# Maternal sleep during pregnancy and adverse pregnancy outcomes: A systematic review and meta-analysis 

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## Keywords

Gestational diabetes mellitus,
Pregnancy outcome, Sleep

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J Diabetes Investig 2022; 13: 12621276
doi: 10.1111/jdi. 13770


#### Abstract

Aims/Introduction: Sleep problems are important public health concern worldwide. We carried out a meta-analysis to quantitatively evaluate whether sleep duration was associated with pregnancy outcomes, and the associations were modified by important characteristics of studies. Materials and Methods: Based on PubMed, Embase and the Cochrane Central Register of Controlled Trials databases, we searched for published literature related to maternal sleep duration and adverse pregnancy outcomes before 30 June 2021. We carried out risk of bias assessment, subgroup analyses and sensitivity analysis. The relative risks or odds ratios with $95 \%$ confidence intervals (Cl) were used to estimate the pooled effects. Results: A total of 5,246 references were identified through a database search, and 41 studies were included in the study. Pregnant women with short sleep duration had 1.81fold $(95 \% \mathrm{Cl} 1.35-2.44, P<0.001)$ the risk of developing gestational diabetes mellitus. The association between short sleep duration and the risk of gestational hypertension, cesarean section, low birthweight, preterm birth and small for gestational age were not significant ( $P>0.05$ ). Furthermore, long sleep duration was significantly correlated with gestational diabetes mellitus (odds ratio1.24. 95\% CI 1.12-1.36, $P<0.001$ ) and CS (odds ratio $1.13 .95 \% \mathrm{Cl} 1.04-1.22, P=0.004$ ), whereas long sleep duration was not linked with gestational hypertension, low birthweight, preterm birth and small for gestational age ( $P>0.05$ ). Conclusions: Short/long sleep duration appeared to be associated with adverse pregnancy outcomes, specifically with an increased risk of gestational diabetes mellitus. Sleep should be systematically screened in the obstetric population.


## INTRODUCTION

Sleep problems frequently beset the majority of pregnant women. Due to considerable changes in hormone levels, physical discomfort, nocturnal awakenings and fertility-related anxiety during pregnancy, pregnant women often suffer from sleep disturbances, which might lead to insufficient sleep time, poor

[^0]sleep quality, insomnia, sleep-disordered breathing (SDB), restless legs syndrome and so on ${ }^{1,2}$. According to the Pittsburgh Sleep Quality Index (PSQI) cut-off score of $\geq 5$, the results from a meta-analysis found that the prevalence of sleep disturbances was $36.5-55.2 \%^{3}$. The rate was higher in some epidemiological studies, which was estimated at $70.5-77.1 \%^{4,5}$. The American Academy of Sleep Medicine and Sleep Research Society developed a consensus recommendation that adults should sleep at least 7 h per night $^{6}$. Actually, it was reported that
approximately $28 \%$ of pregnant women slept less than 7 h per night ${ }^{7}$. In addition, a study reported that the incidence of long sleep time was $14.7-24.4 \%^{8}$.

Significant sleep disturbance is not only common, but also adverse for health ${ }^{9,10}$. Multitudinous studies have researched the relationship between sleep during pregnancy and subsequent maternal and fetal outcomes ${ }^{11,12}$. However, some previous studies reported that sleep had no association with adverse pregnancy outcomes, whereas other emerging evidence suggested that sleep was involved in adverse maternal complications and fetal outcomes. For example, Qiu et al. ${ }^{13}$ reported that deficiency and excess of sleep increased the risk of placental abruption. Morokuma et al. found that the association between bedtime and small for gestational age (SGA) was not significant ${ }^{14}$. However, the data of Weng's study in 2020 showed that short sleep was related to SGA, with 2.14 -fold odds, but its association did not reach statistical significance ${ }^{15}$.

Previous meta-analyses showed the association between sleep disturbances and healthy outcomes. Sleep disturbances were associated with the development of preeclampsia, gestational diabetes mellitus (GDM), cesarean section (CS), depression and preterm birth (PTB) ${ }^{16}$. A significant association between sleep-disordered breathing and GDM was evident in the study by Luque-Fernandez et al. ${ }^{17}$; however, the evidence about the effect of sleep duration on adverse pregnancy outcomes was limited. The outcomes were confined to GDM, PTB and SGA ${ }^{16,18,19}$. Only a recent meta-analysis showed consideration for multifarious adverse outcomes ${ }^{20}$, but the authors did not carry out a subgroup analysis or sensitivity analysis to test the robustness of findings across country, trimester or study design.

Sleep problems are important public health concerns worldwide. With mothers and babies as the key population, it is essential to quantify the risk of sleep time on adverse pregnancy outcomes. In the interest of providing supportive evidence for clinical guidance, we carried out a meta-analysis to examine whether sleep time was associated with pregnancy outcomes, and the associations were modified by important characteristics of studies.

## MATERIALS AND METHODS

## Electronic search

The present study was carried out following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The study protocol was recorded in the National Institute for Health Research Prospero International Prospective Register of Systematic Reviews (PROSPERO) with the number of CRD42020221948. Articles were identified by searching three electronic scientific literature databases, including PubMed, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL). A spacious retrieval method was developed to search for all related articles up to 30 June 2021. In regard to Medical Subject Heading (MeSH) terms and
key words, it combined term "sleep" as the exposure variable; the terms "gestational diabetes mellitus", "gestational hypertension", "cesarean section", "low birthweight", "preterm birth" and "small for gestational age" as the outcome variables; and the term "pregnant" as the target population. Details of the search terms are shown in Table S1.

