Sleep Duration and Risk of Type 2 Diabetes: A Meta-analysis of Prospective Studies

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Diabetes Care 2015;38:529–537 | DOI: 10.2337/dc14-2073

OBJECTIVE

It remains unclear how many hours of sleep are associated with the lowest risk of type 2 diabetes. This meta-analysis was performed to assess the dose-response relationship between sleep duration and risk of type 2 diabetes.

RESEARCH DESIGN AND METHODS

PubMed and Embase were searched up to 20 March 2014 for prospective observational studies that assessed the relationship of sleep duration and risk of type 2 diabetes. Both semiparametric and parametric methods were used.

RESULTS

Ten articles with 11 reports were eligible for inclusion in the meta-analysis. A total of 18,443 incident cases of type 2 diabetes were ascertained among 482,502 participants with follow-up periods ranging from 2.5 to 16 years. A U-shaped dose-response relationship was observed between sleep duration and risk of type 2 diabetes, with the lowest risk observed at a sleep duration category of 7–8 h per day. Compared with 7-h sleep duration per day, the pooled relative risks for type 2 diabetes were 1.09 (95% CI 1.04–1.15) for each 1-h shorter sleep duration among individuals who slept <7 h per day and 1.14 (1.03–1.26) for each 1-h increment of sleep duration among individuals with longer sleep duration.

CONCLUSIONS

Our dose-response meta-analysis of prospective studies shows a U-shaped relationship between sleep duration and risk of type 2 diabetes, with the lowest type 2 diabetes risk at 7–8 h per day of sleep duration. Both short and long sleep duration are associated with a significantly increased risk of type 2 diabetes, underscoring the importance of appropriate sleep duration in the delay or prevention of type 2 diabetes.

According to the International Diabetes Federation, the estimated number of diabetic patients worldwide was 382 million in 2013 and will rise to 592 million by 2035 (1). Given its significant burden, it is imperative to identify modifiable lifestyle factors associated with lower risk of diabetes. Sleep is a biobehavioral phenomenon that is regulated by circadian, homeostatic, and neurohormonal processes (2). In the past few years, suboptimal sleep duration, especially short sleep, as a disorder character rising out of the 24-h lifestyle of modern societies, has increasingly been shown to represent an additional behavioral factor adversely affecting public health (3–7).

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Received 30 August 2014 and accepted 17 November 2014.

This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc14-2073/-/DC1.

META-ANALYSIS

Several studies have reported a U-shaped association between sleep duration and type 2 diabetes (8,9), but other studies have not found a uniform relationship (10,11). One previous meta-analysis suggested that both short and long sleep duration were associated with risk of type 2 diabetes (12). However, the definitions of short and long sleep duration differed between studies, which complicated the interpretation of the pooled results. In addition, without a dose-response analysis, it remains unknown how many hours of habitual sleep are associated with the lowest risk of type 2 diabetes. In the past several years, the number of prospective studies with enough quantitative categories has nearly doubled (13–22). Therefore, we conducted a meta-analysis of prospective studies to determine the overall shape of the relationship between sleep duration and risk of type 2 diabetes.

RESEARCH DESIGN AND METHODS

Data Sources and Searches

We conducted a literature search (up to 20 March 2014) of PubMed (Medline) and Embase for prospective studies examining the association between sleep duration and risk of type 2 diabetes. PubMed search terms were ("Diabetes Mellitus" [Mesh] OR "diabetes" [All Fields]) AND sleep. Similar search terms were used for Embase. In addition, we reviewed references from relevant original papers and review articles to identify additional eligible studies. No language restrictions were imposed. We followed the standard guidelines for conducting and reporting meta-analyses of observational studies (23).

Study Selection

Studies were included in this meta-analysis if they satisfied the following criteria: the study design was prospective, the exposure of interest was sleep duration, the outcome was type 2 diabetes, and the investigators reported relative risks (RRs) with 95% CIs for at least three quantitative categories of short sleep or long sleep duration. We excluded animal studies, clinical trials, cross-sectional studies, case-control studies, reviews, commentaries, letters, and studies that examined other associations. If study populations were reported more than once, we used the result with the longest follow-up duration. Two investigators (Z.S. and M.X.) independently screened all studies by title or abstract and then by a full text evaluation. Any discrepancy between the two authors was solved by discussion with the senior investigator (W.B.).

