Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Phibbs CS, Baker LC, Caughey AB, Danielsen B, Schmitt SK, Phibbs RH. Level and volume of neonatal intensive care and mortality in very-low-birth-weight infants. N Engl J Med 2007;356:2165-75.

WEB-ONLY SUPPLEMENTARY INFORMATION

This appendix contains many technical details that could not be included in the main paper due to space constraints. It includes sections on:

List of Appendix Tables

A-1. Classifying NICU Levels of Care and Growth of NICUs

We used the California Office of Statewide Health Planning and Development (OSHPD) Financial Disclosure Data, which all hospitals are legally required to report on an annual basis. These data include if a hospital has a neonatal intensive care unit (NICU), the number of NICU beds, and the number of NICU patient days. The OSHPD financial data were used to identify which years each hospital was operating a NICU. As an additional validation, we cross-checked this information with similar data elements from the American Hospital Association (AHA) Annual Survey of Hospitals.

We classified all hospitals using the levels of care from the original draft of the new NICU classification system developed by the AAP Committee on the Fetus and Newborn,(1) as follows:

- Level 1: Community hospital with no NICU. Well baby nursery.
- Level 2: Classic intermediate NICU, cares for mildly ill infants, but does not provide any sustained mechanical assisted ventilation.
- Level 3A: Provides assisted mechanical ventilation, with restrictions on type or duration

of mechanical ventilation, or on the types of patients that can receive mechanical ventilation (e.g. does not provide mechanical ventilation to infants with birth weight <1000g).

- Level 3B: No restrictions on the provision of assisted mechanical ventilation, but does not provide major surgery. These units may, but are not required to, provide advanced forms of ventilation (e.g., high-frequency ventilation).
- Level 3C: May provide at least some of the more advanced forms of mechanical ventilation, and provides major neonatal surgery (e.g., emphalocele repair, bowel resection, ventriculoperitoneal shunt), but no open-heart surgery or extracorporeal membrane oxygenation (ECMO).
- Level 3D: Provides cardiac surgery to repair serious congenital heart anomalies that require cardio-pulmonary bypass and/or ECMO.

Since the differences in level of care are largely defined by the provision of assisted mechanical ventilation and surgery, we used the information in the discharge data to classify the levels of care for each hospital over time. The ICD-9-CM procedure codes in the discharge data identified when any given hospital provided major neonatal surgery. Similar use of the ICD-9-CM procedure codes for cardiac surgery and ECMO distinguished the 3Ds from the 3Cs.

The 3As and 3Bs were separated from lower-level hospitals by the ICD-9-CM procedure codes for assisted mechanical ventilation. There are only three ICD-9-CM procedure codes for mechanical ventilation: < 96 hours, > 96 hours, and duration unknown. A hospital that only provided shorter duration ventilation was classified as a 3A. Among hospitals that provided longer duration ventilation, we looked at the patterns over time of the number of infants receiving mechanical ventilation, by duration, and BW categories, to classify NICUs as 3A or 3B.

Senior neonatologists in each region of the state reviewed these classifications to check their accuracy and to confirm the classifications for the few hospitals where the classification from the discharge data was not definitive, especially for distinction between levels 3A and 3B.

Table A-1 shows the growth in the number of NICUs from 1983 to 2000 and the number of hospitals at each level with two measures of low volume in 2000: treated fewer than 51 very low birth weight (birth weight < 1500 g) (VLBW) infants, and an average NICU census (all patients) < 15. It also shows the number of births and the VLBW rate. The number of births increased from 1983 to 1991, but then declined, and was relatively constant for the last half of the 1990s. The VLBW rate was fairly constant over time; the number of VLBW births (not shown) was essentially unchanged from 1991 to 2000. There was an expansion of NICUs over time in California, with most of the growth occurring at levels 3A and 3B. Almost all of the lower-level NICUs were smaller units. None of the 12 NICUs that upgraded to 3C (provide pediatric surgery) between 1991 and 2000 were high-volume NICUs. There were a few (6 with average census > 15, and 9 treated > 50 VLBW in 2000) 3B hospitals that functioned as large perinatal centers, but did not provide any neonatal surgery.

A-2. Identifying In-Hospital Fetal Deaths

The obstetrician author (ABC) developed the criteria for identifying in-hospital fetal deaths. Four

categories of fetal death type were created on the basis of maternal diagnosis codes, procedure codes and pregnancy-related complications, or conditions coded on the fetal death certificate. Table A-3 lists the ICD-9-CM diagnosis and procedure codes, and complications associated with each fetal death category.

