



HHS Public Access

Author manuscript

Am J Obstet Gynecol. Author manuscript; available in PMC 2019 January 14.

Published in final edited form as:

Am J Obstet Gynecol. 2017 April ; 216(4): 399.e1–399.e8. doi:10.1016/j.ajog.2016.11.1051.

A longitudinal study of sleep duration in pregnancy and subsequent risk of gestational diabetes: findings from a prospective, multiracial cohort

Shristi Rawal, PhD¹, Stefanie N. Hinkle, PhD¹, Yeyi Zhu, PhD¹, Paul S. Albert, PhD², and Cuilin Zhang, MD, PhD¹

¹Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20817, USA

²Biostatistics and Bioinformatics Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20817, USA

Abstract

Background—Both short and prolonged sleep duration have been linked to impaired glucose metabolism. Sleep patterns change during pregnancy, but prospective data is limited on its relation to gestational diabetes.

Objective(s)—To prospectively examine the trimester-specific (1st and 2nd trimester) association between typical sleep duration in pregnancy and subsequent risk of gestational diabetes, as well as the influence of compensatory daytime napping on this association.

Study Design—In the prospective, multiracial NICHD Fetal Growth Studies-Singleton Cohort, 2581 pregnant women reported their typical sleep duration and napping frequency in the 1st and 2nd trimesters. Diagnosis of gestational diabetes (n=107; 4.1%) was based on medical records review. Adjusted relative risks (aRRs) [95% confidence interval (CI)] for gestational diabetes were

Corresponding author: Cuilin Zhang, Epidemiology Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, 6710B Rockledge Dr, MSC 7004, Bethesda, MD 20817, USA. Phone/fax: 301-435-6917. zhangcu@mail.nih.gov.

The authors report no conflict of interest.

Part of the findings from this study was presented at the 76th Scientific Sessions of the American Diabetes Association, New Orleans, LA, June 10-14, 2016.

Contribution statement: SR conducted the data analysis and wrote the first draft of the manuscript. SNH contributed to data management, data interpretation and revised the manuscript. YZ contributed to data interpretation and revised the manuscript. PSA contributed to data analysis and interpretation and reviewed the manuscript. CZ contributed to funding, concept and design, data interpretation and revised the manuscript. All authors contributed to the critical interpretation of the results, reviewed the manuscript for important intellectual content, and approved the final version of the manuscript. SR and CZ are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

estimated with Poisson regression, adjusting for demographics, pre-pregnancy body mass index, and other risk factors.

Results—From the 1st to 2nd trimester, sleep duration and napping frequency declined. Sleeping duration in the 2nd but not 1st trimester was significantly related to risk of gestational diabetes. The association between 2nd trimester sleep and gestational diabetes differed by pre-pregnancy obesity status (p-for-interaction=0.04). Among non-obese but not obese women, both sleeping more or less than 8-9 hours were significantly related to risk of gestational diabetes [aRRs (95% CI): 5-6 hours: 2.52 (1.27-4.99); 7 hours: 2.01 (1.09-3.68); 10 hours 2.17 (1.01-4.67)]. Significant effect modification by napping frequency was also observed in the 2nd trimester (p-for-interaction=0.03). Significant and positive association between reduced sleep (5-7 hours) and gestational diabetes was observed among women napping rarely/never [aRR (95% CI): 2.48 (1.20, 5.13)], whereas no comparable associations were observed among women napping most/sometimes.

Conclusions—Our data suggest a U-shaped association between sleep duration and gestational diabetes, and that napping and pre-pregnancy obesity status may modify this association.

Keywords

pregnancy; sleep patterns; glucose metabolism; napping; GDM

Introduction

Gestational diabetes mellitus (GDM), a common pregnancy complication affecting up to 13% of all pregnancies, is linked to several adverse health outcomes in both women and their children.¹ Identifying modifiable risk factors of GDM is hence critical in order to prevent the growing burden of GDM and its long-term adverse health sequelae.

Evidence from experimental and observational studies suggests that both reduced and prolonged sleep duration are linked to impaired insulin sensitivity and glucose metabolism.^{2,3} Several underlying mechanisms have been proposed, including elevated oxidative stress, increased systemic inflammation, dysregulation of energy homeostasis, and chronic activation of the hypothalamic-pituitary-adrenal axis.^{2,3} Pregnant women are particularly vulnerable to sleep disturbances, owing to hormonal changes, physical discomfort, or anxiety surrounding childbirth.^{4,6} Whether sleep duration during pregnancy contributes to GDM risk is not clear as existing studies have been limited and conflicting.⁷⁻¹¹ Prospective studies are particularly scarce, with only one study⁸ to date examining sleep duration in early pregnancy in relation to subsequent GDM risk.