Data Extraction and Quality Assessment

We extracted the following information from each study: authors, year of publication, study name, study location, years of follow-up, sample size (number of participants and incident cases), participant characteristics (age and sex), type 2 diabetes assessment, sleep duration categories, covariates adjusted in the multivariable analysis, and RRs (95% CIs) for all categories of sleep duration.

Quality assessment was performed according to the Newcastle-Ottawa Quality Assessment Scale (NOS) (24), which is a validated scale for nonrandomized studies in meta-analyses. This scale awards a maximum of 9 points to each study: 4 for selection of participants and measurement of exposure, 2 for comparability of cohorts on the basis of the design or analysis, and 3 for assessment of outcomes and adequacy of follow-up. We assigned scores of 0–3, 4–6, and 7–9 for low, moderate, and high quality of studies, respectively. When studies had several adjustment models, we extracted those that reflected the maximum extent of adjustment for potentially confounding variables.

To perform a dose-response meta-analysis, we assigned the median or mean sleep duration in each category of duration to the corresponding RR for each study. If the mean or median duration per category was not reported, the midpoint of the upper and lower boundaries in each category was assigned. When the shortest or the longest category was open-ended, we assumed that the open-ended interval length had the same length as the adjacent interval.

Data Synthesis and Analysis

In this meta-analysis, the RRs and 95% CIs were considered as the effect size for all studies. Since the incidence of type 2 diabetes is sufficiently low, odds ratios were deemed equivalent to RRs.

To analyze the trend of sleep duration and risk of type 2 diabetes, we used both semiparametric and parametric methods. For the semiparametric method, taking the analysis of short sleep duration for example, three groups (namely shortest, second shortest, and reference) were generated. For each included study, the shortest and the reference categories corresponded to the shortest and reference groups, respectively. For studies with three categories, the second categories corresponded to the second shortest group. If the study had more than three categories, one group, other than the shortest and reference, was chosen on the basis of their similarity of the duration of sleep in that category to the second shortest group. For each group, a random-effects model was used to pool the RR of type 2 diabetes. The same method was used in the analysis for long sleep duration and risk of type 2 diabetes.

For the parametric method, we used a random-effects dose-response meta-analysis described by Greenland (25) to calculate the trend from the correlated estimates for log RR across categories of sleep duration. The distributions of cases and participants, and RRs and 95% CIs, in each sleep duration category were extracted according to this method. Additionally, we tested for potential nonlinearity in the association between sleep duration and type 2 diabetes using a fixed-effect restricted cubic spline model with four knots at percentiles 5, 35, 65, and 95% of the distribution. We calculated absolute risk differences as background incidence rate $\times$ (RR $-$ 1).

The heterogeneity among studies was estimated by the Cochran Q test and I^2 statistic. Heterogeneity was considered statistically significant at $P \leq 0.10$. The I^2 statistic describes the percentage of total variation in point estimates that can be attributed to heterogeneity. For the I^2 metric, we considered low, moderate, and high I^2 values to be 25, 50, and 75%, respectively (26). To explore the sources of heterogeneity among studies and to test the robustness of the associations, we conducted subgroup analyses by study location, number of participants, duration of follow-up, and study quality, as well as several sensitivity analyses. The possibility of publication bias was assessed using the Egger regression asymmetry test (27). For sensitivity analysis, we also used the fixed-effects model for all the above analyses. Additional sensitivity analyses were performed

by omitting one study at a time and calculating a pooled estimate for the remainder of the studies to evaluate whether the results were affected markedly by a single study. All statistical analyses were performed with Stata version 12 (Stata Corp), and all tests were two sided with a significance level of 0.05.

RESULTS

Literature Search

Figure 1 shows the results of our literature research and study selection. We identified 610 articles from PubMed and 759 articles from Embase prior to 20 March 2014. After exclusion of duplicates and studies that did not fulfill the inclusion criteria, 14 remaining articles seemed to be relevant for this meta-analysis. After evaluating the full texts of these 14 publications, we further excluded 4 articles (10,11,28,29) due to a lack of sufficient data for estimation of dose-response analysis. In addition, we included the report of the control group, and not the intervention group, in the study by Tuomilehto et al. (18). In the study by Kita et al. (16), the results were separated according to the presence or absence of a family history of diabetes (FHD), so we treated it as two separate reports. In total, our meta-analysis included 10 articles (13–22) with 11 independent reports.

