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Sleep duration and risk of all-cause mortality: a systematic review and meta-analysis

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Abstract

Aims. To determine the association between the sleep duration and the risk of all-cause mortality in adults.
Methods. A search strategy was conducted in the MEDLINE, CENTRAL, EMBASE and LILACS databases. Searches were also conducted in other databases and unpublished literature. Cohort studies were included without language, time or setting restrictions. The risk of bias was evaluated with a modified Cochrane Collaboration's tool. An analysis of random effects was conducted. The primary outcome was all-cause mortality. The measure of the effect was the risk difference (RD) with a 95% confidence interval (CI). The planned comparisons were 7–9 h of sleep *v.* <7 h and the same reference *v.* >9 h.
Results. Thirty-nine studies were included in our qualitative analysis, regarding the quantitative analysis, 19 studies were included in <7 *v.* 7–9 h analysis, and 18 studies in the >9 *v.* 7–9 h. A low risk of bias was shown for most of the study items. The overall RD for all-cause mortality was 0.09 (95% CI 0.07–0.11) favouring the >9 h group compared with our reference. In contrast, no differences were found between the <7 h and the reference sleep duration groups (RD 0.00, 95% CI 0.00–0.01).
Conclusion. We found a probable association of long sleep duration and higher mortality; however, it could reflect an underlying systemic or neurological disease that cause sleep fragmentation, deterioration in quality and micro-awakenings.

Introduction

Although sleep and circadian rhythm are inherent to human body, in recent history, sleep problems have increased and it will keep this trend. The globalisation process and technological advances have led to a 24/7 society and the increasing night-time use of TV, internet and mobile phones prone to inadequate and interrupted sleep (Ferrie *et al.*, 2011). Historically, evidence have shown an association between sleep deprivation and/or fragmentation and bad learning capacity and academic performance (Curcio *et al.*, 2006), and also with public health issues like motor vehicle crashes with high economic impact (Durmer and Dinges, 2005; Pandi-Perumal *et al.*, 2006). All these findings have led medical society to try to establish the association between short sleep duration and medical entities, suggesting that it is associated with increased risk of stroke (Leng *et al.*, 2015), coronary heart disease (Cappuccio *et al.*, 2011), metabolic syndrome (Xi *et al.*, 2014), hypertension (Wang *et al.*, 2012), central adiposity (Sperry *et al.*, 2015), obesity (Wu *et al.*, 2014), type 2 diabetes mellitus (Shan *et al.*, 2015) and a rapid decline in renal function (McMullan *et al.*, 2016). However, short sleep duration is not the only factor related with them. Actually, recent evidence suggests that long sleep duration plays an important role as well, relating it with increased risk of stroke (Leng *et al.*, 2015), coronary heart disease (Cappuccio *et al.*, 2011), colorectal cancer (Lu *et al.*, 2013), type 2 diabetes mellitus (Gottlieb *et al.*, 2005; Shan *et al.*, 2015), impaired glucose tolerance (Gottlieb *et al.*, 2005) and even a cross-sectional observational study suggest that the altered (above or below the median of 7–8 h) usual sleep duration is associated with an increased prevalence of hypertension (Gottlieb *et al.*, 2006).

Additionally, sleep duration has been associated with mortality (Youngstedt and Kripke, 2004; Cappuccio *et al.*, 2010; Shen *et al.*, 2016). Youngstedt and Kripke warned about the U-shaped relationship between the sleep duration and the risk of death and furthermore exposed alternative explanations for this kind of association (Youngstedt and Kripke, 2004). Later this hypothesis was supported by a systematic review (SR) that indicated that both short sleep duration and long sleep duration are predictors of all-cause mortality among adults (Cappuccio *et al.*, 2010). More recently, in a meta-analysis (MA) from prospective cohort studies about this issue, the authors found a U-shaped relationship; therefore, they commented that 7 h/day of sleep duration should be recommended to prevent premature death among adults (Shen *et al.*, 2016).

