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Meta-Analysis of Self-Reported Daytime Napping and Risk of Cardiovascular or All-Cause Mortality

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: Whether self-reported daytime napping is an independent predictor of cardiovascular or all-cause mortality remains unclear. The aim of this study was to investigate self-reported daytime napping and risk of cardiovascular or all-cause mortality by conducting a meta-analysis.

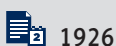
Material/Methods: A computerized literature search of PubMed, Embase, and Cochrane Library was conducted up to May 2014. Only prospective studies reporting risk ratio (RR) and corresponding 95% confidence intervals (CI) of cardiovascular or all-cause mortality with respect to baseline self-reported daytime napping were included.

Results: Seven studies with 98,163 subjects were included. Self-reported daytime napping was associated with a greater risk of all-cause mortality (RR 1.15; 95% CI 1.07–1.24) compared with non-nappers. Risk of all-cause mortality appeared to be more pronounced among persons with nap duration >60 min (RR 1.15; 95% CI 1.04–1.27) than persons with nap duration <60 min (RR 1.10; 95% CI 0.92–1.32). The pooled RR of cardiovascular mortality was 1.19 (95% CI 0.97–1.48) comparing daytime nappers to non-nappers.

Conclusions: Self-reported daytime napping is a mild but statistically significant predictor for all-cause mortality, but not for cardiovascular mortality. However, whether the risk is attributable to excessive sleep duration or napping alone remains controversial. More prospective studies stratified by sleep duration, napping periods, or age are needed.

MeSH Keywords: **Meta-Analysis • Mortality • Sleep Bruxism**

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Background

Napping is a common practice in community-dwelling older adults [1,2], with prevalence up to 68.6% in the elderly population [3]. Daytime napping or siesta is considered to be a healthy habit and linked with good health. A short nap of less than 30 min duration during the afternoon is deemed to have an invigorating effect, helps to restore wakefulness, and improve performance [4,5].

Contrary to the popular view that naps are beneficial to health, longer or frequent naps might be associated with worse long-term health. Daytime napping may be a risk factor for morbidity and mortality in the elderly population. Particularly, these persons requiring naps might have an unrecognized disease or nighttime sleep deprivation. Many studies [6–9] suggested that daytime napping may increase mortality. One study [10] indicated that the greater risk of mortality was only significant in night sleep of more than 9 hours. Others [11,12] did not find these associations. These conflicting findings might be attributable to the different populations, geographic areas, duration of napping time, and cultural habits. Daytime napping as an independent predictor for cardiovascular or all-cause mortality remains controversial.

To our knowledge, no previous meta-analysis has quantitatively evaluated the association between self-reported daytime napping and risk of cardiovascular or all-cause mortality. The aim of this study was to evaluate the findings from the available prospective studies, to determine whether self-reported daytime napping is an independent predictor for cardiovascular or all-cause mortality.

Material and Methods

Literature search

This meta-analysis was conducted according to the reporting items for systematic reviews and meta-analyses (PRISMA) statement. A comprehensive computerized literature search was conducted through PubMed, Embase database, and Cochrane Library up to May 2014. Potentially relevant articles were identified using the following Medical Subject Headings (MeSH): “daytime napping” or “siesta” or “nappers” or “excessive daytime sleepiness” and “death” or “mortality” and “prospective” or “follow-up”. In addition, we searched the reference lists of all identified relevant studies to identify additional eligible studies.

Study selection

Studies meeting the following criteria were included in the meta-analysis: 1) prospective observational study; 2) investigating

baseline daytime napping and subsequent risk of cardiovascular or all-cause mortality as outcomes; 3) reporting multivariate-adjusted risk ratio (RR) or hazard ratio (HR) and corresponding 95% confidence intervals (CI) of cardiovascular or all-cause mortality comparing daytime napping to the non-nappers; and 4) all-cause mortality was obtained from the medical records, or from official death certificates; cardiovascular mortality is grouped by medical diagnostic codes and clinical criteria. The question about napping status was phrased: “Do you normally take a nap during the day?” Daytime napping was defined by the individual study, and the rest were defined as non-nappers. Articles were excluded if: 1) not a prospective observational study; and 2) non-nappers were not considered as control.

