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TITLE

Population-Based Study of Sleep Apnea in Pregnancy and Maternal and Infant Outcomes

RUNNING HEAD

Sleep Apnea and Pregnancy Outcomes

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CONFLICTS OF INTEREST

YSB and JBF have no conflicts of interest to declare. PAC holds an endowed academic chair at the University of Sydney that was funded by ResMed Inc. He has received research and/or equipment support from ResMed Inc, SomnoMed Ltd, Zephyr Sleep technologies, and Exploramed Inc. He has acted as consultant / advisor for Zephr Sleep Technologies, NovoNordisk, and Fisher & Paykel Healthcare.

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ABSTRACT (248/250 words)

Study Objectives: To examine the association between sleep apnea and pregnancy outcomes in a large population-based cohort.

Methods: Population-based cohort study using linked birth and hospital records was conducted in New South Wales, Australia. Participants were all women who gave birth in hospital from 2002 to 2012 (N=636,227). Sleep apnea in the year before pregnancy or during pregnancy was identified from hospital records. Outcomes of interest were gestational diabetes, pregnancy hypertension, planned delivery, caesarean section, preterm birth, perinatal death, 5-minute Apgar score, admission to neonatal intensive care or special care nursery, and infant size for gestational age. Maternal outcomes were identified using a combination of hospital and birth records. Infant outcomes came from the birth record. Modified Poisson regression models were used to examine associations between sleep apnea and each outcome taking into account maternal age, country of birth, socioeconomic disadvantage, smoking, obesity, parity, pre-existing diabetes and hypertension.

Results: Sleep apnea was significantly associated with pregnancy hypertension (adjusted RR 1.68; 95% CI 1.40 – 2.07), planned delivery (1.15; 1.07 – 1.23), preterm birth (1.50; 1.21 – 1.84), 5-minute Apgar <7 (1.60; 1.07 – 2.38), admission to neonatal intensive care/special care nursery (1.26; 1.11 – 1.44), large-for-gestational-age infants (1.27; 1.04 – 1.55) but not with gestational diabetes (1.09; 0.82 – 1.46), caesarean section (1.06; 0.96 – 1.17), perinatal death (1.73; 0.92 – 3.25), or small-for-gestational-age infants (0.81; 0.61 – 1.08).

Conclusions: Sleep apnea is associated with higher rates of obstetric complications and intervention, as well as preterm delivery. Future research should examine if these are independent of obstetric history.

BRIEF SUMMARY

Current Knowledge/Study Rationale: The evidence for an impact of sleep apnea on pregnancy is limited by weak study designs with small clinical samples and poor measurement of sleep apnea. The aim of the current study was to examine if sleep apnea was prospectively associated with maternal and infant outcomes in a population-based cohort, with an indicator of clinically significant sleep apnea.

Study Impact: The study provides evidence that sleep apnea increases risks for a number of pregnancy outcomes. The findings, together with the greater literature, suggest a large-scale intervention study is needed to determine if treatment of sleep apnea can fully ameliorate these risks.

Keywords (min 3, max 10): (1) sleep-disordered breathing, (2) pregnancy, (3) gestational diabetes, (4) pregnancy-induced hypertension, (5) caesarean section, (6) premature birth, (7) small for gestational age, (8) perinatal death, (9) record linkage, (10) cohort study

Manuscript=4123 words, 2 tables, no figures.

INTRODUCTION

Sleep apnea is characterised by pauses in breathing during sleep causing intermittent blood oxygen desaturation and repeated awakening during the night. Snoring, daytime sleepiness and poor daytime function are the main symptoms. Sleep apnea is found disproportionately in men, those of late middle age, and those who are overweight/obese [1]. More recently however, sleep apnea has been observed to occur commonly in pregnant women [2, 3]. While protected by their relative youth and gender, pregnant women are at increased risk for sleep apnea because of the weight gain and hormonal changes associated with pregnancy [4]. Nasal congestion [5], narrowing of the upper airway [6], increased tongue size relative to the oral cavity [7], and enlarged neck circumference [8] during pregnancy are all believed to be contributing factors.