Study Characteristics

Characteristics of all 10 studies were shown in Table 1. The duration of follow-up for incident type 2 diabetes ranged from 2.5 to 16 years, with a median follow-up of 7.5 years. Five studies were conducted in the U.S. (14,17,20–22), two in Europe (15,18), two in Asia (16,19), and one in Australia (13). Sleep duration was assessed by questionnaire in all studies. In six studies (13–15,17,20,21), type 2 diabetes was ascertained by medical records or self-reports; the outcome of four studies (16,18,19,22) was assessed by means of a fasting plasma glucose or a glucose tolerance test. One study was a substudy of a prospective lifestyle intervention trial (18), and the remaining nine were prospective cohort studies. The mean NOS score was 6.7 (of a possible 9 points), suggesting the high quality of the studies included in the meta-analysis.

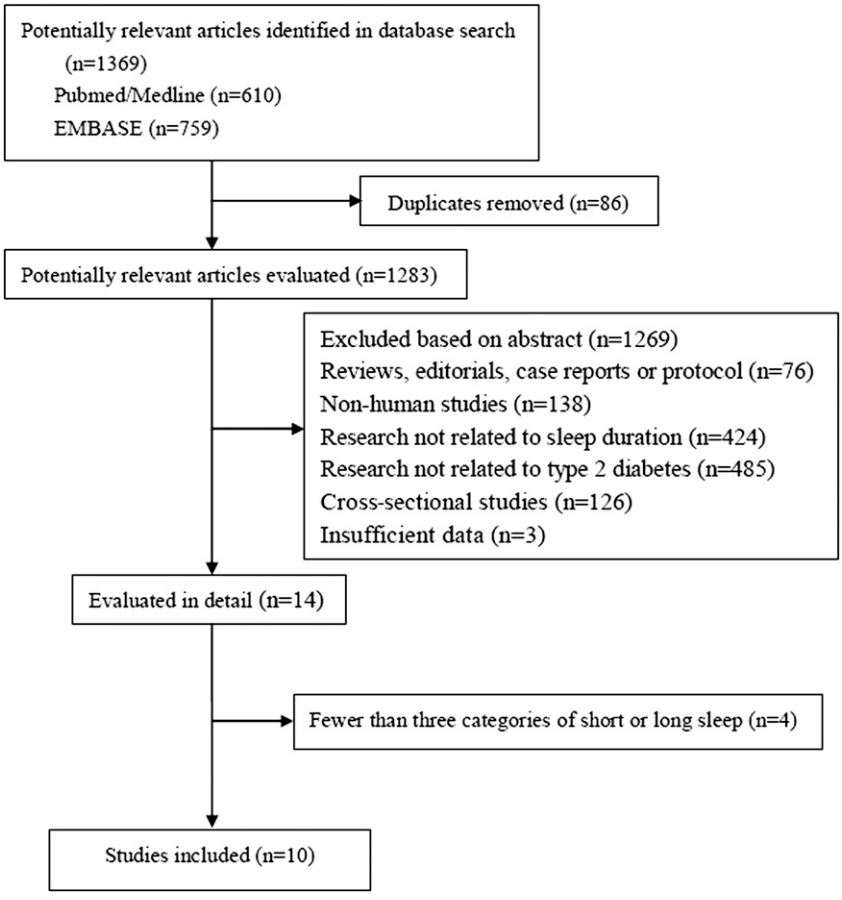

Figure 1—Flow diagram of literature search and study selection.

Overall Sleep Duration and Risk of Type 2 Diabetes

Nine studies with 10 reports were included to explore the overall shape of the relationship between sleep duration and risk of type 2 diabetes (13–18,20–22). A U-shaped association was shown, with the lowest risk of type 2 diabetes at a sleep duration of 7–8 h per day (Fig. 2).

Short Duration of Sleep and Risk of Type 2 Diabetes

The semiparametric analysis included eight articles with nine reports on short sleep and type 2 diabetes risk. Figure 3 shows the RRs for type 2 diabetes with different levels of short sleep duration relative to the reference category. Compared with the reference category of sleep duration (7 h per day), the pooled RR for incident type 2 diabetes was 1.06 (95% CI 1.01–1.11, I^2 = 7.5%, P for heterogeneity = 0.37) for the second shortest (6 h per day) and 1.37 (1.18–1.59, I^2 = 57.1%, P = 0.017) for the shortest (≤5 h per day) category of sleep duration (Supplementary Fig. 1). Thus, there was evidence for substantial between-study heterogeneity in results for the shortest category of sleep duration.

