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Neonatal Morbidity of Small- and Large-for-Gestational-Age Neonates Born at Term in Uncomplicated Pregnancies

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Abstract

Objective—To compare morbidity among small-for-gestational-age (SGA; birthweight [BW] < 10th percentile for gestational age), appropriate-for-gestational-age (AGA; BW 10-90th percentile; reference group), and large-for-gestational-age (LGA; BW > 90th percentile) neonates in apparently uncomplicated pregnancies at term (37 weeks).

Material and Methods—This secondary analysis, derived from an observational obstetric cohort of 115,502 deliveries, included women with apparently uncomplicated pregnancies of non-anomalous singletons who had confirmatory ultrasound dating no later than the second trimester, and who delivered between 37⁰ and 42⁶ weeks. We used two different composite neonatal morbidity outcomes: hypoxic composite neonatal morbidity for SGA and traumatic composite neonatal morbidity for LGA neonates. Log Poisson relative risks (aRR) with 95% confidence intervals (CI), adjusted for potential confounding factors (nulliparity, body mass index, insurance status, and neonatal sex) were calculated.

Results—Among the 63,436 women who met our inclusion criteria, SGA occurred in 7.9% (n=4,983) and LGA in 8.3% (n=5,253). Hypoxic composite neonatal morbidity was significantly higher in SGA (1.1%) vs. AGA (0.7%; aRR 1.44, 95% CI 1.07-1.93) but similar between LGA (0.6%) vs. AGA (aRR 0.84; 95% CI 0.58-1.22). Traumatic composite neonatal morbidity was significantly higher in LGA (1.9%) vs. AGA (1.0%; aRR 1.88, 95% CI 1.51-2.34)) but similar in SGA (1.3%) vs. AGA (aRR 1.28; 95% CI 0.98-1.67).

Conclusions—Among women with uncomplicated pregnancies, hypoxic composite neonatal morbidity is more common with SGA neonates and traumatic–composite neonatal morbidity is more common with LGA neonates.

Introduction

Small for gestational age (SGA) or large for gestational age (LGA) occurs in about 20% of pregnant women and are associated with adverse outcomes (1). Newborns who are SGA (i.e., birthweight [BW] < 10^{th} percentile), compared to those who are appropriate-for-gestational-age (AGA; BW at 10-90th percentile), are at increased risk for stillbirth, seizures, sepsis, intraventricular hemorrhage, necrotizing enterocolitis, hypoxic ischemic encephalopathy and neonatal mortality (2). Newborns who are LGA (i.e., BW > 90th

percentile), are at increased risk of stillbirth, traumatic delivery, mechanical ventilation, brachial plexus palsy and neonatal mortality (1, 3,4)

The frequency of aberrant fetal growth is higher in women with complications of pregnancy. SGA, for example, occurs in 17 to 32% of women with hypertensive diseases and LGA occurs in 24 to 39% of women with diabetes. Additionally, neonatal morbidity is higher in these populations when aberrant growth occurs (5-9). Conversely, although women without apparent pregnancy complications also have newborns with aberrant growth, there are a paucity of data detailing whether these neonates are at increased risk of neonatal morbidity. Resolving this evidence gap has implications with regard to understanding whether sonographic screening for fetal growth among women with uncomplicated pregnancies has the potential to decrease a clinically-significant portion of neonatal morbidity.

Correspondingly, the objective of this analysis was to compare the neonatal morbidity among SGA, AGA, and LGA neonates in women without medical or obstetric complications at term (37 weeks or more). We hypothesized that, compared to AGA neonates, those born SGA would be more likely to have hypoxic morbidity and those born LGA would be more likely to have traumatic morbidity.

Materials and Methods

This is a secondary analysis of an observational obstetric cohort (Assessment of Perinatal Excellence) of women and their neonates born in 25 geographically-dispersed medical centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Maternal demographics, peripartum outcomes, and neonatal morbidities were collected on all women who had a live fetus on admission and delivered a newborn of at least 23 weeks of gestation on randomly selected days representing one third of deliveries over a 3-year period. Data from all charts were abstracted by certified research personnel. Neonatal data were collected until discharge, death or until 120 days of age, whichever came first. Several steps were undertaken to ensure data quality. First, prior to selecting final data collection fields, we conducted a two-week pilot study to evaluate the data collection process, quality of the data, and frequency of missing data. The final data collection fields were based on the information gathered during this pilot phase. During the data collection process, all data were subjected to ongoing data edits to ensure accuracy. The study was approved by the institutional review board at each participating center under a waiver of informed consent. Full details on study methods and the technique of data collection have been previously published. (10)

Women were included in this secondary analysis if they delivered non-anomalous singletons between 37^0 and 42^6 weeks of gestational and had a pregnancy that had been dated by last menstrual period and first or second trimester ultrasound, first or second trimester ultrasound alone, or assisted reproductive technology. A pregnancy was considered complicated if a woman had any of the following: diabetes (pregestational or gestational), chronic hypertension, history of deep venous thrombus or pulmonary embolism, non-obstetric comorbidity (e.g., cardiac disease), thrombophilia, anticoagulant use, placenta previa, placental abruption, or – at admission for delivery – deep venous thrombosis, asthma exacerbation at

delivery, or hypertensive disease of pregnancy (gestational hypertension, preeclampsia, or eclampsia). In the absence of these conditions, women were considered to have apparently uncomplicated pregnancies. Furthermore, a post-hoc sensitivity analysis was conducted excluding women with a diagnosis of suspected intrauterine growth restriction or non-reassuring fetal status at the time of admission.

Size for gestational age was estimated per methods of Alexander et al (11, and personal communication) using neonatal gestational age at delivery, birthweight and sex and maternal race/ethnicity to categorize newborns into three groups: SGA (birthweight less than 10th percentile for gestational age), AGA (birthweight 10th to 90th percentile for gestational age; reference group), and LGA (birthweight greater than 90th percentile for gestational age).

