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CLINICAL REVIEW

Long sleep duration and health outcomes: A systematic review, meta-analysis and meta-regression

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SUMMARY

We examined the dose–response relationship between long sleep duration and health outcomes including mortality and the incidence of diabetes mellitus, hypertension, cardiovascular diseases, stroke, coronary heart diseases, obesity, depression and dyslipidemia. We collected data from 5,134,036 participants from 137 prospective cohort studies. For the independent variable, we categorized participants at baseline as having long sleep duration or normal sleep duration. Risk ratios (RRs) for mortality and incident health conditions during follow-up were calculated through meta-analyses of adjusted data from individual studies. Meta-regression analyses were performed to investigate the association between each outcome and specific thresholds of long sleep. Long sleep was significantly associated with mortality (RR, 1.39; 95% CI, 1.31–1.47), incident diabetes mellitus (1.26, 1.11–1.43), cardiovascular disease (1.25, 1.14–1.37), stroke (1.46, 1.26–1.69), coronary heart disease (1.24, 1.13–1.37), and obesity (1.08, 1.02–1.15). Long sleep was not significantly related to incident hypertension (1.01, 0.95–1.07). Insufficient data were available for depression and dyslipidemia. Meta-regression analyses found statistically significant linear associations between longer sleep duration and increased mortality and incident cardiovascular disease. Future studies should address whether the relationship between long sleep and health outcomes is causal and modifiable.

Introduction

Short and long sleep duration have been associated with a range of adverse health outcomes. The relationship between short sleep duration and health outcomes has been examined more closely. A causal relationship between short sleep duration and adverse health outcomes is supported by meta-analyses of epidemiological and cohort data [1,2], and by laboratory studies of experimental sleep restriction and sleep deprivation [3,4]. Fewer studies have addressed the relationship between long sleep duration and health outcomes, despite the prevalence of long sleep. Long sleep duration, defined more than 9 h of sleep, is prevalent in several developed countries, including Australia (an adjusted proportion of 33% in 2006), Finland (38% in 1999), Germany (40% in 2001), the Netherlands (25.7% in 2005), Sweden (30% in 2000), the U.K. (26% in 2005) and the U.S. (38% in 2007), according to a study using a data from time use survey [5]. A recent survey on behavioral risk factors conducted in the U.S. revealed that approximately 8% of adult respondents reported sleeping nine or longer hours [6].

Several systematic reviews have shown that long sleep duration is associated with important health outcomes including not only mortality [7–10] but also cardiovascular diseases [11], stroke [12,13], and diabetes mellitus [14,15]. However, because these reviews utilized different methodologies, we conducted a systematic review using the same methodology across all health outcomes.

Abbreviations: CER, control event rate; CI, confidence interval; HR, hazard ratio; MOOSE, meta-analysis of observational studies in epidemiology; NOS, Newcastle–Ottawa scale; OR, odds ratio; PRISMA, preferred reporting items for systematic reviews and meta-analyses; RR, risk ratio.

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This approach may allow us to consider the magnitude of long sleep duration effects on different health outcomes.

We have previously examined the association between short sleep duration and important health outcomes, and observed significant associations with outcomes including mortality (risk ratio (RR), 1.12; 95% CI, 1.08–1.16), diabetes mellitus (1.37, 1.22–1.53), hypertension (1.17, 1.09–1.26), cardiovascular diseases (1.16, 1.10–1.23), coronary heart diseases (1.26, 1.15–1.38), and obesity (1.38, 1.25–1.53) [16]. In the present study, we conducted a systematic review, meta-analyses and meta-regression to examine whether long sleep duration is associated with adverse health outcomes using the same methodology. Our method also allowed us to explore the specific sleep duration that is associated with these adverse health outcomes.

Methods

As described in our previous study on short sleep duration [16], we performed the study in accordance with PRISMA (preferred reporting items for systematic reviews and meta-analyses) [17] and MOOSE (meta-analysis of observational studies in epidemiology) [18] guidelines; see Appendices S5 and S6 in Supplementary material for PRISMA and MOOSE checklists.

Two independent researchers (OI and MJ) separately assessed the eligibility, extracted data, and checked the quality of the included studies. Any disagreements were resolved through discussion between these two, with adjudication by a third reviewer (NW) if disagreements persisted.

Data sources and searches

The studies were initially identified on October 17, 2013, through a search of PubMed, PsycINFO, CINAHL and Embase using pre-specified search terms (Appendices S1–S4). The review was not limited to English-language articles. We also hand-searched major medical journals, conference proceedings, and reference lists of included studies and previous systematic reviews for published, unpublished, and ongoing studies. We conducted a search of PubMed using the same search strategy on October 9, 2014 and on May 6, 2016, to identify new studies published during the review process.

Study selection

We included studies that compared individuals with long and "normal" sleep duration on outcomes of mortality and incident health outcomes. All studies included long-term follow-up, used a prospective cohort or randomized controlled trial design, and were conducted in community settings. We limited studies to those with a minimum follow-up duration of 1 y from baseline, and a minimum of 20 participants. Studies were excluded if most participants were aged 20 y or less at baseline, or if participants had been diagnosed with the health outcome at baseline. We also excluded studies that were conducted in inpatient settings and those that involved pharmacological interventions.

The eligibility of each study for inclusion was checked at two stages: 1) review of the title and abstract and 2) review of the full text.

Data extraction and quality assessment

Definition of long duration

Long sleep duration was defined in one of two ways for each paper. For some papers, long sleep duration was defined according to the criteria established by that source paper, given that sleep duration varies among cultures and ethnicities [19,20]. For papers that did not establish a criterion, long sleep was defined as the longest sleep duration range reported for participants in the original article. Durations of sleep in the definition of long sleep were incorporated into subgroup analyses and meta-regression as mediators (see below). When both a self-report (e.g., sleep diary) and objective (e.g., actigraphy or polysomnography) sleep duration were reported, we selected the former as the independent variable. Although self-report may capture a different amount of sleep per night than actigraphy [21] or polysomnography [22], objective measures are less commonly utilized in community settings, making self-report measures more widely applicable. When both sleep duration per night and per 24 h (i.e., including daytime naps) were reported, we selected the former.

The duration of normal sleep was also defined based on each source paper, or defined as the reference range for participants in the original article.

Outcome measures

Outcome measures included mortality and incidence of adverse health outcomes, specifically diabetes mellitus, hypertension, dyslipidemia (hypo or hyperlipidemia), cardiovascular diseases (including events in the heart and brain), coronary heart diseases, stroke, obesity, and depression. When a formal diagnosis was not provided, a surrogate outcome (e.g., coronary artery calcification instead of a diagnosis of coronary artery disease, or a self-report of diabetes mellitus without evidence of formal diagnosis) was included in the primary analyses, but a sensitivity analysis was also conducted (see below).