In pregnancy, sleep patterns change across gestation.^{4, 5} In the first trimester, sleep duration tends to increase, with this trend reversing in the second trimester.^{4, 5} Compared to mid-pregnancy, napping is also more common towards the beginning and end of pregnancy, which may affect the total sleep exposure in a 24-hour period.⁶ Longitudinal assessments of sleeping and napping habits during pregnancy are hence needed to investigate the influence of sleep duration on GDM risk. The trimester-specific association between typical sleep duration and GDM risk, and the influence of compensatory daytime napping on this association has not yet been evaluated. In addition, although obesity is a risk factor for

excessive sleepiness,¹² its influence on the association between sleep duration and GDM during pregnancy is unknown.

In the present study, our objective was to prospectively examine the trimester-specific association between self-reported sleep duration and subsequent GDM risk in a multiracial cohort of pregnant women. As a secondary objective, we examined whether daytime napping modifies the relation between sleep duration and GDM.

Methods

Study Population

This prospective study was conducted on the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Fetal Growth Studies-Singleton Cohort (2009-2013), consisting of 2,334 non-obese pregnant women¹³ and 468 obese pregnant women between the ages of 18-40 years. Sample selection and eligibility criteria have been described in detail previously.¹³ Briefly, women with a history of chronic diseases such as hypertension, diabetes, or cancer were excluded. Eligible women were recruited between 8-13 weeks of gestation from 12 participating clinical sites across the US and followed throughout pregnancy. Institutional review board approval was obtained from all participating sites including NICHD. All participants provided informed consents.

The analytical population was composed of 2,581 women (92.1%) with available medical records and sleep data at enrollment (8-13 weeks); Two percent of the analytical sample (n=51) were lost to follow up at 16-22 weeks.

Exposure Assessment

Structured questionnaires assessed sleep duration and napping frequency during the first (8-13 weeks) and second (16-22 weeks) trimester. At both visits, participants were asked to indicate their typical sleep duration with possible responses including “5 hours or less,” “6 hours,” “7 hours,” “8 hours,” “9 hours,” or “10 hours or more.” Participants were also asked: “how often do you get so sleepy during the day or evening that you have to take a nap?” with possible responses including “most of the time,” “sometimes,” or “rarely or never.”

Outcome assessment

GDM diagnosis was abstracted from medical records (n=107). The diagnosis was based on either the oral glucose tolerance test, using the Carpenter and Coustan's diagnostic criteria¹⁴ or indication of medication-treated GDM on the hospital charge diagnosis (n=12).

Covariates

Several covariates were examined, including socio-demographic variables such as age, race-ethnicity, education, marital status, gestational age at interview, parity, and known risk factors of GDM including family history of diabetes, prior GDM, and pre-pregnancy body mass index (BMI; calculated from self-reported weight and measured height at enrollment, kg/m²). Participants also reported consumption of caffeinated beverages (coffee/tea/soda/energy drinks) during each trimester (cups) and consumption of alcoholic beverages before

pregnancy. Smoking status in the 6 months prior to pregnancy was asked of the obese women; non-obese women who smoked before pregnancy were not eligible for this study.

Statistical Analysis

Participant characteristics across sleep duration categories were compared using the chi-square test for categorical data and one-way ANOVA for continuous variables. Poisson regression models (using log-link) with robust variance estimates were used to estimate adjusted relative risks (aRR) and 95% confidence intervals (CI) for the association between typical sleep duration prior to GDM diagnosis and subsequent risk of GDM. Separate models were fitted for sleep duration in the first and second trimester. Typical sleep duration was categorized as “5-6 hours”, “7 hours”, “8-9 hours” and “10 hours,” with “8-9 hours” as the reference group, to be comparable to prior studies.^{8, 10} In the multivariable model, analyses were adjusted for *a priori* selected covariates including age, gestational age at interview, race-ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian & Pacific Islander), nulliparity (yes, no), education (less, equal to or more than high-school), pre-pregnancy BMI, marital status (married/living with a partner or not), and family history of diabetes (yes, no). A second model further adjusted for napping frequency (most times, sometimes, rarely/never) at the corresponding trimester.

Caffeine consumption during pregnancy and alcohol consumption before pregnancy were not associated with GDM and hence were not considered in the multivariable models. Due to the small number of women (n=17) who smoked before pregnancy, smoking status was not included in the multivariable models. In sensitivity analyses we excluded women who smoked before pregnancy (n=17) and women with prior GDM (n=32). Additionally, we assessed for effect modification by pre-pregnancy obesity status (BMI <30.0 vs. ≥30.0 kg/m²), race-ethnicity, family history of diabetes (yes vs. no), napping frequency (most/sometimes vs. rarely/never), and clinical site.