A hierarchical prioritization approach of categorizing each fetal death as in-hospital, out-of-hospital, or undetermined was applied in each case as follows: Any coding of a category 1 item characterized the fetal death as out-of-hospital. If no category 1 item was coded and a category 3 item was identified, then the fetal death was characterized as in-hospital. If no category 1, 2, or 3 items were coded and a category 4 item was coded, then the fetal death was characterized as in-hospital.

A-3. Definitions of the Congenital Anomalies Excluded from the Main Analysis

The overall strategy for characterizing the risk of congenital anomalies was to group diagnoses that represented the same or similar organ systems that had similar mortality risk. In addition to creating groups of clinically similar problems, these groupings were limited to those anomalies that present elevated mortality risks to neonates. After a thorough analysis of diagnosis codes and conditions related to neonatal mortality, eight major diagnostic risk groups were defined. Subcategories within each risk group were also defined. The eight major diagnostic risk groups included (1) Gastrointestinal, (2) Genitourinary, (3) Central Nervous System, (4) Pulmonary, (5) Cardiovascular, (6), Skeletal, (7) Chromosomal Syndromes, and (8) Other Anomalies. Clinical judgment was used in the creation of these anomaly groups. One of the investigators (RHP) consulted extensively with relevant medical and surgical sub-specialists experienced in treating the various types of anomalies. Specific anomalies that had high correlations with mortality were not included in the groups if clinical judgment indicated that this was just correlation among anomalies, and that the clinical risk was due to other factors. For example, among cardiac anomalies, ventricular septal defect (ICD-9-CM code 745.4) and atrial septal defect (ICD-9-CM code 745.5) were not considered risk factors as the mortality risk associated with these anomalies is almost always due to their co-occurrence with other cardiac defects. Table A-2 lists the major diagnostic risk groups and subcategories along with the ICD-9-CM diagnosis codes used to classify an infant as belonging to a particular group. In addition to utilizing diagnosis codes to classify infants, a hierarchical system of severity was applied to each risk category so that only the condition with the highest mortality risk was coded. This was done to avoid "double coding" related conditions or mutually exclusive conditions that would not likely occur together.

We also created a set of ICD-9-CM codes to identify diagnoses that were incompatible with life, and excluded these cases from all analyses:

- Anencephaly, ICD-9-CM codes 740.0, 740.1, 740.2, 741.19
- Polycystic kidney, ICD-9-CM code 753.13
- Trisomy 13 (Patau's syndrome), ICD-9-CM code 758.1
- Trisomy 18 (Edwards' syndrome), ICD-9-CM code 758.2

A-4. Details of the Statistical Model

Table A-4 shows the ICD-9-CM codes that were used to define the control variables in the model that were derived from information included in the hospital discharge abstracts. For variables not based on ICD-9-CM codes, the table just notes if the data source was birth certificates or

discharge records. Maternal age did not have any measurable independent effect on mortality in the model. The Kotelchuck index was used to calculate adequacy of prenatal care, but the measures of prenatal care use were not statistically significant.(2,3)

The clinical risk variables were limited to factors that were present at birth, or that could be inferred to be present at birth. Clinical factors that arise after birth were only included in the risk model if they were not potentially associated with the quality of care. For example, better infection control practices will reduce the risk of hospital-acquired infections. Including control variables for these types of problems (e.g., infections) would bias the results if quality of care was associated with hospital characteristics, such as patient volume.

In addition to the variables included in the model, we considered several other variables as potential confounders for case-mix or maternal demographics. Table A-4 also provides a complete list of the other variables that were considered for inclusion in the risk model but were rejected at the model testing phase. We excluded the diagnosis of Respiratory Distress Syndrome (RDS, ICD-9-CM code 769) from the model because over 50 percent of the VLBW infants who died did so on the first day of life (many of them in the first few hours of life). An examination of the death certificates showed that the cause of death in these infants was predominately coded as extreme prematurity or a similar cause; a large majority did not have a coded diagnosis of RDS. Thus, if RDS is included in risk models, the odds ratio suggests a protective effect.

A-5. Results of the Full Regression Model

Table A-5 shows the complete results (odds ratios and 95 percent confidence intervals for each parameter estimate) for the regression model reported in Table 3 of the main manuscript. In results not shown, the parameter estimates for the control variables were stable over our sensitivity analyses.