## Selection criteria

The included criteria for the meta-analysis were as follows: (i) original articles of observational studies, including crosssectional studies, case-control studies and cohort studies; (ii) a data analysis of sleep time and any aforementioned outcome; (iii) had a definite measure of sleep time, including PSQI, interview or questionnaire; (iv) were able to classify groups of short sleep duration (SSD), referent sleep duration and long sleep duration (LSD); and (v) presented the relative risks or odds ratios (ORs) and $95 \%$ confidence intervals ( $95 \% \mathrm{CI}$ ), or provided sufficient data to quantify the case of outcomes with different sleep durations. Studies were excluded if they were: (i) case series, case reports, abstracts or randomized controlled trials; or (ii) not reported in English. There were no geographic restrictions for studies.

## Sleep exposure

Based on the latest recommendation and previous literature on pregnancy outcomes, $7-9 \mathrm{~h}$ of sleep is the appropriate sleep duration ${ }^{1,6}$. Short sleep time usually means less than 7 h of sleep per night, whereas long sleep time is usually defined as 9 h or more. However, the cut-off points for sleep duration varied between studies. In some studies, sleep less than 8 h or 6 h were deemed to be $\mathrm{SSD}^{21-23}$. In addition, sleep time might be a binary classification or multiclassification in different studies. To identify relationships and inconsistencies in the literature, when the sleep time was a binary classification, we extracted data as SSD and non-SSD, and when the sleep time was a multiclassification, we tried our best to extract data as SSD, appropriate sleep duration (ASD) and LSD. Both nonSSD and ASD belonged to referent sleep duration. Longitudinal studies showed that sleep quality was poor from the second to the third trimester ${ }^{3}$. Pre-eclampsia symptoms usually start after 20 weeks of pregnancy ${ }^{24}$. When there were data for the second trimester and the third trimester at the same time, the data of the second trimester were used for analysis.

## Data extraction

First, two investigators (Wang and Xu ) independently evaluated the titles and abstracts of all studies. Second, they searched for the potential articles and screened the full texts, which contributed to clearing the final articles for meta-analysis. Another author (Xie) made a judgment when there was an inconsistent decision about inclusion. Third, data extraction was carried out and double-checked. Extracted terms included author, year, country, study design, the measure of sleep time, study population, the definition of SSD, referent sleep duration and LSD,
outcome assessment, the trimester investigating sleep during pregnancy, and the main results of the study, including the number of each outcome in different sleep durations, ORs or relative risks. Importantly, the adjusted ORs with the most adjustment variables received priority. If we failed to extract ORs or relative risks, then we calculated the OR and its $95 \%$ CI using the elaborate count of each outcome for pregnancy, and merged all ORs.

## Assessment of study quality

The Newcastle-Ottawa scale (NOS) was utilized to assess study quality. The NOS is appliable for evaluating case-control studies and cohort studies, through three blocks with a total of eight items, including selection, comparability, exposure evaluation or results evaluation ${ }^{25,26}$. The NOS uses the semiquantitative principle of the star system to evaluate the quality of the publications. The scores range from 0 to 9 . Higher scores indicate better quality. The Agency for Healthcare Research and Quality is suitable for evaluating the overall risk of bias of cross-sectional studies on account of 11 questions ${ }^{27}$. The Agency for Healthcare Research and Quality does not have a specific score, but suggests using high-, medium- and low-risk classification methods. Low-risk means high quality.

## Statistical analysis

The ORs with $95 \%$ CIs for binary results were used to estimate the merging effects. The $I^{2}$ contributed to investigating the heterogeneity of the studies. The higher $I^{2}$ is, the more significant heterogeneity the study shows. When $I^{2}$ was $>50 \%$, a random effects model was used to output the ORs and their $95 \%$ CIs. If not, a fixed effects model was used. Subgroup analyses were carried out for the type of study design (cohort study, cross-sectional study and case-control study), geographical region (Asia and Non-Asia) and referent sleep duration (nonSSD and ASD).

## Publication bias

Begg's and Egger's tests were used to show the publication bias. Some studies believed that the Egger's test was more sensitive than the Begg's test, when the studies included were limited or the publication bias was small ${ }^{28}$. $P$-values $<0.05$ were statistically significant. When publication bias existed, funnel plots and the Duval and Tweedie trim and fill test were carried out.

## Sensitivity analysis

Sensitivity analysis was carried out to deal with high heterogeneity by removing one study and pooled the effects of remaining studies. If the result did not change significantly after the exclusion, it meant that the sensitivity was low, and the result was more robust and reliable. On the contrary, if the result was quite different or even the opposite conclusion after the exclusion, it meant that the sensitivity was high, and the robustness of the result was low. All data analyses were carried out using R version 3.6.1 (https://www.r-project.org/).

## RESULTS

## Characteristics of the retrieved studies

Figure 1 shows a flowchart outlining the selection of eligible literature. There were 5,246 articles initially identified, after removing duplicates and double assessment, 41 of which were ultimately included in the meta-analysis ${ }^{8,14,15,21-23,29-63}$. These studies took place mainly in the USA $(n=13)^{8,31-35,38,39,47,49,50,58,59}$. Most studies were cohorts $(n=32)^{8,14,15,21-23,30-34,36,38-54,58,59,62}$, whereas there were seven case-control studies ${ }^{35,37,55-57,60,61}$ and two cross-sectional studies $^{29,63}$. A total of 16 studies ( $n=24,58.8 \%$ ) reported data for the second trimester. The measurement of sleep time included a questionnaire $(n=28)^{8,14,15,21,22,29,31,33-37,40-46,48-50,54,56,59-61,63}$, PSQI $(n=8)^{23,30,51,53,55,57,58,62}$, structured interview $(n=1)^{47}$, monitor $(n=2)^{38,39}$, sleep $\log (n=1)^{32}$ and one study did not report ${ }^{52}$. Notably, studies were published from 2004 to 2021. The total number of participants was 226,101 . We showed the number, age and essential terms of participants for each study in Table 1. The included articles showed great quality, there was one study with the NOS score $<5$.