Although there are multiple published studies, there is still a lack of high-quality evidence to establish this association as a real one. Furthermore, there are new studies that have not been

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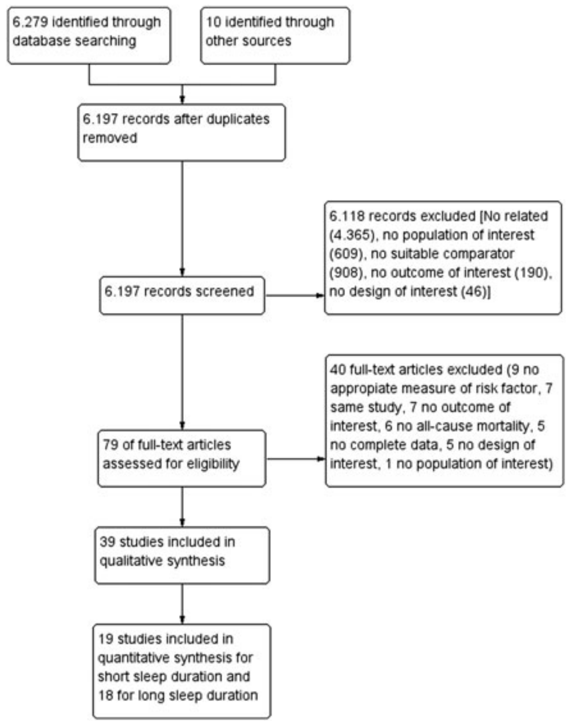

Fig. 1. Flow chart of included studies.

included in previous SR; therefore, we developed this study which aims to determine the association between the sleep duration and the risk of all-cause mortality in adults.

Methods

We performed this review according to the recommendations of the Cochrane Collaboration and following the PRISMA Statement. The PROSPERO registration number is CRD42017076461.

Eligibility criteria

We included both retrospective and prospective cohort studies, which included adults – no pregnant women. The primary outcome was all-cause mortality determined by each study. For all outcomes, studies should have at least 12 months duration for follow-up and the outcome. There were no setting or language restrictions.

Information sources

Literature search was conducted in accordance to recommended (Robinson, 2002). We used medical subject headings (MeSH), Emtree language, Decs and text words related to sleep duration and mortality. We searched MEDLINE (OVID), EMBASE, LILACS and the Cochrane Central Register of Controlled Trials (CENTRAL). To ensure literature saturation, we scanned references from relevant articles identified through the search, conferences, thesis databases, opengray, Google scholar and clinicaltrials.gov, among others. We contacted authors by e-mail in case of missing information.

Data collection

We reviewed each reference by title and abstract. Then we scanned full texts of relevant studies, applied pre-specified inclusion and exclusion criteria and extracted the data. Disagreements were resolved by consensus.

We independently extracted the following information from each article using a standardised form: study design, geographic location, authors names, title, objectives, inclusion and exclusion criteria, number of patients included, losses to follow-up, timing, definition of short, regular and long sleep duration, method to measure sleep duration, definitions of outcomes, outcomes and association measures, sleep duration and funding source.

Risk of bias

The assessment of the risk of bias for each study was made using a modified Cochrane Collaboration tool for assessing the risk of bias, which covers: selection of participants (selection bias), comparability between groups (selection bias), conflict of interest, confounding control, statistical methods, selective reporting (detection and information bias), assessment of the outcome, follow-up long enough and lost to follow-up. Two independent researchers judged about the possible risk of bias from extracted information, rated as 'high risk', 'low risk' or 'unclear risk'.

Data analysis/synthesis of results

The statistical analysis was performed using Review Manager 5.3 (RevMan® 5.3). For categorical outcomes, we reported information about risk differences (RD) with 95% confidence intervals (CI), and we pooled the information with a random-effect MA according to the heterogeneity expected. The results were reported in forest plots of the estimated effects of the included studies with a 95% CI. Heterogeneity was evaluated using the I^2 test. For the interpretation, it was determined that the values of 25, 50 and 75% in the I^2 test correspond to low, medium and high levels of heterogeneity, respectively.

Publication bias

An evaluation was conducted to identify reporting or publication bias using the funnel plot.

Sensitivity analysis

We performed sensitivity analysis extracting weighted studies and running the estimated effect to find differences.

Subgroup analysis

- Gender
- Intervals of sleep duration
- Short or long sleep duration

Results

A total of 6289 studies were found with the designed search strategies, with a total of 6197 after duplicates were removed. Finally, 39 studies were included in our SR; however, to perform an MA, we grouped data into three different groups – <7 h, 7–9 h (reference) and more than 9 h – due to the heterogeneity between studies. We excluded the studies that overlapped these intervals from the MA; thus, 19 studies were included in <7 *v.* 7–9 h MA, and 18 studies in the >9 *v.* 7–9 h MA (Fig. 1).