A-6. Sensitivity Analyses

To facilitate comparison with the resulted reported in the manuscript, the first column of results in Table A-6, labeled "Model 1," repeats the results reported in Table 3. With the exception of when the model was estimated on subsets of low weight infants, the effect of NICU level/volume was similar across all of the models. Model 2 shows how the estimates changed when congenital anomalies with significant mortality risk were included (still excluding the small number of "always lethal" congenital anomalies). Model 3 excluded the anomalies as well as the in-hospital fetal deaths. Models 4 and 5 show the results when the data were restricted to infants with a birth weight between 500 and 999g (Model 4) and between 1000 and 1499g (Model 5). Model 6 adjusted for delivery volume, based on the distribution of delivery volumes (in round numbers) for California hospitals (1-499, 500-999, 1000-1499, 1500-1999, 2000-2999, 300-3999, with 4000 or more as the reference category). Model 7 excluded infants with a gestational age < 24 weeks, and Model 9 includes infants with a birth weight between 400 and 499 g. Model 8 shows how the results changed when the model was modified to include a control for whether infants born at lower levels of care were transferred to a hospital with a higher level NICU. The parameter estimate for being transferred was 0.39 and statistically significant, which was expected, given that an infant must survive the high-risk resuscitation period when many VLBW infants expire. Because of this selection effect, one must be cautious in interpreting the results of this model.

A-7. Details on the Projection of Potentially Excess Mortality

The main model assumptions were:

- The increased regionalization was restricted to geographic areas with at least 100 VLBW deliveries in 2000.
- All deliveries that occurred in hospitals more than 40 km (25 miles) from a large tertiary center were excluded.
- The estimate of projected lives that potentially could be saved was based on the annual average number of deaths over the entire 10-year period, 1,080 deaths.
- Within 40 km (25 miles) of a large tertiary center, we assumed that 90 percent of all VLBW deliveries that currently occur in other hospitals could be shifted to the large tertiary centers. We chose 90 percent based on the highest documented level of regionalization that we could identify. In Western Australia from 1996 through 2000 between 90 and 94 percent of the deliveries at less than 32 weeks gestation occurred in one of the two large tertiary facilities (source, unpublished data, Western Australian Midwives' Notification System, Department of Health, Western Australia). If births to Aboriginals, many of which reside in very remote areas, were excluded, these percentages increased to 91 to 97 percent.
- There are geographically distinct areas of the state that do not currently have a large tertiary center, but do have more than 100 VLBW deliveries. We assumed that VLBW deliveries in these areas could be concentrated at a single hospital. For example, in 2000 there were more than 100 VLBW deliveries in a medium sized city in the Central Valley, with virtually all of them occurring at the 4 hospitals with NICUs, all of which were within 9.6 km (6 miles) of each other. For our projection, we assumed that 90 percent of the VLBW deliveries from the other hospitals could be shifted to the hospital with the highest level of care. Then, in our access calculations, we considered this designated hospital as a large tertiary center, and assumed the 90 percent of the VLBW deliveries from other hospitals within 40 km (25 miles) could be shifted. Further, we applied the 90 percent assumption to the "designated" hospital.

These assumptions resulted in 8 percent of the VLBW deliveries being excluded. Most of the excluded infants were from a few moderate-sized urban areas (Palmdale/Lancaster, Monterey/Salinas, Victorville/Apple Valley, Santa Barbara, San Luis Obispo, Santa Rosa, and Fairfield). Since the overall mortality was above 10 percent, we used the method of Zhang and Yu to convert the odds ratios to relative risks (RR).(4) We took 90 percent of the number of VLBW deliveries at each level of care identified as candidates for regionalization and applied the risk ratios to them. Table A-7 shows these results.

While it is not strictly possible to calculate a confidence interval for the estimated change in mortality with regionalizing NICU care, to provide an idea of the range we recalculated our estimate using the lower and upper limits of the 95 percent confidence intervals for the parameter estimates reported in Table 3. This calculation yielded a range of 10.3 to 32.0 percent. An Excel spreadsheet that includes the formula for these calculations is available from the first author upon request.

Table A-1. Number of Births, VLBW Rate, and Growth in the Number of NICUs in California, 1983, 1991, and 2000.