The primary outcome for SGA was a composite neonatal morbidity (CNM) potentially related to hypoxic events and included any of the following: Apgar score < 5 at 5 min, seizure, bronchopulmonary dysplasia, persistent pulmonary hypertension of the newborn, culture proven sepsis, cardiopulmonary resuscitation within the first 24 hours, hypoxic ischemic encephalopathy (HIE), grade III or IV intraventricular hemorrhage grade (IVH), grade II or III necrotizing enterocolitis, ventilator support within 24 hours, or death before discharge. The primary outcome for LGA newborns, was a CNM potentially related to traumatic events and included any of the following: Apgar score < 5 at 5 min, seizure, cardiopulmonary resuscitation within the first 24 hours, ventilator support within 24 hours, hypoxic ischemic encephalopathy, osseous fracture, intracranial hemorrhage other than IVH, brachial plexus palsy, facial nerve palsy, or death before discharge.

Comparative analyses of aberrant growth category (SGA, AGA, LGA) were performed with the chi-square test or Fisher's exact test for categorical variables and the Wilcoxon rank sum test for continuous variables. Log Poisson relative risks (aRR) with 95% confidence intervals (CI), adjusted for potential confounding factors (nulliparity, body mass index, insurance status, and neonatal sex), were calculated. SAS software version 9.2 was used for the analyses. All tests were two-tailed and p<.05 was used to define statistical significance. No imputation for missing data was performed.

Results

Of the 115, 502 women in the APEX study, 63,436 (55%) had uncomplicated pregnancies at term and were eligible for this analysis (Fig 1). Among these women, 7.9% (N=4,983) had an SGA neonate and 8.3% (N=5,253) had an LGA neonate.

Several maternal characteristics differed significantly based on whether a woman had an SGA, AGA, or LGA neonate. Maternal age, race, ethnicity, cigarette use, cocaine or methamphetamine use, and body mass index at delivery differed for women who delivered an AGA newborn compared to those with aberrant growth (Table 1). Similarly, the gestational age at delivery differed significantly among groups. About 29% of women with an SGA neonate and 42% of women with an LGA neonate delivered at 40 weeks or later. The frequency of cesarean delivery different for women with LGA and AGA neonates (Table 2).

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The absolute frequencies of CNM were less than 2% for the three groups of newborns (Table 3). The three most common morbidities among SGA neonates were ventilator support within 24 hours of birth (0.5%), Apgar score <5 at 5 min (0.4%) and HIE (0.4%). For LGA neonates, the three most common morbidities were fracture (1.0%), brachial plexus palsy (0.4%) and ventilator support (0.3%). Hypoxic CNM was higher in SGA neonates than in AGA neonates, and traumatic CNM was higher in LGA neonates than in AGA neonates (Table 3). After adjusting for confounding factors, the significant differences among groups remained: hypoxic CNM was 44% higher in neonates with SGA than in those with AGA, and traumatic CNM was 88% higher in neonates with LGA than in those with AGA (Table 4). Other factors associated with the CNM outcomes that were studied included nulliparity, male gender and BMI at delivery (Table 4). Private insurance was associated with a lower frequency of the traumatic CNM outcome. The results were similar after women with a diagnosis of intrauterine growth restriction or non-reassuring fetal status at the time of admission were excluded from analysis (Table 5).

Discussion

Our analysis demonstrates that even among women who have an otherwise uncomplicated term pregnancies, hypoxic CNM and traumatic CNM were significantly increased among SGA (1.1%) and LGA (1.9%) neonates, respectively. Specifically, compared to AGA neonates, those who were SGA had a 44% higher risk of hypoxic CNM and those who were LGA had an 88% higher risk of traumatic CNM. Though the CNM, as defined, occurred in less than 2% of newborns with aberrant growth, two points are worth noting. First, adverse outcomes included in the composite are severe with the potential for long-term sequelae. Second, the size of the population at risk for these adverse neonatal outcomes is large with approximately 470,000 SGA and LGA neonates born annually in the United States (12) among women with uncomplicated pregnancies.

This report differs from prior studies on the extremes of fetal growth in that these studies included a general obstetric population (2, 4) or women with comorbidities like hypertensive disease (5-7) or diabetes (8-9). In contrast, our study population was limited to women with uncomplicated pregnancies who delivered at term. Also, unlike most prior reports on abnormal growth, we simultaneously evaluated the outcomes of SGA and LGA neonates in one study population. Additionally, unlike prior publications (13), we were able to define a study group of women with uncomplicated pregnancies that excluded those with a wide variety of potential complicating factors. The criteria for gestational age were based on established criteria, and thus ascertainment of abnormal growth more reliable than that of prior publications that used birth certificate datasets (1).

The limitations of the analysis should be acknowledged. Our analysis was based on the actual birthweight, which is unknowable with exactitude (14) and is not helpful to clinicians managing pregnancy. Though we excluded several conditions that constitute high-risk pregnancies, some unrecognized complications (e.g. thrombophilia) was potentially present in these apparently uncomplicated pregnancies. It is uncertain what proportions of SGA or LGA neonates were detected by clinicians and how antepartum care, including fetal surveillance, and intrapartum management may have been influenced (15-19). Nevertheless,

28% of SGA neonates (Table 2) were delivered at 40 weeks or later, suggesting that many of these cases were not known prior to delivery (i.e., clinicians aware fetal growth restriction typically recommend delivery no later than 39 weeks). The parent dataset did not include stillbirths occurring prior to admission and may thus have excluded the most extreme adverse outcomes for SGA and LGA (2,3). Since the data are observational, it is unknown if increasing the detection of abnormal growth and interventions would improve the CNM (20-22).

Notwithstanding the limitations, the strengths of the analysis include ascertainment of data directly from the charts by trained research personnel from 25 geographically and demographically diverse populations (10). Additionally, uniform definitions of neonatal outcomes were pre-specified and included outcomes that are associated with long-term sequelae.

