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Association between Off-Peak Hour Birth and Neonatal Morbidity and Mortality among Very Low Birth Weight Infants

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Abstract

Objective—To assess the independent association between overnight or “off-peak” hour delivery and 3 neonatal morbidities strongly associated with childhood neurocognitive impairment.

Study design—Retrospective population based cohort study of all infants with birth weights of 500–1499 g born without severe congenital anomalies in California or Pennsylvania between 2002 and 2009. Off-peak hour delivery was defined as birth between 12:00 a.m. and 6:59 a.m. The study outcomes were death; bronchopulmonary dysplasia, retinopathy of prematurity, and severe (grade 3 or 4) intraventricular hemorrhage among survivors; the composite of each morbidity or mortality; and the composite of death or 1 or more of the evaluated morbidities.

Results—Of 47 617 evaluated infants, 9317 (19.6%) were born during off-peak hours. The frequencies of all study outcomes were higher among infants born during off-peak compared with peak hours. After adjusting for maternal, infant, and hospital characteristics, off-peak hour delivery was associated with increased odds of severe intraventricular hemorrhage among survivors (OR 1.39, 95% CI 1.23–1.57) and the composite outcomes of death or severe intraventricular hemorrhage (OR 1.16, 95% CI 1.07–1.25) and death or major morbidity (OR 1.08, 95% CI 1.02–1.15). There was no evidence of subgroup effects based on delivery mode, birth hospital neonatal intensive care level or annual very low birth weight infant delivery volume, or weekday vs weekend off-peak hour delivery for any study outcome.

Conclusions—Very low birth weight infants born between midnight and 7:00 a.m. are at increased risk for severe intraventricular hemorrhage and death or major neonatal morbidity.

Approximately 20% of all births in the US occur between midnight and 7 a.m.¹ Several epidemiological studies raised concern that delivery during overnight or “off-peak” hours may increase mortality risk among preterm infants.^{2–6} Recent data, largely from tertiary

academic centers, suggest that this increased risk is due to differences in case-mix or illness severity among infants born during the day compared with overnight.^{7–9} Whether this is also true in a broader, population-based cohort of preterm infants is uncertain. Moreover, there is limited data on the association between off-peak hour delivery and neonatal morbidities that are predictive of childhood neurodevelopmental impairment. Evaluation of these outcomes is essential to assess the true adverse effects association with off-peak hour delivery.

The objectives of the present study were to compare the risks for death, severe intraventricular hemorrhage, bronchopulmonary dysplasia, and retinopathy of prematurity among very low birth weight (VLBW; birth weight <1500 g) infants born during off-peak vs peak hours in California and Pennsylvania. We used hierarchical regression modeling and mediation analysis to quantify the relative importance of maternal, neonatal, and hospital level factors on any observed differences in outcome risk.

Methods

We conducted a retrospective, population-based cohort study of all infants with birth weights between 500 and 1499 g and born without severe congenital anomalies between January 1, 2002, and December 31, 2009 in California and Pennsylvania. Each state's department of health linked infant birth and death certificates using name and date of birth and deidentified the records. Greater than 98% of these records were then matched to maternal and newborn hospital discharge records using previously described methods.^{10–12} More than 80% of the unmatched birth certificates were missing a hospital identifier, suggesting these infants were delivered at home or at a birthing center. The gestational ages and racial/ethnic distributions were similar between the matched and unmatched records. We excluded records with birth weights greater than 5 SDs from the mean birth weight for the recorded gestational age because of potential recording errors in either variable.¹³ Infants born less than 500 g were also excluded to reduce bias secondary to potential variability in resuscitation strategies among infants born at the limits of viability. The institutional review boards at The Children's Hospital of Philadelphia and the departments of health in California and Pennsylvania approved this study.

The study exposure was delivery during “off-peak” hours defined as birth between 12:00 a.m. and 6:59 a.m. “Peak-hour” births were those that occurred at all other times of the day. We a priori selected this 7-hour overnight period because it is similar to the off-peak periods used in several other studies on this topic and because 7:00 a.m. is a common time that overnight physician and nurse staffing shifts conclude.^{2,5,9,14,15} The study outcomes were death; severe (grade 3 or 4) intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), and retinopathy of prematurity (ROP) among infants who survived to discharge; the individual composites of death or severe IVH, BPD, and ROP; and death or major morbidity, which included 1 or more of the evaluated morbidities.