In the general population, frank sleep apnea confers long-term risk for cognitive impairment [9, 10], hypertension [11], stroke [12, 13], and cardiovascular mortality [13, 14]. In the pregnant population, sleep apnea has been linked to gestational diabetes [2, 3, 15], gestational hypertension, pre-eclampsia and eclampsia [2, 3, 16], low birthweight infants [2, 3], intrauterine growth restriction [3], and neonatal intensive care unit (NICU) admission [3]. Despite a number of independent systematic reviews and meta-analyses [2, 3, 15, 16], conclusions about the impact of sleep apnea on pregnancy are limited by the quality of the primary studies, which have been mainly case-control or cross-sectional in nature. Most have involved small clinical samples susceptible to selection bias and with varying degrees of control for confounding. There are also a number of perplexing results which might be solved by larger and better designed studies. For instance, some studies report that sleep apnea is associated with low birthweight infants, while others report no difference in the mean birthweight of babies born to mothers with and without sleep apnea [2, 3]. Still others show an association between maternal sleep apnea and NICU admission, but paradoxically sleep apnea does not appear related to preterm birth or Apgar scores of infant condition soon after birth which would indicate grounds for admission [3]. Further, the majority of previous studies have used self-reported snoring as indicative of sleep-disordered breathing, even though snoring alone is a poor indicator of clinically significant sleep apnea [17]. Thus the aim of the current study was to examine the association between sleep

apnea and maternal and infant outcomes in a population-based cohort, using routinely collected health records.

METHODS

Data sources

New South Wales (NSW) is the most populous state in Australia and sees approximately 93,000 births each year, which equates to over 30% of all births in the country [18]. Data for this study came from two sets of routinely collected health data: the NSW Perinatal Data Collection (birth records) [19] and the NSW Admitted Patient Data Collection (hospital records).

The birth records describe all births in NSW of at least 20 weeks gestation or at least 400g weight. The birth information is collected by the attending midwife or medical practitioner and includes data on maternal health, pregnancy, labour, delivery, and infant characteristics. The hospital records are a census of discharges, transfers and deaths from NSW public and private hospitals and day procedure centres. Diagnoses and procedures associated with each hospital record are coded by trained medical coders according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) [20] and the Australian Classification of Health Interventions [21]. Up to 20 diagnoses and 20 procedures associated with each admission can be coded, in addition to the principal diagnosis or primary procedure that is the reason for admission.

The birth records and hospital records were linked by the NSW Centre for Health Record Linkage (http://www.cherel.org.au/) using probabilistic record linkage and ChoiceMaker software. Australia does not have a national system of unique individual identifiers so multiple personal identifiers and probabilistic record linkage is used. Probabilistic record linkage involves assigning weights to pairs of records based on the degree of matching on personal identifiers such as names, birth dates, and addresses. Highly-weighted pairs of records are considered matches and lowly weighted pairs are considered non-matches. Clerical review is conducted of middle-weighted pairs and the process is repeated until there are fewer than 5/1,000 false positives and fewer than

5/1,000 false negatives when identifiers are available[22]. The data custodians then remove identifiers to preserve privacy and provide a unique linkage key to researchers to link relevant records for study.

Ethics approval came from the NSW Population and Health Services Research Ethics Committee.

Study population and study period

The study population were all women who gave birth during the period 1st January 2002 to 31st December 2012. There were 636,227 unique women and 1,023,357 babies. We selected only the first birth so that each woman appeared only once in the study population and only the first infant from multiple births were counted in the outcomes. We note that the first birth in the study period is not equivalent to a woman's first delivery, as she may have birthed prior to 2002 and these births are not captured in our data. Parity was recorded and adjusted for in the analyses. Thus there were 636,227 women and 636,227 infants in the study population.