In sensitivity analyses, missing data (9.7%) were imputed with multiple imputation method (M=100)¹⁵, majority of which stemmed from lack of medical chart abstraction. There were no significant differences in age, race-ethnicity, education, parity, pre-pregnancy BMI or family history of diabetes between women who were missing or not missing the medical chart. Women who were non-Hispanic White were more likely to be lost to follow up at 16-22 weeks; none of the other key variables differed between those who were retained or lost to follow up.

All tests were two-tailed and *P*-values <0.05 were considered statistically significant for main effects and <0.15 for interactions. Statistical analyses were completed using SAS version 9.4 (Cary, NC).

Results

From the first to second trimester, the proportion of women sleeping 7 hours or less increased (30.7% vs. 36.2%), whereas the proportion of women sleeping 10 hours declined (24.4% vs. 14.7%) considerably. Compared to the first trimester, fewer women napped most/sometimes (80.4% vs. 54.4%) in the second trimester. Sleep duration in the first trimester

varied significantly across several socio-demographic and lifestyle characteristics (Table 1). For example, women who were younger, Hispanic or nulliparous were more likely to sleep 10 hours, whereas those who were non-Hispanic White, married, or had greater education level were less likely to sleep 10 hours. Interestingly, women who reported napping most frequently in the first trimester were also most likely to sleep the most (10 hours) in a typical day. Similar socio-demographic and lifestyle patterns were observed with sleep duration in the second trimester, except for family history of diabetes, which was only associated with sleep duration in the first trimester.

First trimester sleep duration was not associated with subsequent GDM risk (Table 2). In the second trimester, the association between sleep duration and GDM differed by pre-pregnancy obesity status (p for interaction=0.04) with the association only significant among non-obese women. Among the non-obese, both sleeping more or less than 8-9 hours was associated with approximately two-fold higher risk of GDM (Table 2). The associations persisted after adjusting for other GDM risk factors including age, race, pre-pregnancy BMI, and parity. The associations became slightly attenuated, but were still significant after further adjusting for napping frequency in the second trimester. The highest risk for GDM [aRR=2.52 (1.27, 4.99)] was observed among non-obese women who slept 5-6 hours in the second trimester. In sensitivity analyses, we also stratified the analyses by three BMI categories (normal-weight, overweight, obese); the direction and magnitude of the associations between sleep and GDM were similar among normal-weight and overweight women, which was consistent with a non-significant interaction test observed in the multivariable model.

While napping in itself was not associated with GDM risk in either trimester, it significantly modified the sleep-GDM association (p for interaction=0.03). GDM risk was not significantly related to sleep duration among women who napped most/sometimes, whereas the association was significant among women who rarely or never napped in the second trimester. Specifically, among women who rarely or never napped in the second trimester, those who slept 7 hours or less had a significantly higher risk of GDM compared to women who slept 8-9 hours, even after adjusting for other major risk factors of GDM [aRR (95% CI) = 2.48 (1.20, 5.13)]. Among women who rarely or never napped in the second trimester, those sleeping 10 hours had a marginally increased risk of GDM, compared to women who slept 8-9 hours [aRR (95% CI) = 2.90 (0.97, 8.70)]. In the sub-sample of non-obese women, further stratification by napping frequency (p for interaction=0.049) revealed that the associations between sleep duration and GDM were not significant among non-obese women who napped most/sometimes, but was strongly significant with a U-shaped association among those who never/rarely napped (data not shown).

When considering the joint effect of sleep duration and napping frequency in the second trimester (Table 3), we observed that the women who slept longer (10 hours) and rarely/never napped had the highest risk of GDM [aRR (95% CI) =3.07 (1.02, 9.22)]. We also examined changes in sleep duration from the first to second trimester in association with GDM risk and found no significant associations. There was no suggestion of effect modification by race-ethnicity, family history of diabetes, or clinical site on the association between sleep duration and subsequent GDM risk (data not shown). In sensitivity analyses

we excluded women who smoked before pregnancy (n=17) or those who had a history of prior GDM (n=32), and the results were similar. The analyses with imputed data showed similar results to analyses that excluded women with missing data.

Comment

In this prospective and longitudinal study, we observed a U-shaped association between sleep duration in the second trimester and subsequent risk of GDM, with both less or more sleep than the optimal 8-9 hours per night associated with a higher GDM risk. Moreover, our findings suggested that pre-pregnancy obesity status and napping frequency modified this association as significant associations were only observed among women who were non-obese prior to pregnancy or napped rarely or never during the second trimester. Our findings did not extend to sleep duration in the first trimester, suggesting that the impact of sleep during pregnancy on GDM risk may be more acute than insidious.