## Short sleep duration and adverse pregnancy outcomes

The forest plots showed the pooled results for the connection between short sleep time and the risk of adverse pregnancy outcomes (Figure 2). Involving 597 gestational diabetes patients who has short sleep time in 15 of the included studies, the plot showed that women with a shorter sleep time were more likely to have a GDM than those without, with an OR of 1.81 ( $95 \%$ CI 1.35-2.44, $P<0.001$ ). Significant heterogeneity was noted ( $I^{2}=75.6 \%, P<0.001$ ). At the same time, we could see that women with short sleep time were associated with a higher proportion of hypertension than those without. However, the association was not statistically significant (OR 1.09, 95\% CI 0.93$1.27, P=0.296$ ). No heterogeneity was perceived $\left(I^{2}=0.0 \%\right.$, $P=0.427$ ). Basing on a random effects model with moderate or high heterogeneity, pregnant women with short sleep time were not associated with a significant increased risk of CS (OR 1.17, 95\% CI 0.82-1.66, $P=0.396$ ), low birthweight (LBW; OR 1.19, $95 \%$ CI $074-1.91, P=0.538$ ), PTB (OR 1.12, 95\% CI 0.93-1.34, $P=0.227$ ) and SGA (OR $1.26 ; 95 \%$ CI $0.87-1.84, P=0.127$ ).

## Long sleep duration and adverse pregnancy outcomes

As we can see from Figure 3, the forest plots showed the effect of long sleep time on the risk of adverse pregnancy outcomes. According to the summarized result with low heterogeneity ( $I^{2}=25.2 \%, P=0.228$ ), pregnant women with long sleep time were associated with a significant increased risk of GDM (OR $1.24,95 \%$ CI $1.12-1.36, P<0.001$ ). With two studies in each group, long sleep duration was associated with an increased risk of CS (OR 1.13, $95 \%$ CI $1.04-1.22, P=0.004$ ), whereas no association was found between long sleep time and the risk of gestational hypertension (GH; OR 1.15, 95\% CI 0.59-2.27, $P=0.677$ ) and LBW (OR 0.92, 95\% CI 0.85-1.01, $P=0.070$ ). Meanwhile, paying close attention to pregnant women with or


Figure $\mathbf{1}$ | Flow chart of the identification of eligible studies.
without SGA, we found that no significant difference in long sleep time and group of reference (OR $0.81 ; 95 \%$ CI $0.63-1.06$, $P=0.204$ ). High significant heterogeneity was found among 7 studies ( $I^{2}=87.9 \%, P<0.001$ ).

## Publication bias and sensitivity analysis

As shown in Table S2 and Figure S1, we carried out statistical tests to assess publication bias. The results showed that publication bias existed in studies for the association between SSD and GDM. The Duval and Tweedie trim and fill test showed that seven studies were required. Future subgroup analysis showed that all subgroups studied with the outcome of GDM indicated that sleep time played an adverse role (Table 2). The definition of SSD, referent sleep duration and definition of GDM might be factors for high heterogeneity and publication bias. The effect of SSD on PTB varied in diverse regions, and a non-ideal and statistically significant association was found in non-Asia regions (Table 2). Despite moderate heterogeneity for studies of PTB, it might be explained by the influence of region. It was interesting that a statistically significant association was found between LSD and SGA in cohort studies and cross-sectional studies (Table 3).

Sensitivity analysis was carried out to determine whether the aforementioned results were under the influence of a special
study (Figures S2 and S3). For the outcome of GDM, no matter which study was eliminated, the results were meaningful. For the association between LSD and the outcome of CS and SGA, without the study of Weng et al. and Chaudhary et al., respectively, the pooled effect of LSD on CS and SGA was statistically significant. LSD was a risk factor for CS and a protective risk for SGA.

## DISCUSSION

Good sleep during pregnancy is very important for both the pregnant mother and the fetus, but due to factors, such as hormones and body discomfort, during pregnancy, it is not easy to have healthy sleep. The recognition of the association between poor and excess sleep and pregnancy outcomes is essential. The meta-analysis was carried out to explore the association between gestational sleep duration and adverse pregnancy outcomes. Differing from previous studies, this study was concerned with integrated pregnancy complications and fetal outcomes, including GDM, GH, CS, LBW, PTB and SGA. As suggested by the present study, sleep time was associated with pregnancy complications, specifically with an increased risk of GDM. Short sleep time increased the risk of GDM, whereas long sleep time contributed to the risk of GDM and CS, which reminds us to pay attention to pregnant women's sleep.
Table 1 | Study and participant characteristics for all included studies