The beginning of the study period for each woman was calculated by subtracting 365 days from the estimated date of conception and the end of the study period was demarcated by delivery. The date of conception was estimated by subtracting gestational age in completed weeks from the delivery date and adding 2 weeks (14 days).

Hospital records were linked to the birth records and hospital admissions in the study period for each woman were used to identify the presence of sleep apnea and other medical conditions.

Sleep apnea

Sleep apnea was defined using the ICD-10-AM diagnosis code G47.3 "Sleep apnoea" which included subcategories of central and obstructive sleep apneas (G47.3x). Women with a sleep apnea code in hospital records in the year before or during pregnancy were considered to have sleep apnea while women without a sleep apnea code during this period were considered not to have sleep apnea. Previous validation of hospital records against medical record review has shown that conditions identified in this way have a specificity rate of over 99% [23].

Outcomes

Outcomes for this study were gestational diabetes, pregnancy hypertension, planned delivery, caesarean section, preterm birth, 5-minute Apgar, admission to the neonatal intensive care unit (NICU) or special care nursery (SCN), perinatal death and infant size for gestational age.

Gestational diabetes and pregnancy hypertension (including gestational hypertension, pre-eclampsia or eclampsia) were derived from a combination of hospital and birth record data which have been previously validated against medical records [24, 25]. Information on the type of delivery and infant outcomes came from the birth records.

Planned deliveries and caesarean sections were indicated by check box on the birth record. These outcomes have been shown to correspond well to the maternal medical record [26]. Planned delivery refers to births without spontaneous labour i.e. those requiring induction of labour or caesarean section. Planned delivery indicates a birth required obstetric intervention and is therefore a marker of pregnancy complications. In this context it likely represents comorbidities with sufficient severity to prompt intervention.

All of the infant outcomes were from the birth record. Preterm birth before 37 completed weeks of gestation was determined from gestational age on the birth record, which in turn is based on the best clinical estimate of gestational age using a combination of early ultrasound and date of last menstrual period. Apgar score at 5 minutes was dichotomised into those considered normal ($\geq$7) and those considered low (<7)[27]. Admission to the neonatal intensive care unit (NICU) or the special care nursery (SCN) was combined as changes to data collection over time meant the two could not be considered separately. Perinatal death comprised stillbirths and neonatal death up to 28 days after birth. Small for gestational age (SGA) were infants smaller than the 10th percentile of birth weight for their gestational age and sex, and large for gestational age (LGA) were infants larger than 90th percentile of birth weight for gestational age and sex [28, 29].

Covariates

Information on maternal and pregnancy characteristics came from the birth record. These included maternal age (in years), country of birth (Australia/other), socioeconomic disadvantage (quintiles), smoking during pregnancy (any/none), parity (nulliparous/multiparous), and plurality (singleton/multiple). Socioeconomic disadvantage was defined by the Index of Relative Socio-Economic Disadvantage according to a woman's residential postcode. The index is a standard composite measure created by the Australian Bureau of Statistics for each geographical area and takes into account the proportion of residents who have low income, no educational qualifications, are unemployed or employed in unskilled work, live in overcrowded or low rent housing, who have a disability, poor English, no access to a car, and who are in single parent households [30]. Quintiles for socioeconomic disadvantage were calculated based on the entire population of women giving birth in New South Wales.

Information on the maternal conditions of chronic hypertension and pre-existing diabetes were derived from a combination of hospital and birth records which have been previously validated against medical records [24, 25]. Maternal morbid obesity was identified through hospital admissions records during the study period where an ICD-10-AM code of E65 (localised adiposity) or E66 (obesity) was recorded.

