

The association between sleep deprivation and the risk of cardiovascular diseases: A systematic meta-analysis

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Abstract. Globally, sleep deprivation is a concerning health issue associated with an increased risk of cardiovascular diseases (CVDs). The present study aimed to explore the association between short-term sleep and the risk of CVDs, taking into consideration sex and age groups. A comprehensive review was conducted by assembling cohort studies that are available in the PubMed, Cochrane Library, and Embase databases. Individuals with ≤ 5 or ≤ 6 h of sleep per day were considered as sleep-deprived subjects. To minimize potential bias, two reviewers thoroughly evaluated the selected articles. Relevant data were extracted, and pooled odds ratios (ORs) or relative risks (RRs) were calculated using a random-effects model. In total, 18 cohort studies involving adult subjects were included in the present analysis. The pooled results strongly indicated that sleep deprivation was associated with a greater risk of CVDs [RR: 1.09, 95% confidence interval (CI): 1.02-1.16, $P=0.009$]. However, when the pooled analysis was stratified by sex and age, the following results were observed: short-term sleep women (RR: 1.06, 95% CI: 0.96-1.17, $P=0.27$), short-term sleep men (RR: 1.07, 95% CI: 0.97-1.17, $P=0.17$); ≥ 18 years-old sleep-deprived population (RR: 1.09, 95% CI: 1.00-1.17, $P=0.04$), ≥ 40 years-old sleep-deprived population (RR: 1.09, 95% CI: 0.98-1.22, $P=0.11$), and subjects with co-existing diseases, such as diabetes and hyperlipidemia (RR: 1.06, 95% CI: 0.94-1.20, $P=0.32$). In conclusion, short-term sleep is associated with the increased risk of CVDs. Among subjects who were aged ≥ 18 years-old, there was a strong association with the development of CVDs compared with those who were aged ≥ 40 years-old. Furthermore, men were at a higher risk of CVDs than women. Adequate sleep (7-8 h per day) may play a role in improving cardiac health. The results of the present study may provide valuable support for further

research in public health, highlighting the correlation between sleep deprivation and the risk of CVDs.

Introduction

In recent years, there has been a significant increase in research focusing on the impact of sleep on health. Sleep deprivation has been confirmed to have various detrimental effects on both mental and physical well-being. Studies have revealed that individuals who lack sufficient sleep, experience elevated levels of cortisol, a stress hormone, and increased sympathetic activities (1). Furthermore, extensive research has linked sleep deprivation to a higher risk of cardiovascular disease (CVD), diabetes and hypertension (2). Sleep plays a crucial role in the normal regulation of cardiac functions, both in healthy individuals and those with medical conditions (3). Both the quantity and quality of sleep can influence cellular immunity, and even short-term sleep loss may weaken the immune system (4,5).

In today's fast-paced world, numerous individuals are facing sleep deprivation as they juggle work and other responsibilities that appear to be never-ending. The constant availability of information, entertainment and sports contributes to the temptation of staying awake, leading individuals to willingly sacrifice their health by not getting enough rest. A survey conducted by the National Sleep Foundation in 2009 revealed that $\sim 20\%$ of the United States' population gets < 6 h of sleep on weekdays (6). This trend is concerning, as several cohort studies have shown that short sleep duration is associated with an increased risk of health problems, particularly cardiovascular disorders (7,8). In the present era, cardiac diseases are the leading cause of mortality (9). In the USA, $\sim 2,200$ succumb to cardiovascular-related incidents each day, and $\sim 785,000$ individuals suffer from new myocardial attacks every year (10,11).

In 2012, a study revealed that the average number of sleep h for Americans was 7.18 h/day, while a significant portion of the population, 29.2%, reported getting an average of < 6 h of sleep (12). This pattern of sleep duration was also observed in several other advanced countries, where the average sleep h rate aligns with that of the United States (13). Numerous systematic trials have consistently demonstrated a strong association between sleep deprivation and the development and progression of CVDs. The Morgen study conducted in the Netherlands

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between 1993 and 1997 (14) provided evidence that short sleep duration was associated with a predicted 12-year CVD incidence, while long sleep duration showed no such association. Similarly, findings from the Jichi Medical School Cohort Study in Japan (15) indicated that male participants with sleep duration shorter than 6 h had a higher incidence risk of CVD events compared with those sleeping 7-7.9 h per night. On the other hand, a prospective study in 2015 from the MONICA-Brianza and PAMELA population-based cohorts (16) demonstrated a significant increase in the hazard ratio (HR) of CVD events for participants who slept >9 h compared with those sleeping 7-8 h per night. Contrasting results were found in a study utilizing UK Biobank cohort data (17), where both short (≤ 5 h) and long (≥ 9 h) sleep durations were associated with increased risk of CVD incidence and mortality, even after adjusting for various factors. A previous prospective cohort study from the US (18) showed that individuals sleeping ~ 7 h per night had the lowest CVD-specific mortality, in contrast to those who slept <6 or >8 h.