| Author | Year | Country | Study design | Measure | Population | Trimester |  | Mean age (years) | Outcomes | $\begin{aligned} & \text { NOS/ } \\ & \text { AHRQ } \end{aligned}$ | Adjustment |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Abeysena et al. ${ }^{21}$ | 2009 | Sri Lanka | Cohort | Questionnaire | 690 | 2 |  | $26.4 \pm 5.5$ | SGA | 7 | (-) |
| Abeysena et al. ${ }^{22}$ | 2010 | Sri Lanka | Cohort | Questionnaire | 739 | 1-3 |  | $26.4 \pm 5.5$ | LBW | 7 | (-) |
| Cai et al. ${ }^{23}$ | 2017 | Singapore | Cohort | PSQI | 686 | 2 | (b) | $\begin{gathered} 32.1 \pm 4.8 / \\ 30.3 \pm 5.1 \end{gathered}$ | GDM | 8 | Adjusted for maternal age, ethnicity, education, body mass index at <14 weeks of gestation, history of gestational diabetes and State-Trait Anxiety Inventory total score |
| Chaudhary et al. ${ }^{29}$ | 2021 | Nepal | Crosssectional | Questionnaire | 4,000 | 3 |  | $\geq 20$ | SGA | Medium | $(-)$ |
| Du et al. ${ }^{30}$ | 2020 | China | Cohort | PSQI | 3,692 | 1 |  | 18-45 | GDM | 9 | Adjusted for maternal age, ethnicity, employment, education status, household registration, income, family history of diabetes, history of GDM, stillbirth history, history of induced abortion, parity, gravidity, pre-pregnancy body mass index, gestational weight gain, health-related quality of life, dietary caloric intake, physical activity, smoking, alcohol drinking, type of diet and folicacid supplementation for 3 months before pregnancy |
| Facco et al.31 | 2010 | USA | Cohort | Questionnaire | 182 | 2 | (a) | $\begin{gathered} 30.6 \pm 4.9 / \\ 29.3 \pm 5.7 \end{gathered}$ | GDM | 9 | Adjusted for age, ethno-racial status, BMI and frequent snoring |
| Facco et al.32 | 2017 | USA | Cohort | Sleep log and monitor | 782 | 2 |  | $>18$ | GDM; GH | 9 | Adjusted for maternal age |
| Facco et al. ${ }^{33}$ | 2018 | USA | Cohort | Questionnaire | 7,668 | 2 |  | $>18$ | GDM; GH | 8 | Adjusted for age, body mass index, race/ethnicity, employed and insurance status |
| Facco et al. ${ }^{34}$ | 2019 | USA | Cohort | Questionnaire | 7,658 | 2 |  | $27.0 \pm 5.7$ | PTB | 8 | Adjusted for age and body mass index. |
| Guendelman et al. ${ }^{35}$ | 2013 | USA | Case-control | Questionnaire | 1,023 | 2 |  | >18 | PTB | 8 | Adjusted for race and month of delivery. |
| Howe et al. ${ }^{36}$ | 2015 | New Zealand | Cohort | Questionnaire | 633 | 3 | (c) | $\begin{array}{r} 29.4 \pm 6.1 / \\ 32.8 \pm 4.8 \end{array}$ | SGA | 4 | (-) |
| Kajeepeta et al. ${ }^{37}$ | 2014 | Peru | Case-control | Questionnaire | 959 | 1 | (b) | $\begin{array}{r} 28.2 \pm 6.6 / \\ 28.3 \pm 6.5 \end{array}$ | PTB | 7 | Adjusted for maternal age, pre-pregnancy weight, unplanned pregnancy and no vitamin use during pregnancy |
| Kominiarek et al. ${ }^{38}$ | 2020 | USA | Cohort | Monitor | 83 | 1-3 |  | $26.2 \pm 5.2$ | $\begin{gathered} \text { GDM; GH; } \\ \text { PTB; CS } \end{gathered}$ | 7 | (-) |
| Lee et al. ${ }^{39}$ | 2004 | USA | Cohort | Monitor | 131 | 3 |  | $32.1 \pm 4.5$ | CS | 7 | Adjusted for infant birthweight |

Table 1. (Continued)

| Author | Year | Country | Study design | Measure | Population | Trimester |  | Mean age (years) | Outcomes | $\begin{aligned} & \text { NOS/ } \\ & \text { AHRQ } \end{aligned}$ | Adjustment |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Li et al. ${ }^{40}$ | 2016 | China | Cohort | Questionnaire | 688 | 2 |  | $29.3 \pm 3.9$ | CS; PTB | 8 | Adjusted for maternal age, parity, pre-pregnancy body mass index, exercise habit and birthweight |
| Li et al. ${ }^{41}$ | 2021 | China | Cohort | Questionnaire | 1,082 | 2 |  | $28.7 \pm 4.0$ | PTB; SGA | 8 | Adjusted for maternal age, parity, level of education, method of conception, exercise habits before pregnancy, passive exposure to smoking, pre-pregnancy body mass index, and gestational weight gain |
| Liu et al. ${ }^{42}$ | 2019 | China | Cohort | Questionnaire | 11,311 | 3 | (b) | $\begin{array}{r} 28.3 \pm 4.6 / \\ 28.2 \pm 3.6 \end{array}$ | PTB; SGA | 6 | Adjusted for age, education, annual household income, occupation during pregnancy, cigarette smoking, passive smoking exposure, alcohol drinking, midday nap duration, parity, pre-pregnancy body mass index and pregnancy weight gain |
| Loy et al. ${ }^{43}$ | 2019 | Singapore | Cohort | Questionnaire | 673 | 2 | (a) | $\begin{array}{r} 32.4 \pm 5.6 / \\ 30.7 \pm 4.9 \end{array}$ | GDM; PTB | 7 | Adjusted for age, ethnicity, education, monthly household income, employment status, night-shift, physical activity, early pregnancy body mass index, anxiety score, total eating episodes, total energy intake and infant sex, bedtime, and gestational diabetes mellitus |
| Micheli et a ${ }^{\text {P4 }}$ | 2011 | Greece | Cohort | Questionnaire | 1,091 | 3 |  | 30.6 | $\begin{aligned} & \text { SGA; LBW; } \\ & \text { PTB } \end{aligned}$ | 6 | Adjusted for maternal age, education, pre-pregnancy body mass index and smoking status |
| Morokuma et al ${ }^{14}$ | 2017 | Japan | Cohort | Questionnaire | 7,291 | 2 |  | $30.6 \pm 5.0$ | SGA | 8 | Adjusted risk: maternal age, pre-pregnancy body mass index, gestational age at birth, smoking, hypertension, alcohol consumption and education |
| Murata et al..$^{55}$ | 2021 | Japan | Cohort | Questionnaire | 82,171 | 2 | (a) | $\begin{array}{r} 31.7 \pm 5.5 / \\ 31.7 \pm 4.9 \end{array}$ | PTB; LBW; SGA | 9 | (-) |
| Myoga et al. ${ }^{46}$ | 2019 | Japan | Cohort | Questionnaire | 48,787 | 2 | (b) | $\begin{array}{r} 33.3 \pm 5.0 / \\ 31.1 \pm 5.0 \end{array}$ | GDM | 7 | Adjusted for age, pre-pregnancy body mass index, gestational weight gain, steroid use during pregnancy and previous GDM |
| Okun et al. ${ }^{47}$ | 2012 | USA | Cohort | Structured interview | 217 | 2 |  | $30.1 \pm 5.8$ | PTB | 6 | Adjusted for age, employment, marital status and history of preterm birth |
| Paine et al. ${ }^{48}$ | 2020 | New Zealand | Cohort | Questionnaire | 929 | 3 |  | 32-40 | CS | 6 | Adjusted for ethnicity, age group, area deprivation, parity, clinical indicator and body mass index |

