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Adverse infant outcomes among women with sleep apnea or insomnia during pregnancy: A retrospective cohort study

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ABSTRACT

Objective: To evaluate whether sleep apnea or insomnia among pregnant people is associated with increased risk for adverse infant outcomes.
Design: Retrospective cohort study
Setting: California
Participants: The sample included singleton live births. Sleep apnea and insomnia were defined based on ICD-9 and -10 codes. A referent group was selected using exact propensity score matching on maternal characteristics, obstetric factors, and infant factors among individuals without a sleep disorder.
Measurements: Adverse infant outcomes were obtained from birth certificate, hospital discharge, and death records (eg, Apgar scores, neonatal intensive care unit (NICU) stay, infant death, long birth stay, etc.). Logistic regression was used to calculate odds of an adverse infant outcome by sleep disorder type.
Results: Propensity-score matched controls were identified for 69.9% of the 3371 sleep apnea cases and 68.8% of the 3213 insomnia cases. Compared to the propensity-matched referent group, individuals with a diagnosis of sleep apnea (n = 2357) had infants who were more likely to have any adverse outcome, low 1-min Apgar scores, NICU stay, and an emergency room visit in the first year of life. Infants born to mothers with a diagnosis of insomnia (n = 2212) were at increased risk of few negative outcomes relative to the propensity matched referent group, with the exception of an emergency room visit.
Conclusions: In unadjusted analyses, infants born to individuals with a diagnosis of sleep apnea or insomnia were at increased risk of several adverse outcomes. These were attenuated when using propensity score matching, suggesting these associations were driven by other comorbidities.

Introduction

Sleep disturbance is common among pregnant people, with nearly half experiencing poor sleep quality.[1] More concerning is that a sizeable subset of pregnant people experience more severe and impairing presentations warranting a sleep disorder diagnosis. For example, meta-analytic findings show that sleep apnea occurs in 15% of pregnant people[2] and insomnia symptoms occur in 38% of pregnant people.[3]

Sleep disorders during pregnancy can have significant consequences for both the pregnant person and their infant.[4] For example, sleep apnea is associated with increased risk of gestational hypertension and diabetes, preterm birth, congenital anomaly, resuscitation at birth, intubation at birth, neonatal intensive care unit (NICU) admission, and longer hospital stay.[2,5-7] In contrast, little is known about the impact of maternal insomnia on pregnancy and infant outcomes. We know, for example, that pregnant people with an insomnia diagnosis are 70% more likely (odds ratio [OR] = 1.7, 95% confidence interval [CI] 1.1-2.6) to have an infant born early preterm (<34 weeks

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gestation) relative to propensity score matched pregnant people without an insomnia diagnosis[6] (this is consistent with several smaller studies suggesting associations between sleep disturbance and preterm birth)[8,9]; however, whether insomnia impacts infant outcomes more broadly is unclear.

The aim of the present study was to investigate associations between a diagnosis of sleep apnea or insomnia in pregnant people and a wide spectrum of infant outcomes in a large cohort of nearly 3 million pregnant people and their newborns. We hypothesized that pregnant people with a sleep apnea or insomnia diagnosis would be more likely to give birth to an infant with an adverse outcome than people without a sleep disorder diagnosis. We also examined whether links between sleep disorders and adverse infant outcomes remained after matching on maternal characteristics, obstetric factors, gestational age, and birthweight.

Methods

This was a retrospective cohort sample drawn from all California live born infants between January 1, 2011 and December 31, 2017 (n = 3,448,707). Birth and death certificates, maintained by California Vital Statistics, were linked to hospital discharge, emergency department, and ambulatory surgery records maintained by the California Office of Statewide Health Planning and Development. This administrative database includes detailed information on maternal and infant characteristics, diagnoses at hospital discharge, and procedures that occurred as early as one year prior to delivery for the mother and as late as one year post-delivery for the parent and infant. Data files provided diagnoses and procedure codes based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9)[10] and International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10).[11] The sample was restricted to singleton births with gestations between 22 and 44 weeks with linked birth certificate and hospital discharge records (n = 3,066,016; Fig. 1). This study sample was restricted to infants without ICD codes for chromosomal abnormalities or major structural birth defects on their birth admission or any readmissions during the first year of life and to infants born to mothers with no recorded sleep disorder or only those with insomnia or sleep apnea (n = 2,977,048). Structural birth defects for the study were considered "major" if determined by clinical review as causing major morbidity and mortality or leading to hospitalization during the first year of life.[12] Finally, to remove infants with implausible birthweight and gestational age combinations, infants with birthweights more than 3 standard deviations from the mean were excluded (final sample n = 2,959,204).[13]

Sleep apnea or insomnia diagnosis was defined as an ICD-9 or ICD-10 diagnostic code in the delivery hospital discharge record (Appendix). Other sleep disorders, such as sleep-related movement disorder, occurred so infrequently in the hospital record that meaningful analyses of those data were not possible. Because this analysis was limited to hospital discharge data, information was unavailable about how or when sleep disorders were diagnosed.