Nevertheless, a comprehensive understanding of how sleep duration is precisely related to CVD risk in a community-based general population is still lacking. Major confounding factors, including age and the presence of other diseases (such as diabetes, hypertension and obesity), may influence the findings and contribute to the varying results. Consequently, the risk of CVD could differ based on sleep duration within populations with different health statuses. In the present study, a meta-analysis was conducted in order to investigate the correlation between sleep deprivation and the risk of CVD in subgroups divided by sex, age and co-morbidity status. This may be advantageous in identifying influential factors and provide new insights into the aforementioned correlation.

Materials and methods

Search method. Multiple databases were used to collect data, including Cochrane Library (<https://www.cochranelibrary.com/>), PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) and Embase databases (<https://www.embase.com/>). The Medical Subject Heading (MeSH) terms were 'sleep quality', 'sleep deprivation', 'sleep disturbance' and 'CVD'. 'Related articles' were also utilized as an option in the PubMed to further expand the search, and all retrieved abstracts, studies, and citations were carefully reviewed. The systematic searches in the databases were restricted to only English-language records (19).

Eligibility criteria. The present study included the cohort studies, which determined the correlation between sleep deprivation and the risk of CVDs. The most recently published studies were included. The exclusion criteria were as follows: i) animal research, ii) unpublished data, iii) articles without proper analysis and findings, iv) research studies on children and v) unoriginal data sources, such as review articles. The characteristics of all the included studies are summarized in Table I.

The included studies needed to satisfy the following conditions: i) cohort studies, investigating the correlation between sleep deprivation and the risk of development and progression of CVDs, ii) adult population with sample size

>100 participants, iii) involvement of adult/senior men and women and iv) the most recently published studies with proper analyses and findings (20).

Data extraction. Two investigators (KWT and JJAL) independently extracted the data. Data from the selected studies were collected and organized into a standardized data spreadsheet. The gathered information included author identity, location, publication year, sample size, sex, age, sleep h, follow-up period and the effects on CVDs. The study selection process is illustrated in the PRISMA flow chart (Fig. 1). The relative risk ratio (RR) or HR were extracted and their corresponding 95% confidence interval (CI) from the included studies. In most of the included studies, sleep deprivation was defined as having ≤ 5 or ≤ 6 h of sleep, while normal sleep was considered as 7-8 h per day. Additionally, the overall risk of CVD associated with sleep deprivation was determined by classifying the data based on sex and age (20).

A Microsoft Excel spreadsheet was utilized to create a comprehensive database for the present meta-analysis. Any discrepancies in decision-making were resolved through consultation with another review author (EWL). No language restrictions were imposed during the study selection process.

Statistical analysis. The statistical analysis was performed by Review Manager 5.3 software (Cochrane). Meta-analysis was conducted in accordance with PRISMA protocols. Furthermore, RR or HR of the included studies were extracted to assess the correlation between sleep deprivation and incidence of CVDs using a random-effects model. Pooled RR and 95% CI of the CVDs for sleep deprivation were estimated. The heterogeneity among the included studies was evaluated via the Chi-squared test and the I^2 statistics. A statistically significant heterogeneity was indicated if Cochran's Q-test yielded a $P < 0.10$.

Results

Association between sleep deprivation and the risk of CVDs. A total of 18 cohort studies provided sufficient data for the meta-analysis, allowing for the estimation of the pooled effect size in relation to the association between sleep deprivation and the development and progression of CVDs. The pooled RR was found to be 1.09, with a 95% CI: 1.02-1.16 and a statistically significant $P = 0.009$. The heterogeneity test showed $I^2 = 0\%$ and a $\text{Chi}^2 = 6.77$ (Fig. 2).

Association between sleep deprivation in women and the risk of CVDs. Out of the 18 cohort studies included in the meta-analysis, a total of 9 studies provided sufficient data to calculate the pooled effect size for sleep deprivation in women and its association with the development and progression of CVDs (RR: 1.06, 95% CI: 0.96-1.17, $P = 0.27$; heterogeneity test; $I^2 = 0\%$, $\text{Chi}^2 = 0.69$; Fig. 3).

Association between sleep deprivation in men and the risk of CVDs. Among the 18 cohort studies included in the analysis, a total of 11 studies provided sufficient data to calculate the pooled effect size for sleep deprivation in men and its association with development and progression of CVDs (RR:

Table I. Characteristics of the included studies among sleep-deprived adults.