The aforementioned nine reports were included in the dose-response analysis of short sleep duration and risk of type 2 diabetes. We found no evidence of a curvilinear association between short sleep duration and risk of type 2 diabetes (P = 0.22 for nonlinearity). Compared with 7 h sleep duration per day, the pooled RR for type 2 diabetes was 1.09 (95% CI 1.04–1.15) per 1-h reduction of sleep duration, with evidence of heterogeneity (I^2 = 63.5%, P = 0.005) (Fig. 3*A*). Using the most recent incidence rate of type 2 diabetes for the U.S. population (7.6 cases/1,000 population aged 18–79 years) (30), we estimated that 68 cases of diabetes per 100,000 individuals would occur each year for every 1-h reduction of habitual sleep duration compared with 7 h per day.

Long Duration of Sleep and Risk of Type 2 Diabetes

Seven studies were included in the semiparametric analysis on long sleep

Table 1—Characteristics of prospective studies of sleep duration intake in relation to incident type 2 diabetes

Author	Publication year	Country	Sex of population	Sample size	No. of diabetes cases	Age at baseline (years)	Follow-up (years)	Study outcome and ascertainment	Comparison categories and corresponding RR (95% CI)	Covariates in fully adjusted model	NOS (0–9 points)
Holliday (13)	2013	Australia	Both	156,902	3,641	≥45	2–3	Hospital record	<6, 1.29 (1.08–1.53); 6, 1.00 (0.90–1.12); 7, 1; 8, 1.00 (0.92–1.09); 9, 0.99 (0.88–1.12); ≥10, 1.03 (0.88–1.19)	Age, sex, education, marital status, residential remoteness, alcohol consumption, smoking status, health insurance status, income, BMI, physical activity, and baseline health status	6
Boyko (14)	2013	U.S.	Both	47,093	871	34.9	6	Self-report of physician diagnosis	<5, 2.04 (1.49–2.81); 5, 1.46 (1.15–1.84); 6, 1.19 (0.99–1.43); 7, 1; 8, 1.17 (0.95–1.45); >8, 1.30 (0.93–1.81)	Age, sex, education, BMI, and race/ethnicity	6
von Ruesten (15)	2012	Germany	Both	23,620	841	35–65	7.8	Verified self-report of physician diagnosis	<6, 1.06 (0.80–1.40); 6–7, 0.94 (0.78–1.14); 7–8, 1; 8–9, 0.92 (0.77–1.10); ≥9, 1.05 (0.82–1.33)	Age, sex, sleeping disorders, alcohol intake from beverages, smoking status, walking, cycling, sports, employment status, education, BMI, waist-to-hip ratio, prevalent hypertension at baseline, history of high blood lipid levels at baseline, caffeinated beverages, satisfaction with life, satisfaction with health, and intake of antidepressants	8
Kita (16)	2012	Japan	Both	3,570	121	35–55	4	FPG or prescribed medications	Without FHD ≤5, 5.37 (1.38–20.91); 5–6, 1.38 (0.50–3.79); 6–7, 1.57 (0.64–3.83); >7, 1 With FHD ≤5, 0.25 (0.03–2.42); 5–6, 1.18 (0.43–3.24); 6–7, 0.74 (0.29–1.90); >7, 1	Age, sex, FPG level, BMI, smoking, alcohol intake, physical exercise, education, working hours, shift work, rate of sedentary work, and occupational stress	6
Xu (17)	2010	U.S.	Both	164,399	10,143	50 –71	8	Questionnaire	<5, 1.34 (1.20–1.50); 5–6, 1.06 (1.01–1.11); 7–8, 1; ≥9, 1.09 (0.97–1.22)	Age, sex, race, education, marital status, smoking, coffee and alcohol consumption, calorie intake, FHD, and general health status	7
Tuomilehto (18)	2009	Finland	Both	252	107	40–64	7	WHO criteria	Control group ≤6.5, 1.68 (0.79–3.59); 7–8.5, 1.0; 9–9.5, 2.29 (1.38–3.80); ≥10, 2.74 (1.67–4.50)	Age, sex, BMI, study center, smoking, alcohol intake, hypertension medication, leisure-time physical activity at baseline, and 1-year change in body weight	7