Adverse infant outcomes included 1- and 5-minute Apgar score <7, respiratory distress syndrome, NICU admission, hypoglycemia, infant death, long hospital stay (>2 days for vaginal delivery, >4 days for cesarean delivery), emergency department visit prior to 3 months of age and in the first year of life, hospital admission prior to 3 months of age and in the first year of life, and a composite binary measure indicating whether or not the infant had any adverse outcome. Birthweight and obstetric estimate of gestational age were obtained from birth certificate records. Respiratory distress syndrome and hypoglycemia data were obtained from hospital discharge ICD-9 or ICD-10 codes (see Appendix). Infant death data were obtained from linked death records and hospital discharge status indicating death.

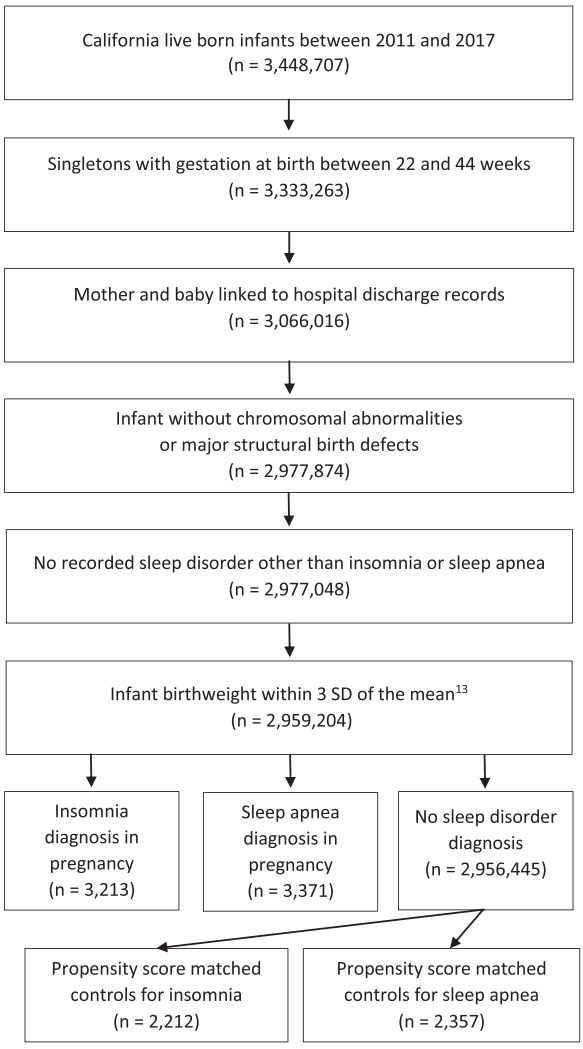

Fig. 1. Sample selection.

Infant year of birth, race/ethnicity, age at term, pre-pregnancy weight and height (used to calculate BMI), education, payer for delivery, enrollment in the Women, Infants, and Children Supplemental Nutrition Program (WIC), smoked during pregnancy, and previous preterm birth were obtained from birth certificate records. Hypertension disorder (including preeclampsia/eclampsia), diabetes, infection during pregnancy, drug use, and alcohol use were obtained from hospital discharge ICD-9 or ICD-10 codes.

Maternal characteristics, clinical factors, and infant factors were compared using chi-square statistics comparing people with sleep apnea or insomnia to people without a sleep disorder. Next, unadjusted logistic regression with a Poisson distribution was used to calculate relative risks (RRs) and 95% CIs for each infant adverse outcome using infants without a recorded sleep disorder as the referent population. Then, logistic regression including infant year of birth, race/ethnicity, age at term, BMI, education, payer for delivery, enrollment in WIC, smoked during pregnancy, previous preterm birth, hypertension disorder, diabetes, infection during pregnancy, drug use, alcohol use, gestational age at delivery, and birthweight for gestational age were used to create propensity scores for women with sleep apnea or insomnia.