Assessment of bias

We employed the Newcastle–Ottawa scale (NOS) [23] to assess the studies' quality. The instrument has three broad categories (patient selection, four criteria; comparability of study groups, one criterion; and assessment of the outcome, three criteria). For the comparability criteria, we allotted two stars according to the depth of statistical adjustment for risk factors in the original studies (e.g., one star for age, sex, and race only; two stars for further factors). Therefore, a study could have a maximum quality rating of nine stars. Although previous meta-analyses [24,25] deemed study quality as high with five or more stars on the NOS criteria, we set a threshold of eight or more stars, to focus on very high quality studies.

We defined adequate follow-up for each disorder in terms of duration and % attrition (i.e., 3 y and 10% attrition for all-cause mortality, cardiovascular diseases, and coronary heart disease; and 2 y and 20% attrition for diabetes mellitus, hypertension, dyslipidemia, obesity, and depression).

Data synthesis and analysis

We analyzed data descriptively and conducted a meta-analysis for each health outcome. In the meta-analysis, we calculated risk ratios (RRs) by pooling adjusted RRs between long and normal sleep provided by the original studies, using a random effects model. If a study provided a point estimate and a p-value but not confidence intervals of RRs, the intervals were obtained using a statistical method with log transformations of the estimate [26]. If hazard ratios (HRs) were reported for a study but RRs were not, the HRs were regarded as RRs. Among studies where odds ratios (ORs) were provided but not RRs, we calculated RRs by using the ORs and control event rates (CERs) in normal duration sleepers reported in the original studies. For studies in which neither RRs nor CERs were reported, and only ORs were provided, CERs were borrowed from a study whose characteristics were similar. For studies in which RRs were provided for subgroups separately (e.g., male and female),

data from subgroups were combined using a fixed-effect meta-analysis.

Statistical heterogeneity between studies was investigated using the I^2 statistic [27], assuming an I^2 of 75% or greater to be an important level of inconsistency, as employed by a previous review [28]. To assess publication bias, we used a funnel plot and Egger's test for all primary outcomes [29]. We used the "trim and fill" method to adjust the funnel plot, then recalculated results [30].

Because subgroup analyses should be interpreted with caution [31], we planned a priori to limit our subgroup analyses to a small number of baseline characteristics such as age and sex (i.e., between 20 and 65 y, or 65 y or more; male, or female).

Sensitivity analyses were planned a priori for the primary analyses set by: 1) excluding studies with surrogate outcomes; 2) limiting studies to those in which sleep duration was reported per night; 3) limiting analyses to studies with eight or more stars in the NOS; 4) limiting studies to those with 10 or more y of follow-up; and 5) excluding studies in which CERs from other studies were used to calculate RRs.

In order to explore possible mediation by the definition of long sleep, additional subgroup analyses were conducted by clustering studies according to the definition of long sleep (e.g., more than 9 h or more than 10 h). When studies were clustered into three or more levels of sleep duration for each outcome, meta-regression analyses were also performed. These analyses examined linear associations between sleep duration and the outcome of interest, using a random-effects model and illustrating the regression line and its 95% prediction intervals.

A p-value of less than 0.05 was chosen to test null hypotheses, despite multiple comparisons, in order to avoid type II over type I errors. For all outcomes, 95% confidence intervals (CIs) were calculated. The data were analyzed using the Comprehensive Meta-Analysis Software (Version 3) [32].

Results

Search results

The initial electronic search yielded 3580 articles, and an additional database search identified 182 studies on October 9, 2014 and 388 on May 6, 2016. In total, 2521 studies remained after removing duplicate articles. A hand-search did not identify any studies that had not been included in the electronic search (Fig. 1). At the first and second eligibility check stages, two independent researchers identified 277 articles and 95 articles, respectively.

Characteristics of included studies

All of the 95 included studies were prospective cohort studies. From these, 137 datasets for nine outcomes (N = 5,134,036) were collected. Most studies were conducted in developed countries (see Table 1 and Tables S1–S9 in Supplementary material). The number of participants in each dataset ranged from 276 to 392,164; the duration of follow-up was from 1 to 34 y; and the total NOS scores ranged from five to nine. Although the definition of long sleep varied among studies, most defined long sleep as greater than 8 or 9 h.

We were unable to pool data from six datasets in meta-analyses because no usable data for meta-analyses were provided (Table S10). The number of datasets included in the meta-analyses for each outcome varied from 8 (hypertension) to 36 (mortality). Table 1 shows the characteristics of studies included for the mortality outcome.

Effect estimates of long sleep compared to normal sleep from meta-analyses

Primary analyses

Compared with normal sleep duration, long sleep duration was associated with a statistically significant increase in all-cause mortality, with an RR of 1.39 (95% CI = 1.31–1.47, P < 0.001, I^2 = 83%, N of datasets = 36; Fig. 2). Qualitatively similar significant results were obtained for incident diabetes mellitus (RR = 1.26, 95% CI = 1.11–1.43, P < 0.001, I^2 = 63%, N = 16), cardiovascular disease (RR = 1.25, 95% CI = 1.14–1.36, P < 0.001, I^2 = 81%, N = 25), stroke (RR = 1.46, 95% CI = 1.26–1.69, P < 0.005, I^2 = 71%, N = 14), coronary heart disease (RR = 1.24, 95% CI = 1.13–1.37, P = 0.003, I^2 = 54%, N = 19), and obesity (RR = 1.08, 95% CI = 1.02–1.15, P = 0.010, I^2 = 0%, N = 13) (Fig. 3). Long sleep duration was not associated with a statistically significant increase in incident hypertension compared to normal sleep duration (RR = 1.01, 95% CI = 0.95–1.07, P = 0.309, N = 8). Substantial heterogeneity between datasets was observed in mortality and cardiovascular disease outcomes. Only one study each was identified for depression and dyslipidemia outcomes, and RRs were not provided in the source studies.

Possible publication bias for primary analyses

No significant publication bias was observed for any outcome in the funnel plots or results from Egger's test (see Figs. S2, S11, S22, S32, S42, S52, and S63 in Supplemental material).

Subgroup analyses for age groups

Subgroup analyses were conducted for participants aged ≥65 y or <65 y at baseline (Fig. 3). Compared to normal sleep duration, long sleep duration was associated with a significant increase in the incidence of cardiovascular disease and coronary heart disease among those ≥65 y, but not among those <65 y. On the other hand, long sleep duration was associated with a significant increase in incident obesity only among participants <65 y, and not among those ≥65 y.