The clinical and sociodemographic data used in this analysis were obtained from infant birth and death certificates and the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis and procedure codes present in the maternal and infant hospital discharge records (Table I; available at www.jpeds.com). The death

outcome includes neonatal deaths that occurred before neonatal intensive care unit (NICU) discharge and in-hospital fetal deaths with a gestational age ≥ 23 weeks gestation or a birth weight ≥ 500 g that met a previous definition of a potentially preventable fetal death.¹¹ We included these fetal deaths to reduce bias against hospitals with high-level obstetrical services capable of rapid cesarean deliveries that resulted in live births that may have otherwise died in utero.^{11,16} Birth hospital NICU level was defined based on the 2004 American Academy of Pediatrics report on levels of neonatal care and was retrospectively applied to deliveries that occurred before 2004 to maintain consistency over the study period.¹⁷

Statistical Analyses

Infant, maternal, and hospital characteristics were summarized with standard descriptive statistics and compared between the infants born during peak and off-peak hours. The proportions of infants born via cesarean and vaginal delivery were calculated for each hour of the day (number of deliveries per hour divided by the total sample size) and reported graphically.

Hourly adjusted delivery rates were also determined to account for maternal and infant factors that may affect the choice of delivery mode. The adjusted rates were calculated using logistic regression and marginal standardization, with delivery mode as the dependent variable and all maternal, infant (excluding gestational age), and birth hospital characteristics listed in Table II as independent variables.¹⁸

We used hierarchical logistic regression to explore the potential association between off-peak hour delivery and the study outcomes. In each model, the outcome of interest was defined as the dependent variable. The first regression model included the year and state of birth only, to account for potential differences across the 2 geographic regions and change in outcome incidence over time. The following prespecified groups of independent covariates were then sequentially added based on the order that they occur during pregnancy: maternal sociodemographic characteristics, chronic comorbidities, and complications of pregnancy (model 2); infant demographic factors present at birth (model 3); and birth hospital characteristics (model 4). This approach to model development permits the mediation analysis described below. Gestational age was not used in the models because of missing data for 6% of the cohort. We used a robust variance estimator for cluster-correlated data in each of the above models to account for possible within-hospital outcome correlation.^{19,20}

We performed subgroup analyses to assess for potential differences in the association between off-peak delivery and the study outcomes based on the following 5 covariates: delivery mode, birth hospital NICU level, birth hospital annual volume of VLBW infant deliveries, and 2 definitions of weekday vs weekend off-peak hour delivery (birth between 12:00 a.m. and 6:59 a.m. on Saturday, Sunday, and Monday and birth between 12:00 a.m. and 6:59 a.m. on Sunday and Monday only). Subgroup effects were assessed by adding an interaction term between the dichotomous off-peak hour delivery variable and the subgroup variable to the full regression model (model 4) described above. To account for multiple comparisons, a *P* value of .0013 was used to identify a statistically significant subgroup effect.²¹

In a secondary analysis, we calculated the risk-aORs for developing the study outcomes based on delivery during each hour of the day. The full regression model (model 4) was used in this analysis. Births between 10:00 a.m. and 10:59 a.m. were used as the reference because more infants were born during this period than any other hour throughout the day.