Statistical Analysis

Characteristics of women with and without sleep apnea were compared using chi-squared tests. Pregnancy outcomes were compared between women with sleep apnea and those without. Modified Poisson regression with robust error variance was used to estimate relative risks with 95% confidence intervals[31]. We chose to analyse the data using modified Poisson regression rather than logistic regression since this approach calculates relative risks directly and these are more easily interpreted than odds ratios. The odds ratios from logistic regression approximate relative risks when the outcome is rare, but the outcomes in this study are not uncommon so the relative risks would be overestimated if logistic regression was applied. Poisson regression is usually applied to count data, therefore the method has been 'modified' to more correctly estimate the standard errors for binary outcomes[31].

The analyses for each outcome were performed with and without adjustment for the covariates of maternal age, country of birth, socioeconomic disadvantage, smoking, obesity, and parity. For gestational diabetes, only these covariates were included in the adjusted model. For pregnancy hypertension, we also controlled for the risk factors of chronic hypertension and pre-existing diabetes. For all other outcomes, we also included chronic hypertension, pregnancy hypertension, pre-existing diabetes, and gestational diabetes in the adjusted models.

The diagnosis of gestational diabetes is only applied to women without pre-existing diabetes, and hence it is not possible to control for pre-existing diabetes in the model for gestational diabetes. However, we also conducted a sensitivity analysis for gestational diabetes which excluded women with pre-existing diabetes.

The models for preterm birth were further stratified by delivery onset (spontaneous labour vs. planned delivery) and the models for NICU/SCN admission were stratified by gestational age (preterm vs. term) to explore the reasons for the observed associations.

All analyses were conducted using SAS 9.3 (SAS Institute, NC).

RESULTS

Of the 636,227 women who delivered in the study period, 519 (0.08%) had a hospital admission with diagnosis of sleep apnea before or during pregnancy. The characteristics of women with and without a hospital record for sleep apnea are presented in Table 1. Women with sleep apnea were older, more likely Australian-born, and more socioeconomically advantaged than those without sleep apnea. Women with sleep apnea also had higher rates of smoking, obesity, pre-existing diabetes, chronic hypertension, and more were in their first pregnancy compared to those without a diagnosis of sleep apnea.

The associations between sleep apnea and the outcomes from the crude and fully-adjusted models are presented in Table 2. In the crude models, women with sleep apnea were not more likely to have gestational diabetes than women without sleep apnea, nor were they more likely to have SGA infants. Sleep apnea was significantly associated with

the other outcomes, although these associations were attenuated when maternal demographics and health risk factors were included in the models.

Sleep apnea remained significantly predictive of pregnancy hypertension, planned delivery, preterm birth, low Apgar5, NICU/SCN admission and LGA infants. The association between preterm birth and sleep apnea was driven by planned deliveries, while risk of NICU/SCN admissions was significantly increased only in term infants. Perinatal death was a rare outcome and although there appears to be a large elevated risk associated with sleep apnea, this was not statistically significant.

When women with pre-existing diabetes were excluded, the result for gestational diabetes was unchanged, i.e. sleep apnea was not significantly associated with risk for gestational diabetes compared to no-apnea (RR 1.27; 0.91 – 1.78).

DISCUSSION

Our study found that a diagnosis of sleep apnea in hospital records in the year before or during pregnancy was associated with adverse pregnancy outcomes in a population-based cohort of women. Women with sleep apnea were more likely to have pregnancy hypertension compared to women without sleep apnea, but they were not more likely to have gestational diabetes. Sleep apnea was associated with increased risk of planned deliveries and preterm births even after taking into account hypertension, diabetes, and other key risk factors. The infants of women with sleep apnea were more likely to be large for gestational age and to be admitted to the NICU or SCN than those born to women without a diagnosis of sleep apnea. However, sleep apnea was not significantly associated with caesarean section, perinatal death or small-for-gestational age infants.

Two previous studies have used population health data to examine the association between obstructive sleep apnea (OSA), the most common form of apnea, and pregnancy outcomes: Chen et al (2012) conducted a population-based case-control study using linked health insurance and birth register records in Taiwan [32] and Louis et al (2014) analysed nationally representative hospital delivery records in the United States [33]. These studies and ours are qualitatively different to the studies that have been reviewed in meta-

analyses on the topic [2, 3, 15, 16] and hence we will discuss the results with particular reference to these studies.