Subgroup analyses for sex

In comparison with normal sleep duration, long sleep duration was associated with a significant increase in mortality and incident diabetes, cardiovascular disease, stroke, and coronary heart disease for both men and women. Long sleep duration was associated with a significant increase in incident obesity only among female (Fig. 3).

Sensitivity analyses

Most sensitivity analyses showed qualitatively similar results to those in the primary analyses (Fig. 3). Analyses limited to high quality studies based on the NOS (>8 stars) and to studies with follow-up greater than 10 y did not show statistically significant findings for incident diabetes (High-quality studies: RR = 1.13, 0.94–1.35, P = 0.191; Long follow-up studies: 1.97, 0.96–4.05, P = 0.064), or incident obesity (High-quality studies: RR 0.94, 0.40–2.24, P = 0.896; Long follow-up studies: 1.04, 0.95–1.13, P = 0.441).

Subgroup analyses and meta-regression for specific values of long sleep duration

Subgroup analyses for specific values of long sleep duration were conducted for outcomes other than depression and dyslipidemia (Fig. 4). In comparison with normal sleep duration, long sleep duration defined as >8 h was associated with a significant increase in mortality, stroke, and coronary heart disease; long sleep defined as >9 h was associated with an increase in incident

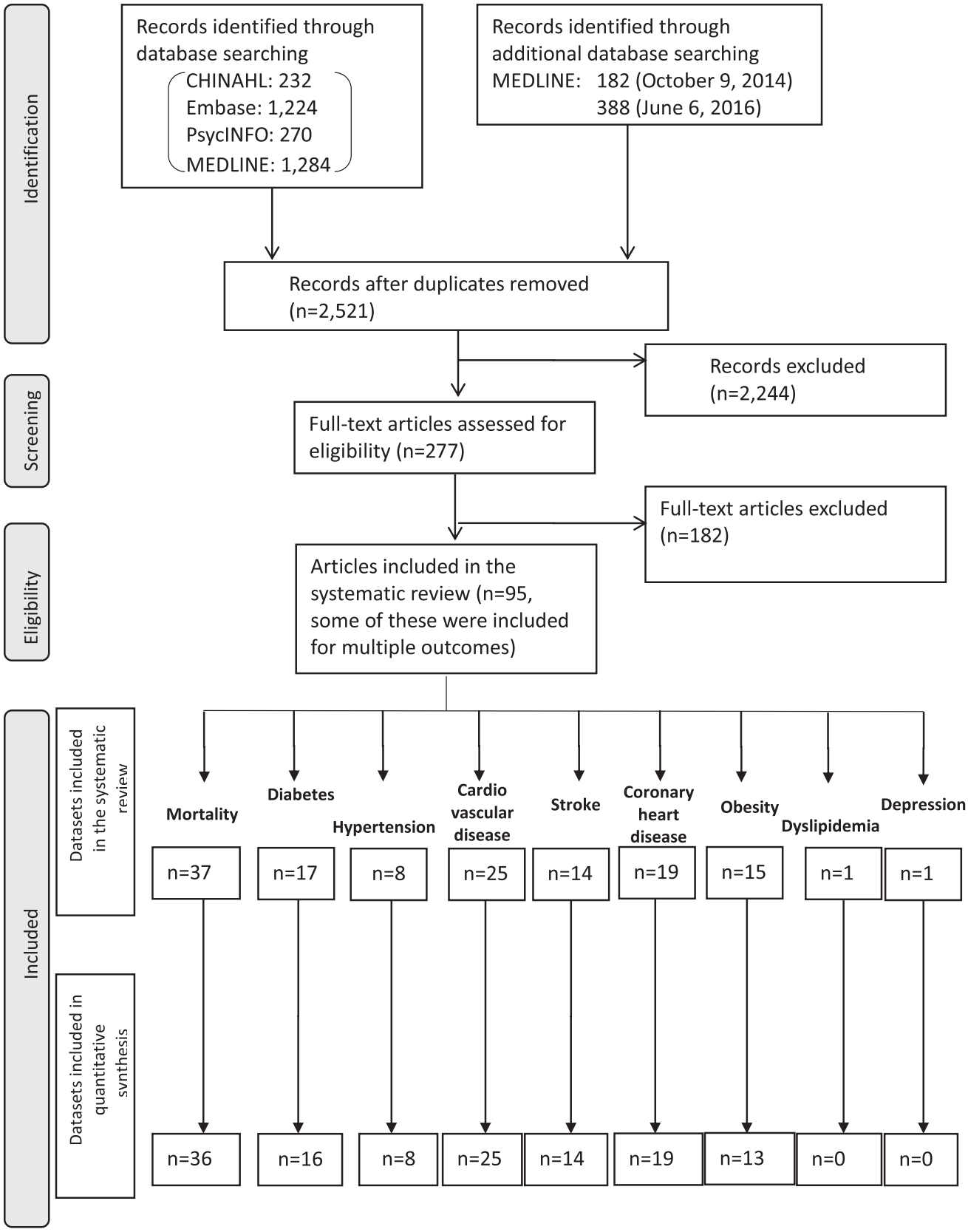


Fig. 1. Flowchart for the included studies. An arrow indicates that the upper limit of the 95% CI is over the scale described here.

Table 1
Characteristics of studies for mortality outcome.