Data extraction and quality assessment

Data were extracted by 2 authors (XK Liu and Q Zhang) independently from each selected study. Data extracted for this study included the first author's surname, publication year, geographic region, study design, sample size, male gender (%), age range of participants, assessment of daytime napping, adjusted RR and HR with 95% CI, duration of follow-up, and adjustment for covariates. Any disagreement was resolved by discussion. Study quality was judged by using the Newcastle-Ottawa Scale (NOS) [13] by 2 authors independently. Quality assessment was conducted in 3 domains: subject selection, comparability of groups, and the ascertainment of outcomes. Using the scale, the total NOS star count ranges from zero to 9. Studies achieving a rating of ≥ 5 stars were judged to be of high quality.

Data synthesis and analysis

Data analyses used most fully multivariate-adjusted RR or HR and 95% CI comparing daytime nappers to the non-nappers. If the publications reported separate RR for different napping duration, we pooled the separate RR for the different items from the individual study. The Cochrane Q statistic and the I^2 statistic were used to assess the heterogeneity of RR across studies. A p-value < 0.10 for the Q statistic or $I^2 > 50\%$ were taken as indicator of severe heterogeneity using a random-effects model, otherwise a fixed-effects model was used [14]. As there was obvious clinical heterogeneity in the durations of napping across the different studies, a random-effects model was used to calculate the pooled RR.

Begg's rank correlation test [15] and Egger linear regression test [16] were used to investigate any possible publication bias. Subgroup analysis was conducted as follows: geographic region (Asia versus No-Asia), follow-up duration (≤ 11 years versus > 11 years), sample sizes (< 5000 versus > 5000), napping duration (< 60 min versus > 60 min), and gender (men versus women).

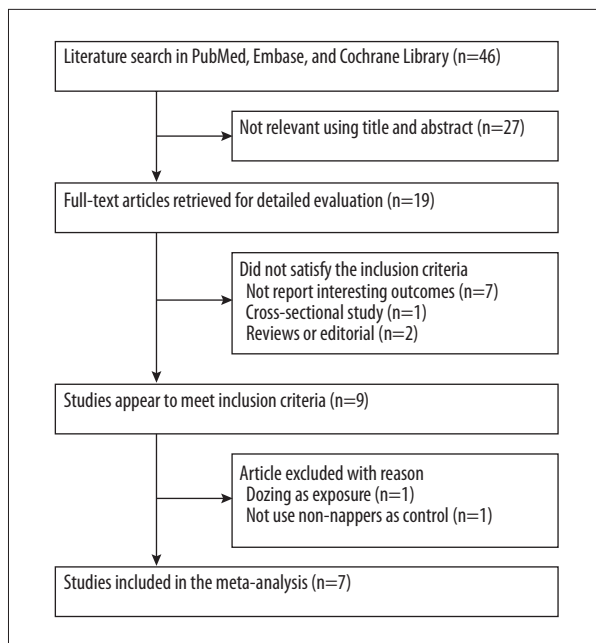


Figure 1. Flow chart of study selection process.

Sensitivity analysis was conducted by excluding 1 study at a time using the metaninf algorithm command in STATA statistical software to investigate the influence of a single study on the overall effect size. All statistical analyses were performed using STATA statistical software, version 12.0 (STATA, College Station, TX, USA). A 2-tailed P value <0.05 was considered as statistically significant.

Results

Literature search and baseline characteristics

Our initial literature search produced 46 citations. Of these citations, 7 studies [6–12] met our predefined inclusion criteria. The detailed study selection process is listed in Figure 1. Table 1 lists the detail characters of the included studies. A total of 98,163 subjects were included. The age of the subjects was over 40 years. The sample sizes of the studies ranged from 455 to 67,129. One study [7] included only women, and others included both men and women. The follow-up duration ranged from 6.9 to 20 years. Overall quality of the included studies was good, and NOS scales ranged from 6 to 7 (Supplemental Table 1).