Table 1. (Continued)

| Author | Year | Country | Study design | Measure | Population | Trimester |  | Mean age (years) | Outcomes | $\begin{aligned} & \text { NOS/ } \\ & \text { AHRQ } \end{aligned}$ | Adjustment |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Qiu et al. ${ }^{49}$ | 2010 | USA | Cohort | Questionnaire | 1,290 | 1 | (b) | $\begin{gathered} 35.2 \pm 5.0 / \\ 33.2 \pm 4.3 \end{gathered}$ | GDM | 6 | Adjusted for maternal age and race/ ethnicity |
| Rawal et al. ${ }^{8}$ | 2019 | USA | Cohort | Questionnaire | 2,530 | 2 | (a) | $\begin{gathered} 28.8 \pm 5.5 / \\ 28.2 \pm 5.4 \end{gathered}$ | GDM | 8 | Adjusted for maternal age, gestational age at interview, race/ethnicity, parity, education, pre-pregnancy body mass index, marital status, family history of diabetes and napping frequency during corresponding weeks |
| Reutrakul et $a^{50}$ | 2011 | USA | Cohort | Questionnaire | 142 | 2 | (b) | $\begin{gathered} 30.1 \pm 5.5 / \\ 27.4 \pm 5.3 \end{gathered}$ | GDM; PTB | 9 | $(-)$ |
| Teong et al. ${ }^{51}$ | 2017 | Malaysia | Cohort | PSQI | 216 | 3 |  | $31.2 \pm 4.5$ | CS; LBW | 7 | $(-)$ |
| Trivedi et al. ${ }^{52}$ | 2021 | India | Cohort | (-) | 1,977 | (-) |  | $24.6 \pm 2.5$ | PTB | 6 | $(-)$ |
| Umeno et al. ${ }^{53}$ | 2020 | Japan | Cohort | PSQI | 87 | 3 | (a) | $\begin{gathered} 31.1 \pm 4.8 / \\ 30.8 \pm 4.6 \end{gathered}$ | CS | 6 | $(-)$ |
| Wang et al. ${ }^{54}$ | 2017 | China | Cohort | Questionnaire | 3,567 | 1 | (a) | $\begin{array}{r} 28.9 \pm 3.3 / \\ 28.9 \pm 3.4 \end{array}$ | LBW; SGA | 8 | Adjusted for maternal age, education level, alcohol consumption, smoking, ethnicity, height, pre-pregnancy body mass index, gestational weight gain, gestational age, average personal income, parity, fetal gender and midday napping |
| Wang et al. ${ }^{55}$ | 2017 | China | Case-control | PSQI | 12,506 | 2 | (b) | $\begin{gathered} 29.4 \pm 3.1 / \\ 28.4 \pm 2.8 \end{gathered}$ | GDM | 8 | Adjusted for maternal age, height, family history of diabetes, parity, Han ethnicity, education, body mass index and systolic blood pressure at first antenatal care visit, multiple pregnancies, weight gain from pre-pregnancy to glucose challenge test, habitual smoking and alcohol consumption before/during pregnancy |
| Wang et al. ${ }^{56}$ | 2021 | China | Case-control | Questionnaire | 500 | 1 | (b) | $\begin{array}{r} 29.0 \pm 3.6 / \\ 27.4 \pm 2.8 \end{array}$ | GDM | 8 | Adjusted for age, ethnicity, education, drinking, smoking, gestational age, parity, progesterone use, midday napping duration and family history of diabetes |
| Wang et al. ${ }^{57}$ | 2021 | China | Case-control | PSQI | 1,300 | 2 |  | $28.1 \pm 3.4$ | GDM | 7 | Adjusted for maternal age, ethnicity, education, pre-pregnancy body mass index, parity, alcohol consumption, smoking, gestational age and family history of diabetes |

Table 1. (Continued)

| Author | Year | Country | Study design | Measure | Population | Trimester |  | Mean age (years) | Outcomes | $\begin{aligned} & \text { NOS/ } \\ & \text { AHRQ } \end{aligned}$ | Adjustment |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Weng et al. ${ }^{15}$ | 2020 | China | Cohort | Questionnaire | 488 | 2 |  | $32.2 \pm 4.1$ | CS; SGA | 6 | Adjusted for maternal age, education, marital status, employment, self-rated family income, parity, abortion history, pregestational body mass index, excessive gestational weight gain and maternal pregnancy complications |
| Whitaker et al. ${ }^{58}$ | 2021 | USA | Cohort | PSQI | 120 | 1-3 | (a) | $\begin{gathered} 31.4 \pm 4.9 / \\ 31.0 \pm 4.7 \end{gathered}$ | GH | 8 | Adjusted for site, age, race, parity, pre-pregnancy body mass index, sedentary behavior trajectory and moderate-to-vigorous intensity physical activity trajectory |
| Williams et al. ${ }^{59}$ | 2010 | USA | Cohort | Questionnaire | 1,272 | 1 |  | $>18$ | GH | 9 | $(-)$ |
| Xu et al. ${ }^{60}$ | 2017 | China | Case-control | Questionnaire | 2,345 | 1-3 |  | 18-45 | GDM | 6 | $(-)$ |
| Yadav et al. ${ }^{61}$ | 2019 | Nepal | Case-control | Questionnaire | 1,104 | 3 | (b) | $\begin{gathered} 19.0 \pm 2.3 / \\ 19.5 \pm 2.3 \end{gathered}$ | LBW | 5 | (-) |
| Yang et al. ${ }^{62}$ | 2021 | China | Cohort | PSQI | 13,015 | 2 |  | $28.5 \pm 2.9$ | CS | 7 | Adjusted for age, body mass index, weight gain from registration to glucose challenge test, gestational age at delivery, habitual smokers before and during pregnancy, alcohol drinkers before and during pregnancy, family history of diabetes in first-degree relatives, parity $\geq 1$, Han nationality, systolic blood pressure at registration for pregnancy, birthweight, neonatal height and gestational diabetes |
| Zafarghand et al. ${ }^{63}$ | 2011 | Iran | Cross-sectional | Questionnaire | 457 | 3 |  | $27.4 \pm 5.7$ | CS; LBW | Medium | (-) |