Study	Sample size	Male%	Mean age ± SD (range) in years at baseline	Years of follow up mean ± SD	Definition of normal sleep duration (h)	Definition of long sleep duration (h)	Newcastle–Ottawa Scale: Selection/Comparability/Outcome
Tsubono 1993 [53]	4318	39.8	61.4 (≥40)	4	7–8/night	≥9/night	★★☆★/★★/★★★
Kojima 2000 [54]	5322	45.8	Male: 46.9 (20–67), Female: 47.7 (20–67)	11.9	7.0–8.9/night	≥10/night	☆★☆★/★★/★★★
Seki 2001 [55]	1065	41.3	65.3 ± 3.6 (60–74)	7.5	7/d	≥9/d	★★☆★/★★/★★★
Heslop 2002 [56]	1st screening: 7028 2nd screening: 3030	1st screening: 85.7 2nd screening: 85.4	Male: (≤65), Female; (≤60)	25	7–8/d	>8/d	★★☆★/★★/★★★
Mallon 2002 [57]	1870	48.4	56 (45–65)	12	6–8/night	>8/night	★★☆★/★☆/★★★
Burazeri 2003 [58]	1842	45.7	Male: median 64 (≥50), Female: median 63 (≥50)	9–11	6–8/night	>8/night	★★☆★/★★/★★★
Goto 2003 [59]	724	34.7	Male: median 73 (65–97), Female: median 74 (65–97)	12	6–7/d	>7/d	★★★★/★★/★★★
Amagai 2004 [60]	11,325	39.0	55.1 (19–93)	8.2 ± 1.5	7.0–7.9/night	≥9/night	★★★★/★★/★★★
Patel 2004 [61]	82,969	0.0	53.4 (40–65)	14	7/d	≥9/d	☆★☆★/★★/★★★
Tamakoshi 2004 [62]	104,010	42.2	56.6 (40–79)	9.9	7/d	≥10/d	★★☆☆/★★/★★★
Ferrie 2007 [63]	Phase 1: 9781 Phase3: 7729	NS	(35–55)	Phase 1: 17.1 Phase 3: 11.8	7/night	≥9/night	☆★☆★/★★/★★★
Lan 2007 [64]	3079	56.8	Male: 71.3 (≥64), Female: 71.9 (≥64)	8.4 ± 3.3	7–7.9/night	≥10/night	★★★★/★★/★★★
Gangwisch 2008 [65]	9789	37.2	Male; 45.0 (32–59), Female; 73.0 (60–86)	≤8, ≤10	7/night	≥9/night	★★★★/★★/★★★
Ikehara, 2009 [66]	98,634	42.1	Male; 58.8 (40–79), Female; 60.2 (40–79)	Median 14.3	7/d	≥10/d	★★☆★/★★/★★★
Stone 2009 [67]	8101	0.0	77.0 (≥69)	6.9	6–8/night	>8/night	★★★★/★★/★★★
Suzuki 2009 [68]	12,601	51.1	74.1 ± 5.4 (65–85)	5.3	7/d	≥10/d	☆★☆★/★★/★★★
Chien 2010 [69]	3430	47.3	(≥35)	15.9 (13.1–16.9)	7/d	≥9/d	★★☆★/★★/★★★
Mesas 2010 [70]	3820	43.8	71.8 ± 7.9 (≥60)	6.8	7/d	≥11/d	★★☆★/★★/★★★
Castro-costa 2011 [71]	1512	38.3	68.9 ± 7.1 (63–75)	7.5 Median: 8.9	7–8/night	≥9/night	★★★★/★★/★★★
Kripke 2011 [72]	434	0.0	67.6 ± 7.9 (50–81)	10.5	5–6.5/d	>6.5/d	★★★★/☆☆/★★★
Kronholm 2011 [73]	23,290	48.8	(25–64)	29–34	7–8/night	≥10/night	★★☆★/★★/★★★
Cohen-Mansfield 2012 [74]	1166	55.5	83.4 ± 5.3 (75–94)	20	7–9/night	>9/night	★★☆★/★★/★★★
Chen 2013 [75]	4064	55.8	73.8 ± 5.7 (≥65)	9	7/night	≥9/night	★★★★/★★/★★★
Garde 2013 [76]	4941	100.0	(40–59)	30	6–7/d	≥8/d	☆★★★/★★/★★★
Hale 2013 [77]	3942	0.0	62.1 (50–79)	11–16	7–8/night	≥9/night	★★☆★/★★/★★★
Kakizaki 2013 [78]	49,256	48.2	(40–79)	10.8	7/d	≥10/d	★★☆★/★★/★★★
Kim 2013 [79]	135,685	45.6	(45–75)	12.9	7/d	≥9/d	★★☆★/★★/★★★
Li 2013 [80]	9455	(38.1)	(20–79)	7	7/night	≥9/night	★★☆★/★★/★★★
Magee 2013 [81]	227,815	46.3	(≥45)	2.8	7/d	≥10/d	★★☆★/★★/★☆★
Yeo 2013 [82]	13,164	41.4	(≥20)	9.44	7/d	≥10/d	★★★★/★★/★★★
Bellavia 2014 [83]	70,973	53.3	(45–83)	15	6.6–7.4/d	>8/d	★★☆★/★★/★★★
Lee 2014 [84]	3427	50.9	(≥65)	5.1 ± 0.9	<10/night	≥10/night	☆★☆★/★★/★★★
Rod 2014 [85]	9098	67.2	45 (35–55)	22	7/night	>9/night	☆★☆★/★★/★★★
Xiao 2014 [86]	239,896	56.2	(51–72)	14	7–8/night	≥9/night	★★☆★/★★/★★☆
Zuurbier 2015 [87]	1734	46.6	62.2 ± 9.3 (45–98)	7.3 ± 1.3	6–7.5/night	>7.5/night	☆★★★/★★/★★★
Hall 2015 [88]	3013	48.6	73.6 ± 2.9 (70–79)	8.2 ± 2 0.3	7–8/night	>8/night	★★★★/★★/★★★
Cai 2015 [89]	113,138	60.1	Male: (40–75) Female: (44–79)	Median: Male: 6.07 Female: 7.12	7/d	≥10/d	★★★★/★★/★★★

