92-1.50), >9h: aHR 1.44 (0.59-3.50). Sleep duration and all-cause mortality in women: ≤5h: aHR 1.21 (0.76-1.91), 6h: aHR 1.14 (0.86-1.52), 7h: aHR 1.00, 8h: aHR 0.91 (0.63-1.30), >9h: aHR 1.48 (0.60-3.65). Sleep duration and CVD mortality: ≤6h: aHR 1.18 (0.87-1.63), 7-8h: aHR 1.00, >9h: aHR 1.61 (0.40-6.59). Poor sleep quality (disturbed sleep) and all-cause mortality in men: aHR 0.85 (0.62-1.16). Poor sleep quality (disturbed sleep) and all-cause mortality in women: aHR 1.03 (0.70-1.52). Poor sleep quality (disturbed sleep) and CVD mortality: aHR 1.04 (0.72-1.49).
Ruigomez 1995 (72)	55.7 months.	All-cause mortality 224/1,219.	Sleep duration and all-cause mortality: <7h: aRR 0.83 (0.56-1.23), 7-9h: aRR 1.00, >9h: aRR 1.37 (0.89-2.11). Sleep duration and all-cause mortality in men: <7h: aRR 1.06 (0.61-1.83), 7-9h: aRR 1.00, >9h: 1.30 (0.71-2.38). Sleep duration and all-cause mortality in women: <7h: aRR 0.66 (0.37-1.16), 7-9h: aRR 1.00, >9h: 1.46 (0.79-2.70).
Ruiter Petrov 2014 (73)	2 years.	Stroke (at least 1 symptom): 224/5,666.	Sleep duration on stroke symptoms: <6h: aHR 1.47 (0.89-2.45), 6h: aHR 1.22 (0.82-1.81), 7h: aHR 1.00, 8h: aHR 1.30 (0.92-1.83), ≥9h: aHR 1.42 (0.82-2.45).
Sands-Lincoln 2013 (74)	10.3 years.	CVD events: 7,257/86,329.	Sleep duration and CVD: ≤5h: aHR 1.06 (0.96-1.16), 6h: aHR 1.00 (0.95-1.06), 7-8h: aHR 1.00, 9h: aHR 0.95 (0.83-1.08), ≥10h: aHR 1.23 (0.89-1.70). Sleep duration and CHD: ≤5h: aHR 1.08 (0.96-1.20), 6h: aHR 1.00 (0.94-1.07), 7-8h: aHR 1.00, 9h: aHR 0.93 (0.80-1.08), ≥10h: aHR 1.33 (0.94-1.88).
Shankar 2008 (75)	13 years.	CHD mortality: 1,416/58,044.	Sleep duration and CHD mortality: ≤5h: aRR 1.57 (1.32-1.88), 6h: aRR 1.13 (0.98-1.31), 7h: aRR 1.00, 8h: aRR 1.12 (0.97-1.29), ≥9h: aRR 1.79 (1.48-2.17).
Song 2016 (76)	7.9 years.	Stroke: 3,135/95,023.	Sleep duration and stroke: <6h: aHR 0.92 (0.81-1.05), 6-8h: aHR 1.00, >8h: aHR 1.29 (1.01-1.64). Sleep duration and stroke in men: <6h: aHR 0.90 (0.78-1.03), 6-8h: aHR 1.00, >8h: aHR 1.24 (0.96-1.60). Sleep duration and stroke in women: <6h: aHR 1.09 (0.75-1.60), 6-8h: aHR 1.00, >8h: aHR 1.91 (0.98-3.74).

Stone 2009 (77)	Up to 4.1 years.	All-cause mortality: 793/6,107.	Sleep duration and all-cause mortality in men: <5h: RH 1.2 (0.8-1.8), 7-8h: RH 1.00. Sleep duration and all-cause mortality in women: <5h: RH 1.8 (1.3-2.5), 7-8h: RH 1.00.
Strand 2016 (78)	9.7 years.	CHD mortality: 711/392,164.	Sleep duration and CHD mortality: <4h: aHR 1.36 (0.88-2.10), 4-6h: aHR 1.03 (0.85-1.24), 6-8h: aHR 1.00, <8h: aHR 1.28 (1.05-1.56). Sleep duration and CHD mortality in men: <4h: aHR 1.03 (0.53-2.00), 4-6h: aHR 1.06 (0.85-1.32), 6-8h: aHR 1.00, <8h: aHR 1.11 (0.88-1.41). Sleep duration and CHD mortality in women: <4h: aHR 1.84 (1.03 -3.29), 4-6h: aHR 0.99 (0.72-1.37), 6-8h: aHR 1.00, <8h: aHR 1.81 (1.28-2.56). Difficulty getting to sleep and CHD mortality: aHR 1.01 (0.80-1.26).