Figure 2 | Forest plots of the association between short sleep time and adverse pregnancy outcomes. ( + ), Women with any outcome in the group of short sleep duration; (-), women without outcome in the group of reference sleep duration; \%W, Weight\%; Case, women with short sleep duration; Control, women with reference sleep duration; CS, cesarean section; GDM, gestational diabetes mellitus; GH, gestational hypertension; LBW, low birthweight; LCl, lower confidence interval; NR, not reported; OR, odds ratio; PTB, preterm birth; Ref, reference sleep duration; SGA, small for gestational age; SSD, short sleep duration; UCI, upper confidence interval.

Studies have also found that pregnant women were more likely to have poor sleep quality and extreme sleep duration. According to a recent meta-analysis, the average PSQI score is 6.07, and approximately half of expectant mothers suffer poor sleep quality. From the second trimester to the third trimester, the average PSQI score increased by 1.68 points, which showed that poor sleep quality was common during pregnancy ${ }^{3}$. Recently, a systematic review confirmed that the prevalence of insomnia in the third trimester of pregnancy is $42.4 \%$, which meant approximately one-third of pregnant women failed to maintain enough sleep ${ }^{64}$. Furthermore, sleep satisfaction and duration decline sharply after delivery, and are difficult to fully recover to pre-pregnancy ${ }^{65}$. It is important to clearly, definitively and comprehensively evaluate the association between gestational sleep time and pregnancy outcomes.

The results of the present study were not exactly consistent with the previous studies. For instance, a meta-analysis clarified that there was a U-shaped relationship between sleep time and PTB, whereas the present study did not ${ }^{66}$. In addition, Zhang et al. ${ }^{67}$ carried out a review showing that pregnant women with 8 h of sleep had lower GDM risk. Whereas in the review by Xu et al. ${ }^{68}$, long but not short sleep time was the risk factor for GDM. A recent systematic review and meta-analysis found that short sleep time was significantly associated with the development of pre-eclampsia, GDM, PTB and stillbirth ${ }^{20}$. In this present study, compared with women with ASD not non-SSD, women with SSD were associated with a significantly higher risk of GH. It is clear that evidence regarding the association between sleep duration and GH, CS and LBW is scant, and these studies reported a wide variation in results. The aforementioned varied findings might result from different study designs, definitions of short and long sleep duration, and group of reference.

In view of the high heterogeneity of the present research, the consideration of variables and the identification of subgroups will contribute to future studies. It is well-known that daytime sleepiness and naps are modifiable risk factors for sleep at night. In the early stages of pregnancy, the hormone progesterone, which contributes to regulating the female reproductive cycle, will increase in large quantities ${ }^{69}$. Progesterone not only makes pregnant women feel extremely sleepy during the day, but also disrupts their nocturnal sleep, which leads to poor or excess sleep time. However, only a few studies have investigated this, and the small sample size is not conducive to analysis. Wang et al..$^{70}$ found women who nap $>1 \mathrm{~h} /$ day had a significantly increased risk of GDM. In addition, depressive symptoms and later gestation were significantly associated with short
sleep time ${ }^{71}$, which emphasized the importance of sleep assessment. It has been previously shown that age, parity, race, education and income were not significantly associated with sleep changes ${ }^{72}$. As a result of lack of statistical power, the aforementioned variables were not significant. Smoking and sugarsweetened beverage consumption can result in poor sleep ${ }^{69,73}$. However, the exploration of these factors during pregnancy is lacking.

Existing studies mentioned the potential mechanisms underlying the link between sleep time and adverse pregnancy outcomes. There was an abundance of evidence to say that sleep interacts with the immune system during pregnancy. Pregnant women with inadequate sleep time appear to have light sleep, which is associated with the increase of inflammatory biomark$\mathrm{ers}^{74}$. For instance, short sleep time is associated with higher Creactive protein levels ${ }^{75}$. As key factors of obstetric complications, inflammation increases during pregnancy will cause poor health related to pregnancy, principally preterm birth and $\mathrm{GH}^{76,77}$. Furthermore, short and long sleep duration interferes with the circadian rhythm. Long-term sleep disorders might cause changes in neuroendocrine function and metabolism, resulting in obesity and insulin resistance, and finally inducing diabetes ${ }^{78,79}$.

Poor sleep duration exerts an adverse effect on placental development and nutrient absorption, leading to LBW and $\mathrm{SGA}^{13}$. As for sleep duration and CS, the underlying pathophysiological mechanisms are unclear. Extreme sleep duration is associated with excessive inflammation, which might be detrimental to pregnancy. A pro-inflammatory environment contributes to triggering contractions and rupture of the membranes, promoting $\mathrm{CS}^{80}$.