Epidemiological studies on the sleep and GDM association are sparse and have just recently begun to emerge. Findings from the few available studies⁷⁻¹¹ have been inconsistent and have provided limited inference due to the retrospective designs and/or small sample sizes. For example, consistent with our study, two other studies^{8, 10} have observed a U-shaped association between sleep duration in pregnancy and GDM risk, although the findings were not always significant for both extremes of sleep duration. In a recent study based on a large cohort of Chinese women¹⁰, both short and prolonged sleep duration were associated with increased GDM risk, but the results were only significant for prolonged sleep duration. However, temporality could not be established from this study¹⁰ as the sleep duration was assessed concurrently with GDM diagnosis. A second prospective, but small study⁸, found that the association between sleep duration in early pregnancy and GDM was statistically significant for very short sleep durations but insignificant for longer sleep duration. This pilot study⁸ however had a relatively few GDM cases (n= 68) and as such, inference from this study was hindered by limited statistical power. Studies^{7, 9} only examining the influence of reduced sleep on GDM have also reported mixed findings. For example, Facco et al.⁷ reported a positive and significant association between short sleep duration and GDM, yet the study only had 10 GDM cases and did not distinguish between women who reported short sleep in early pregnancy or the third trimester, making the findings hard to interpret. Another cross-sectional study⁹ only found a marginal positive association between short sleep duration and GDM diagnosis at the second trimester. Studies^{16, 17} evaluating continuous glucose tolerance test measures instead of clinical endpoint of GDM have also observed inconsistent findings.

The present study extends the previous literature by reporting, for the first time, trimester-specific association between sleep duration in pregnancy and subsequent GDM risk, which is particularly important given the substantial variations in sleep duration across pregnancy. Our findings that the association between sleep duration and GDM risk varied by trimester, pre-pregnancy obesity status, and napping frequency may partly explain the inconsistent reports in the literature. One of the novel findings from this study was that the 2nd trimester sleep duration was associated with an increased GDM risk only among non-obese women. One possible explanation could be that the benefits of optimal sleep are not strong enough to

overcome the influence of pre-pregnancy obesity on GDM risk. In contrast to our study, Qiu et al.⁸ observed that the magnitude of the association between reduced sleep and GDM risk was greater among overweight/obese women as compared to lean women (<25 kg/m²); it is worth noting, however, that the majority of women in their overweight/obese group were overweight and not obese. In the present study, we also observed that the association between short sleep duration in the second trimester and GDM risk was only significant among infrequent nappers, providing for the first time, modest and preliminary evidence that daytime napping may compensate for the adverse effects of insufficient sleep on glucose metabolism.

There are multiple physiological pathways by which sleep disturbances may adversely affect glucose homeostasis. Experimental studies among non-pregnant individuals show that sleep restriction can reduce insulin sensitivity and acute insulin response, which in turn may lead to decreased glucose tolerance.^{2, 18, 19} Sleep deprivation has been linked to elevated oxidative stress and increased inflammatory responses, both of which can affect insulin signaling and adversely impact glucose homeostasis.^{3, 20, 21} Sleep curtailment can also cause increased activation of the sympathetic nervous system, which can disrupt glucose homeostasis and induce insulin resistance by increasing glycogen breakdown and gluconeogenesis.²² Additional proposed mechanisms are disruption of the hypothalamic-pituitary-adrenal axis, elevations in growth hormone and cortisol levels, and diminished glucose uptake in the brain.^{3, 23} The mechanisms by which prolonged sleep can adversely influence glucose tolerance are not well understood. One possibility is that excessive sleep allows for less time to be physically active. Increased sedentary time is linked to adverse cardio-metabolic outcomes and increased insulin resistance.^{24, 25} Additionally, both prolonged and reduced sleep could contribute to insulin resistance in pregnancy by dysregulating appetite hormones such as leptin and ghrelin, which may ultimately disrupt energy homeostasis and cause weight gain.^{3, 23}

Our study had several strengths. To our knowledge, this study is the first to longitudinally examine sleep patterns in pregnancy and investigate trimester-specific associations between sleep duration and subsequent GDM risk. The prospective nature of the present study reduces the possibility of reverse causation. Our follow up rate was quite high (92.2%), decreasing the probability of selection bias. The study sample also had a good representation of multiple race/ethnicities, and was recruited from 12 clinical centers across the US. Compared to existing studies, we had a relatively large number of GDM cases that were based on medical records as opposed to self-report. However, we cannot exclude the possibility that some GDM cases were missed on the available medical record or from those lacking the chart abstraction data. Since excessive or insufficient sleep is associated with several chronic diseases such as type 2 diabetes, and cardiovascular diseases, an additional strength of this study was that it was conducted among relatively healthy women without major chronic diseases.