All-cause mortality

All the included studies reported data on all-cause mortality. As shown in Figure 2, daytime napping was associated with a greater risk of all-cause mortality (RR 1.15; 95% CI 1.07–1.24) comparing with non-nappers in a random-effects model. The

heterogeneity was statistically significant ($I^2=52.1\%$; $P=0.007$). No evidence of publication bias was found by the Begg's rank correlation test ($P=0.284$) and Egger's linear regression test ($P=0.290$).

Cardiovascular mortality

Four studies [7–9,11] reported cardiovascular mortality involving 93,463 subjects. As shown in Figure 3, the pooled estimate of multivariate RR was 1.19 (95% CI 0.97–1.48) comparing daytime napping to non-nappers in a random effect model. Substantial heterogeneity was observed ($I^2=65.4\%$; $P=0.013$). No evidence of publication bias was found using the Begg's rank correlation test ($P=0.707$) and Egger's linear regression test ($P=0.586$).

Subgroup analyses

The detailed results of subgroup analyses are presented in Supplemental Table 2. Daytime napping was associated with a greater risk of all-cause mortality among women (RR 1.21; 95% CI 1.00–1.47), but not men (RR 1.09; 95% CI 0.89–1.34). Sensitivity analyses were performed based on all-cause mortality. In the sensitivity analysis, there was little influence in the quantitative pooled measure of RR or 95% CI when excluding one study at a time (Data not shown).

Discussion

This meta-analysis provides evidence that self-reported daytime napping is a mild but statistically significant risk predictor for all-cause mortality, but not for cardiovascular mortality. Participants with daytime napping had 15% greater risk of all-cause mortality. However, there is likely substantial heterogeneity in the duration of daytime napping. Many of the included studies did not adjust overall sleep duration; therefore, the excess risk of all-cause mortality might be explained by the impact of excessive daytime sleepiness rather than daytime napping itself.

In the current study, a daytime napping duration over 60 min was significantly and independently associated with all-cause mortality in the general population. Subjects with daytime napping showed some trend to increase cardiovascular mortality, in which this association was not statistically significant (RR 1.19; 95% CI 0.97–1.48). A case-control study [17] reported an elevated risk of acute myocardial infarction associated with long-duration daytime napping. In a prospective study [18] conducted in Germany, midday napping was associated with 2.12 times the risk of nonfatal myocardial infarction and sudden cardiac death. Contrary to these findings, 2 studies [19,20] conducted in younger healthy persons in Greece suggested a

Table 1. Summary of clinical studies included in the meta-analysis.