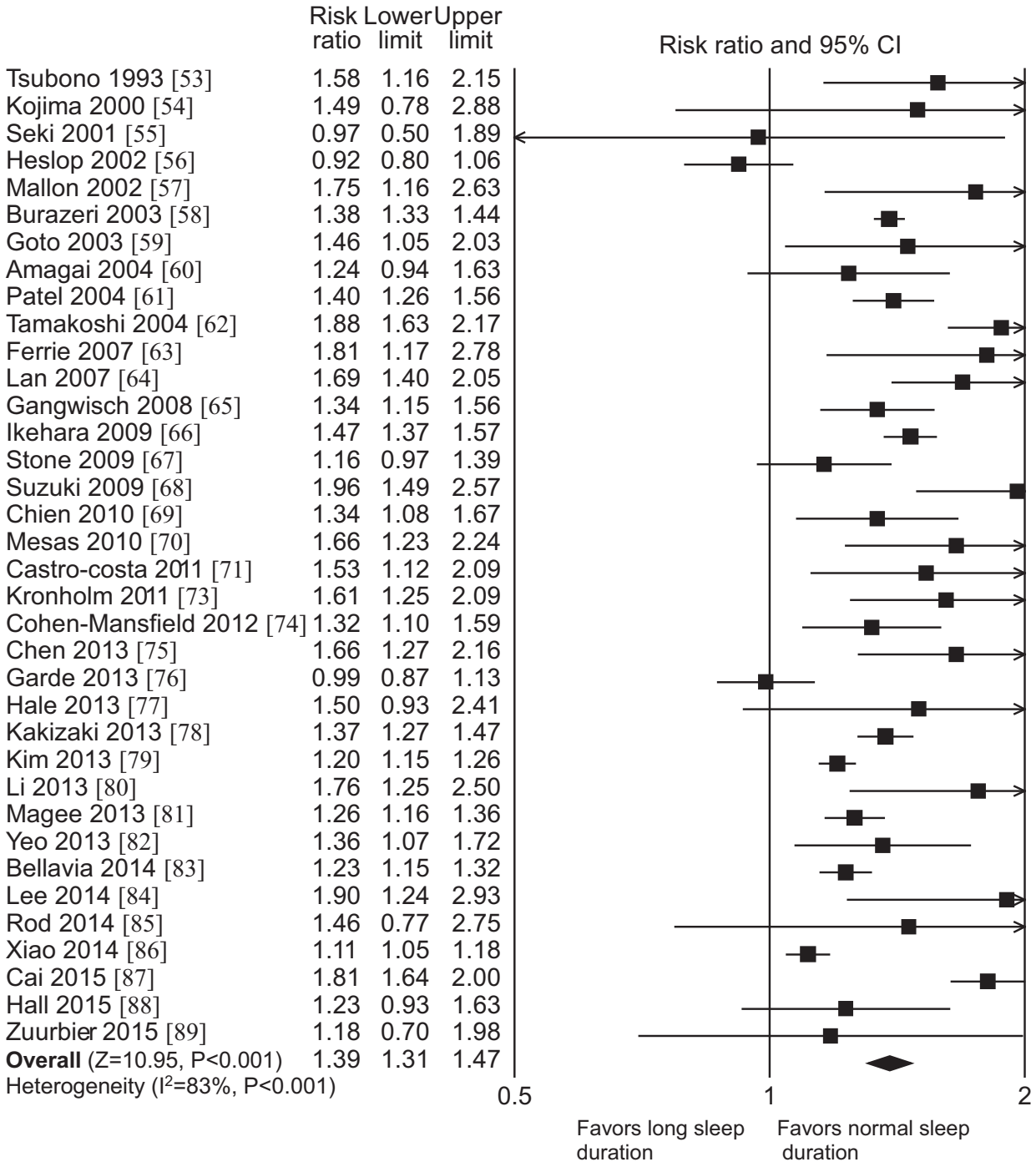


Fig. 2. Mortality outcome comparing long with normal sleepers. An arrow indicates that the upper limit of the 95% CI is over the scale described here.

cardiovascular disease. Similar findings were not observed for diabetes and obesity outcomes.

Meta-regression analyses were performed for mortality, diabetes, cardiovascular disease, stroke, coronary heart disease, and obesity outcomes. Longer sleep duration was significantly associated in a gradient fashion with increased mortality (coefficient = 0.120, P < 0.0001, R^2 analog = 0.03, Fig. 5). The 95% CIs of prediction curves were greater than zero beginning at a sleep duration of >9.5 h. Longer sleep duration was also associated in a gradient fashion with incident cardiovascular disease (coefficient = 0.165, P = 0.002, R^2 analog = 0.05, Fig. S40). No significant gradient associations were observed for the other outcomes.

Discussion

To the best of our knowledge, this is the first systematic review to investigate associations between long sleep duration and multiple health outcomes using the same methodology for each meta-analysis, and to explore the dose–response of long sleep duration on these outcomes using meta-regression analyses. Long sleep duration was associated with greater mortality and increased incidence of multiple health conditions. The strength of association varied across outcomes, with a point estimate RR of 1.46 for stroke, 1.39 for mortality, 1.26 for diabetes mellitus, 1.25 for cardiovascular disease, 1.24 for coronary heart disease and 1.08 for obesity. Long

sleep duration was not significantly associated with increased risk of hypertension, and available evidence was not sufficient to examine depression and dyslipidemia outcomes.

The present results are similar to those from previous systematic reviews. For instance, long sleep duration has been associated with a RR of 1.23 (N of studies = 17) [7] and 1.30 (N = 16) [8] for mortality; with a RR of 1.41 (N = 8) for cardiovascular disease [11]; and with an HR of 1.46 for stroke (N = 11) [12]. Our findings contribute important new information to previous reviews because of our updated comprehensive literature search and our use of the same rigorous methodology for each outcome. However, further epidemiological studies will be needed to investigate the association of long sleep with dyslipidemia and depression.

The lack of a statistically significant association between long sleep duration and hypertension (RR 1.01, 0.95–1.07) is consistent with findings in a previous review (1.02, 0.91–1.14) [33]. On the other hand, our findings differ from previous results for the obesity outcome; we found that long sleep was significantly associated with obesity (RR 1.08, 1.02–1.15, P = 0.010), whereas a previous review did not find a statistically significant association (odds ratio 1.06, 0.98–1.15) [34]. This discrepancy may partly be due to different statistical methodologies, but we also observed narrower confidence intervals, which is likely due to our inclusion of 15 datasets compared to 10 in the previous review.

In subgroup analyses addressing specific thresholds for long sleep duration, values greater than 8 or 9 h were associated with significantly increased mortality and cardiovascular disease in comparison with normal sleep. In meta-regression, longer duration of sleep was linearly associated with increased mortality risk. These findings are again consistent with those in previous studies [9,10]. Although the American Academy of Sleep Medicine and the Sleep Research Society have not published their recommendations for an upper limit of appropriate sleep duration, the National Sleep Foundation issued its recommendations, including 8–10 h for teenagers (aged 14–17 y), 7–9 h for adults (18–64 y) and 7–8 h for older adults (≥65) [35]. Normative total sleep time is reported to decrease with age not only in adolescents but also in adults [36], and most participants included in the present study were aged between 30 and 70 y. The recommendations match well with the results from our analyses.

The findings of the present study complement those of our previous review on short sleep duration [16]. Using identical methodology to that in the current study, we found that sleep duration <6 h is associated with a significant increase in mortality and health outcomes such as diabetes, cardiovascular disease, coronary heart disease, and obesity. In combination, the findings of these two papers are consistent with the "U-shaped" relationship between sleep duration and multiple health outcomes that has been previously described. However, we did not directly test curvilinear relationships in these papers. Moreover, the strength of association with sleep duration varies among the various outcomes, as described above.

Although several theoretical pathways may explain the relationship between long sleep duration and health outcomes [37], our study was unable to examine specific mechanisms. Moreover, we do not have data showing that changing sleep duration modifies health risks. Therefore, while we can confidently state that long sleep duration is a risk factor for adverse health outcomes, we cannot demonstrate that it is a *causal* risk factor [38]. Nevertheless, findings from our studies on the health risks of short and long sleep duration may encourage both mechanistic studies and intervention studies to investigate whether and how sleep duration confers health risk. Regarding education, psychotherapy, and psychosocial interventions, many studies have focused on insomnia and the efficacy of these interventions on the quality of sleep has been reported in recent systematic reviews [39,40]. To the best of our knowledge, there is no evidence base to test these interventions in the community for prevention of the health outcomes. Until such studies are conducted, our findings may be used in education and health literacy efforts to encourage adequate duration of sleep as a key component of overall sleep health [41].