Propensity score matching is a method to create a control group that is as identical to the experimental group as possible, to increase the likelihood that differences between the groups are due to the phenomenon in question. For instance, if people with a sleep disorder

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are more likely to have a preterm birth, but they are also more likely to have hypertension and diabetes (risk factors for preterm birth), we cannot assume the risk of preterm birth is due to the sleep disorder. However, using a control group without a sleep disorder that has an equal number of people with hypertension and diabetes, we can determine whether the risk of preterm birth is due to the sleep disorder. A referent population of women without a sleep disorder was randomly selected at a 1:1 ratio using exact matching of propensity scores without replacement. Although there was no replacement when selecting propensity matched controls for sleep apnea or insomnia, the entire population of women without a sleep disorder was available for each disorder (apnea or insomnia) being analyzed. Women without an exact propensity score matched control were not included in the analysis (n = 1001 people with insomnia; n = 1014 people with sleep apnea). Logistic regression was used to calculate ORs and their 95% CIs for each adverse infant outcome.

All analyses were performed using Statistical Analysis Software version 9.4 (Cary, NC). Proc logistic was used to calculate propensity scores and ORs, proc genmod was used to calculate relative risks. Methods and protocols for the study were approved by the Committee for the Protection of Human Subjects within the Health and Human Services Agency of the State of California.

Results

In this study sample, records identified 3371 individuals who were diagnosed with sleep apnea and 3213 who were diagnosed with insomnia. The majority of these individuals were Hispanic, Black, Asian, or Other race and ethnicity, and between ages 18 and 34 at delivery. Over 50% of individuals had more than 12 years of education and the majority had private health insurance for delivery (Table 1). Individuals with a sleep apnea or insomnia diagnosis differed on many maternal characteristics, obstetric factors, and infant factors relative to those without a sleep disorder diagnosis. For example, those diagnosed with sleep apnea tended to be older (>34 years 39.8% vs. 20.1%), and a larger proportion were obese (70.2% vs. 21.4%), had a hypertension disorder (38.2% vs. 9.0%), had diabetes (34.9% vs. 11.3%), had a mental health diagnosis (45.7% vs. 6.5%), or had an infant large for gestational age (16.1% vs. 9.1%). Of those with sleep apnea, 69.9% (n = 2357) had a propensity score matched control. Individuals diagnosed with insomnia tended to be older (> 34 years 28.7% vs. 20.1%); a larger proportion were obese (24.9% vs. 21.4%), had obtained 12 years or more education (62.1% vs. 54.2%), smoked during pregnancy (13.8% vs. 3.0%), or had a mental health diagnosis (69.2% vs. 6.5%). Of the women with insomnia, 68.8% (n = 2212) had a propensity score matched control.

Infants born to individuals with a diagnosis code for sleep apnea had a higher rate of many adverse outcomes than infants born to individuals without a recorded sleep disorder (Table 2). These infants were more likely to have any adverse outcome (RR 1.2, 95% CI 1.2-1.3), 1-minute Apgar score <7 (RR 2.6, 95% CI 2.4-2.9), and 5-minute Apgar score <7 (3.5, 95% CI 2.9-4.3). They were also at 2.5-fold higher risk for a NICU stay on birth admission, 3.3-fold higher risk for having respiratory distress syndrome, 2.3-fold higher risk of hypoglycemia, and 2.0-fold higher risk of dying prior to age 3 months. Regarding utilization of hospital services, infants born to individuals with a diagnosis code for sleep apnea were more likely to have a long hospital stay and experience an emergency room visit prior to 3 months of age (RRs 1.6, 95% CI 1.5-1.7 and 1.2, 95% CI 1.1-1.3, respectively). However, once the sample was propensity score matched based on maternal characteristics, obstetric factors, gestational age, and birthweight, many of the associations were no longer statistically significant. In this regard, infants born to an individual with a diagnosis code of sleep apnea were more likely to have any adverse outcome, 1-minute Apgar scores <7, a NICU stay, and an ER visit compared to infants born to an individual without a recorded sleep disorder (Table 2).