Study/year	Region	Type of study	Subjects (% men) age range	Assessment of daytime napping	Follow-up (years)	Outcome assessment	Outcome/events number/ RR or HR (95% CI)	Adjustment for covariates
Burazeri et al. [11] 2003	Israel	Prospective cohort study	1859 (45) >50 years	Structured questionnaire Nappers versus non-nappers	9–11	Death certificate ICD-9 codes 390–458	Total death 405 1.36 (0.93–1.97) men 0.91 (0.63–1.31) women CVD(NA) 1.53 (0.84–2.77) men 0.79 (0.45–1.38) women	Age; smoking; BMI; SBP; self-appraised health; homocysteine, glucose and albumin; creatinine; history of CHD, CHF, DB and stroke; and night sleep duration (For women + origin of country, education and smoking)
Bursztyn et al. [6] 2005	Israel	Prospective cohort study	455 (NR) >70 years	2-part questionnaire After nap versus no nap	12	Israeli National Population Register	Total death 147 1.6 (1.0–2.6)	Sex, dependence in activities of daily living, physical activity, self-rated health, DB, hypertension, IHD, malignancy, renal dysfunction, nocturnal sleep satisfaction, smoking, cholesterol, BMI, working status
Lan et al. [12] 2007	Taiwan	Prospective cohort study	3079 (56.8) ≥60 years	Home-based interview	8.4	National death registry at the Department of Health. CVD: ICD-9 codes 390–459	Total death 1338 0.68 (0.37–1.25) <60 min + men 1.06 (0.72–1.55) 60–89 min + men 0.98 (0.60–1.61) 90–119 min + men 1.23 (0.72–2.10) ≥120 min + men 1.24 (0.51–3.04) <60 min + women 0.76 (0.39–1.50) 60–89 min + women 0.47 (0.16–1.41) 90–119 min + women 1.04 (0.46–2.37) ≥120 min + women	Age, marital status, monthly income, cigarettes smoking, alcohol consumption, BMI, exercise, disease history (heart disease, stroke, and cancer), and depression
Stone et al. [7] 2009	USA	Prospective cohort study	8,101 (0) ≥65 years	Self-administered questionnaire or interview. Nappers versus non-nappers	6.9 (mean)	Death certificate ICD-9 codes 401–404, 410–414, 425, 428, 429.2, 430–438, 440–444, and 798	Total death 1922 1.67 (1.26–2.20)* CVD 723 1.96 (1.26–3.06)*	Age, BMI, history of medical condition, including DB, PD, dementia, COPD, non-skin cancer, and osteoarthritis, history of hypertension, walks for exercise, alcohol use, smoking status, depression, cognitive impairment, estrogen use, and benzodiazepine use
Tanabe et al. [8] 2010	Japan	Prospective study	67,129 (41.3) 40–79 years	Self-administered questionnaire. Nappers versus non-nappers	14.3	The Minister for Internal Affairs and Communications	Total death 9643 1.19(1.14–1.24) CVD 2852 1.31 (1.22–1.42)	Age, sex, sleeping duration, treated hypertension, history of DB, any disease under medical treatment, smoking, BMI, weight loss from age 20 years, BP, perceived mental stress, depressive symptoms, working status, educational status and time for walking
Cohen-Mansfield et al. [10] 2012	Israel	Prospective cohort study	1,166 (54.5) 75–94 years	interview	20	Israeli National Population Register	Total death 1108 0.82 (0.67–1.00) <7 night 1.385 (1.07–1.79) >9 night	Age, sex, country of origin, education, financial status, and having children, demographics, health, and function variables.
Leng et al. [9] 2014	UK	Prospective population-based cohort study	16,374 (43.7) 40–79 years	Post questionnaires	13	Death certificate CVD: ICD-9 codes 401–448 or ICD-10 codes I10–I79	CVD 1034 1.00 (0.81–1.22) <60 min 0.92 (0.57–1.48) ≥60 min Total death 3521 1.14(1.02–1.27) <60 min 1.19(1.14–1.24) ≥60 min	Age, sex, social class, education, marital status, employment status, BMI, physical activity, smoking, alcohol, depression, self-reported health, hypnotic drug use, antidepressant use, COPD drug use, time spent in bed at night, self-reported preexisting DB and underlying sleep apnea

NR – not report; BMI – body mass index; HR – hazard risk; RR – risk ratio; BP – blood pressure; SBP – systolic blood pressure; DBP – diastolic blood pressure; DB – diabetes mellitus; CHF – chronic heart failure; CHD – coronary heart disease; COPD – chronic obstructive pulmonary disease; PD – Parkinson’s disease. * Results from the disease-free cohort.

Supplemental Table 1. Quality assessment of studies included in meta-analysis.