Some potential limitations of our study merit discussion. The primary limitation was that sleep duration and napping frequency were self-reported, and thus may be subject to misclassification bias. Self-reported sleep duration is known to be reasonably yet modestly correlated with wrist actigraph-measured sleep duration.²⁶ However, given the study's

prospective design, we expect misclassification if any to be non-differential, which according to our bias analyses²⁷, would yield a bias towards the null. Secondly, our study was focused on the duration of sleep and did not measure other aspects of sleep, such as sleep quality or sleep fragmentation. As such, we could not examine whether co-existing comorbidities such as sleep apnea, could account for the observed association between sleep duration and GDM. Third, we did not evaluate how dietary and lifestyle factors could influence the association between sleep duration and GDM. Fourth, the prevalence of GDM and pre-pregnancy obesity in our sample were slightly lower than national estimates,^{28, 29} presumably due to our relatively healthy cohort. Lastly, due to the lack of data on nap duration, we could not examine whether short or long nap duration had a differential association with GDM risk. Hence, our findings on napping and GDM should be regarded as preliminary.

In summary, the longitudinal and prospective data from our study provides an important contribution to the understanding of the link between sleep duration and GDM risk. Our findings have potential important clinical implications as they suggest that getting optimal amount of sleep in mid-pregnancy, or compensating for insufficient sleep with daytime napping, may help lower GDM risk, which may ultimately reduce adverse health impacts of GDM on both expecting mothers and their newborns. Future studies that assess sleep quality and include objective measures of nocturnal and daytime sleep duration are needed to extend our findings.

Acknowledgments

We acknowledge the contribution of the research teams at our participating clinical centers, including Christina Care Health Systems; University of California, Irvine; Long Beach Memorial Medical Center; Northwestern University; Medical University of South Carolina; Columbia University; New York Hospital Queens; St Peters' University Hospital; University of Alabama at Birmingham; Women and Infants Hospital of Rhode Island; Fountain Valley Regional Hospital and Medical Center; and Tufts University.

Disclosure Statement: This study was supported by *the Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) intramural funding and included American Recovery and Reinvestment Act funding via contract numbers HHSN275200800013C, HHSN275200800002I, HHSN27500006, HHSN275200800003IC, HHSN275200800014C, HHSN275200800012C, HHSN275200800028C, and HHSN275201000009C, and HHSN275201000001Z. The NICHD intramural investigators were involved in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. The work was performed at NICHD and participating clinical centers, including Christina Care Health Systems; University of California, Irvine; Long Beach Memorial Medical Center; Northwestern University; Medical University of South Carolina; Columbia University; New York Hospital Queens; St Peters' University Hospital; University of Alabama at Birmingham; Women and Infants Hospital of Rhode Island; Fountain Valley Regional Hospital and Medical Center; and Tufts University.

References

1. Zhu Y, Zhang C. Prevalence of Gestational Diabetes and Risk of Progression to Type 2 Diabetes: a Global Perspective. *Curr Diab Rep.* 2016; 16:7. [PubMed: 26742932]
2. Reutrakul S, Van Cauter E. Interactions between sleep, circadian function, and glucose metabolism: implications for risk and severity of diabetes. *Ann N Y Acad Sci.* 2014; 1311:151–73. [PubMed: 24628249]
3. Izci-Balserak B, Pien GW. The relationship and potential mechanistic pathways between sleep disturbances and maternal hyperglycemia. *Curr Diab Rep.* 2014; 14:459. [PubMed: 24398662]
4. Hedman C, Pohjasvaara T, Tolonen U, Suhonen-Malm AS, Myllyla VV. Effects of pregnancy on mothers' sleep. *Sleep Med.* 2002; 3:37–42. [PubMed: 14592252]