These findings have implications with regard to whether routine third-trimester sonographic surveillance in women with uncomplicated pregnancies may or may not be clinically beneficial (23,24). Our results suggest that women with uncomplicated pregnancies experience fetal growth aberration which is associated with increased severe neonatal morbidity. This fetal growth aberration (in this and prior studies) is not well ascertained (15,16,25-30) and detection may have be associated with improved outcomes related to antepartum surveillance and interventions (2,4,17,18). Accordingly, it is possible that third-trimester sonography, despite the known vagaries of accurate fetal growth aberration (31) and iatrogenic neonatal morbidity (30,32), could screen for fetal growth aberration in women with uncomplicated pregnancies and guide intervention that improves neonatal outcomes (2,4,17,18,21,22). We, however, emphasize that before such a practice is implemented, evidence from clinical trials is needed to demonstrate that any theoretical benefits is cost-effective and translates to actual clinical improvement.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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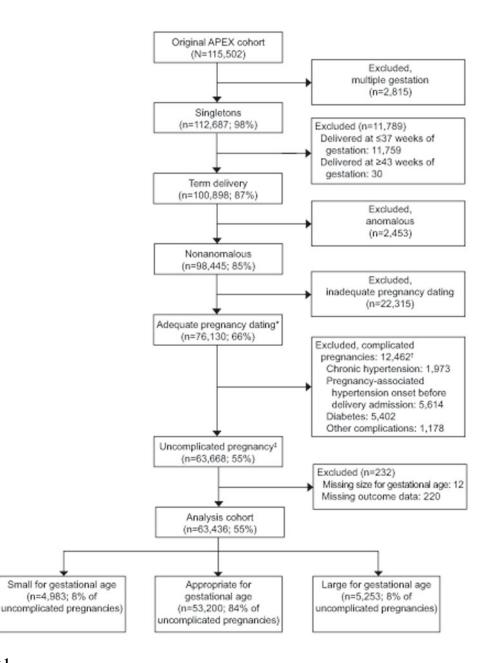


Fig 1.

Analysis cohort inclusion. APEX, Assessment of Perinatal Excellence. *Adequate pregnancy dating was defined as a pregnancy dated by last menstrual period and first- or second-trimester ultrasonogram alone, or assisted reproductive technology. [†]Categories not mutually exclusive. [‡]A pregnancy was considered complicated if the woman had any of the following: diabetes (pregestational or gestational), chronic hypertension, history of deep venous thrombus or pulmonary embolism, hypertensive disease of pregnancy (gestational hypertension or preeclampsia) with an onset before delivery hospital admission, thrombophilia excluding *MTHFR*, anticoagulant use, previa, or any of the following as a reason for delivery hospital admission: vaginal bleeding or abruption, deep venous thrombus, asthma exacerbation, seizures, or other nonobstetric

maternal medical condition. In absence of these conditions, a woman was considered to have an uncomplicated pregnancy.

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	SGA (N=4,983)	AGA (N=53,200)	LGA (n=5,253)	SGA vs. AGA P*	LGA vs. AGA P*
Maternal age (years)	27 (22-31)	28 (23-32)	29 (25-33)	<.001	<.001
Maternal age categories (years)				<.001	<.001
<20	627 (12.6)	4756 (8.9)	236 (4.5)		
20-24.9	1318 (26.5)	11841 (22.3)	911 (17.3)		
25-29.9	1331 (26.7)	15007 (28.2)	1512 (28.8)		
30-34.9	1104 (22.2)	13922 (26.2)	1564 (29.8)		
35	603 (12.1)	7674 (14.4)	1030 (19.6)		
Race / ethnicity				.001	<.001
Non-Hispanic black / African-American	876 (17.6)	9882 (18.6)	924 (17.6)		
Non-Hispanic white	2387 (47.9)	24674 (46.4)	2415 (46.0)		
Non-Hispanic Asian	307 (6.2)	2705 (5.1)	194 (3.7)		
Hispanic / Latino	1197 (24.0)	13372 (25.1)	1448 (27.6)		
Other	180 (3.6)	2083 (3.9)	218 (4.2)		
Not documented	36 (0.7)	484 (0.9)	54 (1.0)		
Primary source of medical care payment $\dot{\tau}$				<:001	<.001
Private insurance	2231 (45.1)	27154 (51.4)	2771 (53.1)		
Government assisted insurance	2240 (45.3)	19897 (37.6)	1811 (34.7)		
Uninsured or self-pay	476 (9.6)	5809 (11.0)	634 (12.2)		
Obstetric history				<.001	<.001
Nulliparous	2506 (50.3)	21231 (39.9)	1497 (28.5)		
Prior vaginal delivery only	1834 (36.8)	23865 (44.9)	2667 (50.8)		
Prior vaginal and cesarean delivery	334 (6.7)	4057 (7.6)	558 (10.6)		
Prior cesarean delivery only	309 (6.2)	4042 (7.6)	530~(10.1)		
Prenatal care (2 visits) $\vec{\tau}$	4792 (99.1)	51408 (99.4)	5092 (99.6)	.02	.13
Cigarette use	837 (16.8)	4441 (8.4)	289 (5.5)	<.001	<.001
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	SGA (N=4,983)	SGA (N=4,983) AGA (N=53,200) LGA (n=5,253)	LGA (n=5,253)	SGA vs. AGA P [*] LGA vs. AGA P [*]	LGA vs. AGA P*
Cocaine or methamphetamine	53 (1.1)	236 (0.4)	13 (0.3)	<.001	.04
BMI at delivery $(kg/m^2)^{\dagger}$	27.8 (25.1-31.6)	27.8 (25.1-31.6) 29.6 (26.6-33.4) 32.6 (29.1-36.8)	32.6 (29.1-36.8)	<.001	<:001
BMI at delivery categories $(kg/m^2)^{\dagger}$				<.001	<:001
<25	1195 (24.4)	6686 (12.8)	203 (4.0)		
25-29.9	2005 (41.0)	20909 (40.0)	1391 (27.0)		
30-34.5	1094 (22.4)	15195 (29.1)	1780 (34.6)		
35-39.9	375 (7.7)	6136 (11.8)	1054 (20.5)		
40	222 (4.5)	3307 (6.3)	716 (13.9)		
Transferred from another hospital	11 (0.2)	159 (0.3)	11 (0.2)	.33	.25
Male fetal sex	2551 (51.2)	26766 (50.3)	2674 (50.9)	.23	.41

Data presented are n (%) or median (interquartile range)

SGA, small for gestational age (birth weight < 10% for gestational age); AGA, appropriate for gestational age (birth weight between 10-89% for gestational age); LGA, large for gestational age (birth weight > 90% for GA); BMI, body mass index

 $\overset{*}{}_{\mathrm{based}}$ on the chi-square test for categorical variables or Wilcoxon rank sum test for continuous variables