Sr. no.	Authors/ country	Year	Study type	Sample size	Age, years	Sex	CVDs effects	Follow-up sleep h	Follow-up period	(Refs.)
1.	Ayas <i>et al</i> Canada	2003	Cohort study	71,671	45-65	Women	Short sleep (≤ 5 h) and long sleep (≥ 9 h) are strongly linked with an increased risk of CVDs	$<5-8$ and >9 h	10 years	(14)
2.	Chandola <i>et al</i> UK	2010	Cohort study	3,413 women and 6,895 men	35-55	Women and men	Greater risk of CVDs in participants having short sleep along with sleep disturbances than persons with just short sleep pattern	$<5-7$ and >8 h	15 years	(15)
3.	Zheng <i>et al</i> China	2019	Cohort study	487,200 (199,241 men and 287,959 women)	30-79	Women and men	Insomnia has found to elevate the risk of CVDs	≤ 5 h	10 years	(16)
4.	Garfield <i>et al</i> UK	2019	Cohort study	4,399	40-69	Men	Sleep disturbances and poor sleep have strongly linked with development and progression of cardiac disorders	≤ 6 h	29 years	(17)
5.	Sabanayagam <i>et al</i> USA	2010	Cohort study	30,397	≥ 18	Women and men	Sleep period <5 and >9 h as compared with 7 h sleep (normal sleep period) have strongly linked with risk of CVDs	$<5-8$ and >9 h	-	(18)
6.	Amagai <i>et al</i> Japan	2010	Cohort study	11,367 (4,413 men and 6,954 women)	50-60	Women and men	Individuals having <6 h of sleep are of high risk of cardiac distresses	$<5-8$ and >9 h	10.7 years	(24)
7.	Shankar <i>et al</i> Singapore	2008	Cohort study	63,257	45-74	Women and men	≤ 5 and ≥ 9 h of sleep have strongly linked with incidence	$<5-8$ and >9 h	4 years	(25)
8.	Wang <i>et al</i> China	2016	Cohort study	101,510	18-98	Men	Insignificant association has been found between short deprivation and long sleep h with CVDs risk	$<5-8$ and >9 h	3.9 years	(28)
9.	Cai <i>et al</i> China	2015	Cohort study	113,138	40-80	Women and men	Longer and shorter sleep durations are associated with cardiac disabilities but subjects with longer sleep h have a high risk than shorter duration	$<5-9$ and >10 h	7.12 years	(29)

Table I. Continued.

Sr. no.	Authors/ country	Year	Study type	Sample size	Age, years	Sex	CVDs effects	Follow-up sleep h	Follow-up period	(Refs.)
10.	Meisinger <i>et al</i> Germany	2010	Cohort study	3,508 men and 3,388 women	45-74	Women and men	<5 sleep h induces cardiac illnesses. However, in women, the risk of developing CVDs is lower compared with males	<5-8 and >9 h	15 years	(30)
11.	Heslop <i>et al</i> UK	2002	Cohort study	6,022 men and 1,006 women	60-65	Women and men	Individuals getting sleep ≤ 7 h found high morbidity rate and risk of CVDs than who take sleep ≥ 8 h per day	≤ 7 and ≥ 8 h	25 years	(31)
12.	Ikehara <i>et al</i> Japan	2009	Cohort study	98,634 (41,489 men and 57,145 women)	40-79	Women and men	Insomnia and long sleep have strongly associated with development of cardiovascular disorders, mortality and neurological disorders	<4-9 and >10 h	14.3 years	(32)
13.	Chen <i>et al</i>	2008	Cohort study	93,175	50-79	Women USA	Longer sleep is strongly linked with the risk of mortality of cardiac disorders	<5-9 and >10 h	7.5 years	(33)
14.	Mallon <i>et al</i> Sweden	2002	Cohort study	266 (165 men and 101 women)	45-65	Women and men	Men having complains of sleep distress have strongly associated with risk of CVDs	<6 and >8 h	12 years	(34)
15.	Eguchi <i>et al</i> Japan	2013	Cohort study	1,255 (476 men and 779 women)	33-97	Women and men	Individuals having <7 h of sleep are prone of developing cardiac distresses	≤ 7 and >7 h	4.5 years	(35)
16.	Qureshi <i>et al</i> USA	1997	Cohort study	7,844 (4,996 women and 2,848 men)	32-75	Women and men	Individuals with sleep duration >8 h have a high risk of CVDs	<6 and >8 h	10 years	(36)
17.	Canivet <i>et al</i> Sweden	2013	Cohort study	4,319	45-64	Women and men	Longer and shorter sleep durations are associated with cardiac disabilities	≤ 6 h >9 h	12 years	(37)
18.	Tao <i>et al</i> UK	2021	Cohort study	407,500	38-73	Women and men	Longer and shorter sleep durations are associated with cardiac disabilities but individuals with longer sleep h have a higher risk than shorter duration	<5-8 and <9 h	9.57 years	(39)