Infants born to individuals with a diagnosis code for insomnia also had a higher rate of many adverse infant birth outcomes than those without a recorded sleep disorder (Table 3). These infants were more likely to have any adverse outcome (RR 1.2, 95% CI 1.2-1.3) and 1 and 5-minute Apgar scores <7 (RRs 2.0, 95% CI 1.8-2.2 and 2.8, 95% CI 2.2-3.5, respectively). These infants were at 2.2-fold higher risk of having a NICU stay, 2.8-fold higher risk of having respiratory distress syndrome, 2.3-fold higher risk of having hypoglycemia, 2.0-fold higher risk of death before 3 months of age, 1.6-fold higher risk of a long birth stay, and 1.3-fold higher risk visiting the emergency room prior to 3-months of age. Again, once the sample was propensity score matched based on maternal characteristics, obstetric factors, gestational age, and birthweight, most associations were no longer statistically significant with the exception of any adverse outcome (OR 1.2, 95% CI 1.1-1.3) and risk of emergency room visit prior to 3 months of age and in the first year of life. Infants born to an individual with a diagnosis code of insomnia had higher odds of an emergency room visit in the first 3 months and first year of life compared to infants born to individuals without a record sleep disorder (ORs 1.2, 95% CI 1.1-1.4 and 1.4, 95% CI 1.2-1.7; Table 3).

Discussion

In a sample derived from nearly 3 million live births, we found that relative to infants born to individuals without a sleep disorder diagnosis, infants born to mothers with a diagnosis of sleep apnea or insomnia had significantly higher odds of any adverse outcome. With respect to sleep apnea, our findings are consistent with other studies showing that maternal sleep apnea is associated with increased risk of low Apgar scores[2] and NICU admission.[2,5] We did not replicate previous findings suggesting a relationship between sleep apnea and longer hospital stay,[5] and our finding that infants born to mothers with a sleep apnea diagnosis were at increased risk of an emergency room visit is a new contribution to the literature. Research on possible mechanisms of the relation between maternal prenatal sleep apnea and poorer birth and infant outcomes associations is small but growing, implicating systemic inflammation and late or prolonged fetal heart rate decelerations.[14,15] Taken together with previous research suggesting that sleep apnea is associated with increased risk of adverse birth outcomes, such as preterm birth,[6] these study findings underscore the importance of utilizing available interventions for treating sleep apnea. Continuous positive airway pressure (CPAP) therapy is the preferred treatment for addressing sleep apnea in the general population and is effective in reducing some of the medical risks associated with sleep apnea.[16-18] Surprisingly, little is known about the benefits of CPAP therapy in pregnancy.[19] However, given the health benefits conferred by CPAP therapy in nonpregnant samples, it is the hope that CPAP therapy will similarly reduce the negative health consequences of sleep apnea in pregnancy.[20]

Research on associations between insomnia diagnosis during pregnancy and adverse infant outcomes is sparse, with the exception of a meta-analysis documenting associations between insomnia diagnosis during pregnancy and risk for infant that is large for gestational age.[21] A population-based study found that individuals treated with Zolpidem, a hypnotic medication commonly prescribed to treat insomnia, were more likely to have children born preterm, with low birth weight, and with congenital abnormalities than individuals who were not prescribed Zolpidem.[22] Unfortunately, such studies cannot disentangle whether these associations are due to the insomnia or the active effects of the drug, which is known to cross into the placenta.[23] Thus, our finding that infants born to mothers with an insomnia diagnosis were at increased risk of only emergency room visit but no other analyzed infant outcomes, is important and novel.

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Table 1
Maternal characteristics, obstetric factors, and infant factors among women without a recorded sleep disorder diagnosis vs. women with a sleep apnea or insomnia diagnosis