 $\stackrel{f}{7}$ number of missing values: insurance (413); prenatal care (1771); BMI (1168)

Intrapartum characteristics

Reno for brokeling (00)		SGA (N=4,983)	AGA (N=53,200)	LGA (n=5,253)	SGA vs. AGA P*	LGA vs. AGA P^*
ey 4915 (98.6) 5201 (99.4) 5200 (99.4) ution, observation, or treatment for intranctive growth restriction 12 (0.2) 12 (0.3) 15 (0.3) 15 (0.3) ution observation, or treatment for onder reasons 210 (0.5) 12 (0.3) 15 (0.3) 15 (0.3) totion observation, or treatment for onder reasons 27 (0.6) 12 (0.3) 15 (0.3) 15 (0.3) totion observation, or treatment for onder reasons 27 (0.4) 18 (0.0) 0.000 -000 totion observation 61 (1.3) 2834 (9.3) 32 (0.6) -000 totion observation 61 (1.3) 2840 (1.3) 32 (0.6) -000 tessent 4761 (9.5) 1304 (5.5) 1304 (5.5) 2200 (9.4) -000 tessent 4761 (5.7) 1304 (5.5) 1304 (5.5) 2200 (9.6) -200 tessent 4761 (5.7) 1304 (5.5) 1204 (5.5) 2200 (9.6) -2001 tessent 1204 (5.5) 1204 (5.5) 1204 (5.5) 2200 (5.6) 2206 t	Reason for hospital admissio				<.001	4
ation observation, observation, observation, or treatment for intranterine growth treation $12(0.2)$ $4(0.0)$ $0(0.0)$ ution, observation, or treatment for intranterine growth treation $2(0.5)$ $15(0.3)$ $15(0.3)$ $15(0.3)$ ution, observation, or treatment for other treatons $23(0.6)$ $213(0.4)$ $18(0.0)$ $10(0.0)$ for bow and delivery admission $46(0.9)$ $18(0.0)$ $18(0.0)$ $0(0.0)$ -000 treatons $470(0.5)$ $5234(0.5)$ $530(0.6)$ -000 -000 treatons $470(0.5)$ $538(0.7)$ $530(0.6)$ -000 -000 treatons $470(0.5)$ $510(0.7)$ $530(0.6)$ -000 -000 treatons $470(0.5)$ $510(0.70)$ $530(0.6)$ -000 treatons $470(0.5)$ $510(0.70)$ $530(0.6)$ -000 treatons $470(0.5)$ $530(0.6)$ -000 -000 treatons $470(0.5)$ $530(0.6)$ -000 -000 treatons $470(0.5)$ $530(0.6)$	Delivery	4915 (98.6)	52811 (99.3)	5220 (99.4)		
ution observations (non-reassaring feal status) 24 (0.5) 17 (0.5) 15 (0.3) ution observations or treatment for observations $32 (0.6)$ $31 (0.6)$ $18 (0.3)$ ~ 001 for blow and delivery admission $45 (0.6)$ $18 (0.0)$ $0 (0.0)$ ~ 001 term agrowth verticion $46 (0.9)$ $34 (0.7)$ $34 (0.7)$ $33 (0.6)$ ~ 001 term agrowth verticion $67 (1.3)$ $34 (0.7)$ $33 (0.6)$ ~ 001 term agrowth verticion $67 (1.3)$ $34 (0.7)$ $33 (0.6)$ ~ 001 term agrowth verticion $67 (1.3)$ $34 (0.7)$ $33 (0.6)$ ~ 001 term agrowth verticion $47 (0.5)$ $34 (0.7)$ $32 (0.6)$ ~ 001 term agrowth verticion $21 (0.4)$ $21 (0.6)$ ~ 001 ~ 001 term agrowth verticion $21 (0.5)$ $21 (0.5)$ $23 (0.6)$ ~ 001 term agrowth verticion $21 (0.5)$ $21 (0.5)$ $21 (0.5)$ ~ 001 term agrowth verticion $21 (0.5)$ $21 (0.5)$ $21 (0.5)$ <	Evaluation, observation, or treatment for intrauterine growth restriction	12 (0.2)	4 (0.0)	0 (0.0)		
ation observation, or treatment for oher reasons 2 (0.6) 13 (0.4) 18 (0.3) < 001 for hour and delivery admission 46 (0.9) 18 (0.0) 0 (0.0) < 001 atering greath restriction 47 (1.3) 34 (0.7) 33 (0.6) < 001 atering field status 67 (1.3) 348 (0.7) 33 (0.6) < 001 atering field status 67 (1.3) 549 (9) 530 (9) < 001 atering field status 67 (1.3) 540 (9) 530 (9) < 001 atering field status 147 (9,57) 510 (9,72) 500 (9,70) < 200 atering the attering	Evaluation, observation, or treatment for non-reassuring fetal status	24 (0.5)	172 (0.3)	15 (0.3)		
for labor and lelivery admission <	Evaluation, observation, or treatment for other reasons	32 (0.6)	213 (0.4)	18 (0.3)		
atering growth verticition 46 (0.9) 18 (0.0) 0 (0.0) reasoning fetal status 67 (1.3) 34 (0.7) 33 (0.6) reasoning fetal status 487 (97.7) 5284 (99.2) 520 (99.4) reasoning fetal status 487 (197.7) 5283 (197.0) 5001 status 476 (195.7) 51601 (197.2) 501 (197.2) 501 status 476 (195.7) 51601 (197.2) 501 (197.2) 501 status 476 (195.7) 51601 (197.2) 501 (197.2) 501 status 21 (1.6) 181 (1.5) 517 (1.5.4) 517 (1.5.4) 520 (1.6.7) before 21 (1.6) 181 (1.5.7) 181 (1.5.7) 181 (1.5.7) 520 (1.6.7) before 21 (1.6) 181 (1.5.7) 181 (1.5.7) 182 (1.5.1) 182 (1.5.1) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520 (1.6.7) 520	Reason for labor and delivery admission				<.001	ŕ
casarring feal status $67(1.3)$ $34(0.7)$ $33(0.6)$ $320(0.9.4)$ reasons $4870(97.7)$ $5284(9.9.3)$ $520(0.9.4)$ <001 ation $120(0.7, 0)$ $5081(97.0)$ <001 x $192(3.9)$ $1304(2.5)$ $5081(97.0)$ <001 x $192(3.9)$ $1304(2.5)$ $127(2.4)$ <001 x $192(3.9)$ $1304(2.5)$ $127(2.4)$ <001 x $192(3.9)$ $1304(2.5)$ $127(2.4)$ <001 x $192(3.9)$ $121(1.8, 9)$ $32(6.6)$ 2.8 x $1007(2)$ $121(1.8, 9)$ $32(6.6)$ 2.8 x $1002(2.1)$ $1037(2.4)$ $1002(2.6)$ $1002(2.6)$ x $1002(2.6)$ $102(2.6)$ $1002(2.6)$ $1002(2.6)$ x $117(3.6)$ $1822(3.6, 1)$ $1002(2.6)$ $1002(2.6)$ x $117(3.6)$ $1237(2.4)$ $118(27.0)$ $1002(2.6)$ x $117(3.6)$ $1237(2.4)$ $118(27.0)$ $1002(2.6)$ x $117(3.6)$ $1237(2.4)$ $118(27.0)$ $118(27.0)$ x $117(3.6)$ $1237(2.4)$ $118(27.0)$ $1000(0)$ x $117(3.6)$ $1237(2.4)$ $118(27.0)$ $1000(0)$ x $117(3.6)$ $1237(2.4)$ $118(27.0)$ $1000(0)$ x $117(3.6)$ $1237(2.6)$ $118(27.0)$ $1000(0)$ x $112(2.6)$ $1237(2.6)$ $118(27.0)$ $1000(0)$ x $118(2.0)$ $1000(0)$ $118(2.0)$ 10	Intrauterine growth restriction	46 (0.9)	18 (0.0)	0 (0.0)		