Table 1. Characteristics of included studies

Author	Cohort name	Country	Age	Gender	Follow-up	*N*
Pollak *et al.* (1990)		USA	65–98 y	M-F	3.5 y	1855
Rumble and Morgan (1992)	Nottingham Longitudinal Study of Activity and Ageing (NLSAA)	England	⩾65 y	M-F	5 y	567
Tsubono *et al.* (1993)	Japan Collaborative Cohort Study (JACC)	Japan	⩾40	M-F	4 y	4318 (1717M-2601F)
Ruigomez *et al.* (1995)	Health Interview Survey of Barcelona (HISB)	Spain	⩾65 y	M-F	5 y	989 (395M-594F)
Kojima *et al.* (2000)	Shirakawa Town	Japan	20–67 y	M-F	12 y	5322 (2438M-2884F)
Heslop *et al.* (2002)		Scotland	⩽65 y	M-F	25 y	3030 (2588M-442F)
Mallon *et al.* (2002)		Sweden	45–65 y	M-F	12 y	1870 (906M-964F)
Burazeri *et al.* (2003)	Kiryat Yovel Community Health Study (3rd round)	Israel	⩾50 y	M-F	9–11 y	1842 (841M-1001F)
Tamakoshi and Ohno (2004)	Japan Collaborative Cohort Study (JACC)	Japan	40–79 y	M-F	9.9 y	102 021 (42 784M-59 237 F)
Amagai (2004)	Jichi Medical School Cohort Study	Japan	19–93 y	M-F	9 y	11 325 (4419M-6906F)
Patel *et al.* (2004)	Nurses' Health Study	USA	30–55 y	F	16 y	82 969
Hublin *et al.* (2007)	Finnish Twin Cohort	Finland	⩾24 y	M-F	21 y	19 794 (9529M-10 265F)
Ferrie *et al.* (2007)	White Hall II	England	35–55	M-F	17.1 y	9781
Lan *et al.* (2007)	Survey of Health and Living Status of the Elderly in Taiwan	Taiwan	⩾64 y	M-F	8.4 y	2834 (1602M-1232F)
Gangwisch *et al.* (2008)	NHANES I	USA	32–86 y	M-F	8–10 y	9789
Suzuki *et al.* (2009)	Shizuoka Study	Japan	65–85	M-F	7 y	12 601(6423M-6178 F)
Vgontzas *et al.* (2010)	Penn State Cohort	USA	>20 y	M-F	14 y M and 10 y F	1741 (741M-1000 F)
Castro-Costa *et al.* (2011)	Bambui Health and Ageing Study (BHAS)	Brazil	>60 y	M-F	7.5 y	1512
Chien *et al.* (2010)	Chin-Shan Community Cardiovascular Cohort study	Taiwan	⩾35 y	M-F	15.9 y	3430
Mesas *et al.* (2010)		Spain	⩾60 y	M-F	8 y	3820
Kutner *et al.* (2013)	Comprehensive Dialysis Study	US	>18 y	M-F	5 y	1440
Rhee *et al.* (2012)	Seoul Male Cohort Study	South Korea	40–59 y	M	16 y	14 095
Kakizaki *et al.* (2013)	Ohsaki Cohort Study	Japan	40–79 y	M-F	10.8 y	49 256 (23 749M-25 507F)
Cohen-mansfield and Perach (2012)	Cross-Sectional and Longitudinal Aging Study (CALAS)	Israel	75–94 y	M-F	20 y	933
Chen *et al.* (2013)	Shih-Pai Sleep Study	Taiwan	>65	M-F	9 y	4064
Yeo *et al.* (2013)	Korean Multi-center Cancer Cohort (KMCC)	South Korea	>20	M-F	9.44 y	13 164 (5447M-7717F)
Kim *et al.* (2014)	Multiethnic Cohort Study	USA	45–75 y	M-F	12.9 y	135 685 (61 936M-73 749)
Li *et al.* (2013)	The SAKUCESS (Saku Cancer Etiology Surveillance) study	Japan	20–79 y	M-F	7 y	9455
Garde *et al.* (2014)	Copenhagen Male Study	Denmark	40–59 y	M	30 y	4941
Bellavia *et al.* (2014)	Cohort of Swedish Men and the Swedish Mammography Cohort.	Sweden	45–83 y	M-F	15 y	70 973
Magee *et al.* (2013)	The 45 and Up Study	Australia	⩾45 y	M-F	2.8 y	227 810
Jung *et al.* (2013)	Rancho Bernardo Study	USA	>60 y	M-F	19 y	2001 (889M-1112F)