We found no association between sleep apnea and gestational diabetes which was surprising given meta-analyses of clinical studies show a pooled odds ratio ranging from 1.9 – 3.0 between sleep-disordered breathing and gestational diabetes [2, 3, 15]. The two previous population-based studies also reported higher risk of gestational diabetes associated with OSA (ORs 1.6 and 1.9 respectively) despite reporting low rates of sleep apnea and controlling only for ICD code of obesity, as in the current study [32, 33]. It is unclear what might account for this disparity, especially since gestational diabetes was not associated with sleep apnea in our population even before control for confounding. It may be the case that sleep apnea does not contribute independently to risk for gestational diabetes despite the two conditions being commonly comorbid. A meta-analysis by Ding and colleagues[3] supports this view, as a significant association between sleep apnea and gestational diabetes was only found in non-prospective studies (pooled OR from 5 studies: 2.11, 95% CI: 1.60 - 2.80), but the association was not significant for prospective studies (pooled OR 1.20, 95% CI: 0.93, 1.53). Another meta-analysis by Xu and colleagues [16] of cohort studies on the relationship between OSA and gestational diabetes reported a modest but non-significant increase in the risk for gestational diabetes (pooled RR 1.40; 95% CI: 0.62 - 3.19). This would be consistent with the finding that sleep apnea does not predict incident diabetes in the general population although diabetes does appear to predict subsequent sleep-disordered breathing [34, 35].

In contrast, the observed association between sleep apnea and pregnancy hypertension is consistent with both clinical and population-based studies. These have shown sleep apnea is associated with a greater than two-fold odds ratio for pregnancy-related hypertension, and a roughly two-fold odds ratio for pre-eclampsia [2, 3, 32, 33]. Sleep apnea is similarly predictive of hypertension in the general population [11] and treatment of sleep apnea has demonstrated improvements in blood pressure [11, 36], which raises the question of whether treatment or prevention of sleep apnea may improve hypertensive disorders in pregnancy. Two small intervention studies have shown that continuous positive airway pressure improves blood pressure in pregnant women with pre-eclampsia

[37, 38], although impact on pregnancy outcomes were not examined and this will need to be addressed in future research.

A novel finding in the present study was that sleep apnea was not significantly associated with perinatal death, although the risk was elevated. Previous clinical studies have been precluded from recruiting mothers with stillbirths due to ethical considerations. Louis and colleagues examined the association between OSA and stillbirth and found no significant association based on maternal delivery records [33]. That study was able to take into account more maternal comorbidities than the present study, hence the increased risk seen here may be due to residual confounding by maternal cardiovascular, renal, or pulmonary disease. However, Louis and colleagues examined only stillbirths and not neonatal deaths, which are also included in perinatal mortality here. Given the rarity and gravity of the outcome, the association between sleep apnea and perinatal death warrants further study.

An increase in preterm birth could be one reason for a tendency to more infant deaths. The increased risk for preterm births in mothers with sleep apnea observed in the current study is consistent with previous population and clinical studies [3, 32, 33]. However, our subgroup analysis showed that the association is mainly driven by planned deliveries, suggesting that sleep apnea is linked to other complications that call for obstetric intervention, but does not increase the risk of spontaneous preterm delivery. We also found that sleep apnea was associated with a small increase in the risk for planned delivery, although this was not reflected in greater likelihood of any caesarean section. This is in contrast to a previous study from the US which showed caesarean section was more likely in mothers who snored [39] and those with diagnosed OSA [33].

We observed an association between sleep apnea and admission to the NICU/SCN for term but not preterm babies. Preterm infants may be admitted to the NICU/SCN on the basis of prematurity alone, whilst it appears maternal sleep apnea increases the likelihood of NICU/SCN admission for term infants. In the current study, this is consistent with the tendency to lower Apgar scores for these infants, reflecting poorer condition of the baby soon after birth.