resons470 (97.7)5534 (90.3)520 (99.4)ation $ -$ ation $ -$ <td< td=""><td>Non-reassuring fetal status</td><td>67 (1.3)</td><td>348 (0.7)</td><td>33 (0.6)</td><td></td><td></td></td<>	Non-reassuring fetal status	67 (1.3)	348 (0.7)	33 (0.6)		
with attent < 001 x < 761 (95.7) 51601 (97.2) < 5081 (97.0)h < 192 (39) 51601 (97.2) < 5081 (97.0)h < 192 (39) < 192 (39) < 320.60 h < 100.3 < 210.40 < 320.60 < 28 h < 100.3 < 210.40 < 320.60 < 28 h < 464 (9.3) < 111.89 < 320.60 < 28 h < 464 (9.3) < 191.00 < 320.60 < 28 h < 100.3 < 120.3 < 100.3 < 200.3 h < 1717 (34.5) $18327 (34.4)$ $1510 (28.8)$ < 28 h $< 1717 (34.5)$ $18327 (34.4)$ $1510 (28.8)$ < 200.3 h $< 1717 (34.5)$ $18327 (34.4)$ $1510 (28.8)$ < 200.3 h $< 1717 (34.5)$ $18327 (34.4)$ $1510 (28.8)$ < 200.3 h $< 1717 (34.5)$ $18327 (34.4)$ $1510 (28.8)$ < 200.3 h $< 1717 (34.5)$ $18327 (34.4)$ $1510 (28.8)$ < 200.3 h $< 1263 (28.4)$ $1327 (24.9)$ < 120.3 < 100.3 h $< 1263 (28.4)$ $1327 (24.9)$ < 120.3 < 100.3 h $< 1260 (28.4)$ $1360 (23.6)$ < 100.3 < 100.3 h $< 1260 (28.4)$ $1260 (28.6)$ < 120.3 < 100.3 h $< 1260 (28.6)$ $1260 (28.6)$ < 100.3 < 100.3 h $< 1260 (28.6)$ $1260 (28.6)$ < 100.3 < 100.3 h $< 1260 (28.6)$ <	Other reasons	4870 (97.7)	52834 (99.3)	5220 (99.4)		
x 4761 51601 5081 670 h 127 127 127 127 127 h 120 120 120 120 120 h 120 120 121 120 120 h 1217 1217 1202 1202 1202 h 1217 1237 1202 1202 1202 h 1271 1227 1202 1202 1202 h 1271 12272 1202 1202 1202 h 12717 1271 1202 1202 1202 h 12717 127172 1202 1202 1202 h 12372 12712 1202 1202 1202 h 12372 12712 1202 1202 1202 h 12372 12712 1202 1202 1202 h 1202 1272 1202 1202 1202 h 1202 1202 1202 1202 1202 <tr< td=""><td>Presentation</td><td></td><td></td><td></td><td><.001</td><td>.008</td></tr<>	Presentation				<.001	.008
h192 (3.9)130 (2.5)127 (3.4)breech malpresentation21 (0.4)181 (0.3)32 (0.6).28breech malpresentation464 (9.3)4711 (8.9)35 (6.8).28labor464 (9.3)643 (12.1)1035 (197).001labor549 (1.0)643 (12.1)1035 (197).001labor1717 (34.5)1832 (34.4)1510 (28.8).001consummented1263 (25.4)1571 (28.5)1290 (24.6).consummented1454 (29.2)13270 (24.9)1418 (27.0).consummented1454 (29.2)13270 (24.9)1418 (27.0).conduction3529 (70.8)3930 (75.1)335 (73.0).conduction3529 (70.8)3930 (75.1)335 (73.0).conduction384 (77)150 (0.3)0 (0.0).decide382 (13)150 (32.0)100 (31).consummenter88 (1.8)650 (1.2)51 (1.0).consuming feat status0 (0.0)138 (0.3)109 (2.1).consuminoticitie0 (0.0)133 (23.2)123 (23.2)125 (24.0)consuminoticitie92 (197)123 (23.2)126 (24.0).consuminoticitie147 (3.0)237 (34.2)237 (34.0).consuminoticitie92 (197)133 (23.2)126 (24.0).consuminoticitie123 (23.2)123 (23.2)126 (24.0).consuminoticitie123 (23.2)123 (23.2)con	Vertex	4761 (95.7)	51601 (97.2)	5081 (97.0)		
breech malpresentation $21 (0.4)$ $181 (0.3)$ $32 (0.6)$ $.28$ bech malpresentation $464 (9.3)$ $471 (89)$ $358 (6.8)$ $.28$ labor $.464 (9.3)$ $.471 (89)$ $.358 (6.8)$ $.28$ labor $.401 (10.6)$ $.435 (12.1)$ $.1035 (19.7)$ $.001$ consumption to induction) $.549 (110)$ $.643 (12.1)$ $.1035 (19.7)$ $.001$ consumption to induction) $.171 (34.5)$ $.1832 (34.4)$ $.151 (28.8)$ $.001$ consumption to induction $.1263 (25.4)$ $.1517 (28.5)$ $.120 (24.6)$ $.77$ consumption to the toton $.164 (29.2)$ $.1327 (24.9)$ $.181 (27.0)$ $.77$ consumption to the toton $.164 (29.2)$ $.1327 (24.9)$ $.141 (27.0)$ $.77$ consumption to the toton $.1263 (75.1)$ $.129 (75.1)$ $.77$ $.77$ consumption to the toton $.352 (70.8)$ $.3930 (75.1)$ $.3835 (73.0)$ $.77$ consumption to the toton $.384 (7.7)$ $.150 (0.3)$ $.00.0)$ $.77$ consumption to the toton $.98 (1.8)$ $.650 (1.2)$ $.100 (0.0)$ consumption to the toton $.138 (0.3)$ $.109 (2.1)$ $.109 (2.1)$ consumption $.127 (2.0)$ $.1232 (23.2)$ $.128 (24.0)$ consumption $.127 (2.0)$ $.201 (2.0)$ $.001$	Breech	192 (3.9)	1304 (2.5)	127 (2.4)		