Finally, we assessed for mediation of the association between off-peak hour delivery and the study outcomes by the evaluated maternal, infant, and hospital level factors. Mediation analysis divides the association between an exposure and an outcome (total effect) into the proportion of the association attributable to the study exposure itself (direct and/or residual effects) and the proportion of the association attributable to mediating factors (indirect effects). (Figure 1; available at www.jpeds.com) In the present analysis, the direct or residual effect indicates the proportion of the association between off-peak hour delivery and the study outcomes not accounted for by the evaluated maternal, infant, and hospital level factors. Observed residual effect may be due to unmeasured mediation by the evaluated factors. It may also result, at least in part, from hospital structural factors (ie, capabilities of hospital professionals, staff, and the overall health care delivery system) that are not captured in our dataset and that differ between peak and off-peak hours. The mediation analysis was performed using the counterfactual framework described by Robins, Greenland, and Pearl and generalized for a logit model by Buis.^{22–24} The mediation percentage for each group of successively added factors was calculated as $([\text{indirect effects}_{\text{successive model}} - \text{indirect effects}_{\text{prior model}}] / \text{total effect})$. The 95% CIs were calculated using nonparametric bootstrap techniques by rerunning the regression models on 500 random samples of 47 617 births drawn with replacement. The CIs that did not include zero were considered statistically significant. All analyses were performed with Stata 13.1 (StataCorp, College Station, Texas).

Results

Of the 47 617 VLBW infants included in the study cohort, 9317 (19.6%) were born during off-peak hours (between 12:00 a.m. and 6:59 a.m.). Mothers who gave birth during off-peak hours were more frequently diagnosed with placental abruption, chorioamnionitis, premature rupture of amniotic membranes, and precipitous labor (Table II). Preeclampsia and oligohydramnios were more common among mothers who delivered during peak hours. The infants born during off-peak hours had modestly lower mean birth weights and gestational ages and were more likely to be male and result from a multiple gestation pregnancy (Table II). Small for gestational age infants were more commonly born during peak than off-peak hours. A higher proportion of off-peak births occurred in teaching hospitals compared with peak hour deliveries (Table II).

The probability of delivering by cesarean but not vaginal birth varied throughout the day (Figure 2). Diagnoses of multiple gestation pregnancy, preeclampsia, umbilical cord prolapse, and fetal distress were associated with higher odds of an operative delivery (Table III; available at www.jpeds.com). In contrast, off-peak hour delivery was one of the strongest negative predictors of birth by cesarean delivery (aOR 0.65, 95% CI 0.61–0.69).

All study outcomes occurred with greater frequency among the infants born during off-peak compared with peak hours (Table II). Table IV shows the results of the hierarchical regression analysis. After adjusting for the year and state of birth (model 1), delivery during off-peak hours was associated with increased odds of all study outcomes. After additional adjustment for the maternal characteristics and complications of pregnancy listed in Table II (model 2), the ORs associated with off-peak hour delivery were attenuated for each outcome and were no longer significantly increased for the outcome of death. Once infant factors were accounted for (model 3), off-peak hour delivery was only associated with increased risk for severe IVH among survivors and the composite outcomes of death or severe IVH and death or major morbidity. Additional adjustment for hospital level factors (model 4) did not affect the results. We did not find evidence of important subgroup differences for any of the evaluated outcomes (interaction term *P* values ranged from 0.07 to 0.96). In the secondary analysis conducted for each hour of the day, delivery between 3:00 a.m. and 3:59 a.m. was associated with the highest risk-adjusted odds of developing severe IVH among survivors (aOR 1.83, 95% CI 1.24–2.72; Figure 3; available at www.jpeds.com). There were minimal differences in the hourly risk-adjusted odds for the other study outcomes.

Figure 4 shows the percentage that the evaluated factors mediated the association between off-peak hour delivery and the study outcomes. Maternal factors mediated the largest proportion for each outcome except for severe IVH among survivors. For the outcome of death, maternal factors were the only statistically significant mediators, explaining 72.5% (95% CI 55.5–100) of the total association. The mediation proportion attributed to infant factors ranged from 8.6% (95% CI 2.7–14.6) for severe IVH among survivors to 27.1% (95% CI 7.1–53.6) for BPD among survivors. The evaluated hospital factors did not significantly mediate the association between off-peak hour delivery and any of the study outcomes after maternal and infant factors were considered. Residual mediation independently associated with off-peak hour delivery was observed for severe IVH among survivors (71.9%, 95% CI 60.8–80.6) and the composites of death or severe IVH (35.8%, 95% CI 22.8–46.8) and death or major morbidity (29.7, 95% CI 14.1–43.0).