	Births*	**VLBW%***	**Level 2**	**Level 3A**	**Level 3B**	**Level 3C**	**Level 3D**	**All Levels**
1983	437,843	1.2%	59	4	14	18	14	109
1991	607,2019	1.0%	62	19	40	20	15	156
2000	531,285	1.1%	49	27	46	31	15	167
2000 treated < 51 VLBW			47	24	37	11	0	119
2000 census<15			49	25	40	13	0	130

Levels were empirically determined by the authors from a modified version of the American Academy of Pediatrics definitions(1): Level 2: intermediate NICU, no mechanical ventilation; Level 3A: mechanical ventilation with restrictions (e.g., only BW > 1000 g); Level 3B: no restrictions on mechanical ventilation, no major surgery; Level 3C: major neonatal surgery, no cardiac surgery or extra-corporeal membrane oxygenation (ECMO); Level 3D: cardiac surgery and/or ECMO.

* Data on the number of births and VLBW rate are from the California Center for Health Statistics, www.dhs.ca.gov/hisp/chs.

Table A-2. Diagnosis, Procedure, and Complications Codes Associated with Fetal Death Categorization.

	Type of Data	Specific Codes
Category I	**ICD-9-CM diagnosis codes**	646.01, papyraceous fetus 651.31, 651.33, twin pregnancy with fetal loss 651.41, triple pregnancy with fetal loss 651.61, other multiple pregnancy with fetal loss 655.71, decreased fetal movements 656.43, intrauterine death 663.20, cord entanglement w/ compression 663.31, cord entanglement w/o compression 665.01, rupture of uterus before labor
	ICD-9-CM procedure codes	69.93, insertion of laminaria 74.91, hysterotomy to terminate pregnancy
Category II	**ICD-9-CM diagnosis codes**	656.40, 656.41, intrauterine death
Category III	**ICD-9-CM diagnosis codes**	656.31, fetal distress 660.41, shoulder systocia 662.31, delayed delivery of second twin 663.51, vasa previa 669.71, cesarean delivery w/o indication
	ICD-9-CM procedure codes	74.0, classical cesarean section 74.1, low cervical cesarean section 74.4, other cesarean section 74.99, unspecified cesarean section 75.2, intrauterine transfusion 75.32, fetal EKG (scalp) 75.33, fetal blood sampling and biopsy 75.35, other diagnostic procedures on fatus and amnion
	Death certificate complications/conditions	Amniocentesis Tocolysis Fetal distress Unsuccessful attempt of VBAC Birth injury
Category IV	**ICD-9-CM diagnosis codes**	656.81, other specified fetal and placental problems 663.01, prolapse of cord 663.21, cord entanglement w/ compression

		665.11, rapture of uterus during labor
	ICD-9-CM procedure codes	68.0, hysterotomy 75.34, fetal monitoring not otherwise specified
	Death certificate complications/conditions	Electronic fetal monitoring Cord prolapse

No differentiation made for 5th digits of ICD-9-CM diagnoses codes.

Table A-3. Congenital Anomaly Diagnostic Risk Groups and Their Frequency in California for 1998-2000.

Diagnostic Risk Group	ICD-9-CM Diagnosis Codes	N (1998-2000) and (% of All Coded Risks)
Gastrointestinal		
Abdominal wall defect	756.70, 756.79	986 (0.054)
Tracheoesophageal fistula	750.3, 750.4	365 (0.020)
Small bowel or upper GI anomalies		
(1) Anomalies NOS including pyloric stenosis	750.5, 750.7, 750.8, 750.9, 751.1, 751.5, 751.8, 751.9	745 (0.040)
(2)	751.5	903 (0.049)
(3) Volvulus or intestinal fixation problem	560.2, 751.4	224 (0.012)
Meckel's syndrome	751.0	67 (0.004)
Large bowel		
(1) Atresia, etc.	751.2	647 (0.035)
(2) Hirschprung's	751.3	214 (0.012)
(3) Meconium obstruction	771.1	1479 (0.080)
Liver, bile duct, pancreas		
(1) Biliary atresia or Pancreatic anomaly	751,61, 751.7	100(0.005)
(2) Bile, liver, pancreas	751.60, 751.69	246 (0.013)
Genitourinary		
Renal		
(1) Agenesis	753.0	434 (0.024)
(2) Polycystic	753.12, 753.14, 753.15	294 (0.016)
(3) Other cystic	753.10, 753.19	244 (0.013)
(4) Other anomalies	753.3, 753.4	430 (0.023)
Obstructions		
(1) High obstruction	753.21, 753.22, 753.23	2154 (0.117)
(2) Low obstruction	753.6, 753.7, 753.8, 753.9, 753.20 756.71	450 (0.024)
(3) Prune belly, etc.		28 (0.002)
Central Nervous System		
Spina bifida, etc.		
(1) Spina bifida	741.00, 741.01, 741.02, 741.03, 741.90, 741.91, 741.92, 741.93, 742.59	441 (0.024)
(2) Encephalocele	742.0	86 (0.005)
Brain		
(1)	742.1, 742.4	1080 (0.059)
(2)	742.2, 742.3	757 (0.041)
(3)	742.8, 742.9	252 (0.014)
Pulmonary		
Congenital Diaphragmatic Hernia	519.4, 553.3, 748.9, 750.6, 756.6	588 (0.032)
Airway	748.3, 748.9	933 (0.051)
Cyst, etc.		
(1)	748.4, 748.60	435 (0.024)
(2)	748.69, 748.8	126 (0.007)