5. Lee KA, Zaffke ME, McEnany G. Parity and sleep patterns during and after pregnancy. *Obstet Gynecol.* 2000; 95:14–8. [PubMed: 10636494]
6. Mindell JA, Jacobson BJ. Sleep disturbances during pregnancy. *J Obstet Gynecol Neonatal Nurs.* 2000; 29:590–7.
7. Facco FL, Grobman WA, Kramer J, Ho KH, Zee PC. Self-reported short sleep duration and frequent snoring in pregnancy: impact on glucose metabolism. *Am J Obstet Gynecol.* 2010; 203:142e1–5. [PubMed: 20510182]
8. Qiu C, Enquobahrie D, Frederick IO, Abetew D, Williams MA. Glucose intolerance and gestational diabetes risk in relation to sleep duration and snoring during pregnancy: a pilot study. *BMC women's health.* 2010; 10:17. [PubMed: 20470416]
9. Reutrakul S, Zaidi N, Wroblewski K, Kay HH, Ismail M, Ehrmann DA, et al. Sleep disturbances and their relationship to glucose tolerance in pregnancy. *Diabetes care.* 2011; 34:2454–7. [PubMed: 21926292]
10. Wang H, Leng J, Li W, Wang L, Zhang C, Liu H, et al. Sleep duration and quality, and risk of gestational diabetes mellitus in pregnant Chinese women. *Diabet Med.* 2016
11. Naud K, Ouellet A, Brown C, Pasquier JC, Moutquin JM. Is sleep disturbed in pregnancy? *J Obstet Gynaecol Can.* 2010; 32:28–34. [PubMed: 20370977]
12. Panossian LA, Veasey SC. Daytime sleepiness in obesity: mechanisms beyond obstructive sleep apnea--a review. *Sleep.* 2012; 35(5):605–15. [PubMed: 22547886]
13. Buck Louis GM, Grewal J, Albert PS, Sciscione A, Wing DA, Grobman WA, et al. Racial/ethnic standards for fetal growth: the NICHD Fetal Growth Studies. *Am J Obstet Gynecol.* 2015; 213:449e1–e41. [PubMed: 26410205]
14. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 30, September 2001 (replaces Technical Bulletin Number 200, December 1994). Gestational diabetes. *Obstet Gynecol.* 2001; 98:525–38. [PubMed: 11547793]
15. Graham JW, Olchowski AE, Gilreath TD. How many imputations are really needed? Some practical clarifications of multiple imputation theory. *Prev Sci.* 2007; 8:206–13. [PubMed: 17549635]
16. Herring SJ, Nelson DB, Pien GW, Homko C, Goetzl LM, Davey A, et al. Objectively measured sleep duration and hyperglycemia in pregnancy. *Sleep Med.* 2014; 15:51–5. [PubMed: 24239498]
17. Izci Baserak B, Jackson N, Ratcliffe SA, Pack AI, Pien GW. Sleep-disordered breathing and daytime napping are associated with maternal hyperglycemia. *Sleep Breath.* 2013; 17:1093–102. [PubMed: 23354511]
18. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet.* 1999; 354:1435–9. [PubMed: 10543671]
19. Buxton OM, Pavlova M, Reid EW, Wang W, Simonson DC, Adler GK. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. *Diabetes.* 2010; 59:2126–33. [PubMed: 20585000]
20. Vgontzas AN, Zoumakis E, Bixler EO, Lin HM, Follett H, Kales A, et al. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. *J Clin Endocrinol Metab.* 2004; 89:2119–26. [PubMed: 15126529]
21. Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. *Arch Intern Med.* 2006; 166:1756–62. [PubMed: 16983055]
22. Schmid SM, Jauch-Chara K, Hallschmid M, Schultes B. Mild sleep restriction acutely reduces plasma glucagon levels in healthy men. *J Clin Endocrinol Metab.* 2009; 94:5169–73. [PubMed: 19837925]
23. O'Keeffe M, St-Onge MP. Sleep duration and disorders in pregnancy: implications for glucose metabolism and pregnancy outcomes. *Int J Obes (Lond).* 2013; 37(6):765–70. [PubMed: 22945608]
24. Mayer-Davis EJ, D'Agostino R Jr, Karter AJ, Haffner SM, Rewers MJ, Saad M, et al. Intensity and amount of physical activity in relation to insulin sensitivity: the Insulin Resistance Atherosclerosis Study. *JAMA.* 1998; 279:669–74. [PubMed: 9496984]

25. Assah FK, Brage S, Ekelund U, Wareham NJ. The association of intensity and overall level of physical activity energy expenditure with a marker of insulin resistance. *Diabetologia*. 2008; 51:1399–407. [PubMed: 18488189]
26. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? *Epidemiology*. 2008; 19:838–45. [PubMed: 18854708]
27. Lash, T, Fox, M, Fink, A. *Applying Quantitative Bias Analysis to Epidemiologic Data*. New York, NY: Springer-Verlag; 2009.
28. DeSisto CL, Kim SY, Sharma AJ. Prevalence Estimates of Gestational Diabetes Mellitus in the United States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2007-2010. *Prev Chronic Dis*. 2014; 11:E104. [PubMed: 24945238]
29. Fisher SC, Kim SY, Sharma AJ, Rochat R, Morrow B. Is obesity still increasing among pregnant women? Prepregnancy obesity trends in 20 states, 2003-2009. *Prev Med*. 2013; 56:372–8. [PubMed: 23454595]

Abbreviations

GDM	Gestational diabetes mellitus
NICHD	<i>Eunice Kennedy Shriver</i> National Institute of Child Health and Human Development

Table 1
Participant characteristics by sleep duration at 8-13 gestational weeks and 16-22 gestational weeks, the NICHD Fetal Growth Studies-Singleton Cohort (2009-2013)