Lastly, we found sleep apnea was associated with infants that were large, rather than small, for gestational age. This was unexpected as the intermittent hypoxia

associated with sleep apnea has been hypothesised to result in small infants [40] and in previous studies has been linked to low birthweight [2, 3] and intrauterine growth restriction [3]. However, there are a number of studies that have found no difference in the average weight of infants born to mothers with and without sleep apnea [2, 3]. We cannot discount the possibility that sleep apnea was associated with larger than expected infants due to residual confounding by obesity since we were only able to account for morbid obesity in the analyses. It is important to note however that the two previous population-based studies were similarly constrained in their ability to control for obesity but still reported an increased risk for small infants associated with OSA (ORs 1.2 and 1.3) [32, 33]. These studies did not explore an association with large infants and our results require replication in a cohort able to control for pre-pregnancy BMI.

Strengths and limitations

Strengths of the present study include the use of linked datasets from a large and population-based sample of mothers and infants, the use of objective sleep apnea as the exposure, and validated information on the outcomes and risk factors. The evidence for the relationship between sleep apnea and maternal outcomes can be considered cross-sectional associations, while associations between sleep apnea and the nature of delivery and infant outcomes are longitudinal, which provides stronger evidence for a causal link between sleep apnea and the outcomes than previous cross-sectionally or retrospectively collected data.

Many previous studies investigating sleep apnea in pregnancy have been limited by selected samples, cross-sectional or case-control study designs, and reliance on self-reported snoring as the main measure of sleep apnea. The present study was able to examine the associations between objective report of sleep apnea and outcomes for a population-based cohort of women and their infants, which has the advantages of a representative sample, large sample size, and the ability to control for multiple risk factors.

Previous studies have relied heavily on self-reported snoring as an indicator of sleep-disordered breathing, although only a small subset of those who snore will have significant sleep apnea[41]. The use of sleep apnea diagnosis from hospital records as our

exposure therefore improves on previous studies. The hospital records have been shown to have high specificity (over 99%) for a range of medical conditions when compared to medical record review [23], meaning that the sleep apnea group likely contains true cases of clinically significant sleep-disordered breathing. This is further supported by our finding that 70% of those with sleep apnea had it as their principal diagnosis (and the reason for hospital or clinic admission) and 61% of those with sleep apnea also had a procedure code in the hospital records indicating they underwent a sleep test in the study period.

We included all types of sleep apnea in the current study because the purported effects on pregnancy outcomes derive from symptoms common to both obstructive and central apneas i.e. pauses in breathing causing hypoxaemia. More practically, there is a lack of specificity in the medical coding of sleep apnea such that unspecified sleep apnea constitutes 79% of all cases in the current study, with 20% specified as obstructive and <1% specified as central (see Supplementary Table 1 for details).

The rate of sleep apnea determined through hospital records was very low at 0.08%, although studies based on health records in the Taiwan and the United States report similarly low rates (0.03% and 0.01% respectively) [32, 33]. The hospital data likely underestimates the prevalence of sleep apnea in the study population. We assumed that women without a sleep apnea code in their hospital record did not have sleep apnea. Some of these women may have had sleep apnea that was (i) not recorded on their hospital records or (ii) not recorded because they were not admitted to hospital prior to or during the course of their pregnancy. However, the inclusion of women with unrecognized sleep apnea in the group with "no sleep apnea" should bias the results conservatively towards the null.

We did not have information on the severity of sleep apnea to determine if more severe sleep apnea was correlated with worse pregnancy outcomes. Such information would be important to collect in future studies and would be strong evidence for a causal effect of sleep apnea on maternal and infant health.