Study/year	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome was not present at study start	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Enough follow-up periods (>11 years)	Adequacy of follow-up of cohorts	Overall NOS scores
Burazeri et al. [11] 2003	*	*	*		*	*		*	6
Bursztyn et al. [6] 2005	*	*	*		*	*	*	*	7
Lan et al. [12] 2007	*	*	*		*	*		*	6
Stone et al. [7] 2009		*	*	*	*	*		*	6
Tanabe et al. [8] 2010	*	*	*		*	*	*	*	7
Cohen-Mansfield et al. [10] 2012	*	*	*		*	*	*	*	7
Leng et al. [9] 2014	*	*	*		*	*	*	*	7

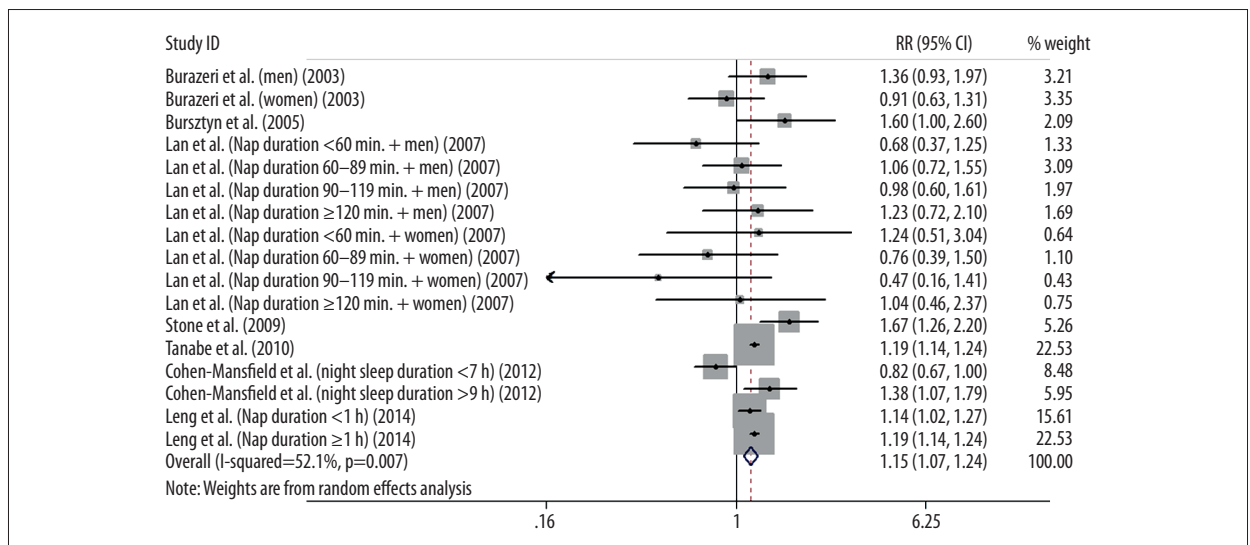


Figure 2. RR and 95% CI of all-cause mortality comparing daytime nappers to non-nappers in a random-effects model.

protective effect of afternoon siesta against coronary mortality. Naps longer than 30 min can cause sleep inertia and are usually not recommended [21]. These results indicated that daytime napping might have different impact on younger and elderly persons. However, we could not conduct subgroup analysis by age due to most of the subjects were elderly persons.

A more recently published study [22] suggested that daytime napping with duration >30 min was significantly and independently associated with all-cause mortality in men but not in

women. However, our subgroup analysis based on gender did not found gender-specific association between daytime napping and mortality. Therefore, the gender-specific association between daytime napping and mortality needs further study.

Although the biological mechanisms by which daytime napping results in a higher mortality risk are not completely elucidated, a possible explanation is that abrupt increase in blood pressure and heart rate upon awakening from a nap results in sympathetic nervous activation [23]. The morning has the highest risk