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Table 1—Continued

Author	Publication year	Country	Sex of population	Sample size	No. of diabetes cases	Age at baseline (years)	Follow-up (years)	Study outcome and ascertainment	Comparison categories and corresponding RR (95% CI)	Covariates in fully adjusted model	NOS (0–9 points)
Gangwisch (20)	2007	U.S.	Both	8,992	430	32–86	8–10	Self-report of physician diagnosis, hospital diagnosis, or cause of death	≤5, 1.47 (1.03–2.09); 6, 1.08 (0.80–1.47); 7, 1; 8, 1.09 (0.83–1.43), ≥9, 1.52 (1.06–2.17)	Age, physical activity, depression, alcohol consumption, ethnicity, education, marital status, overweight/obesity, and hypertension	6
Hayashino (19)	2007	Japan	Both	6,509	230	19–69	4.2	Multiple methods	<6, 1.15 (0.76–1.74); 6–7, 1; 7–8, 1.15 (0.84–1.59); >8, 1.03 (0.62–1.70)	Age, BMI, sex, history of smoking, history of hypertension, history of high cholesterol, potential history of diabetes, exercise quartiles, and assigned intervention	8
Yaggi (21)	2006	U.S.	Male	1,139	90	40–70	15–17	Self-report of physician diagnosis	≤5, 1.95 (0.95–4.01); 6, 1.95 (1.06–3.58); 7, 1; 8, 1.41 (0.78–2.55); >8, 3.12 (1.53–6.37)	Age, education, hypertension, smoking, self-rated health status, and waist circumference	7
Ayas (22)	2003	U.S.	Female	70,026	1,969	40–65	10	Verified self-report of physician diagnosis	≤5, 1.18 (0.96–1.44); 6, 1.10 (0.97 –1.25); 7, 1.02 (0.91 –1.16); 8, 1; ≥9, 1.29 (1.05–1.59)	BMI, shiftwork, hypercholesterolemia, hypertension, smoking, snoring, exercise, alcohol, depression, postmenopausal hormone use, and FHD	6

FPG, fasting plasma glucose; WHO, World Health Organization.

duration and risk of type 2 diabetes. The pooled RR for type 2 diabetes was 1.11 (95% CI 0.97–1.28, I^2 = 59.0%, P = 0.023) for the second longest (8 h per day) and 1.40 (1.08–1.80, I^2 = 75.8%, $P < 0.001$) for the longest (≥9 h per day) category of sleep duration (Supplementary Fig. 2). Substantial between-study heterogeneity was shown in results for both categories of long sleep duration.

For the dose-response analysis of long sleep duration with diabetes, six studies above except one were included. No potentially nonlinear dose-response relationship was detected (P = 0.90 for nonlinearity). The pooled RRs for type 2 diabetes were 1.14 (95% CI 1.03–1.26) per 1-h increment of sleep duration compared with 7 h, with evidence of heterogeneity (I^2 = 79.1%, $P < 0.001$) (Fig. 3*B*). The corresponding absolute risk difference was estimated to be 106 cases of type 2 diabetes per 100,000 individuals per year per 1-h increase of sleep duration compared with 7 h per day.

Subgroup and Sensitivity Analysis

Supplementary Table 1 shows the different subgroup dose-response analyses. The associations between short and long sleep duration and risk of type 2 diabetes did not differ substantially by study location, number of participants, duration of follow-up, or study quality.

To explore potential source of heterogeneity across studies, we carried out several sensitivity analyses. After excluding the study of Boyko et al. (14) from short sleep analysis, the heterogeneity decreased dramatically (I^2 = 63.5–23.5%), but no similar impact of a single study was observed on the heterogeneity of long sleep analysis. From the results of the subgroup analyses by number of participants (≥10,000 or <10,000), it was implied that the number of participants might be a potential source of heterogeneity for long sleep duration analysis (Supplementary Table 2).

To further confirm the robustness of the results, the dose-response analyses were repeated using a fixed-effects model; the pooled estimates were consistent for short and long sleep duration in relation to risk of type 2 diabetes. Sensitivity analyses omitting one study at a time did not substantially alter the pooled results for short sleep duration and risk of type 2 diabetes, but the

