



Original Article

Sleep duration and total cancer mortality: a meta-analysis of prospective studies

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ABSTRACT

Objective: Epidemiological evidence suggests a possible association between sleep duration and cancer-related mortality, but the reported findings are inconsistent. We conducted a meta-analysis of prospective studies to evaluate the relationships between sleep duration and cancer mortality.

Methods: Potentially relevant studies were identified by searching PubMed and Embase databases in addition to manual searches of references of retrieved full publications. The summary relative risks (RRs) with 95% confidence intervals (CIs) were computed using a random-effect model. The meta-regression analyses were performed to explore any potential effect modifier.

Results: A total of 17 reports from 11 independent prospective studies were included in this meta-analysis. When comparing with reasonable sleep duration (mostly defined as 7 or 7–8 h), the summary RR for long sleep duration (mostly defined as ≥ 9 or ≥ 10 h) and short sleep duration (mostly defined as ≤ 6 or ≤ 5 h) was 1.11 (95% CI = 1.05–1.18) and 1.05 (95% CI = 0.99–1.11), respectively, with little evidence of heterogeneity. There was evidence of publication bias for the association of long sleep duration with cancer mortality, and the summary RR was slightly attenuated to be 1.10 (95% CI = 1.02–1.18) after using a statistical method to correct for the bias.

Conclusion: This meta-analysis of prospective studies suggests that long, not short sleep duration is associated with significantly increased risk of total cancer mortality.

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1. Introduction

Over the past two decades, the potential influences of sleep duration on health outcomes have received great interest. Collectively, evidence shows that both long and short sleep durations are associated with all-cause mortality and certain conditions such as cardiovascular diseases and type 2 diabetes [1–4]. The evidence with respect to the impacts of sleep duration on total cancer mortality has been less consistent. A 2009 meta-analysis [5] pooling data from published prospective studies showed that long sleep duration, but not short sleep duration, was associated with increased risk of cancer mortality. However, these results were based on only three studies, and may be of a limited statistical power. A number of large prospective studies [6–12] have been published since the 2009 meta-analysis, but their results are

inconsistent and inconclusive. To better understand the relationship between long and short sleep durations and risk of cancer mortality, we performed this meta-analysis of prospective studies. Since individual studies varied by study and population characteristics, we also conducted a meta-regression analysis to explore potential effect modifiers.

2. Methods

2.1. Literature search

We searched for potentially relevant literature in the databases of PubMed (from 1966 to December 2015) and Embase (from 1980 to December 2015) using the search strategy as follows: ((sleep duration) OR (sleep)) AND (cancer) AND ((mortality) OR (survival) OR (death)) AND ((cohort study) OR (follow-up study) OR (prospective study)). There was no language restriction imposed. In addition, the references of the obtained full reports and previous meta-analyses were also carefully checked for any further studies.

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2.2. Selection criteria

To be included, the studies had to meet the following criteria: (1) had a prospective study design, (2) had long or short sleep duration as the exposure of interest, (3) had cancer-related mortality as the outcome of interest, (4) used night sleep duration only, without insomnia or other sleep disorders reported; and (5) included the relative risks (RRs) with corresponding 95% confidence intervals (95% CIs). The studies were searched independently by two authors, and differences were solved by discussion and confirmed by another author.

2.3. Data extraction

We used a data-collecting form to extract the following information from each study, which included the following: first author's name, year of publication, study location, population age, cohort name, follow-up duration, numbers of participants and cancer death, definitions of long, short, and appropriate sleep durations, relative risks (RRs) and 95% confidence intervals (95% CIs) of cancer mortality associated with long or short sleep duration, and potential confounding factors adjusted for in the statistical models.