464 (9.3) $4711 (8.9)$ $388 (6.8)$ 28 $1abor$ -601 -601 -601 $1abor$ $549 (11.0)$ $6435 (12.1)$ $1035 (19.7)$ -601 $ccearean without labor or induction)549 (11.0)6435 (12.1)1035 (19.7)-601carean without labor or induction)549 (11.0)549 (11.0)1517 (28.5)1290 (24.6)-7carean symmeted1263 (25.4)1517 (28.5)1290 (24.6)-7-7carean symmeted1454 (29.2)1377 (24.9)1418 (27.0)-7carean symmeted1454 (29.2)1370 (24.9)1418 (27.0)-7carean symmeted1454 (29.2)1370 (24.9)1418 (27.0)-7carean symmeted3529 (70.8)3930 (75.1)335 (73.0)-7carean symmetric non384 (7.7)150 (0.3)0 (0.0)-7carean symmetric non384 (7.7)150 (0.3)0 (0.0)-7carean symmetric non384 (7.7)150 (0.3)0 (0.0)-7carean symmetric non-88 (1.8)650 (1.2)51 (1.0)-7carean symmetric non-92 (24.2)-109 (2.1)-7carean symmetric non-123 (23.2)-128 (24.0)-701carean symmetric non-123 (23.2)-237 (2.0)-701$	Non-breech malpresentation	21 (0.4)	181 (0.3)	32 (0.6)		
< 001bor or induction) $549 (11.0)$ $6435 (12.1)$ $1035 (19.7)$ bor or induction) $549 (11.0)$ $6435 (12.1)$ $1035 (19.7)$ $1717 (34.5)$ $18323 (34.4)$ $1510 (28.8)$ $1263 (25.4)$ $1571 (28.5)$ $1290 (24.6)$ $1263 (25.4)$ $1571 (28.5)$ $1290 (24.6)$ $1454 (29.2)$ $13270 (24.9)$ $118 (27.0)$ $1454 (29.2)$ $13270 (24.9)$ $1418 (27.0)$ $< 1263 (25.4)$ $13270 (24.9)$ $1418 (27.0)$ $< 1269 (72)$ $3930 (75.1)$ $3835 (73.0)$ $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $3835 (73.0)$ 7 $< 1200 (75.1)$ $982 (19.7)$ $190 (2.1)$ $< 1200 (75.1)$ $1233 (23.2)$ $109 (2.1)$ $< 1200 (75.1)$ $1233 (23.2)$ $1238 (23.0)$ $< 1200 (75.1)$ $1233 (23.2)$ $123 (20.0)$ $< 1200 (75.1)$ $1237 (23.2)$ $1238 (20.0)$ $< 1200 (75.1)$ $1233 (23.2)$ $123 (20.0)$ $< 1200 (75.1)$ $1233 (23.2)$ $123 (20.0)$ $< 1200 (75.1)$ $123 (75.1)$ $123 (75.0)$ $< 1200 (75.1)$ $123 (75.1)$ $123 (75.1)$ <td>PROM</td> <td>464 (9.3)</td> <td>4711 (8.9)</td> <td>358 (6.8)</td> <td>.28</td> <td><.001</td>	PROM	464 (9.3)	4711 (8.9)	358 (6.8)	.28	<.001
bor or induction)549 (11.0) $6435 (12.1)$ $1035 (19.7)$ $1717 (34.5)$ $18323 (34.4)$ $1510 (28.8)$ $1717 (34.5)$ $1823 (34.4)$ $1510 (28.8)$ $1263 (25.4)$ $15171 (28.5)$ $1290 (24.6)$ $1263 (25.4)$ $13270 (24.9)$ $1290 (24.6)$ $1454 (29.2)$ $13270 (24.9)$ $1418 (27.0)$ $1454 (29.2)$ $13270 (24.9)$ $1418 (27.0)$ $147 (29.2)$ $3329 (75.1)$ $3355 (73.0)$ 1200 $384 (7.7)$ $3930 (75.1)$ $384 (7.7)$ $150 (0.3)$ $0 (0.0)$ 1200 $384 (7.7)$ $150 (0.3)$ 1200 $384 (7.7)$ $150 (0.3)$ 1200 $138 (0.3)$ $0 (0.0)$ 1200 $138 (0.3)$ $0 (0.0)$ 1200 $138 (0.3)$ $100 (2.1)$ 1200 $1232 (23.2)$ $1238 (24.0)$ $127 (120)$ $1233 (23.2)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (23.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120)$ $1238 (20.0)$ $1238 (20.0)$ $127 (120$	Type of labor				<.001	<.001
1717 (34.5) $18323 (34.4)$ $1510 (28.8)$ $1263 (25.4)$ $15171 (28.5)$ $1290 (24.6)$ $1263 (25.4)$ $15171 (28.5)$ $1290 (24.6)$ $1454 (29.2)$ $13270 (24.9)$ $1418 (27.0)$ 7	None (cesarean without labor or induction)	549 (11.0)	6435 (12.1)	1035 (19.7)		
1263 (25.4) 15171 (28.5) 1290 (24.6) 1454 (29.2) 13270 (24.9) 1418 (27.0) 1454 (29.2) 13270 (24.9) 1418 (27.0) 7	Spontaneous	1717 (34.5)	18323 (34.4)	1510 (28.8)		
1454 (29.2) 13270 (24.9) 1418 (27.0) 1454 (29.2) 13270 (24.9) 1418 (27.0) 145 1529 (70.8) 3930 (75.1) $335 (73.0)$ 140 1529 (70.8) 150 (0.3) 0 (0.0) 150 150 (0.3) 0 (0.0) 0 (0.0) 150 150 (1.2) 151 (1.0) 100 (2.1) 150 103 (1.3) 109 (2.1) 109 (2.1) 150 1233 (23.2) 1258 (24.0) 100 147 (3.0) 2247 (4.2) 263 (5.0) <00	Spontaneous, augmented	1263 (25.4)	15171 (28.5)	1290 (24.6)		
\dot{r} 3529 (70.8) 3930 (75.1) 3835 (73.0) sint 384 (7.7) 150 (0.3) 0 (0.0) s 384 (7.7) 150 (0.3) 0 (0.0) s 88 (1.8) 650 (1.2) 51 (1.0) o 0.0 138 (0.3) 109 (2.1) 922 (19.7) 1332 (23.2) 1258 (24.0) 947 (4.2) 2247 (4.2) 263 (5.0) <01	Induced	1454 (29.2)	13270 (24.9)	1418 (27.0)		
3529 (70.8) $3930 (75.1)$ $3835 (73.0)$ sion $384 (7.7)$ $150 (0.3)$ $0 (0.0)$ s $88 (1.8)$ $650 (1.2)$ $51 (1.0)$ s $0 (0.0)$ $138 (0.3)$ $109 (2.1)$ $922 (19.7)$ $1233 (23.2)$ $1258 (24.0)$ $147 (3.0)$ $2247 (4.2)$ $263 (5.0)$ <001	Reason for induction				7	4
tion384 (7.7)150 (0.3)0 (0.0)s88 (1.8)650 (1.2)51 (1.0)0 (0.0)138 (0.3)109 (2.1)922 (19.7)12332 (23.2)1258 (24.0)147 (3.0)2247 (4.2)263 (5.0)	Not induced	3529 (70.8)	39930 (75.1)	3835 (73.0)		
s 88 (1.8) 650 (1.2) 51 (1.0) 0 (0.0) 138 (0.3) 109 (2.1) 982 (19.7) 12332 (23.2) 1258 (24.0) 147 (3.0) 2247 (4.2) 263 (5.0) <.001	Intrauterine growth restriction	384 (7.7)	150~(0.3)	0 (0.0)		
$\begin{array}{ccccccc} 0 & 0.00 & 138 (0.3) & 109 (2.1) \\ \\ 0 & 0.01 & 0.02247 (4.2) & 1258 (24.0) \\ 147 (3.0) & 2247 (4.2) & 263 (5.0) & < 001 \\ \end{array}$	Non-reassuring fetal status	88 (1.8)	650 (1.2)	51 (1.0)		
982 (19.7) 12332 (23.2) 1258 (24.0) 147 (3.0) 2247 (4.2) 263 (5.0) <.001	Macrosomia	0 (0.0)	138 (0.3)	109 (2.1)		
147(3.0) $2247(4.2)$ $263(5.0)$ <001	Other reasons	982 (19.7)	12332 (23.2)	1258 (24.0)		
	Suspected chorioamnionitis	147 (3.0)	2247 (4.2)	263 (5.0)	<.001	.008