Cardiovascular		
Aortic valve	746.3, 746.4, 424.1	216 (0.012)
Aortic arch		
(1)	747.10, 747.21, 747.29	436 (0.024)
(2)	747.11, 747.22, 746.81	135 (0.007)
Hypoplastic Left Heart Syndrome	746.7	321 (0.017)
Endocardial fibroelastosis	425.3	149 (0.008)
Mitral valve		
(1) Stenosis	746.5	42 (0.002)
(2) Other mitral	424.0, 746.6, 746.84	436 (0.024)
Transpositions	745.10, 745.19, 745.12	360 (0.020)
Coronary/Myocardial	746.85, 425.1	105 (0.006)
Common Right Ventricle, etc.	745.3, 745.11, 745.0	450 (0.024)
Pulmonary valve — tricuspid		
(1)	746.01, 746.83, 746.2	325 (0.018)
(2)	746.09, 745.2, 746.1	693 (0.038)
Cushion, etc.	745.60, 745.61, 745.69	346 (0.019)
Pulmonary veins, etc.	746.82, 747.41, 747.42	177 (0.010)
Great vein	747.40, 747.49	94 (0.005)
Skeletal	756.50, 756.51, 756.55, 756.59	115 (0.006)
Chromosomal Syndromes		
(1)	758.3, 758.5, 758.89, 758.9, 759.89, 759.9	1484 (0.081)
(2)	759.7	107 (0.006)
(3) Conjoined twins	759.4	15 (0.001)
Other		
(1) Non-immune hydrops	778.0	385 (0.021)
(2) Hamartoses	759.6	34 (0.002)
(3) Congenital anemia	776.5	1846 (0.100)

Table A-4. Definitions of Variables Included in the Final Model and Variables that Were Considered as Potential Control Variables but Not Included in the Final Model.

Variable	ICD codes
Variables derived from ICD-9-CM codes	
Included in the final model	
Small for gestational age	764.1, 764.2, 764.9
Large for gestational age	766.0, 766.1, 775.0
Hydrops due to isoimmunization	773.3
Hemolytic disorders	773.0, 773.2
Fetal distress	768.6, 768.3, 768.4
Fetus affected by maternal condition	760.0, 760.7, 760.72, 760.73
Oligohydramnios	761.2, 761.3
Other high risk maternal condition	760.3, 761.0
Placenta hemorrhage.	762.1, 762.2
Premature rupture of membrane	762.7, 761.1, 760.2
Prolapsed cord	762.4, 762.0
Excluded from final model	
Respiratory distress syndrome	769.0
Birth injury	767.1, 767.3
Other umbilical cord compression	762.6, 762.5, 763.1
Birth trauma	767.8, 767.9
Severe birth trauma/asphyxia	772.2, 767.0, 772.5, 768.5, 779.0, 768.9, 285.1, 345.3, 458.9, 459.0, 459.89, 459.9, 785.59, 788.5, 794.01, 997.1, 997.3, 958.4, 796.3, 733.10, 799.0, 785.50
Maternal Demographic Variables	
Included in the final model	
Race/ethnicity (reference White, non-Hispanic)	
Black	Codes from birth certificates
Mother's education	
8 or fewer years	Codes from birth certificates
9-11 years	Codes from birth certificates
Insurance	
Medicaid	Codes from discharge records
Self-pay	Codes from discharge records
HMO	Codes from discharge records
Excluded from final model	
Race/ethnicity (reference White, non-Hispanic)	
White-Hispanic	Codes from birth certificates
Asian	Codes from birth certificates
Native American	Codes from birth certificates
Maternal education (reference, college graduate)	
High school graduate	Codes from birth certificates
Some post-secondary education, but no 4-year degree	Codes from birth certificates
Prenatal care, from Kotelchuck index(2,3)	Codes from birth certificates

Table A-5. Complete Regression Results for Information Reported on Table 3 of the Manuscript.