Suzuki 2009 (11)	6 years.	All-cause mortality: 1,004/14,001. CVD mortality: 310/14,001.	Sleep duration and all-cause mortality: ≤5h: aHR 0.92 (0.66-1.28), 6h: aHR 1.06 (0.80-1.39), 7h: aHR 1.00, 8h: aHR1.36 (1.09-1.70), 9h: aHR 1.41 (1.05-1.90), ≥10h: aHR 1.96 (1.49-2.57). Sleep duration and all-cause mortality in men: ≤5h: aHR 1.08 (0.72-1.61), 6h: aHR 1.05 (0.75-1.47), 7h: aHR 1.00, 8h: aHR 1.36 (1.04-1.78), 9h: aHR 1.52 (1.08-2.15), ≥10h: aHR 1.86 (1.34-2.56). Sleep duration and all-cause mortality in women: ≤5h: aHR 0.71 (0.39-1.29), 6h: aHR 1.08 (0.67-1.74), 7h: aHR 1.00, 8h: aHR 1.39 (0.92-2.09), 9h: aHR 1.15 (0.64-2.09), ≥10h: aHR 2.27 (1.37-3.76). Sleep duration and CVD mortality: ≤5h: aHR 1.10 (0.62-1.93), 6h: aHR 0.85 (0.50-1.45), 7h: aHR 1.00, 8h: aHR 1.52 (1.01-2.29). 9h: aHR 1.55 (0.91-2.63), ≥10h: aHR 1.95 (1.18-3.21). Sleep duration and CVD mortality in men: ≤5h: aHR 0.97 (0.46-2.05), 6h: aHR 0.75 (0.38-1.48), 7h: aHR 1.00, 8h: aHR 1.05 (0.63-1.75). 9h: aHR 1.26 (0.65-2.45), ≥10h: aHR 1.71 (0.94-3.11). Sleep duration and CVD mortality in women: ≤5h: aHR 1.48 (0.59-3.67), 6h: aHR 1.08 (0.44-2.66), 7h: aHR 1.00, 8h: aHR 2.83 (1.39-5.76). 9h: aHR 2.32 (0.93-5.77), ≥10h: aHR 2.31 (0.91-5.82). Poor sleep quality (frequent awakening) and all-cause mortality: aHR 0.99 (0.83-1.18). Poor sleep quality (frequent awakening) and all-cause mortality in men: aHR 1.00 (0.81-1.24). Poor sleep quality (frequent awakening) and all-cause mortality in women: aHR 0.96 (0.69-1.31). Poor sleep quality (frequent awakening) and CVD mortality: aHR 0.91 (0.66-1.26). Poor sleep quality (frequent awakening) and CVD mortality in men: aHR 0.97 (0.64-1.48). Poor sleep quality (frequent awakening) and CVD mortality in women: aHR 0.81 (0.49-1.35).
Tamakoshi 2004 (79)	9.9 years.	All-cause mortality: 11,071/104,010.	Sleep duration and all-cause mortality in men: ≤4h: aRR 0.88 (0.44-1.78), 5h: aRR 1.07 (0.83-1.38), 6h: aRR 1.11 (0.95-1.28), 7h: aRR 1.00, 8h: aRR 1.19 (1.07-1.32), 9h: aRR 1.27 (1.08-1.48), ≥10h: aRR 1.75 (1.46-2.09). Sleep duration and all-cause mortality in women: ≤4h: aRR 1.83 (1.20-2.81), 5h: aRR 1.18 (0.90-1.53), 6h: aRR 1.17 (0.99-1.39), 7h: aRR 1.00, 8h: aRR 1.35 (1.17-1.56), 9h: aRR 1.57 (1.26-1.96), ≥10h: aRR 2.12 (1.67-2.68).
Tsubono 1993 (80)	4 years.	All-cause mortality: 207/4,318.	Sleep duration and all-cause mortality: ≤6h: aRR 1.26 (0.81-1.97), 7-8h: aRR 1.00, ≥9h: aRR 1.58 (1.16-2.15).