	SGA (N=4,983)	AGA (N=53,200)	LGA (n=5,253)	SGA vs. AGA P*	LGA vs. AGA P*
Antibiotics for chorioamnionitis	115 (2.3)	1868 (3.5)	223 (4.3)	<.001	.006
Abruption	8 (0.2)	70 (0.1)	5 (0.1)	.59	.48
Cesarean delivery	1290 (25.9)	13603 (25.6)	2016 (38.4)	.62	<.001
Reason for cesarean				*	<.001
Not delivered via cesarean	3693 (74.1)	39597 (74.4)	3237 (61.6)		
Non-reassuring fetal status	403 (8.1)	2031 (3.8)	174 (3.3)		
Macrosomia	0 (0.0)	128 (0.2)	181 (3.5)		
Other reasons	887 (17.8)	11444 (21.5)	1661 (31.6)		
Received anesthesia of any kind	4486 (90.0)	47846 (89.9)	4835 (92.0)	.84	<.001
Received regional epidural anesthesia	3469 (77.3)	36759 (76.8)	3359 (69.5)	.45	<.001
Received regional spinal anesthesia	1260 (28.1)	13797 (28.8)	1736 (35.9)	.29	<.001
Received general anesthesia	93 (2.1)	452 (0.9)	56 (1.2)	<.001	.15
Gestational age (weeks)	39.3 (38.4-40.0)	39.4 (38.9-40.3)	39.7 (39.1-40.6)	<.001	<.001
Gestational age categories (weeks)				<.001	<.001
37,0-37,6 weeks	589 (11.8)	4124 (7.8)	183 (3.5)		
38,0-38,6 weeks	1079 (21.7)	9679 (18.2)	747 (14.2)		
39,0-39.6 weeks	1889 (37.9)	20109 (37.8)	2109 (40.2)		
40,0-40.6 weeks	1077 (21.6)	13663 (25.7)	1480 (28.2)		
41,0-41.6 weeks	334 (6.7)	5320 (10.0)	677 (12.9)		
42,0-42.6 weeks	15 (0.3)	305 (0.6)	57 (1.1)		
Birthweight (g)	2683 (2515-2822)	3379 (3146-3630)	4189 (4045-4363)	<.001	<.001
Birthweight (g)				+	+
<2500	1136 (22.8)	50 (0.1)	0 (0.0)		
2500-3999	3847 (77.2)	51688 (97.2)	952 (18.1)		
4000	0 (0.00)	1462 (2.8)	4301 (81.9)		