	Odds Ratio	95% Confidence Interval*	p-value*
Singleton Female			
500-599g	28.97	(24.24, 34.62)	p<0.00
600-699g	10.17	(8.56, 12.08)	p<0.00
700-799g	4.63	(3.88, 5.52)	p<0.00
800-899g	3.17	(2.65, 3.79)	p<0.00
900-999g	2.24	(1.85, 2.70)	p<0.00
1000-1249g	1.36	(1.16, 1.59)	p<0.00
1250-1499g	0.83	(0.70, 0.98)	p=0.03
Singleton Male			
500-599g	50.93	(42.34, 61.26)	p<0.00
600-699g	17.12	(14.22, 20.61)	p<0.00
700-799g	7.62	(6.59, 8.83)	p<0.00
800-899g	4.61	(3.87, 5.48)	p<0.00
900-999g	3.02	(2.56, 3.56)	p<0.00
1000-1249g	1.85	(1.61, 2.13)	p<0.00
Multiple Birth			
500-599g	37.77	(29.81, 47.86)	p<0.00
600-699g	12.24	(10.00, 14.97)	p<0.00
700-799g	7.27	(6.01, 8.79)	p<0.00
800-899g	3.28	(2.58, 4.17)	p<0.00
900-999g	2.81	(2.23, 3.56)	p<0.00
1000-1249g	1.45	(1.20, 1.74)	p<0.00
1250-1499g	0.47	(0.38, 0.58)	p<0.00
Gestation Age			
<24 weeks	3.22	(2.76, 3.75)	p<0.00
24-25 weeks	1.55	(1.35, 1.78)	p<0.00
26-27 weeks	0.97	(0.85, 1.10)	p=0.62
28-29 weeks	0.83	(0.73, 0.94)	p<0.00
30-31 weeks	0.90	(0.79, 1.02)	p=0.09
32-33 weeks	1.01	(0.86, 1.17)	p=0.93
Level 1			
treat 1-10 VLBW infants	2.72	(2.37, 3.13)	p<0.00
treat >10 VLBW infants	2.39	(1.91, 3.00)	p<0.00
Level 2			
treat 0-10 VLBW infants	2.53	(2.02, 3.18)	p<0.00
treat 11-25 VLBW infants	1.88	(1.56, 2.26)	p<0.00
treat ≥26 VLBW infants	1.22	(0.98, 1.52)	p=0.08
Level 3A			
treat ≤25 VLBW infants	1.69	(1.28, 2.24)	p<0.00
treat 26-50 VLBW infants	1.78	(1.35, 2.34)	p<0.00
treat >50 VLBW infants	1.08	(0.96, 1.21)	p=0.22
Level 3B, 3C			
treat ≤25 VLBW infants	1.51	(1.17, 1.95)	p<0.00
treat 26-50 VLBW infants	1.30	(1.13, 1.50)	p<0.00
Level 3B, 3C, 3D			
treat 51-100 VLBW infants	1.19	(1.04, 1.37)	p=0.01

Race[a]			
Black	0.75	(0.68, 0.82)	p<0.00
Mother's Education[b]			
8 or fewer years	0.96	(0.87, 1.06)	p=<0.38
9-11 years	1.08	(0.99, 1.17)	p=0.07
Insurance			
Medicaid	1.00	(0.92, 1.10)	p=0.95
Self-pay	1.20	(1.04, 1.39)	p<0.02
HMO	0.98	(0.91, 1.06)	p=0.63
Fetal and Infant Clinical Conditions			
Small for gestational age[c]	0.30	(0.24, 0.38)	p<0.00
Large for gestational age	0.64	(0.46, 0.89)	p<0.00
Hydrops due to isoimmunization[d]	46.31	(23.94, 89.57)	p<0.00
Hemolytic disorders	0.43	(0.31, 0.58)	p<0.00
Maternal Conditions			
Fetal distress	0.71	(0.61, 0.83)	p<0.00
Fetus affected by maternal condition[e]	0.58	(0.51, 0.66)	p<0.00
Oligohydramnios	2.71	(2.12, 3.46)	p<0.00
Other high risk maternal condition[f]	1.72	(1.25, 2.37)	p<0.00
Placenta hemorrhage	3.47	(2.89, 4.17)	p<0.00
Premature rupture of membrane	1.28	(1.11, 1.48)	p<0.00
Prolapsed cord	1.19	(0.97, 1.46)	p=0.09
Year			
1991	2.21	(1.92, 2.54)	p<0.00
1992	1.84	(1.59, 2.13)	p<0.00
1993	1.54	(1.33, 1.78)	p<0.00
1994	1.33	(1.16, 1.53)	p<0.00
1995	1.24	(1.06, 1.44)	p<0.01
1996	1.24	(1.07, 1.44)	p<0.01
1997	1.18	(1.04, 1.35)	p=0.01
1998	1.11	(0.97, 1.27)	p=0.14
1999	1.04	(0.91, 1.19)	p=0.57