A limitation of the current study is that we have no information on treatment of sleep apnea or compliance with treatment. It is likely that diagnosed sleep apnea in hospital records would be accompanied by treatment, although we have no way of determining the severity of the apnea, the provision of treatment, or the degree of

compliance with treatment. However, compliance with treatment would be expected to reduce any association between sleep apnea and pregnancy outcomes.

We were able to control for a number of major confounding factors, including age, smoking, hypertension, diabetes, and socioeconomic status. In addition, the data on diabetes and hypertension diagnoses and delivery outcomes have been previously validated [24-26]. However, we cannot rule out residual confounding, such as by obstetric history or obesity. Although we attempted to control for the effects of obesity by identifying mothers with a record of morbid obesity (BMI>30kgm^{-2}), this was found in <1% of the sample compared to estimated total overweight/obesity rates of 18 - 52% in NSW women of reproductive age from health surveys [43].

Implications and conclusions

We found that sleep apnea was associated with pregnancy hypertension, planned delivery, preterm birth, 5-minute Apgar <7, admission to NICU/SCN, and large-for-gestational-age infants. Although the results are not conclusive of a causal link, they show that women with sleep apnea are at increased risk of adverse outcomes and suggest it may be important to identify and manage sleep apnea in pregnancy, especially as other studies have shown sleep apnea symptoms become more common and increase in severity over the course of pregnancy.

Future research should investigate if the associations between sleep apnea and pregnancy outcomes are independent of obesity and other obstetric risk factors, and if intervention for sleep apnea can reduce risk of adverse pregnancy outcomes.

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Table 1. Demographic, health, and pregnancy characteristics of 636,227 pregnant women with and without sleep apnea.

	Sleep apnea n=519 (n, col%)	**No sleep apnea** n=635,708 (n, col%)
Maternal age		
<20 years	57 (11.0)	32,086 (5.1)
20-34 years	286 (55.1)	477,366 (75.1)
35+years	176 (33.9)	126,071 (19.8)
Born in Australia	430 (82.9)	426,821 (67.1)
Disadvantage quintile (SEIFA)		
Most disadvantaged	77 (14.8)	117,799 (18.5)
Disadvantaged	93 (17.9)	119,679 (18.8)
Average	106 (20.4)	130,082 (20.5)
Advantaged	129 (24.9)	124,155 (19.5)
Most advantaged	114 (22.0)	135,132 (21.3)
Smoking during pregnancy	70 (13.5)	80,414 (12.7)
Morbid obesity	61 (11.8)	3,775 (0.6)
Pre-existing diabetes	35 (6.7)	3,577 (0.6)
Chronic hypertension	23 (4.4)	7,270 (1.1)
Nulliparous	400 (77.1)	418,816 (65.9)
Multiple pregnancy	9 (1.7)	9,942 (1.6)

All differences between sleep apnea and no-apnea groups are statistically significant at $p<0.01$, with the exception of plurality (multiple pregnancy) where $p=0.75$.

Table 2. Comparison of maternal and infant outcomes in 636,227 pregnant women with and without sleep apnea.