SGA, small for gestational age (birth weight < 10% for gestational age); AGA, appropriate for gestational age (birth weight between 10-89% for gestational age); LGA, large for gestational age (birth weight > 90% for GA); NA, not applicable

 $_{\star}^{*}$ based on the chi-square test for categorical variables or Wilcoxon rank sum test for continuous variables

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		SGA (N=4,983)	()	AGA N=53,200)		LGA (N=5,253)	3)
	u (%)	uRR*(95% CI)	aRR↑ (95% CI)	u (%)	u (%)	uRR*(95% CI)	aRR † (95% CI)
Hypoxic composite neonatal morbidity	55 (1.1)	1.57 (1.18-2.08) [‡]	1.44 (1.07-1.93) <i>§</i>	374 (0.7)	31 (0.6)	0.84 (0.58-1.21)	0.84 (0.58-1.22)
Traumatic composite neonatal morbidity	65 (1.3)	1.33 (1.03-1.72) 🕌	1.28 (0.98-1.67)	523 (1.0)	102 (1.9)	1.98 (1.60-2.44)¶	1.88 (1.51-2.34)¶
Bronchopulmonary dysplasia ${\cal H}$	0 (0.0)			2 (0.0)	1 (0.0)		
Persistent pulmonary hypertension of the newborn ${\cal H}$	11 (0.2)			36 (0.1)	9 (0.2)		
Proven newborn sepsis H	6 (0.1)			44 (0.1)	5 (0.1)		
Necrotizing enterocolitis stage II or III H	0 (0.0)			3 (0.0)	0 (0.0)		
Intraventricular hemorrhage grade (IVH) III or IV H	0 (0.0)			1 (0.0)	0 (0.0)		
Apgar score < 5 at 5 min $H. T$	19 (0.4)			93 (0.2)	6 (0.1)		
Ventilator support within 24 hrs. H T	25 (0.5)			191 (0.4)	16 (0.3)	-	
Seizure H,T	7 (0.1)			39 (0.1)	3 (0.1)		
Cardiopulmonary resuscitation within first 24 hrs. H_{i} T	7 (0.1)			30 (0.1)	2 (0.0)		
Hypoxic ischemic encephalopathy $H_{\rm r}T$	20 (0.4)			92 (0.2)	9 (0.2)		
Death before discharge H, T	3 (0.1)			7 (0.0)	2 (0.0)		
Fracture (skull, depressed skull, clavicle, other) ${\cal T}$	6 (0.1)			135 (0.3)	54 (1.0)		
Intracranial hemorrhage (other than IVH) T	7 (0.1)			70 (0.1)	4 (0.1)		
Brachial plexus injury T	1 (0.0)			24 (0.1)	19 (0.4)		
Facial nerve palsy T	3 (0.1)			5 (0.0)	2 (0.0)		
Data as n (%)							

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SGA, small for gestational age; AGA, appropriate gestational age; LGA, large for gestational age; aRR, adjusted relative risk; CI, confidence interval

H____a component of hypoxic CNM;

* Compared with AGA and unadjusted

 $\dot{ au}$ Compared with AGA and adjusted for insurance status, nulliparity, body mass index, and male fetal sex; number with complete data in the multivariable model is 61905 $^{\ddagger}_{\rm P=.002}$

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^{\$}P=.02 ∥P=.03 ¶P<.001

Table 4

Full multivariable models for hypoxic and traumatic neonatal morbidity and growth

	Hypoxic CN	M	Traumatic C	NM
	aRR*(95% CI)	Р	aRR*(95% CI)	Р
SGA	1.44 (1.07-1.93)	.02	1.28 (0.98-1.67)	.07
LGA	0.84 (0.58-1.22)	.37	1.88 (1.51-2.34)	<.001
Private insurance	0.85 (0.70-1.02)	.08	0.70 (0.60-0.82)	<.001
Nulliparous	2.18 (1.81-2.64)	<.001	1.59 (1.36-1.85)	<.001
Male fetal sex	1.50 (1.24-1.81)	<.001	1.28 (1.10-1.49)	.001
BMI, per unit increase in kg/m ²	1.04 (1.02-1.05)	<.001	1.03 (1.02-1.05)	<.001

SGA, small for gestational age; AGA, appropriate gestational age; LGA, large for gestational age; aRR, adjusted relative risk; CI, confidence interval; BMI, body mass index (at delivery)

adjusted for all variables in the table; number with complete data in the multivariable model is 61905

Table 5

Sensitivity analysis evaluating hypoxic and traumatic neonatal morbidity and growth after excluding women with a diagnosis of intrauterine growth restriction or non-reassuring fetal status at the time of admission

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		SGA (N=4,852)	(3	AGA N=52,739)		LGA (N=5,213)	()
	(%) u	uRR $^{*}(95\% \text{ CI})$ aRR $^{*}(95\% \text{ CI})$	aRR*(95% CI)	u (%)	u (%)	uRR [*] (95% CI) aRR [*] (95% CI)	$aRR^*(95\% CI)$
Hypoxic composite neonatal morbidity	51 (1.1)	51 (1.1) 1.55 (1.15-2.08) \ddagger 1.40 (1.03-1.90) $\$$	$1.40\ (1.03-1.90)$	358 (0.7)	31 (0.6)	31 (0.6) 0.88 (0.61-1.26) 0.89 (0.62-1.29)	0.89 (0.62-1.29)
Traumatic composite neonatal morbidity $62 (1.3)$ 1.33 (1.02-1.73)	62 (1.3)	1.33 (1.02-1.73) //	1.27 (0.97-1.67)	507 (1.0)	102 (2.0)	102 (2.0) 2.04 (1.65-2.52) 1 1.94 (1.56-2.42)	1.94 (1.56-2.42)¶

* Compared with AGA and unadjusted

 $\dot{\tau}$ Compared with AGA and adjusted for insurance status, nulliparity, body mass index, and male fetal sex; number with complete data in the multivariable model is 61290

 $f_{\rm P=.004}$ $f_{\rm P=.03}$ // $f_{\rm P=.03}$

¶P<.001