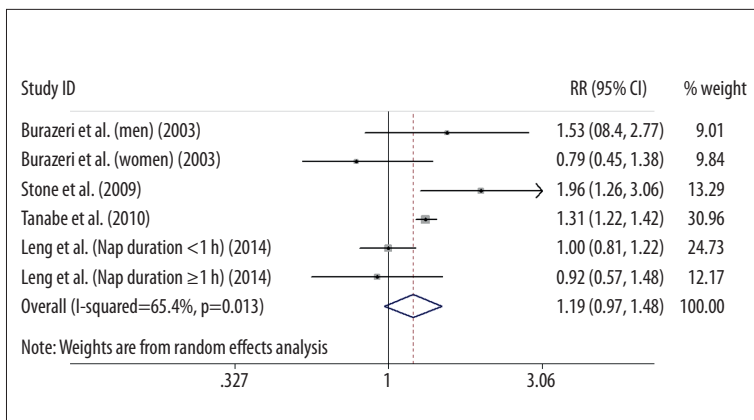


Figure 3. RR and 95% CI of cardiovascular mortality comparing daytime nappers to non-nappers in a random-effects model.

Supplemental Table 2. Subgroup analyses of self-reported daytime napping and risk of all-cause mortality.

Group	Number of studies	Event/total number	Pooled risk ratio	95% CI
Region				
Asia	2	10,981/70,208	1.12	1.01–1.26
No Asia	5	4,616/27,955	1.19	1.05–1.34
Follow-up duration				
≤11 years	3	3,665/13,039	1.08	0.89–1.32
>11 years	4	12,746/85,124	1.16	1.08–1.25
Sample size				
<5000	4	3,812/6,559	1.05	0.89–1.24
>5000	3	12,599/91,604	1.19	1.14–1.26
Nap duration				
<60 min	3	2,777/21,312	1.10	0.92–1.32
>60 min	3	2,777/21,312	1.15	1.04–1.27
Gender				
Men	3	6,676/30,347	1.15	1.09–1.21
Women	4	6,632/49,821	1.15	0.92–1.43

for cardiovascular events. Another explanation is that the prothrombotic effects after daytime napping may trigger thrombotic cardiovascular events [24]. Moreover, napping was also linked to depression [25,26] and obstructive sleep apnea (OSA) [27], cancer [28], Parkinson’s disease [29], and type 2 diabetes [30,31], all of which may increase risk of mortality. In addition, daytime napping might be a consequence of nighttime sleep disturbance, which was associated with greater risk of mortality [32].

Several potential limitations of this study should be addressed. First, a major limitation is the reliance on self-reported daytime napping. Data relating to daytime rest without sleep were unavailable. All the included studies measured napping by using subjective questionnaires, which are more prone to misclassification. However, self-reports are the primary methods for evaluating napping in our daily life. Second, duration of napping, working status, culture, educational background, climate, and age are the common confounding factors accounting for napping and mortality risk. However, the study did not adjust confounding variables in a consistent way. Lack of adjustment or

over-adjustment for these variables might lead to a slight overestimation or underestimation of the real risk estimate. Third, most of the subjects were older persons (age over 40 years), which limited generalizability to young populations. Moreover, a tendency to underreport napping habits was found in older persons [33], and this may result in underestimation of the relationship. Fourth, the information on nighttime sleep duration, as well as napping duration or times, is not sufficient. Long or short sleep duration are likely to increase the risk of mortality [34], and most of the included studies did not consider these potential factors.

Afternoon napping is common in many countries and is considered a healthy activity. A short nap during the day can aid the return of normal cellular immune function [35]. However, the protective effect of afternoon nap is yet to be proven in different populations. Daytime napping may reflect a low quality of nighttime sleep and might be a marker of undiagnosed health problems. Given the close link between OSA and mortality [36], daytime napping might be used as a surrogate measure of OSA. Therefore,

objective measures of sleep are needed to determine whether sleep apnea contributes to these relationships. Further detection of the possibility of OSA is warranted in these populations.

Conclusions

Self-reported daytime napping is a mild but statistically significant risk predictor for all-cause mortality but not for

cardiovascular mortality. However, whether the risk is attributable to excessive daytime sleepiness or daytime napping alone remains unclear. More well-designed prospective studies based on younger populations are required to determine whether daytime napping is an independent predictor for mortality.

Conflict of interest

None declared.

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