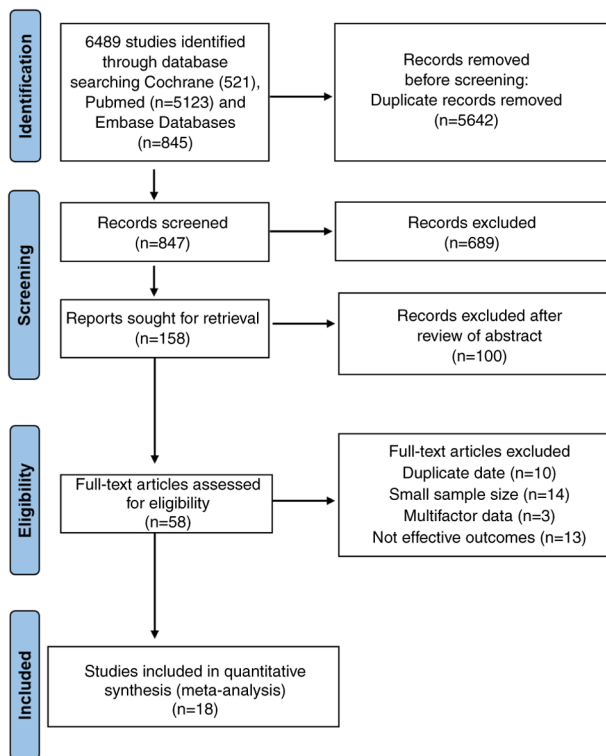


Figure 1. Systemic PRISMA flowchart for meta-analysis.

1.07, 95% CI: 0.97-1.17, $P=0.17$; heterogeneity test; $I^2=0\%$, $\text{Chi}^2=0.86$; Fig. 4).

Association between sleep deprivation and participants with comorbidities. Out of the 18 cohort studies included in the analysis, a total of 6 studies provided sufficient data to calculate the pooled effect size for the association of sleep deprivation in cases suffering from other diseases with the development and progression of CVDs (RR: 1.06, 95% CI: 0.94-1.20, $P=0.32$; heterogeneity test; $I^2=0\%$, $\text{Chi}^2=0.28$; Fig. 5).

Association between sleep deprivation in subjects aged ≥ 18 years old and the risk of CVDs. Out of the 18 cohort studies included in the analysis, a total of 7 studies provided sufficient data to calculate the pooled effect size for the association of sleep deprivation in individuals who were aged ≥ 18 years-old with the development and progression of CVDs (RR: 1.09, 95% CI: 1.00-1.17, $P=0.04$; heterogeneity test; $I^2=0\%$, $\text{Chi}^2=5.30$; Fig. 6).

Association between sleep deprivation in subjects aging ≥ 40 years-old and the risk of CVDs. Out of the 18 cohort studies included in the analysis, all 18 studies reported adequate data to calculate the pooled effect size for the association of sleep deprivation in individuals who were aged ≥ 40 years old with development and progression of CVDs (RR: 1.09, 95% CI: 0.98-1.22, $P=0.11$; heterogeneity test; $I^2=0\%$, $\text{Chi}^2=1.51$; Fig. 7).

Discussion

Sleep is essential for physical health and mental well-being, facilitating bodily restoration and cognitive functions. Sleep

deprivation can have adverse effects on both physical and mental health, leading to fatigue, reduced concentration, increased stress and irritability. Additionally, sleep disturbances and short sleep duration have been associated with reduced productivity, impaired decision-making, and various health issues, including diabetes mellitus, cardiac disorders and depression (21). Over the past century in the United States, the average time spent sleeping has significantly decreased, from 9 h in 1910 to 7.5 h in 1975 and 6.8 h in 2005 (22). In Japan, 21.4% of the population suffers from insomnia (23). Investigational studies have indicated that sleeping disorders may contribute to the development of CVDs (24). Both long- and short-term sleep have been noted to be associated with an increased risk of CVDs. However, it has been reported that, in comparison to insomnia, long-term sleep is more strongly associated with an increased risk of cardiac illnesses (14,25). A comprehensive meta-analysis was conducted to explore the correlation between short sleep and the risk of CVDs, categorizing the data into subgroups based on sex and age. The present study is the first to provide insights into the relationship between sleep deprivation and CVD risk using population-based cohort studies of adults. The findings of the present study indicate an increased risk of CVDs among both sleep-deprived women and men. However, the association varied depending on age groups and sex. Among women, the pooled analysis showed a weak and statistically insignificant link between sleep deprivation (sleeping <5 or 6 h) and an increased risk of development and progression of CVDs. By contrast, for sleep-deprived men, the association with the risk of CVDs was even weaker than in women. Moreover, among the population aged >18 years, the pooled analysis demonstrated a strong association with a greater risk of development and progression of CVDs. However, among those aged >40 years, the association with the risk of CVD was weak and statistically insignificant. Out of the 18 studies, six cohort studies provided RR of CVD risk among sleep-deprived individuals who also suffered from other health complications, including hypertension, diabetes mellitus and hyperlipidemia. The pooled analysis among these individuals showed a weak and statistically insignificant association with a greater risk of progression and development of CVDs