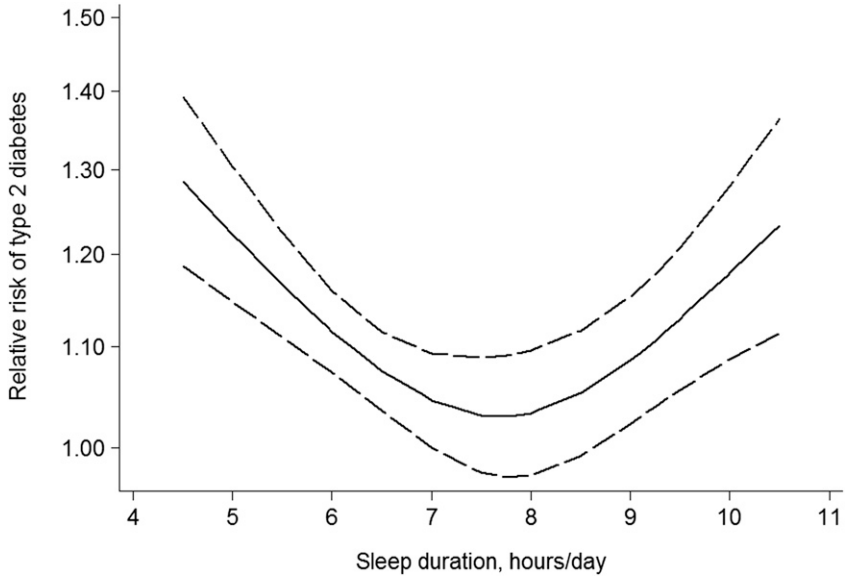

Figure 2—The relationship between sleep duration and risk of type 2 diabetes.

pooled results of the remaining studies were borderline (1.09 [0.99–1.12]) by omission of the study by Tuomilehto et al. (18) for long sleep duration and risk of type 2 diabetes (Supplementary Fig. 3).

Assessment of Publication Bias

Begg and Egger regression tests provided no evidence of substantial publication bias ($P > 0.05$ for both tests).

CONCLUSIONS

In this meta-analysis of prospective studies, we found that the association between sleep duration and risk of type 2 diabetes followed a U-shaped manner; both short and long sleep duration were associated with a significantly elevated risk of type 2 diabetes. Compared with 7 h per day, an hour decrease was associated with a 9% and an hour increase of sleep duration was associated with a 14% increased risk of diabetes in the overall population.

Results in Relation to Other Studies

There has been some debate about the relationship between sleep duration and type 2 diabetes, and the results of published epidemiologic studies have been inconsistent (31). One possible reason is that categories of sleep duration differed across studies. For example, the definitions of short sleep duration ranged from ≤5 to ≤7 h per day (10,21,29). Consistent with our results, a previous meta-analysis indicated both short and long sleep duration were associated with an increased risk of type 2 diabetes, but they did not use a dose-response analysis to determine the overall shape of the association (12). In our analysis, we found a U-shaped association between sleep duration and risk of type 2 diabetes, with the lowest risk of type 2 diabetes at a sleep duration of 7–8 h per day in our analysis, which could contribute to recommendations regarding appropriate sleep duration for future intervention studies. A recent study has shown that both habitual short and long sleep duration were indicated to be associated with risk of obesity in younger (<40 years) but not in older women (>40 years) (32). However, the U-shaped association was still observed when we restricted to the studies that were conducted in subjects older than 40 years. Furthermore, racial/ethnic and sex differences have been reported in the risk of type 2 diabetes by sleep duration (10,11), but we could not investigate these differences due to limited data from the original studies.

Potential mechanisms linking sleep to diabetes may differ between short and long sleep. Several potential biologic mechanisms may contribute to the relation of short sleep duration and diabetes. First, laboratory studies have corroborated and extended the decreases in glucose tolerance and insulin sensitivity after sleep restriction, as shown by increased hepatic glucose production and reduced peripheral glucose disposal (33–37). A recent research indicated that slow wave sleep suppression but not rapid eye movement sleep disturbance during nocturnal sleep plays a key role in the regulation of glucose (38). Changes in the activity of neuroendocrine systems seem to be major mediators of the detrimental metabolic effects of insufficient sleep (31). Increased sympathetic nerve activity may result in reduced β-cell responsiveness and inadequate pancreatic insulin secretion (33,39), while increased uptake of glucose by total sleep– or slow wave sleep–deprived brain could result in increased circulating levels of glucose and postprandial insulin-to-glucose ratio (38). Both inadequate insulin and enhanced glucose could lead to the development of insulin resistance and type 2 diabetes. Meanwhile, sleep disruption during the night is associated with decreased testosterone and melatonin secretion, and it was possible that sleep disruption was related to diabetes via a mechanism of testosterone or melatonin (40,41). However, a recent study also found that restricting sleep could result in an insulin-resistant state in human adipocytes through reduction of phosphorylation of AKT, which indicated that sleep might be an important regulator of energy metabolism in peripheral tissues (42). AKT signaling plays a central role in insulin-stimulated glucose uptake in both muscle and adipose tissue, which was established in rat and human studies (43,44). Reduced phosphorylation of AKT is linked to insulin resistance through negative insulin receptor substrate functions (45), reduced phosphatidylinositol 3-kinase (PI3K) activity (46), and impaired phosphorylation of the AKT substrate AS160 (47). Second, associated with hunger/appetite and caloric intake due to increases in ghrelin and decreases in leptin, short sleep may lead to greater time to eat as well as fatigue leading to lower physical activity levels, thereby increasing risk of weight gain and subsequent health risks (39,48). Meanwhile, short sleep duration was associated with depressive symptoms, low socioeconomic status, low education, and other risk factors of diabetes (8,49). Individuals with sleep loss, especially shift workers, also have irregular sleep schedules, which could result in circadian misalignment and augment markers of insulin resistance