(*Continued*)

Table 1. (*Continued.*)

Author	Cohort name	Country	Age	Gender	Follow-up	*N*
Xiao *et al.* (2014)	NIH-AARP Diet and Health Study	USA	51–72	M-F	14 y	239 896
Rod *et al.* (2014)	The White Hall II	England	35–55 y	M-F	22 y	9098 (6114M-2984F)
Zuurbier *et al.* (2014)	Rotterdam Study	The Netherlands	⩾45 y	M-F	7.3 y	1734
Kubota *et al.* (2015)	Japan Collaborative Cohort Study (JACC)	Japan	40–79 y	M-F	21 y	2914 (1674M-1240 F)
Hall *et al.* (2015)	Health, Aging, and Body Composition (Health ABC) study	USA	70–79 y	M-F	8.2 y	3013
Cai *et al.* (2015)	Shanghai Women's and Men's Health Studies	China	44–79 y M and 40–75 y F	M-F	14 y F and 8 y M	113 138(44 590M-68 548F)
Wang *et al.* (2016)	The Kailuan Study	China		M-F	3.98 y	95 903

y, years; M, male; F, female.

Included studies

Although our starting inclusion criterion was to include clinical trials additionally to cohort studies, none of them was found (Fig. 1). Thirty-nine studies were included in our SR; the reference for normal sleep duration was heterogeneous and the definition for short and long sleep duration varies between studies. Other characteristics were also heterogeneous, for instance included patients that vary from 567 to 135.685, follow-up durations going from 2.8 to 30 years and Africa was the only continent without representation in our study (Table 1). Furthermore, three studies excluded the deaths within 2 years after baseline (Tamakoshi and Ohno, 2004; Lan *et al.*, 2007; Castro-Costa *et al.*, 2011), and in these cases, these data were included; other study (Heslop *et al.*, 2002) made two measurements and reported the results for who did not change the sleep duration, and in this case, these data were included.

We excluded Gale and Martyn's study because the risk to measure was time in bed, and no sleep duration was reported (Gale and Martyn, 1998). Other studies were excluded because they did not report the sleep duration adequately (scales or short and long sleep duration pooled together) (Wingard, 1982; Wingard *et al.*, 1982; Martínez-Gómez *et al.*, 2013; Ding *et al.*, 2015; Stamatakis *et al.*, 2015).

Risk of bias

The risk of bias was assessed with a modified Cochrane Collaboration tool (explained above). Although the item for comparability between groups was warning, we have to remark the control they offered for confounding; besides a multivariate analysis in almost all the studies. The assessment of the outcome was graded as low risk in almost all the studies, since they used a good strategy to identify mortality within each population; furthermore, low risk was predominant in remaining items (Table 2).

Sleep duration and all-cause mortality

The results varied among studies, but most of them reported a higher mortality in long sleep duration groups, while short sleep duration was more controverted (Table 3). Tsubono *et al.* (1993) and Kubota *et al.* (2015) had the same cohort (Japan Collaborative Cohort Study), both showed the basic data; however, Kubota *et al.* (2015) had more participants and longer follow-up period; therefore, we excluded Tsubono *et al.*'s (1993) data from our MA. Additionally Ferrie *et al.* (2007) and Rod *et al.* (2014) also had the same cohort (The White Hall II), but in this case, Ferrie *et al.* (2007) did not show the basic data, thus this (Ferrie *et al.*, 2007) was the excluded study.

We found an overall RD of 0.09 (95% CI 0.07–0.11) (Table 4) (Fig. 2) favouring mortality in the >9 h group. In contrast, no differences were found between the <7 h and the reference sleep duration groups (RD 0.00, 95% CI 0.00–0.01) (Fig. 3). Similar outcomes were found in the subgroup gender analysis (Table 4).

Discussion

Summary of the main results

All-cause mortality

Previous SR and MA showed a U-shaped association between sleep duration and mortality (Cappuccio *et al.*, 2010; Shen *et al.*, 2016); however, in our study, we did not find a real association with short sleep duration. We might say that it was an unexpected finding but a really interesting one. Regarding previous SR, Cappuccio *et al.* in their MA (Cappuccio *et al.*, 2010) did not establish a well-defined parameter for short or normal sleep duration; thus, the comparison was made with many different definitions depending on each study; on the other hand, long sleep duration results were reproducible in our study. Shen *et al.* in a recent MA (Shen *et al.*, 2016) found an association with both short and long sleep duration, but for longer duration, the association is clearly stronger, and for short duration, the association might be questioned, since it may have occurred for overlapping hours. Therefore, we grouped the studies according to definitions, by exact hours of sleep to prevent overlapping.