Limitations of the study

Although our findings are internally consistent and consistent with previous studies, we acknowledge several limitations.

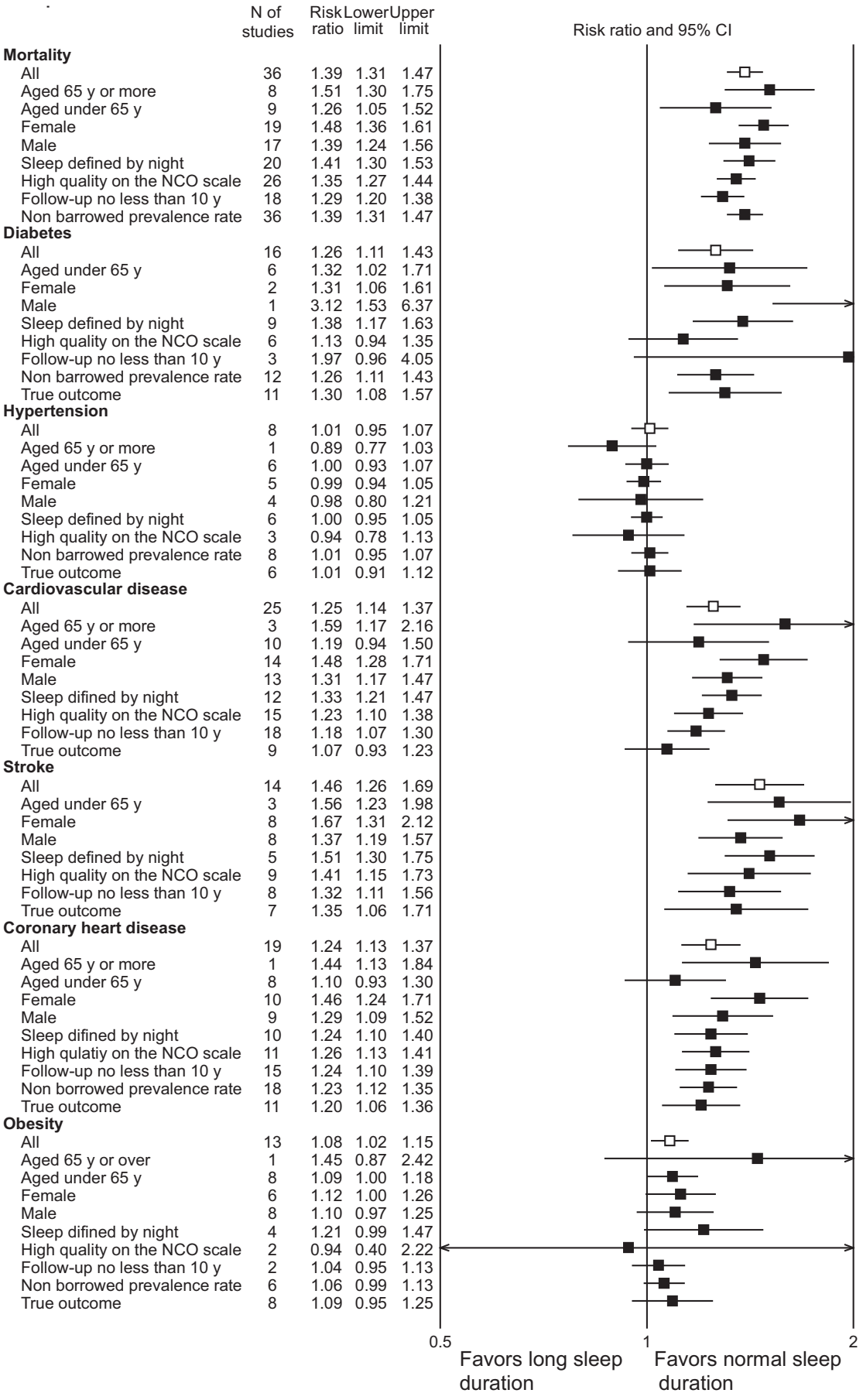
First, our analyses focused on night-time sleep rather than on 24-h sleep. Given the number of primary, subgroup, and sensitivity analyses, we were concerned about inflating the risk of type I errors. A previous systematic review conducted meta-analyses using both night-time and 24-h sleep [9], and reported similar findings with regard to all-cause mortality. Therefore, we believe that our decision to focus on night-time sleep is unlikely to have had a major effect on our conclusions.

Secondly, we collected most of the data on sleep duration based on results from an interview question or a questionnaire, or from a sleep diary, but not from objective measures (e.g., actigraphy or polysomnography), because we believed that self-reported measures were more widely utilized and applicable than objective measures in community settings. However, sleep duration assessment based on a simple question, sleep diary, and objective measures have been reported to be inconsistent [42,43]. In addition, the term "sleep duration" has been sometimes used as the amount of time in bed in previous epidemiological studies [44]. The definition of sleep duration utilized in our systematic review relies on the definition used in original studies and different measurement approaches might lead to discrepancies among the included studies, although we have extracted data on actual sleep duration with the utmost care and attention.

Thirdly, we did not investigate the impact of other dimensions of sleep, such as subjective or objective sleep quality, on health outcomes. Although previous studies have reported an association between sleep problems such as insomnia and mortality [45,46], we intended to focus on the duration of sleep because it is likely that sleep duration is more easily recognized and accurately reported by participants rather than the quality of sleep, in community surveys. However, we believe that interventions to reduce unwanted health outcomes should include information not only about sleep duration but also about the quality of sleep, because the latter may be an important factor in mechanisms linking sleep and subsequent health outcomes.

Fourthly, we have done our meta-analyses by pooling adjusted RRs between long and normal sleep as provided by the original studies. However, we were dependent on the original studies as to whether types of confounders had been adjusted or not, and some important confounders, including employment status, depression and excessive amounts of time in bed, were not adjusted in all studies (Tables S1–S9). This is a limitation of meta-analyses pooling aggregated data.