Characteristics	Sleep duration at 8-13 Gestational Weeks					Sleep duration at 16-22 Gestational Weeks					P*
	Over all	5-6 hours	7 hours	8-9 hours	10 hours	Over all	5-6 hours	7 hours	8-9 hours	10 hours	
Age	2581 (5.5)	28.5 (5.5)	29.4 (5.3)	28.5 (5.3)	26.5 (5.6)	2530 (5.5)	28.8 (5.5)	29.5 (5.2)	28.2 (5.4)	25.5 (5.4)	<0.0001
Race/ethnicity											<0.0001
Non-Hispanic White	27.2	22.5	31.3	34.0	15.4	27.7	19.7	36.5	31.2	11.6	
Non-Hispanic Black	27.7	38.0	23.9	19.4	28.5	27.6	40.3	20.2	22	43.3	
Hispanic	28.7	27.4	25.0	28.5	32.3	28.6	27.4	23.2	29.7	33.6	
Asian/Pacific Islander	16.3	12.1	19.7	17.9	13.8	16.2	12.6	20.2	17.1	11.6	
Education											<0.0001
Less than high school	11.4	11.1	8.2	9.9	16.2	11.3	11.3	5.3	10.5	22.3	
High- school graduate or equivalent	18.4	21.6	10.8	16.7	24.1	18.3	18.5	11.2	18.4	28.0	
More than high school	70.2	67.3	81.1	73.4	59.8	70.4	70.3	83.5	71.2	49.7	
Married/living with a partner	74.4	69.0	79.5	79.6	65.2	74.4	68.6	80.8	78.3	58.1	<0.0001
Nulliparity	46.8	35.3	39.5	48.3	55.9	47.0	35.1	46.6	50.0	49.7	<0.0001
Smoking before pregnancy	0.7	0.2	0.8	0.9	0.5	0.6	1.3	0.8	0.5	0.3	0.26
Family history of diabetes	21.8	28.7	22.9	19.7	20.5	21.8	23.4	20.4	21.8	21.9	0.75
Alcoholic beverage consumption before pregnancy	64.6	62.2	71	66	59.8	64.8	62.1	73.2	64.5	57.0	<0.0001
Pre-pregnancy BMI,kg/m ²	25.5 (5.2)	26.3(5.8)	25.1 (5.0)	25.2 (5.0)	25.5 (5.2)	25.5 (5.2)	26.1 (5.5)	25.2(5.3)	25.3 (5.1)	25.8 (5.4)	0.016
Pre-pregnancy BMI categories											0.02
17.87-24.99 kg/m ²	56.4	51.0	59.4	57.6	56.0	56.5	51.2	60.8	57.2	53.5	
25.0-29.99 kg/m ²	26.5	27.1	26.8	26.7	25.4	26.3	27.9	23.7	27.2	25.5	
30.00-48.83 kg/m ²	17.1	21.9	13.8	15.7	18.7	17.2	20.9	15.5	15.6	20.9	
Need day nap during corresponding weeks											
Most of the time	42.9	41.0	34.0	35.4	63.4	20.8	27.2	13.9	15.0	43.7	<0.0001
Sometimes	37.6	39.1	38.7	42.0	27.7	35.6	31	33.5	38.2	35	

Characteristics	Sleep duration at 8-13 Gestational Weeks					Sleep duration at 16-22 Gestational Weeks					P*
	Over all	5-6 hours	7 hours	8-9 hours	10 hours	Over all	5-6 hours	7 hours	8-9 hours	10 hours	
Rarely or never	2581	(16%)	(14.7%)	(44.8%)	(24.4%)	2530	(15.4%)	(20.8%)	(49.1%)	(14.7%)	
Gestational age during interview (weeks)	19.5	19.9	27.4	22.6	8.9	43.5	41.8	52.7	46.9	21.3	
	12.7 (1.0)	12.7 (0.9)	12.8 (0.9)	12.7 (1.0)	12.6 (1.0)	19.7 (2.4)	19.7 (2.4)	20.1 (2.5)	19.7 (2.4)	19.4 (2.4)	0.001
Caffeinated beverages consumed (cups)	0.41 (0.8)	0.46 (0.9)	0.33 (0.7)	0.36 (0.7)	0.37 (0.9)	0.41 (0.8)	0.43 (0.8)	0.40 (0.7)	0.40 (0.8)	0.44 (0.9)	0.8

Data are presented as % for categorical variables and mean (SD) for continuous variables.

* P values for differences in participant characteristics across categories of sleep duration were obtained by χ^2 test for categorical variables and one way -ANOVA for continuous variables.