	No sleep disorder	Sleep apnea		Insomnia	
	n (%)	n (%)	*p*-value[a]	n (%)	*p*-value[a]
Sample	2,952,660	3371		3213	
Infant year of birth					
2011	436,877 (14.8)	248 (7.4)	<.0001	237 (7.4)	<.0001
2012	438,812 (14.9)	423 (12.6)	.0002	360 (11.2)	<.0001
2013	426,397 (14.4)	416 (12.3)	.0005	474 (14.8)	.6157
2014	433,289 (14.7)	449 (13.3)	.0263	481 (15.0)	.6357
2015	417,852 (14.2)	563 (16.7)	<.0001	599 (17.4)	<.0001
2016	409,555 (13.9)	535 (15.9)	.0008	564 (17.6)	<.0001
2017	389,878 (13.2)	737 (21.9)	<.0001	538 (16.7)	<.0001
Race and ethnicity					
White not Hispanic	782.541 (26.5)	1018 (30.2)	<.0001	1379 (42.9)	<.0001
Hispanic	1,447,581 (49.0)	1303 (38.7)	<.0001	1089 (33.9)	<.0001
Black	144,887 (4.9)	374 (11.1)	<.0001	249 (7.8)	<.0001
Asian	432,667 (14.7)	355 (10.5)	<.0001	225 (7.0)	<.0001
Other	144,984 (4.9)	321 (9.5)	<.0001	271 (8.4)	<.0001
Maternal age at term					
<18 years	50,003 (1.7)	16 (0.5)	<.0001	29 (0.9)	.0005
18-34 years	2,307,765 (78.2)	2015 (59.8)	<.0001	2263 (70.4)	<.0001
>34 years	594,781 (20.1)	1340 (39.8)	<.0001	921 (28.7)	<.0001
Missing	111 (0.0)	0 (0.0)	.7218	0 (0.0)	.7282
Body mass index					
Underweight	112,311 (3.8)	23 (0.7)	<.0001	111 (3.5)	.3013
Normal weight	1,344,875 (45.6)	352 (10.4)	<.0001	1389 (43.2)	.0084
Overweight	741,117 (25.1)	502 (14.9)	<.0001	769 (23.9)	.1276
Obese	631,692 (21.4)	2366 (70.2)	<.0001	832 (25.9)	<.0001
Missing	122,665 (4.2)	128 (3.8)	.2988	112 (3.5)	.0577
Maternal education					
<12 years	505,985 (17.1)	270 (8.0)	<.0001	327 (10.2)	<.0001
12 years	721,774 (24.4)	750 (22.3)	.0030	744 (23.2)	.0893
>12 years	1,600,365 (54.2)	2136 (63.4)	<.0001	1996 (62.1)	<.0001
Missing	124,536 (4.2)	215 (6.4)	<.0001	146 (4.5)	.3578
Payment for delivery					
Private	1,406,381 (47.6)	2242 (66.5)	<.0001	1922 (59.8)	<.0001
Medi-Cal[b]	1,358,235 (46.0)	1041 (30.9)	<.0001	1163 (36.2)	<.0001
Other	90,389 (3.1)	72 (2.1)	.0018	99 (3.1)	.9477
Mother enrolled in WIC	1,500,063 (50.8)	1535 (45.5)	<.0001	1404 (43.7)	<.0001
Smoked during pregnancy	88,557 (3.0)	278 (8.3)	<.0001	442 (13.8)	<.0001
Previous preterm birth	30,203 (1.0)	92 (2.7)	<.0001	85 (2.7)	<.0001
Hypertension disorder	267,051 (9.0)	1292 (38.2)	<.0001	615 (19.1)	<.0001
Diabetes	332,364 (11.3)	1176 (34.9)	<.0001	482 (15.0)	<.0001
Infection during pregnancy	306,888 (10.4)	687 (20.4)	<.0001	822 (25.6)	<.0001
Drug/alcohol abuse	59,030 (2.0)	201 (6.0)	<.0001	488 (15.2)	<.0001
Mental health diagnosis	19,2778 (6.5)	1539 (45.7)	<.0001	2223 (69.2)	<.0001
Gestational age at delivery (weeks)					
22-28	7844 (0.3)	37 (1.1)	<.0001	24 (0.8)	<.0001
29-31	12,898 (0.4)	57 (1.7)	<.0001	50 (1.6)	<.0001
32-36	164,841 (5.6)	416 (12.3)	<.0001	349 (10.9)	<.0001
37-38	717,424 (24.3)	980 (29.1)	<.0001	822 (25.6)	.0894
39-42	2,048,622 (69.4)	1881 (55.8)	<.0001	1968 (61.3)	<.0001
43-44	1031 (0.0)	0 (0.0)	.2779	0 (0.0)	.2894
Birthweight for gestational age[c]					
SGA	251,788 (8.5)	234 (6.9)	.0010	322 (10.0)	.0024
AGA	2,432,987 (82.4)	2594 (77.0)	<.0001	2585 (80.5)	.0038
LGA	268,211 (9.1)	543 (16.1)	<.0001	310 (9.7)	.2657
Missing	696 (0.0)	0 (0.0)	.3727	0 (0.0)	.3841

WIC, Women Infants and Children's Program; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age.
[a] vs. no sleep disorder.
[b] California's Medicaid.
[c] SGA is < 10th percentile, AGA is 10th to 90th percentile, and LGA is > 90th percentile. Calculations are made based on gestational age and sex, per the reference Talge et al., 2014.[13]