Long sleep duration

It is notable that in spite of long sleep duration seems a predictor of mortality, causality is unlikely. We cannot establish if there is any condition that predisposes to greater sleep duration. Magee *et al.* (2013) found a higher mortality in the <6 and ⩾10 h durations in the entire cohort, but additionally they performed a healthy and unhealthy groups analysis. In the healthy group, no association was found, meaning that sleep duration would be

Table 2. Risk of bias assessment of included studies

Author	Selection of participants (selection bias)	Comparability between groups (selection bias)	Conflict of interest	Confounding control	Statistical methods	Selective reporting (information and detection bias)	Assessment of the outcome	Follow-up long enough (5 years)	Lost to follow-up (20%)
Pollak *et al.* (1990)	Low risk	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	High risk	Low risk
Rumbleand Morgan (1992)	Low risk	Unclear risk	Low risk	Low risk	High risk (intervals very wide)	Low risk	Unclear risk	Low risk	Low risk
Tsubono *et al.* (1993)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk
Ruigomez *et al.* (1995)	Low risk	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kojima *et al.* (2000)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Heslop *et al.* (2002)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mallon *et al.* (2002)	Low risk	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Burazeri *et al.* (2003)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Tamakoshi and Ohno (2004)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Amagai (2004)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Patel *et al.* (2004)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Hublin *et al.* (2007)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ferrie *et al.* (2007)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Lan *et al.* (2007)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Gangwisch *et al.* (2008)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Suzuki *et al.* (2009)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High Risk
Vgontzas *et al.* (2010)	Low risk	Unclear risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Castro-Costa *et al.* (2011)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Chien *et al.* (2010)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Mesas *et al.* (2010)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Kutner *et al.* (2013)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk
Rhee *et al.* (2012)	Low risk	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kakizaki *et al.* (2013)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Cohen-mansfield and Perach (2012)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Chen *et al.* (2013)	Low risk	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Yeo *et al.* (2013)	Low risk	High risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kim *et al.* (2014)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Li *et al.* (2013)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Garde *et al.* (2014)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bellavia *et al.* (2014)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Magee *et al.* (2013)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk
Jung *et al.* (2013)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Xiao *et al.* (2014)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Rod *et al.* (2014)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zuurbier *et al.* (2014)	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kubota *et al.* (2015)	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear risk
Hall *et al.* (2015)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Cai *et al.* (2015)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wang *et al.* (2016)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk

Table 3. Results within studies

Author	Reference group (h)	Duration used (h)	Outcome
Pollak *et al.* (1990)		0–4, 5, 6, 7, 8, ⩾9	No association in adjusted analysis
Rumble and Morgan (1992)	4–9.9	<4, 4–9.9, ⩾10	No association
Tsubono *et al.* (1993)	7–8	⩽6, 7–8, ⩾9	⩾9 h was associated with higher mortality
Ruigomez *et al.* (1995)	7–9	<7, 7–9, >9	No association in adjusted analysis
Kojima *et al.* (2000)	7–8.9	<7, 7–8.9, 9–9.9, ⩾10	Short sleep duration was associated with higher mortality in males
Heslop *et al.* (2002)	7–8	<7, 7–8, >8	No association in fully adjusted analysis
Mallon *et al.* (2002)	6–8	<6, 6–8, >8	>8 h was associated with higher mortality
Burazeri *et al.* (2003)	<6	<6, 6–8, >8	>8 h was associated with higher mortality in males
Tamakoshi and Ohno (2004)	7	⩽4, 5, 6, 7, 8, 9, ⩾10	⩾8 h was associated with higher mortality in males and females; ⩽4 h in females
Amagai (2004)	7–7.9	<6, 6–6.9, 7–7.9, 8–8.9, ⩾9	<6 h was associated with higher mortality in males
Patel *et al.* (2004)	7	⩽5, 6, 7, 8, ⩾9	⩾8 h was associated with higher mortality
Hublin *et al.* (2007)	7–8	<7, 7–8, >8	Short and long sleep duration was associated with higher mortality
Ferrie *et al.* (2007)	7	⩽5, 6, 7, 8, ⩾9	No association in the phase 1; in phase 3 ⩾9 h was associated with higher mortality
Lan *et al.* (2007)	7–7.9	<7, 7–7.9, 8–8.9, 9–9.9 ⩾10	⩾10 h was associated with higher mortality in males; ⩾8 h in females
Gangwisch *et al.* (2008)	7	⩽5, 6, 7, 8, ⩾9	⩾8 h was associated with higher mortality
Suzuki *et al.* (2009)	7	⩽5, 6, 7, 8, 9, ⩾10	⩾8 h was associated with higher mortality in general population and males; ⩾10 h in females
Vgontzas *et al.* (2010)	⩾6. No insomnia	<6 and ⩾6. Insomnia and no insomnia	<6 h with insomnia is associated with higher mortality
Castro-Costa *et al.* (2011)	7–7.9	<6, 6–6.9, 7–7.9, 8–8.9, ⩾9	⩾8 h was associated with higher mortality
Chien *et al.* (2010)	7	⩽5, 6, 7, 8, ⩾9	⩾9 h was associated with higher mortality
Mesas *et al.* (2010)	7	⩽5, 6, 7, 8, 9, 10, ⩾11	⩽5 and ⩾8 h were associated with higher mortality
Kutner *et al.* (2013)	6–7	<6, 6–7, 7–9, >9	>9 h was associated with higher mortality
Rhee *et al.* (2012)	⩾8	⩽5, 6–7, ⩾8	⩽5 h was associated with higher mortality
Kakizaki *et al.* (2013)	7	⩽6, 7, 8, 9, ⩾10	⩾8 h was associated with higher mortality
Cohen-mansfield and Perach (2012)	7–9	<7, 7–9, >9	>9 h was associated with higher mortality
Chen *et al.* (2013)	7	⩽4, 5, 6, 7, 8, ⩾9	⩾8 h was associated with higher mortality
Yeo *et al.* (2013)	7	⩽5, 6, 7, 8, 9, ⩾10	⩽5 and ⩾9 h were associated with higher mortality
Kim *et al.* (2014)	7	⩽5, 6, 7, 8, ⩾9	⩽5 and ⩾8 h were associated with higher mortality in males; ⩽5 and ⩾9 h in females
Li *et al.* (2013)	7	⩽5, 6, 7, 8, ⩾9	⩾9 h was associated with higher mortality in males and females
Garde *et al.* (2014)	6–7	<6, 6–7, ⩾8	No association in fully adjusted analysis
Bellavia *et al.* (2014)	6.6–7.4	<6, 6–6.5, 6.6–7.4, 7.5–8, >8	⩽6.5 and >8 h were associated with higher mortality
Magee *et al.* (2013)	7	<6, 6, 7, 8, 9, ⩾10	<6 h and ⩾10 h were associated with higher mortality
Jung *et al.* (2013)	7–7.9	<6, 6–6.9, 7–7.9, 8–8.9, ⩾9	⩾9 h was associated with higher mortality in females
Xiao *et al.* (2014)	7–8	<5, 5–6, 7–8, ⩾9	Short and long sleep duration was associated with higher mortality
Rod *et al.* (2014)	7	⩽5, 6, 7, 8, ⩾9	6 h was associated with higher mortality, but ⩽5 h was not
Zuurbier *et al.* (2014)	6–7.5	<6, 6–7.5, >7.5	No association in fully adjusted analysis
Kubota *et al.* (2015)	7	⩽5, 6, 7, 8, ⩾9	⩽5 and ⩾9 h were associated with higher mortality in males; in females just ⩾9 h
Hall *et al.* (2015)	7	<6, 6, 7, 8, >8	No association in fully adjusted analysis
Cai *et al.* (2015)	7	4–5, 6, 7, 8, 9, ⩾10	⩽5 and ⩾8 h were associated with higher mortality in females; in males ⩾9 h
Wang *et al.* (2016)	7	⩽5, 6, 7, 8, ⩾9	⩽5 and ⩾9 h were associated with higher mortality

h, hours.