The present meta-analysis had some advantages. Based on extensive literature searches and the inclusion of more than 20,000 pregnant women, our findings are consistent with previous assumptions. Short sleep duration and long sleep duration are associated with GDM. It is worthy to further investigate the dose-response relationship between sleep duration and GDM to clearly and definitively identify the best sleep duration. Focusing on common adverse pregnancy outcomes, we extracted and showed important information in detail. Taking into account the heterogeneity of the results, we carried out a subgroup analysis and sensitivity analysis to preliminarily explore the potential influencing factors, which provide ideas for future research. In particular, we carefully divided the referent sleep duration into non-SSD and ASD, which further clarifies the effect of SSD on pregnancy outcomes.

Outcome:GDM


| Author | Year | LSD | Ref |  |  |  |  |  |  |  |  |  | OR | ICI | UCI | \%W | \%W |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Author | Year | LSD | Ref | (+) | (-) | (+) | (-) |  |  |  |  |  | OR | LCI | UCI | (fixed) | (random) |
| Whitaker, et al | 2021 | 7.5 h | 5 h | 17 | 79 | , | 21 |  |  |  |  |  | 1.51 | 0.40 | 5.63 | 26.2 | 26.2 |
| Williams, et al | 2010 | $\geq 10 \mathrm{~h}$ | 5-6 h | 13 | 122 | 14 | 138 |  |  |  |  |  | 1.05 | 0.48 | 2.32 | 73.8 | 73.8 |
| Fixed effect model ( $p=0.677$ ) |  |  |  |  |  |  |  |  |  |  |  |  | 1.15 | 0.59 | 2.27 | 100.00\% |  |
| Random effect model ( $p=0.677$ ) |  |  |  |  |  |  |  |  |  |  |  |  | 1.15 | 0.59 | 2.27 | - | 100.00\% |
| Heterogeneity: I-squared $=0 \%, p=0.643$ |  |  |  |  |  |  |  | 0.2 | 0.5 |  | 2 | 5 |  |  |  |  |  |

Outcome:CS


| Author | Year | LSD | Ref | Case |  | Control |  |  | OR |  | OR | LCI | UCI | $\begin{gathered} \% W \\ \text { (fixed) } \end{gathered}$ | \%W(random) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | (+) | (-) | (+) | (-) |  |  |  |  |  |  |  |  |
| Murata, et al | 2021 | 9-9.9 h | 6-7.9 h | 837 | 11139 | 3101 | 34843 |  |  |  | 0.92 | 0.84 | 1.00 | 98.1 | 98.1 |
| Wang, et al | 2017 | $\geq 9 \mathrm{~h}$ | 8-9 h | 29 | 1261 | 34 | 1529 |  |  |  | 1.10 | 0.59 | 2.05 | 1.9 | 1.9 |
| Fixed effect model ( $p=0.070$ ) |  |  |  |  |  |  |  |  |  |  | 0.92 | 0.85 | 1.01 | 100.00\% |  |
| Random effect model ( $p=0.070$ ) |  |  |  |  |  |  |  |  |  |  | 0.92 | 0.85 | 1.01 | - | 100.00\% |
| Heterogeneity: I-squared=0\%, $\boldsymbol{p}=0.578$ |  |  |  |  |  |  |  | 0.5 | 1 | 2 |  |  |  |  |  |



| Author | Year | LSD | Ref |  | se | Con | trol |  | OR |  | OR |  |  | \%W | \%W |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Author | Year | LSD | Ref | (+) | (-) | ( + | (-) |  | OR |  | OR | LCI | UCI | (fixed) | (random) |
| Chaudhary, et al | 2021 | 10-14 h | 8-9 h | 112 | 1109 | 418 | 1644 | * |  |  | 0.40 | 0.32 | 0.50 | 10.1 | 17.2 |
| Howe, et al | 2015 | $\geq 9 \mathrm{~h}$ | 6-9 h | 1 | 1 | 1 | 1 |  | + |  | 1.60 | 0.80 | 3.20 | 1.0 | 8.4 |
| Liu, et al | 2019 | 9.1-10 h | 7.1-9 h | 1 | 1 | 1 | 1 |  | + |  | 0.83 | 0.71 | 0.98 | 19.3 | 18.2 |
| Morokuma, et al | 2017 | 9-12 h | 7-7.9 h | 77 | 1198 | 187 | 2212 |  |  |  | 0.80 | 0.60 | 1.08 | 5.8 | 15.7 |
| Murata, et al | 2021 | 9-9.9 h | 6-7.9 h | 558 | 11418 | 1951 | 35993 |  |  |  | 0.91 | 0.83 | 1.00 | 59.7 | 19.1 |
| Wang, et al | 2017 | $\geq 9 \mathrm{~h}$ | 8-9 h | 85 | 1205 | 100 | 1463 |  |  |  | 0.98 | 0.72 | 1.34 | 5.2 | 15.4 |
| Weng, et al | 2020 | $>8 \mathrm{~h}$ | 7-8 h | 1 | 1 | 1 | 1 |  |  |  | 1.05 | 0.43 | 2.57 | 0.6 | 6.1 |
| Fixed effect model ( $p<0.001$ ) |  |  |  |  |  |  |  |  |  |  | 0.83 | 0.77 | 0.89 | 100.00\% |  |
| Random effect model ( $p=0.204$ ) |  |  |  |  |  |  |  |  |  |  | 0.81 | 0.63 | 1.06 | - | 100.00\% |
| Heterogeneity: I-squared=87.9\%, p<0.001 |  |  |  |  |  |  |  | 0.5 | 1 | 2 |  |  |  |  |  |

Figure $\mathbf{3} \mid$ Forest plots of the association between long sleep time and adverse pregnancy outcomes. (+), Women with any outcome in the group of long sleep duration; (-), women without outcome in group of referent sleep duration; \%W, Weight\%; Case, women with long sleep duration; Control, women with referent sleep duration; CS, cesarean section; GDM, gestational diabetes mellitus; GH, gestational hypertension; LBW, low birthweight; LCl, lower confidence interval; LSD, long sleep duration; NR, not reported; OR, odds ratio; PTB, preterm birth; Ref, reference sleep duration; SGA, small for gestational age; UCI, upper confidence interval.