C-statistic (area under the ROC curve) = 0.86.

* Standard errors are corrected for clustering of patients within hospitals.

The excluded categories were Male 1250-1499 g for birth weight, private, not HMO for type of insurance, 2000 for year, > 33 weeks for gestational age, and hospital with a level 3B, 3C, or 3D NICU that treated > 100 VLBW infants for NICU level/volume category.

The data include in-hospital fetal deaths, and excluded infants with congenital anomalies that had significant mortality risk. Infants with a BW < 500 g are excluded.

The VLBW patient volumes represent total patients treated at each hospital, including patients transferred to, or received from other facilities.

Levels were empirically determined by the authors from a modified version of the American Academy of Pediatrics definitions(1): Level 2: intermediate NICU, no mechanical ventilation; Level 3A: mechanical ventilation with restrictions (e.g., only BW > 1000 g); Level 3B: no

restrictions on mechanical ventilation, no major surgery; Level 3C: major neonatal surgery, no cardiac surgery or extra-corporeal membrane oxygenation (ECMO); Level 3D: cardiac surgery and/or ECMO.

a. The other racial and ethnic groups (Asian, Native American, and Hispanic) had no significant effect on mortality and were excluded from the final model. Based on maternal self-report from the birth certificate.
b. The other education categories (12 years and < 4 years of college) had no significant effect on mortality and were excluded from the final model. Based on maternal self-report from the birth certificate.
c. Small and large for gestational age were based on ICD-9-CM codes for these conditions (764 and 766, respectively).
d. Non-immune hydrops was excluded with the congenital anomalies. Cases with hemolytic disease who didn't receive a diagnosis of hydrops are included in the "hemolytic disorders" variable.
e. Maternal hypertensive disorders and noxious substances (ICD-9-CM codes 760.0, 760.7, 760.72, 760.73).
f. Chronic maternal circulatory and respiratory diseases and incompetent cervix (ICD-9-CM codes 760.3, 761.0).

Table A-6. Sensitivity Tests of Model Assumptions.

NICU Level / Number of VLBW Infants Treated Per Year	Model 1: Base Model	Model 2: Include Anomalies	Model 3: Exclude Fetal Deaths	Model 4: 500-999g	Model 5: 1000-1499g	Model 6: Add Delivery Volume	Model 7: Delete GA < 24	Model 8: Add Transfer Up	Model 9: Add BW 400-499g
Level 1									
treat ≤ 10 VLBW infants	2.72**	2.51**	2.08**	2.72**	2.56**	2.83**	2.78**	4.56**	2.28**
treat > 10 VLBW infants	2.39**	2.16**	1.92**	2.54**	2.10**	2.47**	2.48**	3.77**	1.93**
Level 2									
treat ≤ 10 VLBW infants	2.53**	2.27**	2.04**	2.68**	2.18**	2.68**	2.41**	3.89**	2.15**
treat 11 to 25 VLBW infants	1.88**	1.78**	1.68**	2.04**	1.55**	1.95**	1.87**	2.76**	1.63**
treat > 25 VLBW infants	1.22 ns	1.17 ns	1.17 ns	1.18 ns	1.32**	1.20 ns	1.22*	1.65**	1.10 ns
Level 3A									
treat ≤ 25 VLBW infants	1.69**	1.56**	1.54**	2.13**	1.10 ns	1.70**	1.56**	2.08**	1.96**
treat 26 to 50 VLBW infants	1.78**	1.60**	1.76**	1.92**	1.48*	1.76**	1.66**	2.06**	1.91**
treat > 50 VLBW infants	1.08 ns	1.04 ns	1.04 ns	1.14 ns	0.78*	1.04 ns	1.06 ns	1.28*	1.04 ns
Level 3B or 3C									
treat ≤ 25 VLBW infants	1.51**	1.45**	1.32 ns	1.60**	1.39 ns	1.56**	1.45**	1.68**	1.51**
treat 26 to 50 VLBW infants	1.30**	1.28*	1.27**	1.36**	1.26*	1.29**	1.26**	1.36**	1.26**
Level 3B, 3C, or 3D									
treat 51 to 100 VLBW infants	1.19*	1.17*	1.15 ns	1.24**	1.11 ns	1.18*	1.20**	1.20**	1.20**
treat > 100 VLBW infants	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
ROC c-statistic	0.86	0.87	0.88	0.83	0.72	0.87	0.82	0.87	0.87