Discussion

In this 2 US state population based cohort of over 47 000 VLBW infants, birth during off-peak (between 12:00 a.m. and 6:59 a.m.) compared with peak hours (between 7:00 a.m. and 11:59 p.m.) was associated with higher frequencies of death, severe IVH, BPD, and ROP. After adjustment for 25 clinical, sociodemographic, and hospital level covariates, off-peak hour delivery was associated with a 39% increase in the odds of severe IVH among infants who survived to discharge. For the composite outcomes of death or severe IVH and death or major morbidity (severe IVH, BPD, and/or ROP), off-peak hour delivery was associated with a 16% and 8% increased odds, respectively. After adjusting for differences in maternal and infant characteristics, off-peak hour delivery was no longer associated with increased risk for the other study outcomes. There was no evidence of subgroup effects based on delivery mode, birth hospital neonatal intensive care unit level or annual VLBW infant delivery volume, or weekday vs weekend off-peak hour delivery for any of the study outcomes.

The independent association between off-peak hour delivery and severe IVH but not the other evaluated adverse outcomes may reflect the degree that injury around the time of birth contributes to the pathophysiology of this morbidity. IVH in preterm infants typically originates in the periventricular germinal matrix during the first 24–48 hours of life when this highly vascularized region is particularly sensitive to disturbances in cerebral blood flow because of hypoxia, hypercarbia, and acidosis.²⁵ Infants born overnight compared with during the day more commonly have an umbilical cord pH <7.1 and are at increased risk for perinatal asphyxia even after adjusting for multiple potential confounders.^{26,27}

Prior studies proposed several clinical and structural factors that may contribute to the higher rates of adverse outcomes among infants born overnight compared with during the daytime.^{2–5} One such factor is differences in case mix or illness severity occurring between day and night deliveries. In our cohort, infants born during off-peak compared with peak hours had modestly lower mean birth weights and gestational ages. They were also more likely to be male and result from a multiple gestation pregnancy. The mothers of infants born overnight were more commonly diagnosed with chorioamnionitis, placental abruption, premature rupture of amniotic membranes, and precipitous labor. After adjustment for these and other maternal and infant characteristics, off-peak hour delivery was not associated with increased risk for death, BPD, or ROP but remained associated with increased risk for severe IVH. When considered in the temporal order that they occur during pregnancy, maternal medical and sociodemographic factors mediated the largest proportion of the association between off-peak hour delivery and each of the study outcomes except for severe IVH among survivors. These findings suggest that differences in case-mix explained most of the increased morbidity risk observed among infants born during off-peak hours. The remaining independent association between off-peak hour delivery and severe IVH risk may be due to residual mediation or confounding from unmeasured clinical characteristics or other factors that are unrelated to illness severity.

Two structural factors that may contribute to the higher IVH risk among infants born overnight are lower staffing levels or less availability of in-house physicians during off peak hours and greater nighttime fatigue leading to lower provider mental alertness. A recent survey of California childbirth hospitals found that only 64% were capable of performing a cesarean delivery within 30 minutes at all times of the day, and only 56% had a pediatrician, family practitioner, or neonatologist available in-house to attend nighttime deliveries.²⁸ Unfortunately, our dataset does not include information on hospital staffing levels. As surrogate measures, we included categorical variables for birth hospital NICU level, annual volume of VLBW infant deliveries, and hospital teaching status in our risk-adjustment models. Birth hospital NICU level and annual volume of VLBW infant deliveries predict neonatal morbidity and mortality risk and NICU level correlates modestly well with 24-hour availability of high-risk obstetrical and neonatal care.^{11,28,29} We found that after accounting for maternal and infant covariates, further adjustment for these hospital factors did not change the ORs associated with off-peak hour delivery for any of the study outcomes. However, we acknowledge that these hospital covariates may not completely capture variation in overnight staffing and that residual hospital level confounding may exist. For example, 2 studies from tertiary perinatal centers with well-established 24-hour care models

reported that preterm infants born overnight were not at increased risk for mortality or morbidity, including severe IVH.^{7,9}