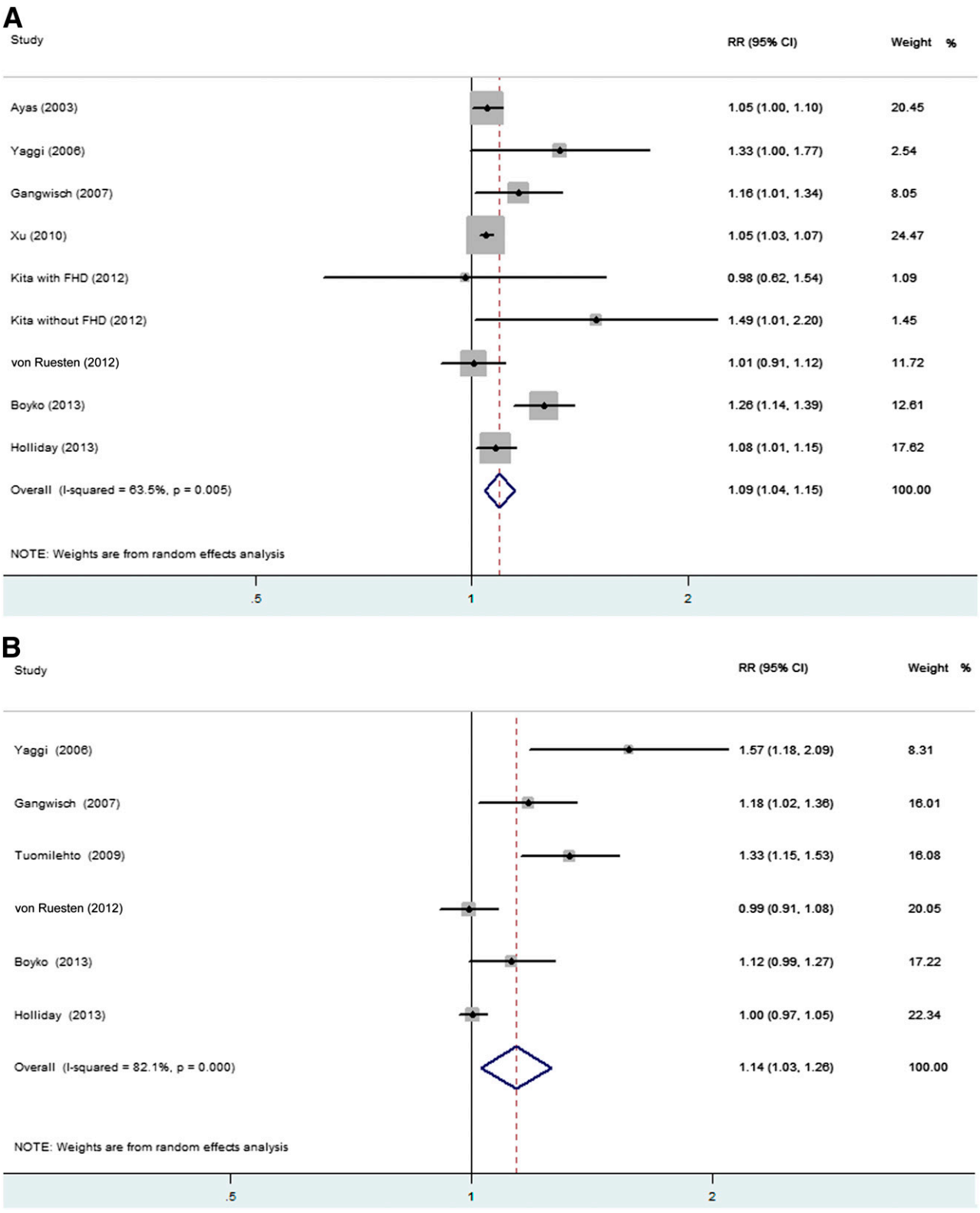

Figure 3—The dose-response relationship plot between sleep duration (per hour) and risk of type 2 diabetes for short sleep (*A*) and long sleep (*B*).

and inflammation independently of sleep loss (50). Finally, short sleep duration has been associated with increases of inflammatory markers (51), such as C-reactive protein and interleukin-6 (IL-6), which indicate low-level systemic inflammation and play a role in diabetes development (52).