Tu 2012 (81)	4 years.	Unclear.	Sleep duration and CHD in women: ≤4h: aOR 1.46 (1.26-1.70), 5h: aOR 1.28 (1.15-1.43), 6h: aOR 1.11 (1.02-1.21), 7h: aOR 1.00, 8h: aOR 0.95 (0.86-1.03), 9h: aOR 1.07 (0.92-1.25), ≥10h: aOR 1.41 (1.19-1.67). Sleep duration and stroke in women: ≤4h: aOR 1.75 (1.49-2.07), 5h: aOR 1.37 (1.21-1.55), 6h: aOR 1.16 (1.05-1.29), 7h: aOR 1.00, 8h: aOR 1.05 (0.94-1.17), 9h: aOR 1.07 (0.89-1.29), ≥10h: aOR 1.88 (1.56-2.27).
Twig 2016 (82)	6.4 years.	Coronary artery disease 92/26,023.	Poor sleep quality (highest vs lowest quartile) and coronary artery disease: aHR 2.38 (1.37-4.11).
Von Ruesten 2012 (83)	8 years.	Stroke 169/23,620. MI 197/23,620.	Sleep duration and MI: <6h: aHR 1.44 (0.85-2.43) 6h: aHR 0.80 (0.53-1.20), 7h: aHR 1.00, 8h: aHR 0.82 (0.56-1.19), ≥9h: aHR 0.89 (0.54-1.49). Sleep duration and strokes: <6h: aHR 2.06 (1.18-3.59), 6h: aHR 1.13 (0.72-1.77), 7h: aHR 1.00, 8h: aHR 1.16 (0.77-1.73), ≥9h: aHR 1.65 (1.00-2.73).
Wang 2016 (84)	3.98 years	MI: 423/101,510. All-cause mortality: 1,793/101,510.	Sleep duration and MI: ≤5h: aHR 0.89 (0.60-1.30), 6h: aHR 0.84 (0.61-1.16), 7h: aHR 1.00, 8h: aHR 0.86 (0.66-1.13), ≥9h: aHR 1.12 (0.58-2.16). Sleep duration and all-cause mortality: ≤5h: aHR 1.23 (1.03-1.80), 6h: aHR 1.95 (0.81-1.12), 7h: aHR 1.00, 8h: aHR 1.06 (0.92-1.20), ≥9h: aHR 1.65 (1.22-2.22).
Werle 2011 (85)	9 year.	All-cause mortality: 141/187. CV mortality: 56/187.	Incremental increase in hours of sleep and all-cause mortality: aHR 0.95 (0.89-1.02). Incremental increase in hours of sleep and CV mortality: aHR 0.83 (0.73-0.95).
Westerlund 2013 (8)	13 year.	CVD mortality: 857/41,192. Stroke: 1,685/41,192. MI: 1,908/41,192.	Sleep duration and CVD mortality: ≤5h: aHR 1.11 (0.76-1.64), 6h: aHR 1.17 (0.88-1.55), 7h: aHR 1.00, ≥8h: aHR 1.12 (0.85-1.47). Sleep duration and CVD: ≤5h: aHR 1.05 (0.88-1.26), 6h: aHR 0.97 (0.86-1.09), 7h: aHR 1.00, ≥8h: aHR 1.00 (0.89-1.13). Sleep duration and stroke: ≤5h: aHR 1.05 (0.80-1.37), 6h: aHR 0.95 (0.79-1.14), 7h: aHR 1.00, ≥8h: aHR 0.87 (0.72-1.04). Sleep duration and MI: ≤5h: aHR 1.19 (0.92-1.55), 6h: aHR 1.05 (0.88-1.25), 7h: aHR 1.00, ≥8h: aHR 1.19 (1.00-1.41). Poor sleep quality (difficulty maintaining sleep) and CVD mortality: mostly/always aHR 0.97 (0.77-1.20).
Wingard 1983 (86)	9 year.	All-cause mortality: 369/6,928.	Sleep duration and all-cause mortality in men: ≤6h: 52/352, 7-8h: 142/1735, ≥9h: 15/132. Sleep duration and all-cause mortality in women: ≤6h: 35/386, 7-8h: 107/1902, ≥9h: 17/200.
Xiao 2014 (87)	14 years.	All-cause mortality: 44,100/239,896. CVD mortality: 11,635/239,896.	Sleep duration and all-cause mortality: <5h: aRR 1.16 (1.11-1.26), 5-6h: aRR 1.04 (1.02-1.06), 7-8h: aRR 1.00, ≥9h:aRR 1.11 (1.06-1.19). Sleep duration and CVD mortality: <5h: aRR 1.25 (1.13-1.38), 5-6h: aRR 1.06 (1.02-1.10), 7-8h: aRR 1.00, ≥9h: aRR 1.07 (0.97-1.17).