At the same time, insomnia during pregnancy is associated with other adverse birth and maternal outcomes, such as preterm birth and depression,[6,24] and thus important to assess and intervene upon. Several randomized clinical trials support the positive benefits of cognitive behavioral therapy for insomnia (CBTI), which is recommended as first line treatment for insomnia in nonpregnant samples,[25] and for significantly reducing insomnia symptoms in pregnant individuals.[26-28] For example, Felder and colleagues demonstrated that 6 weekly sessions of CBTI, delivered digitally, resulted in twice the reduction in insomnia symptoms 10 weeks later than usual care.[26] It is currently unknown whether CBTI is associated with improved birth outcomes.

In our initial crude analyses, both sleep apnea and insomnia were associated with most of the analyzed infant outcomes. The majority

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Table 2
Infant outcomes for women with ICD-9/10 code for sleep apnea during pregnancy

	Whole population			Matched sample		
	Sleep apnea during pregnancy n (%)	No sleep disorder during pregnancy n (%)	RR (95% CI)	Sleep apnea during pregnancy n (%)	No sleep disorder during pregnancy n (%)	OR (95% CI)
Sample	3371	2,952,660		2357	2357	
Complications						
Any adverse outcome						
No	1358 (40.3)	1,553,904 (52.0)	Reference	1095 (46.5)	1176 (49.9)	Reference
Yes	2013 (59.7)	1,418,756 (48.1)	**1.2 (1.2, 1.3)**	1262 (53.5)	1181 (50.1)	**1.1 (1.0, 1.3)**
1-minute Apgar[c]						
<7	430 (12.8)	144,497 (4.9)	**2.6 (2.4, 2.9)**	226 (9.6)	148 (6.3)	**1.6 (1.3, 2.0)**
≥7	2936 (87.1)	2,799,961 (94.8)	Reference	2129 (90.3)	2202 (93.4)	Reference
5-minute Apgar[c]						
<7	102 (3.0)	25,328 (0.9)	**3.5 (2.9, 4.3)**	49 (2.1)	34 (1.4)	1.4 (0.9, 2.2)
≥7	3264 (96.8)	2,918,295 (98.8)	Reference	2307 (97.9)	2315 (98.2)	Reference
Infant NICU stay on birth admission						
No	2907 (86.2)	2,791,512 (94.5)	Reference	2158 (91.6)	2208 (93.7)	Reference
Yes	464 (13.8)	161,148 (5.5)	**2.5 (2.3, 2.8)**	199 (8.4)	149 (6.3)	**1.4 (1.1, 1.7)**
Respiratory distress syndrome						
No	3215 (95.4)	2,911,080 (98.6)	Reference	2320 (98.4)	2327 (98.7)	Reference
Yes	156 (4.6)	41,580 (1.4)	**3.3 (2.8, 3.8)**	37 (1.6)	30 (1.3)	1.2 (0.8, 2.0)
Hypoglycemia						
No	3233 (95.9)	2,900,268 (98.2)	Reference	2294 (97.3)	2296 (97.4)	Reference
Yes	138 (4.1)	52,392 (1.8)	**2.3 (2.0, 2.7)**	63 (2.7)	61 (2.6)	1.0 (0.8, 1.5)
Infant death						
No	3355 (99.5)	2,945,637 (99.8)	Reference	2352 (99.8)	2350 (99.7)	Reference
Yes	16 (0.5)	7023 (0.2)	**2.0 (1.2, 3.3)**	5 (0.2)	7 (0.3)	0.7 (0.2, 2.3)
< 3 months	13 (0.4)	5586 (0.2)	**2.0 (1.2, 3.5)**	[a]	[a]	[b]
Utilization						
Long birth stay						
No	2783 (82.6)	2,629,812 (89.1)	Reference	2087 (88.5)	2078 (88.2)	Reference
Yes	588 (17.4)	322,848 (10.9)	**1.6 (1.5, 1.7)**	270 (11.5)	279 (11.8)	1.0 (0.8, 1.2)
ER visit						
No	2071 (61.4)	1,970,343 (66.7)	Reference	1487 (63.1)	1566 (66.4)	Reference
Yes	1300 (38.6)	982,317 (33.3)	**1.2 (1.1, 1.2)**	870 (36.9)	791 (33.6)	**1.2 (1.0, 1.3)**
<3 months	513 (15.2)	380,215 (12.9)	**1.2 (1.1, 1.3)**	339 (14.4)	317 (13.5)	1.1 (1.0, 1.3)
Hospital admission						
No	2985 (88.6)	2,672,001 (90.5)	Reference	2144 (91.0)	2118 (89.9)	Reference
Yes	386 (11.5)	280,659 (9.5)	**1.2 (1.1, 1.3)**	213 (9.0)	239 (10.1)	0.9 (0.7, 1.1)
<3 months	282 (8.4)	193,889 (6.6)	**1.3 (1.1, 1.4)**	156 (6.6)	169 (7.2)	0.9 (0.7, 1.1)