Table 4. Subgroup analysis

Group	Sleep duration					
	<4 h	<5 h	<6 h	<7 h	7–9 h	>9 h
General mortality	0.05 (−0.04, 0.13)	0.04 (0.02, 0.05)*	0.01 (0.00, 0.01)	0.00 (0.00, 0.01)	Ref	0.09 (0.07, 0.11)*
Male		0.00 (−0.09, 0.09)	−0.01 (−0.06, 0.05)	−0.01 (−0.04, 0.02)	Ref	0.07 (0.01, 0.12)*
Female		−0.01 (−0.06, 0.04)	−0.01 (−0.03, 0.02)	−0.01 (−0.02, 0.00)	Ref	0.08 (0.03, 0.12)*

h, hours; Ref, reference.
*Statistically significant.

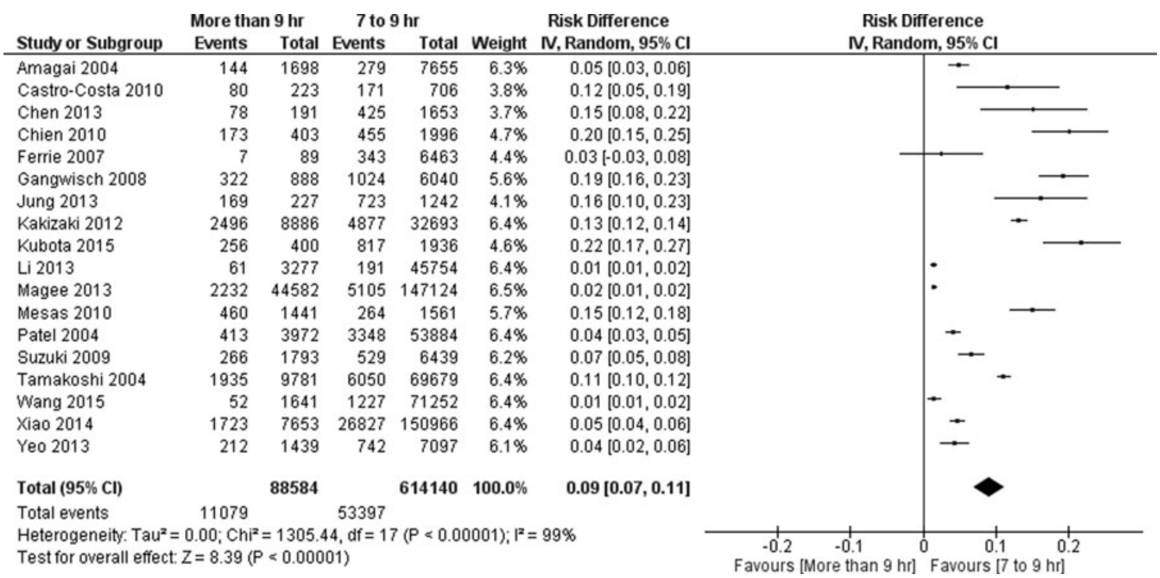

Fig. 2. Meta-analysis of included studies for long sleep duration. Outcome: mortality.