Table 2 | Pooled results for subgroup of short sleep duration and adverse pregnancy outcomes

| Outcomes of interest | Study design |  |  | Region |  | Reference sleep duration |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Cohort | Cross-sectional | Case-control | Asia | Non-Asia | SSD vs non-SSD | SSD vs ASD |
| GDM | 1.39 (1.14, 1.71) | - | 2.74 (1.21, 6.20) | 1.78 (1.25, 2.52) | 1.74 (1.15, 2.64) | 1.71 (1.14, 2.56) | 1.80 (1.26, 2.56) |
| GH | 1.09 (0.93, 1.27) | - | - | - | 1.09 (0.93, 1.27) | 1.04 (0.89, 1.23) | 1.85 (1.04, 3.28) |
| CS | 1.26 (0.84, 1.88) | 0.80 (0.46, 1.39) | - | 1.16 (0.76, 1.75) | 1.27 (0.51, 3.18) | 1.16 (0.70, 1.91) | 1.09 (0.83, 1.44) |
| LBW | 1.05 (0.60, 1.84) | 2.98 (1.49, 5.94) | 0.86 (0.42, 1.76) | 1.29 (0.75, 2.24) | 0.70 (0.34, 1.46) | - | 1.19 (0.74, 1.91) |
| PTB | 1.07 (0.86, 1.32) | - | 1.30 (0.93, 1.34) | 1.07 (0.76, 1.51) | 1.20 (1.04, 1.38) | - | 1.12 (0.93, 1.34) |
| SGA | 1.07 (0.87, 1.31) | 2.13 (2.13, 3.08) | - | 1.39 (0.92, 2.12) | 0.83 (0.54, 1.27) | - | 1.26 (0.87, 1.84) |

Data are presented as the odds ratio (95\% confidence interval). -, Not enough data to be pooled; ASD, appropriate sleep duration; CS, cesarean section; GDM, gestational diabetes mellitus; GH, gestational hypertension; LBW, low birthweight; PTB, preterm birth; SGA, small for gestational age; SSD, short sleep duration. All the bold values are statistically significant, with $P<0.05$.

Table $\mathbf{3}$ | Pooled results for the subgroup of long sleep duration and adverse pregnancy outcomes

| Outcomes of interest | Study design |  |  | Region |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  | Cohort | Cross-sectional | Case-control | Asia | Non-Asia |
| GDM | 1.13 (1.00, 1.29) | - | 1.37 (1.19, 1.58) | 1.23 (1.11, 1.35) | 1.56 (0.92, 2.63) |
| GH | 1.15 (0.59, 2.27) | - | - | - | 1.15 (0.59, 2.27) |
| CS | 1.13 (1.04, 1.22) | - | - | 1.13 (1.04, 1.22) | - |
| LBW | 0.92 (0.85, 1.01) | - | - | 0.92 (0.85, 1.01) | - |
| PTB | 1.07 (0.95, 1.20) | - | 1.14 (0.66, 1.99) | 1.07 (0.95, 1.20) | 1.14 (0.66, 1.99) |
| SGA | 0.90 (0.83, 0.96) | 0.40 (0.32, 0.50) | - | 0.77 (0.58, 1.01) | 1.60 (0.63, 1.06) |

Data are presented as the odds ratio ( $95 \%$ confidence interval). - Not enough data to be pooled; CS, cesarean section; GDM, gestational diabetes mellitus; GH, gestational hypertension; LBW, low birthweight; PTB, preterm birth; SGA, small for gestational age. All the bold values are statistically significant, with $P<0.05$.

The present study had a number of limitations. First, the studies included were observational studies, so heterogeneous bias is a concern for them ${ }^{81}$. Second, the heterogeneity of pooled results was high, which might be due to different diagnostic criteria of outcomes, investigation of sleep time for nocturnal sleep or $24-\mathrm{h}$ sleep, the definition of short sleep time and so on. To explore and explain high heterogeneity, random effects models and subgroups for study design and region are carried out. Third, a general limitation is that our meta-analysis was limited to English studies. The subgroup analysis showed that the risk of PTB in pregnant women with SSD varied in different regions (Asia or non-Asia). The potential influence of culture should be addressed in the future. Fourth, ORs exacted from the studies included were adjusted by different variables. Therefore, further studie3s are required to better eliminate the potential impact of residual confounding.

Short sleep duration and long sleep duration have cacoethic effects on pregnant women and infants. As sleep time is a potentially important and modifiable behavioral target in pregnancy, systematical prenatal screening should focus on sleep. During counseling, prenatal healthcare and subsequent interventions, clinical professionals should screen the sleep of pregnant women and guide proper sleep habits according to the estimates of risks quantified by the present meta-analysis.

## ACKNOWLEDGMENTS

This work was supported by the National Social Science Foundation of China (No. 20BRK037) and the Key Research and Development Program of Shaanxi (No. 2019SF-100). The funder was not involved in the design, collection, analysis, interpretation of data and writing of the study. We appreciate all authors of publications included in the meta-analysis.

## DISCLOSURE

The authors declare no conflict of interest.
Approval of the research protocol: The study protocol was recorded in PROSPERO with the number of CRD42020221948. Informed consent: N/A.
Approval date of registry and the registration no. of the study: The approval date of Registry is 2 March 2021; the registration number is CRD42020221948.
Animal studies: N/A.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 | Details of search strategy.
Table S2 | Results of Begg's and Egger's test.
Figure S1 | Funnel plot for outcome of gestational diabetes mellitus.
Figure S2 | Plot for sensitivity analysis of short sleep duration and adverse pregnancy outcomes.
Figure S3 | Plot for sensitivity analysis of long sleep duration and adverse pregnancy outcomes.


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    Received 16 September 2021; revised 26 January 2022; accepted 11 February 2022