** p<0.01; * p<0.05; ns = p>0.05.

* This model also controls for birth weight, gestational age, sex, plurality, Black race, maternal education, type of insurance, year, and a range of obstetric and neonatal risk factors. See Methods above for additional details. The base model is reported in full in Table A-5.

The data include in-hospital fetal deaths, and excluded infants with congenital anomalies that had significant mortality risk. Infants with a BW < 500 g are excluded.

The VLBW patient volumes represent total patients treated at each hospital, including patients transferred to, or received from other facilities.

Levels were empirically determined by the authors from a modified version of the American Academy of Pediatrics definitions(1): Level 2: intermediate NICU, no mechanical ventilation; Level 3A: mechanical ventilation with restrictions (e.g., only BW > 1000 g); Level 3B: no restrictions on mechanical ventilation, no major surgery; Level 3C: major neonatal surgery, no cardiac surgery or extra-corporeal membrane oxygenation (ECMO); Level 3D: cardiac surgery and/or ECMO.

Table A-7. Estimate of the Potentially Preventable Deaths if 90 Percent of VLBW Deliveries in Large Urban Areas Occurred at Hospitals with a Level 3B, 3C, or 3D NICU that Treats More than 100 VLBW Infants per Year.

NICU Level / Number of VLBW Infants Treated Per Year	Risk Ratio for Mortality	2000 VLBW Market Share[1]	2000 Share of Births > 40 km (25 Miles) From a Tertiary NICU[2]	% Increase in Overall Mortality[3]	Deaths Potentially Preventable
Level 1					
treat ≤ 10 VLBW infants	2.08	4.9	30.7	3.3%	28
treat >10 VLBW infants	1.91	4.0	10.1	3.0%	25
Level 2					
treat ≤10 VLBW infants	1.98	1.3	40.0	0.7%	6
treat 11 to 25 VLBW infants	1.62	4.6	12.3	2.3%	19
treat >25 VLBW infants	1.17	6.4	8.4	0.9%	8
Level 3A					
treat ≤25 VLBW infants	1.50	0.9	26.1	0.3%	3
treat 26 to 50 VLBW infants	1.56	4.5	7.6	2.1%	18
treat >50 VLBW infants	1.06	3.5	0	0.2%	2
Level 3B or 3C					
treat ≤25 VLBW infants	1.38	3.5	6.6	1.1%	10
treat 26 to 50 VLBW infants	1.23	19.1	18.0	3.3%	28
Level 3B, 3C, or 3D					
treat 51 to 100 VLBW infants	1.15	25.8	0.0	3.5%	30
treat >100 VLBW infants	Ref	21.5			
Hypothetical Potential Change in Mortality				20.6%	175

The VLBW patient volumes represent total patients treated at each hospital, including patients transferred to, or received from other facilities.

Levels were empirically determined by the authors from a modified version of the American Academy of Pediatrics definitions(1): Level 2: intermediate NICU, no mechanical ventilation; Level 3A: mechanical ventilation with restrictions (e.g., only BW > 1000 g); Level 3B: no restrictions on mechanical ventilation, no major surgery; Level 3C: major neonatal surgery, no cardiac surgery or extra-corporeal membrane oxygenation (ECMO); Level 3D: cardiac surgery and/or ECMO.

[1] Percentage of VLBW deliveries at each NICU/volume level in 2000.

[2] Tertiary NICUS include existing large NICUs and "virtual" large NICUs that were assigned for geographic areas with more than 100 VLBW deliveries spread across several hospitals. Deliveries more than 40 km from these NICUs were excluded from the simulation.

[3] Calculated by comparing the mortality for each NICU volume/level versus predicted mortality if 90 percent of the deliveries in large urban areas occurred in the highest NICU level/volume category.

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