Physicians and nurses perform psychomotor activities less proficiently and are more prone to commit medical errors at night than during the day.^{30–33} Physician-patient contact may also decrease at night, even on wards where providers are present 24 hours a day. In 2 older studies, Tyson et al^{34,35} showed that physician bedside care in the NICU declined throughout the night and that this was associated with less management of the mechanical ventilator in intubated babies and higher nighttime rates of neonatal acidosis and mortality. Our finding that the hourly risk-aORs for severe IVH increased among VLBW infants born between 12:00 a.m. and 4:00 a.m. raises concern that physician fatigue and/or inadequate attention to a nonreassuring fetus or neonate may independently contribute to the risk for this morbidity. The circadian variation in cesarean but not vaginal delivery rates also demonstrates significant manipulation of birth timing. It is possible that nighttime delay of medically indicated cesarean deliveries prolongs fetal exposure to a poor intra-uterine environment and increases risk for severe IVH.

We acknowledge several study limitations. Maternal and infant comorbidities and study outcomes were classified using ICD-9-CM codes. Several studies have evaluated the reliability of various maternal and infant ICD-9-CM diagnosis and procedure codes.^{36–42} In general, these reported high specificity and variable sensitivity, which may result in underestimation of morbidity rates.^{36–42} The use of ICD-9-CM codes also prevents adjustment for disease severity. Unmeasured differences because of illness acuity may be present. There are no ICD-9-CM codes for important medications such as antenatal corticosteroids or surfactant. Although there are codes for some interventions such as mechanical ventilation, we do not have data on the timing of therapy initiation. Finally, we were only able to risk stratify based on the factors available in our dataset.

In conclusion, this population-based study assessed the association between off-peak hour delivery of VLBW infants and neonatal morbidities that are strongly predictive childhood neurodevelopmental delay. Overnight delivery was associated with increased risk for death and severe IVH, BPD, and ROP among survivors. After risk adjusting for 25 different maternal, infant, and hospital level factors using a 2 US state administrative database, off-peak hour birth remained associated with increased risk for severe IVH. If these findings are confirmed in future population based cohorts, further research should explore strategies to decrease the risk for neurologic injury among VLBW infants born at night.

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Glossary

BPD	Bronchopulmonary dysplasia
ICD-9-CM	<i>International Classification of Diseases, Ninth Revision, Clinical Modification</i>

IVH	Intraventricular hemorrhage
NICU	Neonatal intensive care unit
ROP	Retinopathy of prematurity
VLBW	Very low birth weight

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Figure 1.
Mediation analysis conceptual framework.

Figure 2.

Cesarean and vaginal delivery rates. Hourly delivery rates are shown as a proportion of the total number of deliveries over the 24-hour day. Off-peak hours are defined as births occurring between 12:00 a.m. and 6:59 a.m. Peak hours are births occurring at all other times of the day. Delivery rates adjusted for the maternal, infant (excluding gestational age), and birth hospital characteristics listed in Table II.

Figure 3.

Risk-aORs for the individual (*top panels*) and composite (*bottom panels*) study outcomes by hour of birth. Off-peak hours are defined as births occurring between 12:00 a.m. and 6:59 a.m. Peak hours are births occurring at all other times of the day. Outcome probabilities and ORs with 95% CIs adjusted for the maternal, infant (excluding gestational age), and birth hospital characteristics listed in Table II.

Figure 4.

Outcome mediation proportions. Mediation proportion and 95% CI are shown for the maternal and infant (excluding gestational age) factors listed in Table II. Noncomposite morbidity outcomes represent disease among survivors. The mediation proportions attributable to hospital level factors were not statistically significant for any of the study outcomes.