Outcome	**Sleep apnea** n=519 (n, col%)	**No sleep apnea** n=635,261 (n, col%)	**RR** (95% CI)	**adjusted RR** (95% CI)
Gestational diabetes	42 (8.1%)	39,559 (6.2%)	1.30 (0.97 – 1.74)	1.09 (0.82 – 1.46)
Pregnancy hypertension	102 (19.7%)	55,076 (8.7%)	**2.27 (1.91 – 2.70)**	**1.40 (1.15 – 1.70)**
Labour onset				
Spontaneous	201 (38.7%)	369,583 (58.1%)	Ref	Ref
Planned delivery	316 (60.9%)	266,010 (41.8%)	**1.46 (1.36 – 1.56)**	**1.15 (1.07 -1.23)**
Type of delivery				
Vaginal	299 (57.6%)	449,052 (70.6%)	Ref	Ref
Caesarean	217 (41.8%)	186,411 (29.3%)	**1.43 (1.30 – 1.59)**	1.06 (0.96 – 1.17)
Preterm birth (≤36 weeks)	75 (14.5%)	43,812 (6.9%)	**2.10 (1.70 – 2.58)**	**1.50 (1.21 – 1.84)**
Spontaneous	22 (11.0%)	24,718 (6.7%)	**1.63 (1.10 – 2.42)**	1.26 (0.84 – 1.88)
Planned	52 (16.5%)	19,087 (7.2%)	**2.29 (1.78 – 2.94)**	**1.61 (1.25 – 2.06)**
Low Apgar at 5 minutes (<7)	24 (4.6%)	15,358 (2.4%)	**1.91 (1.29 – 2.83)**	**1.60 (1.07 – 2.38)**
Preterm	11 (14.7%)	6,188 (14.1%)	1.04 (0.60 – 1.80)	1.11 (0.64 – 1.92)
Term	13 (2.9%)	9,170 (1.6%)	**1.89 (1.11 – 3.23)**	1.65 (0.96 – 2.82)
NICU/SCN admission	145 (27.9%)	101,906 (16.0%)	**1.74 (1.52 – 2.00)**	**1.26 (1.11 – 1.44)**
Preterm	55 (73.3%)	30,128 (68.6%)	1.07 (0.93 – 1.23)	0.99 (0.87 – 1.13)
Term	90 (20.3%)	71,778 (12.1%)	**1.67 (1.40 – 2.01)**	**1.26 (1.06 – 1.48)**
Perinatal death	10 (1.9%)	5,617 (0.9%)	**2.18 (1.18 – 4.03)**	1.73 (0.92 – 3.25)
Small for gestational age	43 (8.3%)	68,598 (10.8%)	0.77 (0.58 – 1.03)	0.81 (0.61 – 1.08)
Large for gestational age	79 (15.2%)	57,805 (9.1%)	**1.68 (1.37 – 2.06)**	**1.27 (1.04 – 1.55)**

RR = relative risk from Poisson regression models. CI = confidence interval. Adjusted models include the covariates of maternal age, country of birth, smoking, obesity, parity, socioeconomic disadvantage, chronic hypertension, pre-existing diabetes, gestational diabetes and pregnancy hypertension. Adjusted model for gestational diabetes only included the covariates of maternal age, country of birth, smoking, obesity, parity, and socioeconomic disadvantage. Adjusted model for pregnancy hypertension included these plus chronic hypertension and pre-existing diabetes.

Supplementary Table 1. ICD-10-AM codes used in the identification of sleep apnea.

ICD-10-AM code	**Description**	**Number of women (% of all cases in study)**
G47.30	Sleep apnoea, unspecified	170 (32.8%)
G47.31	Central sleep apnoea syndrome (Central sleep hypopnoea syndrome)	6 (1.2%)
G47.32	Obstructive sleep apnoea syndrome (Obstructive sleep hypopnoea syndrome)	336 (64.7%)
G47.33	Sleep hypoventilation syndrome	1 (0.2%)
G47.39	Other sleep apnoea	6 (1.2%)
	Total	519 (100.0%)

Note: ICD-10-AM refers to the Australian Modification of the ICD-10. These codes differ from those in the ICD-10.

Supplementary Table 2. ICD-10-AM codes used in the identification of obesity.

ICD-10-AM code	**Description**	**Number of records (% of all records of obesity)**
E65	Localised adiposity	156
E66.0	Obesity due to excess calories	12
E66.1	Drug-induced obesity	1
E66.2	Extreme obesity with alveolar hypoventilation	None
E66.8	Other obesity (Morbid obesity)	1282
E66.9	Obesity, unspecified (Simple obesity Not Otherwise Specified)	2388
	Total	3839 (100.0%)

Note: There are 3 more obesity records than women with obesity (N=3836) because 2 women had both E65 and E66.9, and 1 woman had both E66.1 and E66.9.