Regarding the association between sleep deprivation and CVD risk, several underlying mechanisms may be involved. Sleep deprivation can disrupt the body's hormonal balance, leading to alterations in hormone secretion. Specifically, inadequate sleep may result in increased levels of cortisol, commonly known as the stress hormone. Elevated cortisol levels can contribute to insulin resistance, inflammation and hypertension, all of which are risk factors for CVD. Chronic sleep deprivation can trigger a state of chronic low-grade inflammation in the body. This sustained inflammatory response is associated with the development and progression of atherosclerosis, a condition characterized by the buildup of plaque in the arteries. Inflammation plays a key role in promoting the formation of arterial plaques and increasing the risk of cardiovascular events. Sleep deprivation can disrupt the balance between the sympathetic and parasympathetic branches of the autonomic nervous system. This imbalance can lead to increased sympathetic activity, which is linked to elevated heart rate, blood pressure and reduced heart rate variability, all of which contribute to

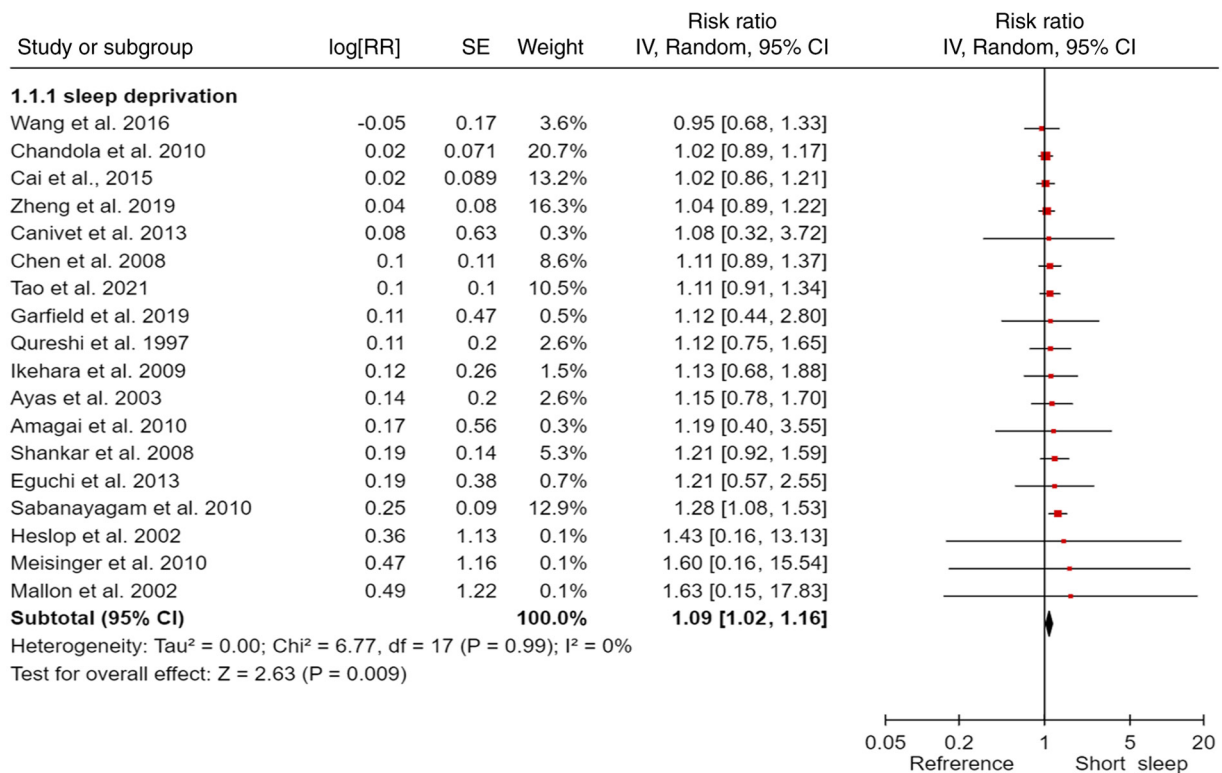


Figure 2. Correlation between sleep deprivation and the risk of cardiovascular diseases. CI, confidence interval.