Table 1

Diagnoses and corresponding ICD-9-CM codes

Diagnoses	ICD-9-CM codes
Study outcomes	
BPD	770.7
IVH (grade 3 or 4)	772.13, 772.14
ROP	362.2x
Infant characteristics	
Small for gestational age	656.5, 760.4, 764.0, 764.1
Multiple gestation	651.x
Maternal chronic comorbidities	
Chronic hypertension	642.0x, 642.1x, 642.2x
Diabetes mellitus	250, 250.x, 357.2, 360.2, 362.0x, 366.41, 648.0x
Pregnancy complications	
Gestational diabetes	648.8x
Preeclampsia/gestational hypertension	642.3x, 642.4x, 642.5x, 642.7x
Placental abruption	641.2
Placenta previa	641.0, 641.1
Chorioamnionitis	646.6x, 658.4x, 659.2x, 659.3x
Oligohydramnios	658.0, 658.0x
PROM	658.1x, 658.2x
Induction of labor	73.4, 659.0x, 659.1x
Precipitous labor	661.3x
Eclampsia	642.6
Umbilical cord prolapse	663.0, 762.4,
Fetal distress	656.3x, 656.8x, 659.7x
Cesarean delivery	74.x, 74.9x
Excluded congenital anomalies	
Congenital heart disease	424.0, 424.1, 425.1, 425.3, 745.1x, 745.2, 745.3, 745.6x, 746.x, 747.1, 747.2x, 747.4x
Chromosomal abnormality	758.3, 758.5, 758.89, 758.9, 759.4, 759.7, 759.89, 759.9
CNS malformation	741.0x, 741.9x, 742.0-4, 742.59, 742.8, 742.9
Dermatologic malformation	757.1
Gastrointestinal malformation	560.2, 750.3-9, 751.1x, 756.7, 756.79, 777.1
Genitourinary malformation	753.0, 753.1x, 753.2x, 753.3-9, 756.71
Pulmonary malformation	519.4, 533.3, 748.3, 748.4, 748.6x, 748.8, 748.9, 750.6, 756.6
Skeletal malformation	756.6x
Other malformations	759.6, 776.5, 778.0

CNS, central nervous system; *PROM*, premature rupture of membranes; x, any number.

Table II

Infant, maternal, and hospital characteristics and study outcomes

Characteristics/outcomes	Off-peak hour delivery (n = 9317)	Peak hour delivery (n = 38 300)	P value
Infant characteristics			
Birth weight, g—mean (SD)	1057 (293)	1074 (288)	<.001
Gestational age, wk—mean (SD)	28.5 (3.9)	29.1 (4.0)	<.001
Male, n (%)	4899 (52.6)	19 330 (50.5)	.001
SGA, n (%)	2420 (26.0)	12 161 (31.8)	<.001
Multiple gestation, n (%)	1954 (25.2)	9635 (21.0)	<.001
Maternal characteristics			
Age, y—mean (SD)	28.2 (6.9)	28.6 (6.9)	<.001
Race, n (%)			<.001
White	3282 (35.2)	14 304 (37.4)	
Black	1568 (16.8)	5924 (15.5)	
Hispanic	3204 (34.4)	13 233 (34.5)	
Asian/other	1263 (13.6)	4839 (12.6)	
Insurance status, n (%)			.004
Fee for service	554 (6.0)	2082 (5.4)	
HMO	3953 (42.4)	17 054 (44.5)	
Public	4484 (48.1)	17 932 (46.8)	
Other	297 (3.2)	1129 (3.0)	
Uninsured	29 (0.3)	103 (0.3)	
Chronic comorbidities			
Chronic hypertension, n (%)	214 (2.3)	1080 (2.8)	.005
Diabetes mellitus, n (%)	158 (1.7)	814 (2.1)	.009
Pregnancy complications			
Gestational diabetes, n (%)	584 (6.3)	2467 (6.4)	.54
Preeclampsia/gestational hypertension, n (%)	1577 (16.9)	9270 (24.2)	<.001
Placental abruption, n (%)	1379 (14.8)	4859 (12.7)	<.001
Placenta previa, n (%)	305 (3.3)	1188 (3.1)	.39
Chorioamnionitis, n (%)	1740 (18.7)	6390 (16.7)	<.001
Oligohydramnios, n (%)	409 (4.4)	2767 (7.2)	<.001
PROM, n (%)	2958 (31.8)	9649 (25.2)	<.001
Induction of labor, n (%)	435 (4.7)	1615 (4.2)	.05
Precipitous labor, n (%)	330 (3.5)	787 (2.1)	<.001
Eclampsia, n (%)	68 (0.7)	328 (0.8)	.23
Umbilical cord prolapse	146 (1.6)	636 (1.7)	.52
Fetal distress, n (%)	2369 (25.4)	10 085 (26.3)	.08
Cesarean delivery, n (%)	5507 (59.1)	27 490 (71.8)	<.001
Birth hospital characteristics			
NICU level, n (%)			.03
I	783 (8.4)	2862 (7.5)	