Bold indicates $p < .05$.
[a] Not displayed when n < 5.
[b] Not calculated when n < 5.
[c] Numbers do not add up to 100% because Apgar scores were missing for some infants.

of these associations were attenuated after matching on maternal characteristics, obstetric factors, gestational age, and birthweight. This suggests that these associations may be due to other characteristics and comorbidities, though we are not able to identify statistically which characteristics drove the initial higher rates of adverse infant outcomes.

The mechanisms underlying the associations between sleep apnea and insomnia and adverse infant outcomes have yet to be fully elucidated. Sleep apnea, which is marked by recurrent total or partial collapse of the upper airway and results in frequent nocturnal arousals and hypoxemia, is also associated with elevated inflammation, oxidative stress, and endothelial dysfunction.[29] Similarly, a meta-analytic review of the sleep literature demonstrated a significant link between insomnia symptoms and elevated levels of pro-inflammatory mediators (eg, interleukin-6).[30] Dysregulation of inflammatory processes has been proposed as an important pathway in understanding adverse birth outcomes, as well as the role of sleep in pregnancy complications.[31-33] Research prospectively monitoring biological processes implicated in adverse birth outcomes among individuals with and without sleep disorders is warranted.

There are several strengths of this study that extend the current literature. The use of a large population-based sample provided a sufficient number of cases to test our study hypotheses, which is often challenging in smaller studies. Further, the use of ICD-9 and 10 codes highlights the questions that can be tackled using available medical record data. That said, there are several inherent limitations to using medical record data that should be noted. For example, because this study relied solely on medical records, it remains unclear how routinely sleep disorders were queried by providers. In our sample <0.1% of individuals had an ICD-9 or ICD-10 code of either sleep apnea or insomnia, which is significantly lower than would be expected based on self-report prevalence data. For example, the rates of objectively-defined sleep disordered breathing are approximately 4% in early pregnancy and 8% in mid pregnancy,[34] and the rates of insomnia disorder are 20% at the end of the third trimester.[35] Reasons for these low numbers may include providers tending not to assess sleep concerns during prenatal care and patients omitting sleep complaints. Indeed, survey data indicate that only about one-third of pregnant individuals discuss sleep with their health care providers.[36] Consequently, the findings presented here may reflect more severe cases of insomnia and sleep apnea, and may not represent the population of individuals with diagnosed sleep apnea or insomnia during pregnancy generally. Future research is

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Table 3
Infant outcomes for women with ICD-9/10 code for insomnia during pregnancy