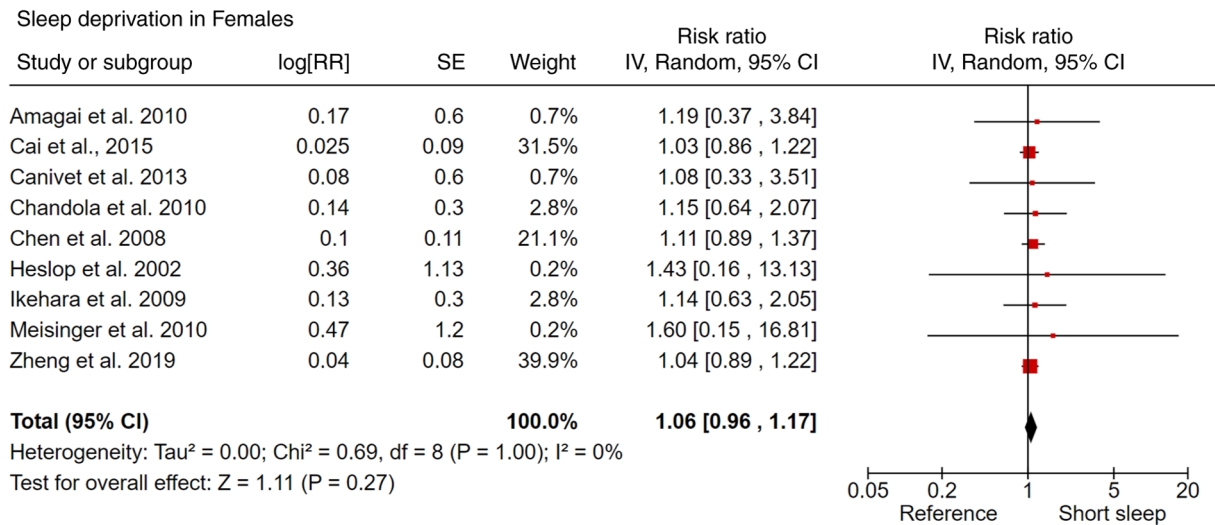


Figure 3. Correlation between sleep deprivation and the risk of cardiovascular diseases in women. CI, confidence interval.

cardiovascular dysfunction. Sleep deprivation has been shown to impair endothelial function, which refers to the health and responsiveness of the cells lining the blood vessels. Endothelial dysfunction can result in reduced vasodilation capacity and increased vascular resistance, further promoting CVD development. Chronic sleep deprivation is associated with disturbances in glucose metabolism and insulin sensitivity, which can contribute to the development of type 2 diabetes. Diabetes is a significant risk factor for CVD, as it accelerates the progression of atherosclerosis and increases the likelihood of cardiovascular events (41-43).

Sleep deprivation has been strongly linked to an increased risk of developing cardiovascular disorders. Numerous studies have shown that individuals who do not get enough sleep or experience frequent sleep disturbances are at a higher risk of developing conditions, such as coronary artery disease (CAD), myocardial infarction, stroke, high blood pressure and diabetes (26-28). Furthermore, lack of sleep has been associated with elevated levels of inflammation and stress hormones, which can further contribute to the risk of cardiovascular disorders. Additionally, insomnia and other sleep disorders have been found to be linked to feelings of

Sleep deprivation in Males

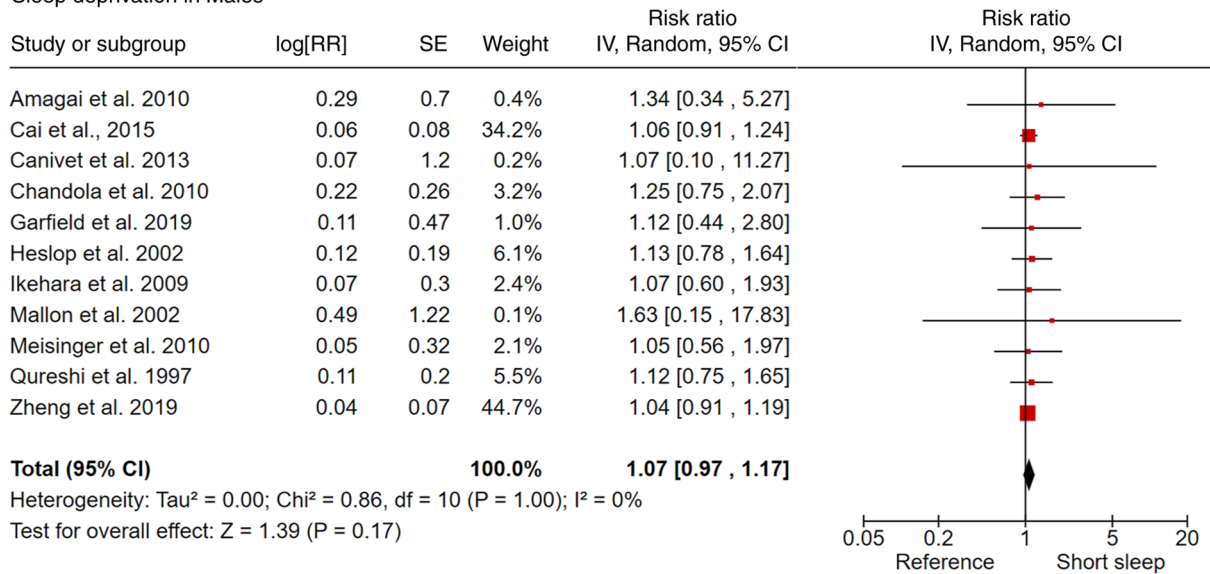


Figure 4. Correlation between sleep deprivation and the risk of cardiovascular diseases in men. CI, confidence interval.