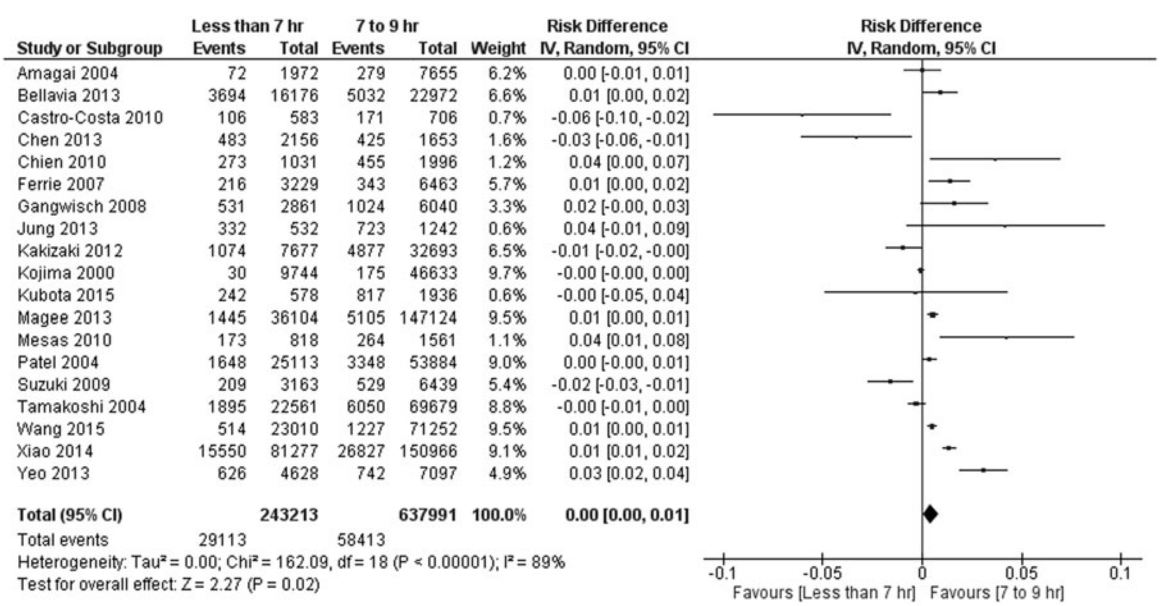

Fig. 3. Meta-analysis of included studies for short sleep duration. Outcome: mortality.

influenced by other conditions, which are the real reasons of higher mortality; however, other studies found association regardless of health status (Patel *et al*., 2004; Mesas *et al*., 2010). It is also possible that in this study, long sleep duration group has a greater number of old people; however, most of included studies in our analysis had adjusted analysis with a large number of variables

– including age – and association was more consistent with this group. Therefore, these results suggested that long sleep duration should be an independent predictor of all-cause mortality.

The explanations to this association are still in theoretical field. Proposed mechanisms for mortality associated with long sleep include (Grandner and Drummond, 2007; Shen *et al*., 2016): (1) long sleep is linked to increased sleep fragmentation that is associated with a number of negative health outcomes; (2) long sleep is associated with feelings of fatigue and lethargy that may decrease resistance to stress and disease; (3) changes in cytokine levels associated with long sleep increase mortality risk; (4) long sleepers experience a shorter photoperiod that could increase the risk of death in mammalian species; (5) a lack of physiological challenge with long sleep decrease longevity; (6) underlying disease processes mediate the relationship between long sleep and mortality.

Some patients with neurologic and/or systemic alterations, which modify the quality of dream, could compensate with an increase in total sleep duration, being a marker of disease and, indirectly at least from a theoretical point of view, of mortality.

Short sleep duration

Alterations in the circadian cycle including sleep restriction have been documented in various mammalian and non-mammalian animal models as a risk factor for mortality (Snyder *et al*., 2013).

Sleep restriction has been associated with different metabolic alterations. The reduction of total sleep duration increases blood pressure, induces insulin resistance and is associated with weight gain and obesity (Grandner *et al*., 2014). Consequently, sleep restriction is a recognised risk factor for cerebrovascular disease, an important cause of mortality (Eguchi *et al*., 2008). Sleep restriction has also been associated with dysfunction of the immune system, negative nitrogen balance and protein catabolism (Friese, 2008). In addition, chronic sleep deprivation is fatal in humans, as is the case in patients suffering from fatal familial insomnia, a degenerative brain disorder that results in death between 6 and 24 months from the onset (Manetto *et al*., 1992). In this study, no increased risk was identified in the group of <7 h of sleep, with boundary hours to 7 being unlikely to represent a risk and to be part of the variability of normal sleep time in the general healthy population. The observed effect of increased risk of mortality with sleep deprivation is best identified with lower total sleep time (<5 h). However, with <4 h of sleep, there are no differences, probably in association with the low number of studies.

Strengths and limitations

The main strength of our study was the well-defined comparison groups. Previous studies used the particular definition from each study to determine the association between sleep duration and mortality; however, we have noticed that many patients were lost to analysis since they were in groups that overlapped with our definition, or – in some studies – the data were shown with measures of association, and the number of patients was not provided. Although all the studies were cohorts, it is unlikely that clinical trials could be performed on this topic due to ethic and methodological issues. Additionally, we suggest that more studies must be performed to evaluate sleep quality, sleep disturbances and other dimensions because sleep duration is just one of sleep-related variables and perhaps molecular studies would be important trying to explain this outcome and the association with mortality.

Conclusion

According to the results, we found a probable association of long sleep duration and higher mortality; however, it could reflect an underlying systemic or neurological disease that causes sleep fragmentation, deterioration in quality and micro-awakenings. We recommend further high-quality studies to establish a well-defined association between sleep duration and mortality since we found many gaps in the literature.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S2045796018000379.

Data. Data have not been published. The authors could share it if anybody requests it.

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Conflict of interest. None.

Ethical standards. This systematic review and meta-analysis accomplishes all the ethics requirements according to Helsinki declaration and all international statements.

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