	Whole population			Matched sample		
	Insomnia during pregnancy n (%)	No sleep disorder during pregnancy n (%)	RR (95% CI)	Insomnia during pregnancy n (%)	No sleep disorder during pregnancy n (%)	OR (95% CI)
Sample	3213	2,952,660		2212	2212	
Complications						
Any adverse outcome						
No	1327 (41.3)	1,553,904 (52.0)	Reference	1040 (47.0)	1135 (51.3)	Reference
Yes	1886 (58.7)	1,418,756 (48.1)	**1.2 (1.2, 1.3)**	1172 (53.0)	1077 (48.7)	**1.2 (1.1, 1.3)**
1-minute Apgar[c]						
< 7	312 (9.7)	144,497 (4.9)	**2.0 (1.8, 2.2)**	158 (7.1)	146 (6.6)	1.1 (0.9, 1.4)
≥ 7	2885 (89.8)	2,799,961 (94.8)	Reference	2049 (92.6)	2058 (93.0)	Reference
5-minute Apgar[c]						
< 7	77 (2.4)	25,328 (0.9)	**2.8 (2.2, 3.5)**	2178 (98.5)	2184 (98.7)	1.3 (0.8, 2.4)
≥ 7	3121 (97.1)	2,918,295 (98.8)	Reference	28 (1.3)	21 (1.0)	Reference
Infant NICU stay on birth admission						
No	2825 (87.9)	2,791,512 (94.5)	Reference	2068 (93.5)	2074 (93.8)	Reference
Yes	388 (12.1)	161,148 (5.5)	**2.2 (2.0, 2.4)**	144 (6.5)	138 (6.2)	1.0 (0.8, 1.3)
Respiratory distress syndrome						
No	3085 (96.0)	2,911,080 (98.6)	Reference	2178 (98.5)	2184 (98.7)	Reference
Yes	128 (4.0)	41,580 (1.4)	**2.8 (2.4, 3.4)**	34 (1.5)	28 (1.3)	1.2 (0.7, 2.0)
Hypoglycemia						
No	3082 (95.9)	2,900,268 (98.2)	Reference	2151 (97.2)	2160 (97.7)	Reference
Yes	131 (4.1)	52,392 (1.8)	**2.3 (1.9, 2.7)**	61 (2.8)	52 (2.4)	1.2 (0.8, 1.7)
Infant death						
No	3197 (99.5)	2,945,637 (99.8)	Reference	2209 (99.9)	2207 (99.8)	Reference
Yes	16 (0.5)	7023 (0.2)	**2.1 (1.3, 3.4)**	[a]	5 (0.2)	[b]
< 3 months	12 (0.4)	5586 (0.2)	**2.0 (1.1, 3.5)**	[a]	[a]	[b]
Utilization						
Long birth stay						
No	2650 (82.5)	2,629,812 (89.1)	Reference	1958 (88.5)	1970 (89.1)	Reference
Yes	563 (17.5)	322,848 (10.9)	**1.6 (1.5, 1.7)**	254 (11.5)	242 (10.9)	1.1 (0.9, 1.3)
ER visit						
No	1982 (61.7)	1,970,343 (66.7)	Reference	1390 (62.8)	1497 (67.7)	Reference
Yes	1231 (38.3)	982,317 (33.3)	**1.2 (1.1, 1.2)**	822 (37.2)	715 (32.3)	**1.2 (1.1, 1.4)**
< 3 months	517 (16.1)	380,215 (12.9)	**1.3 (1.2, 1.4)**	341 (15.4)	264 (11.9)	**1.4 (1.2, 1.7)**
Hospital admission						
No	2890 (90.0)	2,672,001 (90.5)	Reference	2004 (90.6)	2010 (90.9)	Reference
Yes	323 (10.1)	280,659 (9.5)	1.1 (0.9, 1.2)	208 (9.4)	202 (9.1)	1.0 (0.8, 1.3)
< 3 months	221 (6.9)	193,889 (6.6)	1.1 (0.9, 1.2)	138 (6.2)	143 (6.5)	1.0 (0.8, 1.2)

Bold indicates $p < .05$.
[a] not displayed when n < 5.
[b] not calculated when n < 5.
[c] Numbers do not add up to 100% because Apgar scores were missing for some infants.

needed to determine whether severity of insomnia and sleep apnea is associated with infant outcomes. Previous survey data suggest that prenatal insomnia is likely undertreated,[36] and treatment rates for prenatal sleep apnea are unknown. A second limitation is that treatment for sleep disorders is not available in this dataset. Thus, it is possible that a portion of individuals with a sleep apnea diagnosis received treatment, which may attenuate associations with adverse infant outcomes. Another limitation is that because we relied on hospital discharge records, we cannot know for certain whether the sleep disorders were diagnosed for the first time during pregnancy or whether the diagnosis preceded pregnancy. This information will be important for clarifying the impact of timing and chronicity of sleep disorders on infant outcomes and identifying key opportunities for intervention.

Sleep apnea and insomnia may be windows into the overall health of pregnant individuals and offer low-stigma targets for assessment of risk of adverse infant outcomes. Given the growing evidence of the health consequences of sleep apnea and insomnia, there is an increasing need for clinicians to assess and address sleep disorders in pregnancy and for researchers to test whether targeting sleep apnea and insomnia reduces these adverse infant outcomes.

Declaration of conflict of interest

The authors report no conflicts of interest.

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Author contribution

JF, AP, RB, LR, KR, and LJP conceived of the study. RB carried out the analyses. JF wrote the initial draft of the manuscript and all authors contributed to editorial changes and approved the final manuscript.

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Supplementary materials

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