Sleep deprivation in participants with co-morbidities

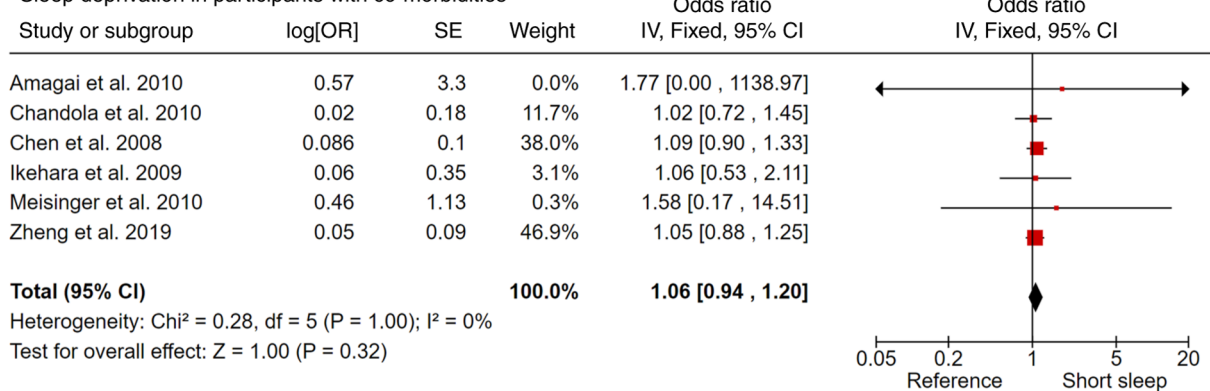


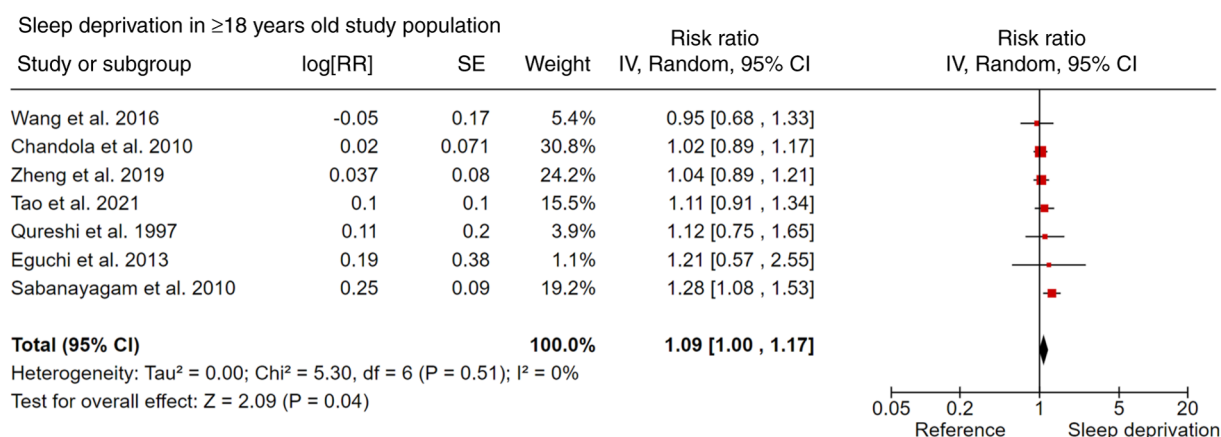
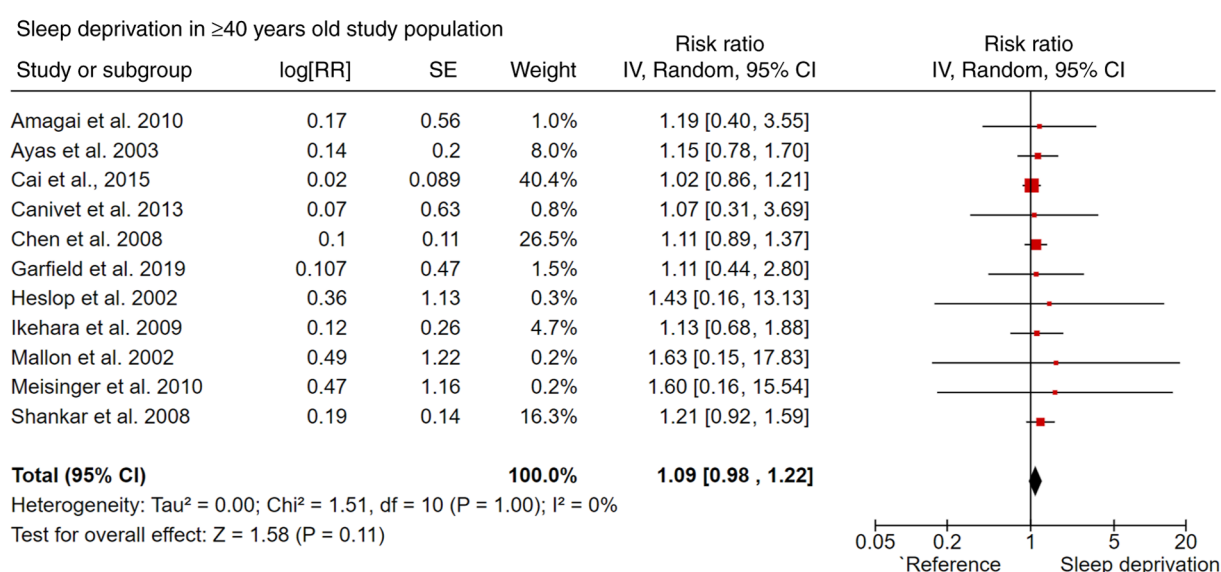
Figure 5. Correlation between sleep deprivation and the risk of cardiovascular diseases in participants with co-morbidities. CI, confidence interval.