Yeo 2013 (88)	9 years.	All-cause mortality: 1,580/13,164. CVD mortality: 363/13,164.	Sleep duration and all-cause mortality: ≤5h: aHR 1.21 (1.03-1.41), 6h: aHR 1.10 (0.95-1.27), 7h: aHR 1.00, 8h: aHR 1.03 (0.89-1.19), 9h: aHR 1.36 (1.11-1.67), ≥10h: aHR1.36 (1.07-1.72). Sleep duration on CVD mortality: ≤5h: aHR 1.40 (1.02-1.93), 6h: aHR 1.25 (0.92-1.69), 7h: aHR 1.00, 8h: aHR 1.04 (0.76-1.42), 9h: aHR 1.26 (0.81-1.96), ≥10h: aHR 1.37 (0.82-2.29).
Zawisza 2015 (89)	10.8 years.	All-cause mortality 2,093/2,449.	Incremental increase in hours of sleep and all-cause mortality: aHR 1.04 (1.003-1.075).
Zuubier 2015 (90)	7.3 years.	All-cause mortality: 154/1,734.	Sleep duration and all-cause mortality: <6h: aHR 1.12 (0.77-1.65), 6-7.5h: aHR 1.00, ≥7.5 h: 1.18 (0.70-1.98).

Figure 1: Flow diagram of study inclusion

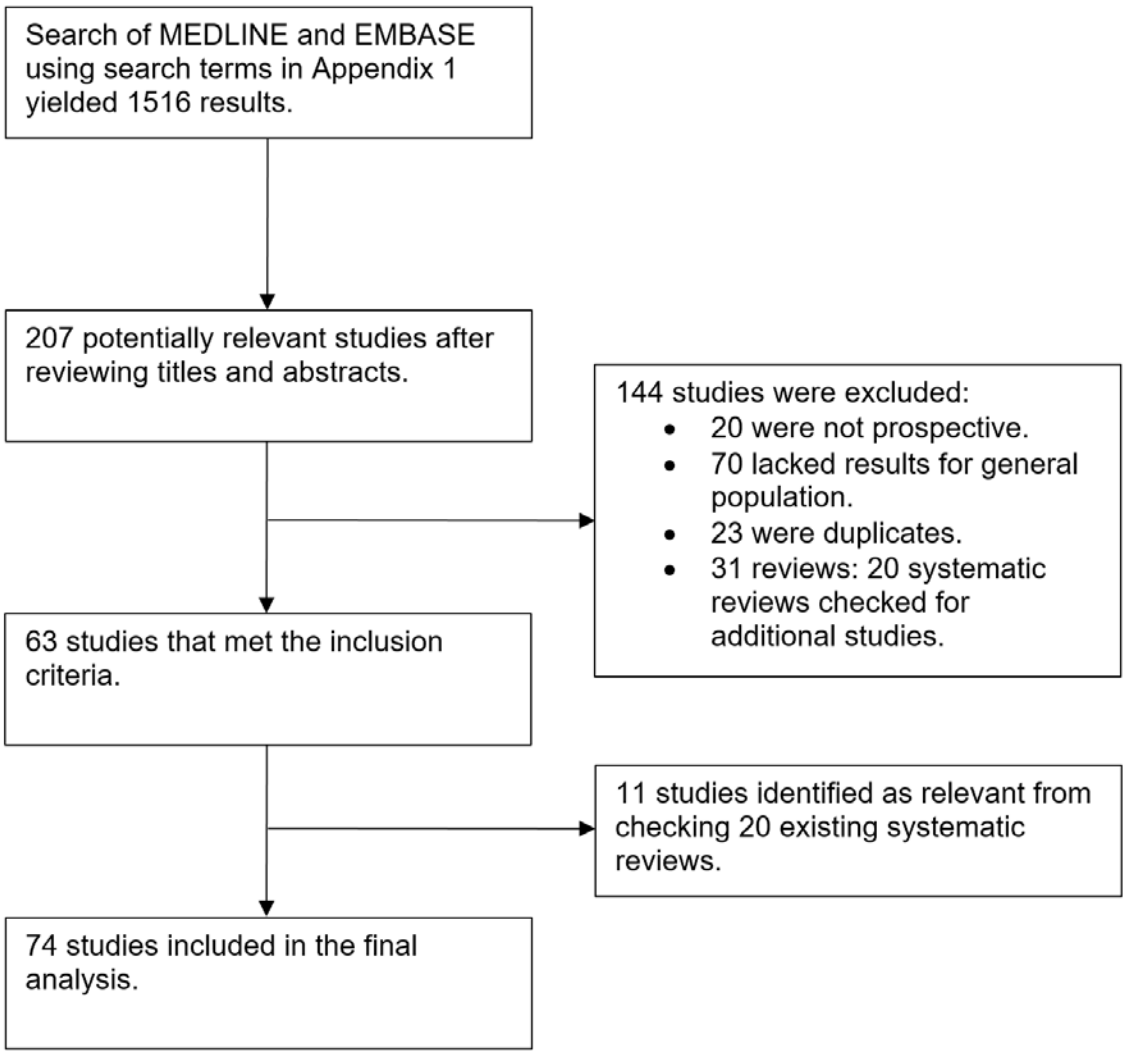


Figure 2: Sleep duration and risk of all-cause mortality with linear and cubic splines

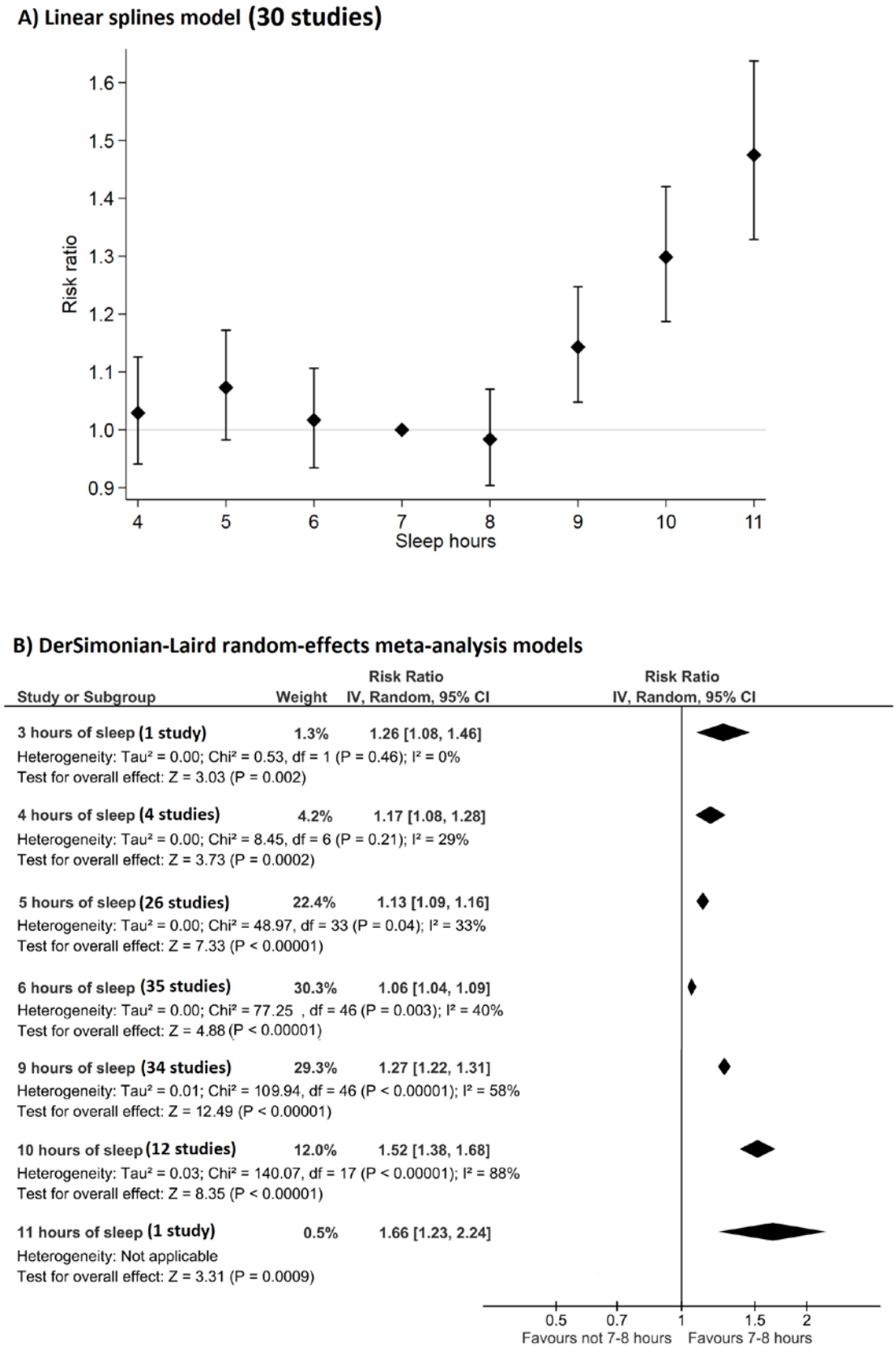
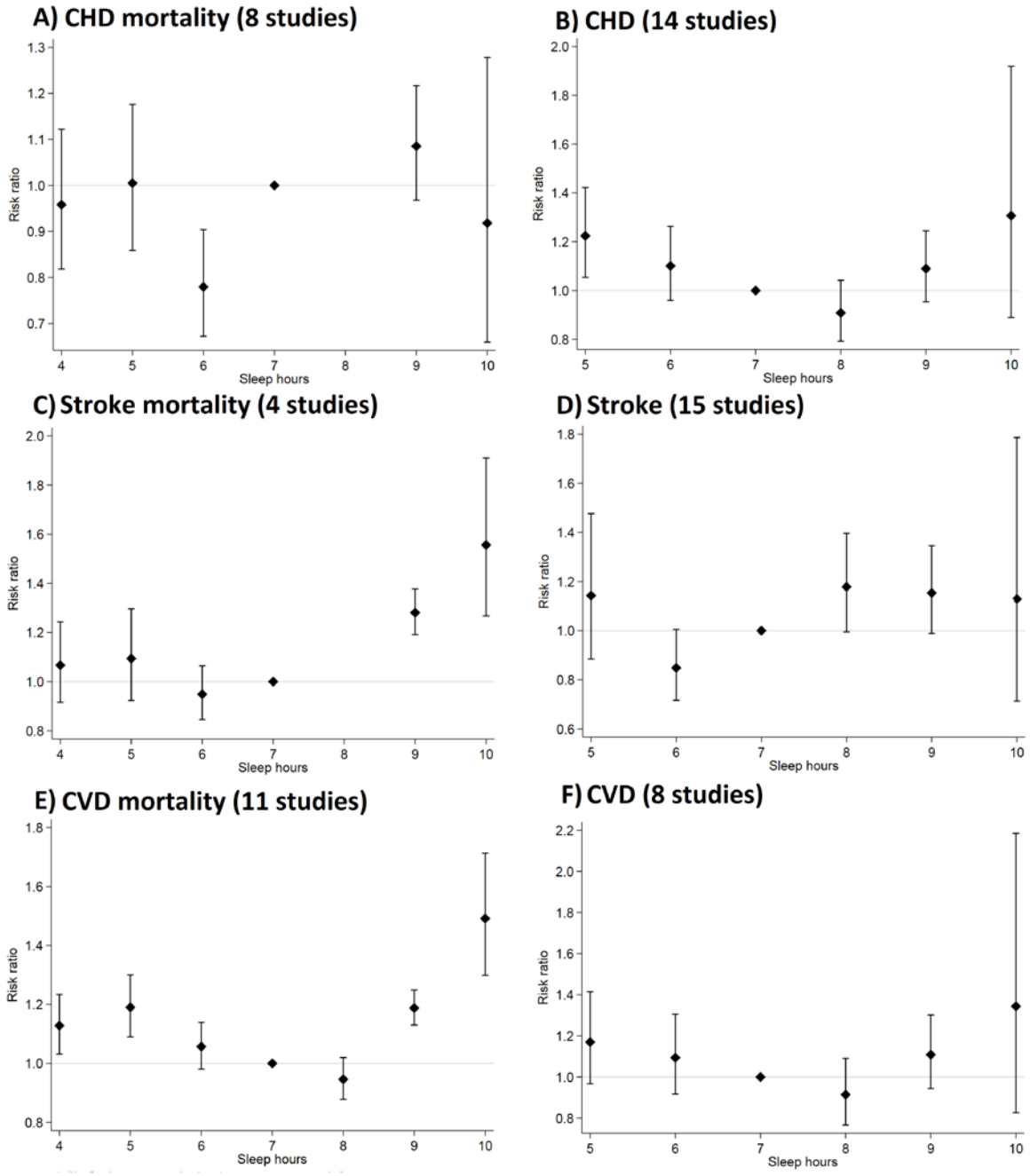


Figure 3: Linear models for adverse cardiovascular events



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