2.4. Statistical analysis

The most covariate-adjusted risk estimates were used in the meta-analysis. Men and women were considered independent reports among studies that reported sex-specific results. The pooled RRs with 95% CIs were obtained with a random-effect model [13]. Subgroup and meta-regression analyses were performed to explore the potential sources of heterogeneity according to geographic region, sex of participants, duration of follow-up, and definitions of long, short, and appropriate sleep durations. A sensitive analysis was conducted by excluding one study each turn. Heterogeneity was estimated and quantified by Q and I^2 statistics [14]. For the Q statistic, $p < 0.1$ was considered as statistically significant. For the I^2 statistic, the following cut-off points were used: $<30\%$ (little or no heterogeneity), $30\text{--}75\%$ (moderate heterogeneity), and $>75\%$ (high heterogeneity). Potential publication bias was investigated using both the Begg rank correlation test and Egger linear regression test [15,16]. In case of publication bias, the “trim-and-fill” method [17] was applied to correct such bias. All statistical analyses were performed using STATA software, version 11.0 (STATA Corp., College

Station, TX, USA). All p values were two-sided, and the level of significance was at <0.05 unless explicitly stated otherwise.

3. Results

3.1. Search results and study characteristics

The initial database and manual search identified 748 unique hits, of which 729 items were excluded after screening the titles and abstracts (Fig. 1). After reviewing the full texts, six reports were excluded because the outcome of interest was not cancer mortality. Also excluded were two publications that reported only the death rate of cancer [18,19], and one publication that did not distinguish between long and short sleep durations [20]. Finally, a total of 10 publications that contained 11 independent prospective cohort studies were included in this meta-analysis (two independent cohorts were reported in one publication [8]).

Two studies [8,21] among the 11 studies included only women, and one study [8] included only men; six studies [7,9,11,12,22,23] remained in which results were separated by sex, and two studies combined results for men and women [6,10]. Therefore, there were 17 individual reports in this meta-analysis. Three of the 11 studies were conducted in China, three studies in Japan, two studies in the United States, and the remaining three studies were in Korea, the United Kingdom, and Sweden, respectively. The included studies reported different definitions for appropriate, long, and short sleep durations, with the appropriate sleep duration defined as 7 h [8–11,21], 7–8 h [6,7,12,23], or 6–8 h per night [22]; long sleep duration was defined as ≥ 9 h [6,7,21,23], ≥ 10 h [8–12], or >8 h per night [22]; and short sleep duration was defined as <6 h [7,10,22,23], <5 h [6,9,21], <7 h [12], <4 h [11], or 4–5 h per night [8]. A total of 622,429 participants were included in these studies. The characteristics of the included studies are shown in Table 1.

3.2. Long sleep duration and cancer mortality

A total of 17 independent reports from 11 prospective studies were included in the meta-analysis of long sleep duration and total cancer mortality. Results of the meta-analysis showed that subjects with a long sleep duration had 11% increased risk of cancer mortality when compared with those with an appropriate sleep duration ($RR = 1.11$, 95% CI = 1.05–1.18), with little evidence of heterogeneity among studies ($p = 0.42$, $I^2 = 2.7\%$) (Fig. 2).

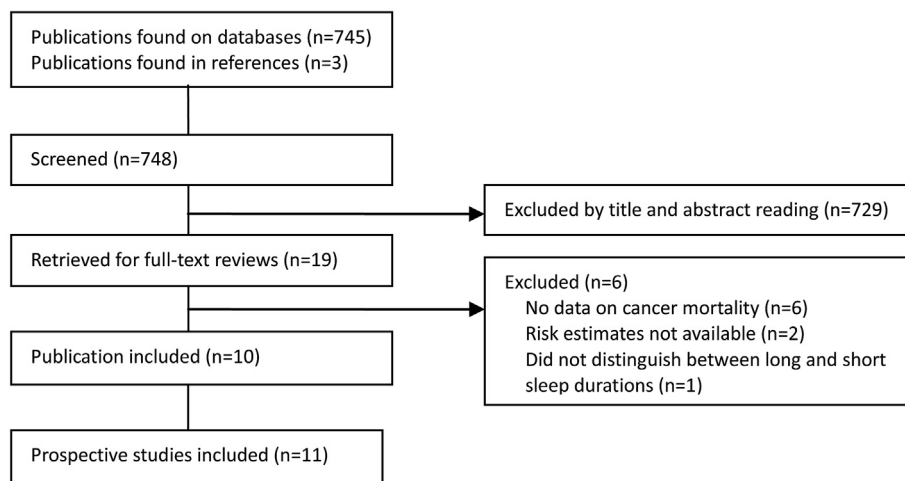


Fig. 1. Literature search for the meta-analysis.

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