GDM, gestational diabetes mellitus

Table 2
Relative risk (95% confidence interval) of gestational diabetes mellitus (GDM) in association with self-reported sleep duration during the first and second trimester of pregnancy, the NICHD Fetal Growth Studies-Singleton Cohort (2009-2013)

Sleep Duration	n GDM/total n	Unadjusted RR (95% CI)	Adjusted Model A* RR (95% CI)	Adjusted Model B† RR (95% CI)
<u>First trimester (8-13 weeks)</u>				
All women				
8-9 hours	51/1157	1	1	1
5-6 hours	16/413	0.88 (0.51, 1.52)	0.87 (0.49, 1.55)	0.87 (0.49, 1.54)
7 hours	15/380	0.90 (0.51, 1.57)	0.91 (0.51, 1.60)	0.90 (0.51, 1.60)
10 hours	25/631	0.90 (0.56, 1.44)	1.07 (0.67, 1.71)	1.04 (0.65, 1.68)
Non-obese				
8-9 hours	33/977	1	1	1
5-6 hours	11/323	1.01 (0.52, 1.97)	1.06 (0.53, 2.13)	1.06 (0.53, 2.12)
7 hours	12/328	1.08 (0.57, 2.07)	1.02 (0.52, 1.98)	1.02 (0.52, 1.98)
10 hours	16/514	0.92 (0.51, 1.66)	1.17 (0.64, 2.14)	1.09 (0.59, 2.02)
Obese				
8-9 hours	18/180	1	1	1
5-6 hours	5/90	0.56 (0.21, 1.45)	0.60 (0.22, 1.62)	0.58 (0.22, 1.56)
7 hours	3/52	0.58 (0.18, 1.88)	0.70 (0.22, 2.19)	0.69 (0.22, 2.15)
10 hours	9/117	0.77 (0.36, 1.65)	1.00 (0.48, 2.05)	1.07 (0.50, 2.29)
<u>Second trimester (16-22 weeks)</u>				
All women				
8-9 hours	44/1242	1	1	1
5-6 hours	19/390	1.38 (0.81, 2.33)	1.49 (0.87, 2.57)	1.51 (0.89, 2.60)
7 hours	26/526	1.40 (0.87, 2.24)	1.37 (0.84, 2.22)	1.38 (0.85, 2.23)
10 hours	16/372	1.21 (0.69, 2.13)	1.55 (0.89, 2.71)	1.49 (0.82, 2.68)
Non-obese				
8-9 hours	24/1042	1	1	1
5-6 hours	14/306	1.99 (1.04, 3.79)	2.57 (1.31, 5.05)	2.52 (1.27, 4.99)
7 hours	20/442	1.96 (1.10, 3.52)	2.00 (1.09, 3.66)	2.01 (1.09, 3.68)
10 hours	12/291	1.79 (0.91, 3.54)	2.36 (1.14, 4.88)	2.17 (1.01, 4.67)
Obese				
8-9 hours	20/192	1	1	1
5-6 hours	5/81	0.59 (0.23, 1.52)	0.61 (0.25, 1.47)	0.62 (0.25, 1.50)
7 hours	6/81	0.71 (0.30, 1.71)	0.80 (0.32, 1.96)	0.79 (0.32, 1.95)
10 hours	4/77	0.50 (0.18, 1.41)	0.72 (0.28, 1.86)	0.76 (0.28, 2.05)

* In Model A, relative risks (aRR) and 95% confidence intervals (CI) were estimated with Poisson regression adjusting for maternal age (years), gestational age at interview (weeks), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian & Pacific Islander), parity (nulliparous or not), education (less, equal to or more than high-school), pre-pregnancy body mass index (kg/m^2), marital status (married/living with a partner vs. not), and family history of diabetes (yes/no).

[†]In Model B, relative risks (aRR) and 95% confidence intervals (CI) were estimated with Poisson regression adjusting for variables in Model 1+napping frequency during corresponding weeks.

GDM, gestational diabetes mellitus

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3
Relative risk (95% confidence interval) of gestational diabetes mellitus (GDM) in association with joint status of self-reported sleep duration and napping frequency at weeks 16-22 of pregnancy, the NICHD Fetal Growth Studies-Singleton Cohort (2009-2013)

Sleep duration/Napping Status	n GDM/total n	Unadjusted RR (95% CI)	Adjusted Model A* RR (95% CI)
8-9 hours & Rarely/Never	12/582	1	1
5-7 hours & Rarely/Never	26/440	2.61 (1.46, 5.62)	2.56 (1.28, 5.10)
10+ hours & Rarely/Never	4/79	2.41 (0.81, 7.43)	3.07 (1.02, 9.22)
5-7 hours & Some/Most times	19/476	1.95 (0.95, 3.95)	2.11 (1.03, 4.32)
8-9 hours & Some/Most times	32/660	2.23 (1.22, 4.52)	2.21 (1.16, 4.24)
10+ hours & Some/Most times	12/292	2.00 (0.91, 4.38)	2.44 (1.12, 5.29)

* In Model A, relative risks (aRR) and 95% confidence intervals (CI) were estimated with Poisson regression adjusting for maternal age (years), gestational age at interview (weeks), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Asian & Pacific Islander), parity (nulliparous or not), education (less, equal to or more than high-school), pre-pregnancy body mass index (kg/m^2) marital status, and family history of diabetes (yes/no)

GDM, gestational diabetes mellitus