Characteristics/outcomes	Off-peak hour delivery (n = 9317)	Peak hour delivery (n = 38 300)	P value
II A/B	495 (5.3)	2051 (5.4)	
III A	1167 (12.5)	4847 (12.7)	
III B/C	6872 (73.8)	28 540 (74.5)	
Annual VLBW infant delivery volume, n (%)			.01
10	500 (5.4)	1832 (4.8)	
11–25	957 (10.3)	3941 (10.3)	
26–50	1793 (19.2)	7839 (20.5)	
>50	6067 (65.1)	24 688 (64.5)	
Teaching hospital, n (%)	2925 (31.4)	10 677 (27.9)	<.001
Study outcomes			
Death, n (%)	1270 (13.6)	4291 (11.2)	<.001
Severe IVH, n (%) [*]	390 (4.9)	1084 (3.2)	<.001
BPD, n (%) [*]	1562 (19.4)	5941 (17.5)	<.001
ROP, n (%) [*]	1942 (24.1)	7704 (22.7)	.005
Death or severe IVH, n (%)	1660 (17.8)	5375 (14.0)	<.001
Death or BPD, n (%)	2832 (30.4)	10 232 (26.7)	<.001
Death or ROP, n (%)	3212 (34.5)	11 995 (31.3)	<.001
Death or major morbidity, n (%) [†]	4194 (45.0)	15 665 (40.9)	<.001

HMO, health maintenance organization; PROM, premature rupture of amniotic membranes; SGA, small for gestational age.

^{*} This outcome was determined for 42 056 infants who survived to discharge (8047 born during off peak- hours and 34 009 born during peak hours).

[†] Major morbidity includes severe IVH, BPD, or ROP.

Table III

Characteristics by delivery mode and aORs for cesarean birth

Characteristics	Cesarean birth (n = 32 997)	Vaginal birth (n = 14 620)	aOR* (95% CI) for cesarean birth
Off-peak hour delivery	5507 (16.7)	3810 (26.1)	0.65 (0.61–0.69)
Infant characteristics			
Birth weight, g—mean (SD)	1086 (275)	1037 (315)	1.02 (1.01–1.03) [†]
Male, n (%)	16 531 (50.1)	6856 (46.9)	0.97 (0.93–1.02)
SGA, n (%)	11 397 (34.5)	3184 (21.8)	1.28 (1.20–1.36)
Multiple gestation, n (%)	9994 (30.3)	1595 (10.9)	5.75 (5.15–6.42)
Maternal characteristics			
Age, y—mean (SD)	29.2 (6.8)	27.0 (6.8)	1.03 (1.02–1.04)
Race, n (%)			
White	12 722 (38.6)	4864 (33.3)	Reference
Black	4843 (14.7)	2649 (18.1)	0.88 (0.81–0.95)
Hispanic	11 205 (34.0)	5232 (35.8)	1.00 (0.93–1.07)
Asian/other	4227 (12.8)	1875 (12.8)	0.87 (0.80–0.94)
Insurance status, n (%)			
Fee for service	1921 (5.8)	715 (4.9)	Reference
HMO	15 323 (46.4)	5684 (38.9)	0.93 (0.81–1.06)
Public	14 753 (44.7)	7663 (52.4)	0.88 (0.77–1.01)
Other	926 (2.81)	500 (3.4)	0.88 (0.72–1.08)
Uninsured	74 (0.2)	58 (0.4)	0.51 (0.80–0.94)
Chronic comorbidities			
Chronic hypertension, n (%)	1060 (3.2)	234 (1.6)	2.25 (1.90–2.66)
Diabetes mellitus, n (%)	760 (2.3)	212 (1.5)	1.42 (1.18–1.72)
Pregnancy complications			
Gestational diabetes, n (%)	2364 (7.2)	687 (4.7)	1.20 (1.07–1.34)
Gestational hypertension, n (%)	9898 (30.0)	949 (6.5)	11.6 (10.3–13.0)
Placental abruption, n (%)	4634 (14.0)	1604 (11.0)	1.69 (1.00–2.86)
Placenta previa, n (%)	1337 (4.1)	156 (1.1)	5.37 (3.27–8.82)
Chorioamnionitis, n (%)	4993 (15.1)	3137 (21.5)	1.03 (0.96–1.11)
Oligohydramnios, n (%)	2765 (8.4)	411 (2.8)	2.54 (2.23–2.88)
PROM, n (%)	7858 (23.8)	4749 (32.5)	0.98 (0.92–1.04)
Induction of labor, n (%)	935 (2.8)	1115 (7.6)	0.10 (0.09–0.12)
Precipitous labor, n (%)	100 (0.3)	1017 (7.0)	0.04 (0.03–0.06)
Eclampsia, n (%)	376 (1.1)	20 (0.1)	19.6 (11.1–34.6)
Umbilical cord prolapse	665 (2.0)	117 (0.80)	4.83 (3.69–6.32)
Fetal distress, n (%)	10 527 (31.9)	1927 (13.2)	3.77 (3.40–4.19)
Birth hospital characteristics			
NICU level, n (%)			
I	2194 (6.7)	1451 (9.9)	Reference