Fifthly, we recognize that the role of individual differences regarding sleep duration preferences is still uncertain [47], and that the reasons for different durations of sleep vary from person to person. Previous epidemiological studies have shown that short sleep duration is associated with characteristics such as being unmarried [48], more frequent binge drinking [49], lower socioeconomic status [49,50], lower education levels [50], working multiple jobs [51], pre- and post-sleep activities including socializing, self-care and hygiene, and watching TV [51] and African, Asian and


N of studies
Risk ratio
Lower limit
Upper limit
Risk ratio and 95% CI
Mortality
All 36 1.39 1.31 1.47
Aged 65 y or more 8 1.51 1.30 1.75
Aged under 65 y 9 1.26 1.05 1.52
Female 19 1.48 1.36 1.61
Male 17 1.39 1.24 1.56
Sleep defined by night 20 1.41 1.30 1.53
High quality on the NCO scale 26 1.35 1.27 1.44
Follow-up no less than 10 y 18 1.29 1.20 1.38
Non barrowed prevalence rate 36 1.39 1.31 1.47
Diabetes
All 16 1.26 1.11 1.43
Aged under 65 y 6 1.32 1.02 1.71
Female 2 1.31 1.06 1.61
Male 1 3.12 1.53 6.37
Sleep defined by night 9 1.38 1.17 1.63
High quality on the NCO scale 6 1.13 0.94 1.35
Follow-up no less than 10 y 3 1.97 0.96 4.05
Non barrowed prevalence rate 12 1.26 1.11 1.43
True outcome 11 1.30 1.08 1.57
Hypertension
All 8 1.01 0.95 1.07
Aged 65 y or more 1 0.89 0.77 1.03
Aged under 65 y 6 1.00 0.93 1.07
Female 5 0.99 0.94 1.05
Male 4 0.98 0.80 1.21
Sleep defined by night 6 1.00 0.95 1.05
High quality on the NCO scale 3 0.94 0.78 1.13
Non barrowed prevalence rate 8 1.01 0.95 1.07
True outcome 6 1.01 0.91 1.12
Cardiovascular disease
All 25 1.25 1.14 1.37
Aged 65 y or more 3 1.59 1.17 2.16
Aged under 65 y 10 1.19 0.94 1.50
Female 14 1.48 1.28 1.71
Male 13 1.31 1.17 1.47
Sleep difined by night 12 1.33 1.21 1.47
High quality on the NCO scale 15 1.23 1.10 1.38
Follow-up no less than 10 y 18 1.18 1.07 1.30
True outcome 9 1.07 0.93 1.23
Stroke
All 14 1.46 1.26 1.69
Aged under 65 y 3 1.56 1.23 1.98
Female 8 1.67 1.31 2.12
Male 8 1.37 1.19 1.57
Sleep defined by night 5 1.51 1.30 1.75
High quality on the NCO scale 9 1.41 1.15 1.73
Follow-up no less than 10 y 8 1.32 1.11 1.56
True outcome 7 1.35 1.06 1.71
Coronary heart disease
All 19 1.24 1.13 1.37
Aged 65 y or more 1 1.44 1.13 1.84
Aged under 65 y 8 1.10 0.93 1.30
Female 10 1.46 1.24 1.71
Male 9 1.29 1.09 1.52
Sleep difined by night 10 1.24 1.10 1.40
High qulatiy on the NCO scale 11 1.26 1.13 1.41
Follow-up no less than 10 y 15 1.24 1.10 1.39
Non borrowed prevalence rate 18 1.23 1.12 1.35
True outcome 11 1.20 1.06 1.36
Obesity
All 13 1.08 1.02 1.15
Aged 65 y or over 1 1.45 0.87 2.42
Aged under 65 y 8 1.09 1.00 1.18
Female 6 1.12 1.00 1.26
Male 8 1.10 0.97 1.25
Sleep difined by night 4 1.21 0.99 1.47
High quality on the NCO scale 2 0.94 0.40 2.22
Follow-up no less than 10 y 2 1.04 0.95 1.13
Non borrowed prevalence rate 6 1.06 0.99 1.13
True outcome 8 1.09 0.95 1.25
0.5
1
2
Favors long sleep duration
Favors normal sleep duration