depression and anxiety, which can act as additional inducers of CVDs (29-31).

The findings of the present study are consistent with previous meta-analysis studies on the association between sleep duration and the risk of CVDs. In a meta-analysis review conducted in 2011, it was demonstrated that short-term sleep was associated with elevated incidence rates of various CVDs, including stroke and coronary heart disease (CHD) (32-34). Furthermore, another meta-analysis concentrated on investigating the relationship between sleep duration and the risk of cardiac illnesses, and it provided evidence that short-term sleep was strongly associated with an increased risk of heart failure (HF) and stroke (35-37). Cheong *et al* (38) confirmed that concentration on the interactions between the host and gut microbiota may be promising for the prevention or treatment of CVD. Previous observational studies, supported by meta-analyses, have consistently indicated an association between short sleep duration and increased risk of CVDs, such as CAD, HF and stroke (39-42). Additionally, short sleep duration has been linked to various cardiovascular risk factors, including type 2

diabetes and overweight (43-46). Moreover, meta-analyses of observational studies have further confirmed that short sleep duration could serve as an independent risk factor for CHD and is associated with higher risks of all-cause and cardiovascular mortalities (47-49). Regarding stroke, observational studies have suggested that short sleep duration is associated with an elevated risk of stroke (50-53), and a meta-analysis of such studies further substantiated this finding (54). However, a more recent dose-response meta-analysis (55) reported contrasting results, showing an association between long sleep duration and an increased risk of stroke.

Therefore, it has been suggested that achieving a sleep duration of 7-8 h per day could potentially yield positive impacts on cardiac health. However, it is essential to acknowledge the limitations to the present study, which could potentially compromise its accuracy. Certain of these limitations include the reliance on self-reported sleep duration in numerous of the included studies, variations in follow-up periods, different analytical measurement approaches (for example, questionnaires) used across the studies, and the absence of subjective

Figure 6. Correlation between sleep deprivation and the risk of cardiovascular diseases in individuals who aged ≥ 18 years-old. CI, confidence interval.Figure 7. Correlation between sleep deprivation and the risk of cardiovascular diseases in individuals who aged ≥ 40 years-old. CI, confidence interval.

estimates of sleep length in certain studies. Additionally, a methodological quality assessment of the included studies was not conducted, which may influence the overall reliability of the present findings.

There are still numerous research directions about sleep deprivation and the risk of CVDs. For example, future research may focus on the degree of sleep deprivation on the increased risk of CVDs, and whether the detrimental effect of sleep deprivation on cardiac health is reversible. In addition, the exact mechanism of an increased risk of CVDs after sleep deprivation also remains to be investigated in the future.

In conclusion, the present study indicated that sleep deprivation, characterized by ≤ 5 or ≤ 6 h of sleep per day, increased the risk of CVDs. Notably, it was revealed that the risk of CVDs was higher in men compared with women. Furthermore, subjects who were aged ≥ 18 years-old exhibited a significant association with development of CVDs, whereas the association was weaker in those who were aged ≥ 40 years old. Based on these findings, it was suggested that sleep-deprived individuals consider extending their sleep duration to the recommended 7-8 h per day to potentially improve their cardiac health. The

results of the present study may provide valuable support for further research in public health, highlighting the correlation between sleep deprivation and the risk of CVDs.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YP and WL conceived and designed the study. WL provided administrative support. YP, YZ, XS and SH collected data.

All authors participated in data analysis and interpretation, writing process, reading and approval of the final version of the manuscript. YP and WL confirm authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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