Characteristics	Cesarean birth (n = 32 997)	Vaginal birth (n = 14 620)	aOR* (95% CI) for cesarean birth
II A/B	1721 (5.2)	825 (5.6)	1.05 (0.87–1.26)
III A	4098 (12.4)	1916 (13.1)	1.03 (0.85–1.24)
III B/C	24 984 (75.7)	10 428 (71.3)	1.12 (0.99–1.28)
Annual VLBW infant delivery volume—mean (SD)	83.3 (59.6)	81.8 (62.3)	0.99 (0.98–1.00) [‡]
Teaching hospital, n (%)	9211 (27.9)	4391 (30.0)	0.85 (0.75–0.96)

HMO, health maintenance organization; SGA, small for gestational age.

* aORs calculated from a logistic regression model inclusive of all variables present in the Table.

[‡] OR calculated for 100-g increments.

[‡] OR calculated for 10-infant increments.

Table IVHierarchical regression analysis, OR (95% CI)^{*}

Outcomes	Model 1: birth year and state	Model 2: model 1 + maternal factors	Model 3: model 2 + infant factors	Model 4: model 3 + hospital factors
Individual				
Death	1.26 (1.17–1.37)	1.07 (0.99–1.16)	1.05 (0.95–1.15)	1.05 (0.96–1.15)
Severe IVH [†]	1.55 (1.37–1.75)	1.43 (1.26–1.62)	1.39 (1.24–1.57)	1.39 (1.23–1.57)
BPD [†]	1.14 (1.06–1.22)	1.09 (1.01–1.17)	1.06 (0.98–1.15)	1.06 (0.98–1.14)
ROP [†]	1.11 (1.04–1.18)	1.07 (1.01–1.14)	1.05 (0.99–1.12)	1.06 (0.99–1.14)
Composite				
Death or severe IVH	1.34 (1.25–1.44)	1.16 (1.08–1.25)	1.16 (1.07–1.25)	1.16 (1.07–1.25)
Death or BPD	1.20 (1.15–1.26)	1.09 (1.04–1.14)	1.06 (0.99–1.13)	1.06 (1.00–1.12)
Death or ROP	1.18 (1.12–1.24)	1.08 (1.03–1.14)	1.06 (0.99–1.13)	1.07 (1.00–1.14)
Death or major morbidity	1.20 (1.14–1.25)	1.11 (1.05–1.16)	1.08 (1.02–1.15)	1.08 (1.02–1.15)

C-statistics for model 4: death 0.88, severe IVH 0.78, BPD 0.81, ROP 0.79, death or severe IVH 0.86, death or BPD 0.85, death or ROP 0.83, death or major morbidity 0.83.

^{*} Models sequentially adjusted for the maternal, infant (excluding gestational age), and hospital factors listed in Table II.

[†] Outcome determined for 42 056 infants who survived to discharge (8047 born during off peak-hours and 34 009 born during peak hours).