The potential mechanisms underlying the association between long sleep duration and increased diabetes risk are currently considered more speculative.

First, long sleep duration was suggested to be associated with some risk factors of incidence of diabetes such as depression, low socioeconomic status, undiagnosed medical disease, poor physical health, and low physical activity (49,53). However, using the maximum extent of adjustment for potentially confounding variables in our study, the pooled result between long sleep duration and risk of diabetes is still significant. Second, obstructive sleep apnea is a known cause of increased need for sleep and has been identified as a risk factor for insulin resistance and diabetes (54). Finally, short and long sleep duration were associated with increased levels of inflammation markers (55,56), and it is possible that sleep disruption is related to diabetes via a mechanism of low-grade systemic inflammation. However, it is also possible that long sleep is a consequence of the sleep-inducing effects of the inflammatory state (57).

Strengths and Limitations

This meta-analysis has several strengths. All studies included in our meta-analysis used a prospective design; thus, the differential misclassification of sleep duration attributable to recall bias was minimized. The mean NOS score of 6.7 ensured the relatively high quality of the included studies. Moreover, we investigated a dose-response relation between sleep duration and risk of type 2 diabetes, allowing us to examine the shape of this possible association. Linear and nonlinear relations were also tested to quantify the associations.

Several limitations of our study should also be acknowledged. First, we may not have identified some studies that were unpublished or published in other languages. Second, all the studies relied on self-reported sleep duration, whereas actigraphy and polysomnography (the gold standard) may provide more objective measures. However, objective measures of sleep duration are expensive and therefore they may not be feasible in large prospective cohort studies. In addition, a previous validation study observed a moderate correlation ($r = 0.47$) between self-reported sleep duration and measured sleep duration using wrist actigraphy (58). In addition, only one included study defined diabetes based upon formal glucose tolerance testing. Third, sleep duration was assessed at one time point in most studies, and participants may have changed their sleep pattern during the follow-up. Thus, it is possible that a single measure of exposure may not fully capture the sustained effects of sleep duration over time on long-term risk of type 2 diabetes. Fourth, a meta-analysis of observational data, though prospective, cannot directly control for residual or unmeasured confounding. We made an attempt to allow for multiple confounding by including adjusted estimates from multivariate models from each contributing study. However, due to limited data from the original studies, we were unable to stratify studies by race/ethnicity and sex, although this represents an important area for future research. Finally, sleep quality affected by factors like sleep apnea is an independent predictor of diabetes risk (12), but it was not assessed in our study.

Conclusion

In summary, our dose-response meta-analysis of prospective studies shows a U-shaped relationship between sleep duration and risk of type 2 diabetes, with the lowest type 2 diabetes risk at 7–8 h per day of sleep duration. Both short and long sleep duration are associated with an elevated risk of type 2 diabetes. Longer-term randomized controlled trials are needed to establish causality and to elucidate the underlying mechanisms.

Funding. This work was funded by the National Science and Technology Support Program (2012BAI02B02).

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. Z.S. conceived the study, searched the databases and checked them according to the eligible criteria and exclusion criteria, analyzed the data, and wrote the draft of the manuscript. H.M. and P.Y. helped extract quantitative data from some papers and contributed to writing, reviewing, or revising the manuscript. M.X. searched the databases and checked them according to the eligible criteria and exclusion criteria and contributed to writing, reviewing, or revising the manuscript. Y.G. provided advice on meta-analysis methodology. W.B. provided advice on meta-analysis methodology, analyzed the data, and contributed to writing, reviewing, or revising the manuscript. Y.R. analyzed the data and contributed to writing, reviewing, or revising the manuscript. C.L.J. and F.B.H. contributed to writing, reviewing, or revising the manuscript. L.L. conceived the study, helped develop search strategies, and contributed to writing, reviewing, or revising the manuscript.

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