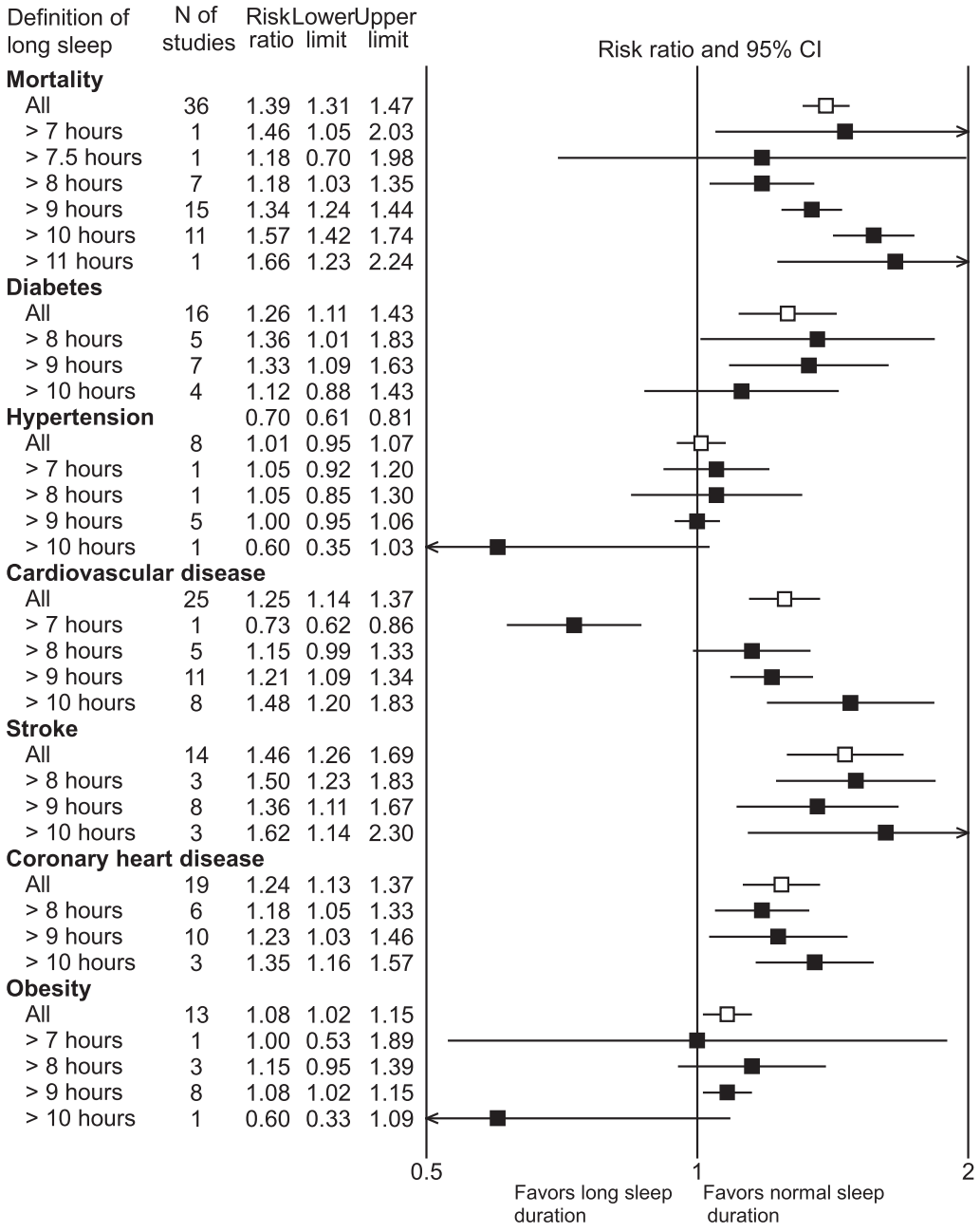


Fig. 4. Subgroup analyses for duration thresholds of long sleep. An arrow indicates that the upper limit of the 95% CI is over the scale described here.

Hispanic ethnicity [50]. On the other hand, characteristics related to long sleep duration include Mexican ethnicity, public liability insurance [50], and less weekly physical activity [52]. Some of these characteristics, such as working multiple jobs, may present barriers for possible interventions aimed at sleep duration because of economic disincentives. However, other characteristics associated with sleep duration may be more amenable to change, including frequent binge drinking, the amount of physical activity, and using smart phones and television viewing prior to sleeping. Future studies focusing on sleep duration must also account for individual preferences.

Finally, shorter or longer periods of sleep duration are unlikely to link directly to sleep disorders such as sleep apnea or insomnia. Therefore, our findings are likely to have limited comparability with findings derived from patients seeking treatment in clinical settings.

Fig. 3. Relative risks of mortality and health outcomes comparing long with normal sleepers. NCO scale, Newcastle–Ottawa Scale. For the outcomes of dyslipidemia and depression, no meta-analyses were performed. An arrow indicates that the upper limit of the 95% CI is over the scale described here.

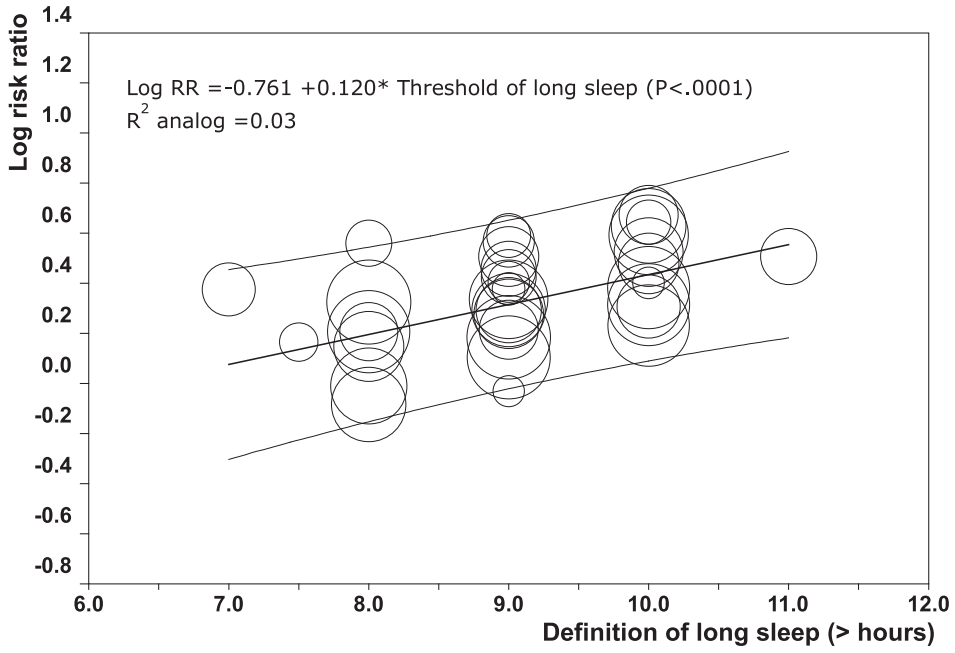


Fig. 5. Meta-regression for specific values of long sleep duration in mortality.

Conclusions

Long sleep duration was associated with a significant increase in risk for mortality and incident diabetes, cardiovascular disease, stroke, coronary heart disease, and obesity. Future studies should address potential mechanisms underlying the relationship between long sleep duration and adverse health outcomes. Whether interventions to reduce long sleep duration also reduce health risk remains an open question.

Practice points

1). Long sleep duration is associated with greater mortality and increased incidence of mortality, diabetes mellitus, cardiovascular disease, stroke, coronary heart disease, and obesity.
2). The strength of association with long sleep duration varies among these outcomes
3). Longer duration of sleep is linearly associated with increased mortality risk.
4). Currently, whether interventions to reduce long sleep duration also reduce health risk remains an open question.

Research agenda

1). Future studies should address potential mechanisms underlying the relationship between long sleep duration and adverse health outcomes.
2). Studies on interventions aimed at sleep duration should be conducted to investigate whether adverse health risks decrease in community settings.

Authors' contributions

All authors contributed to the manuscript as follows:

OI designed the study, developed technical materials, acquired data, and interpreted the data.

MJ designed the study, developed technical materials, acquired data, and interpreted the data.

NW designed the study, interpreted the data, and drafted the manuscript.

DJB interpreted the data, and drafted the manuscript.

YK obtained funding, conceived the study, designed the study, and interpreted the data.

All authors have revised the important intellectual content critically, have read and approved the final manuscript, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.

Institution at which the work was performed

Nihon University, Oita University, and Kyoto University, Japan, and University of Pittsburgh, USA.

Disclosure of conflicts of interests

The authors have no conflicts of interests to declare, that may be affected by the publication of the paper. Other conflicts of interests are as follows:

OI has research funds from the Japanese Ministry of Health Labor and Welfare and the Japanese Ministry of Education, Science, and Technology.

MJ has research funds from the Japanese Ministry of Health Labor.

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DJB has served as a paid consultant for the following companies over the past 5 y, each at a level of less than $5000 per 12-mo period: Bayer HealthCare, BeHealth Solutions, Cereve, CMEOutfitters, Emmi Solutions, Medscape, Merck, and Purdue.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.smrv.2017.06.011.

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