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A Comparison of Wisconsin Neonatal Intensive Care Units with National Data on Outcomes and Practices

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ABSTRACT

Context: Improvements in neonatal care over the past 3 decades have increased survival of infants at lower birthweights and gestational ages. However, outcomes and practices vary considerably between hospitals.

Objective: To describe maternal and infant characteristics, neonatal intensive care units (NICU) practices, morbidity, and mortality in Wisconsin NICUs, and to compare outcomes in Wisconsin to the National Institute of Child Health and Human Development network of large academic medical center NICUs.

Methods: The Newborn Lung Project Statewide Cohort is a prospective observational study of all very low birthweight (≤1500 grams) infants admitted during 2003 and 2004 to the 16 level III NICUs in Wisconsin. Anonymous data were collected for all admitted infants (N=1463). Major neonatal morbidities, including bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), and retinopathy of prematurity (ROP) were evaluated.

Results: The overall incidence of BPD was 24% (8%-56% between NICUs); IVH incidence was 23% (9%-41%); the incidence of NEC was 7% (0%-21%); and the incidence of grade III or higher ROP was 10% (0%-35%).

Conclusion: The incidence rates of major neonatal morbidities in Wisconsin were similar to those of a national network of academic NICUs.

INTRODUCTION

The Newborn Lung Project is a unique regional cohort of very low birthweight (VLBW), ≤1500 grams, children based on births in Wisconsin. This study, started in 1987, has followed up on health, behavior, and academic outcomes of cohort children for almost 2 decades. The first cohort includes all VLBW children admitted to 6 Neonatal Intensive Care Units (NICU) between 1988 and 1991, covering a contiguous region of Wisconsin and Iowa.[1-3] The most recent Newborn Lung Project (Project) cohort covers the entire state of Wisconsin and includes all VLBW admissions during 2003 and 2004. Reflecting a trend toward decentralization of NICU care, there are now 16 level III NICUs in the state. This recent population-based cohort gives us the opportunity to compare VLBW infants in Wisconsin to infants born at centers that are part of a prominent national network of NICUs.

National vital statistics show that the percentage of births that are VLBW has increased from 1.3% to 1.5% since 1990.[4] In Wisconsin, the percentage of births that are VLBW has increased from 1.1% to 1.3% since 1995.[5] The Wisconsin infant mortality rate across all birthweights declined steadily until 2004, and has leveled off in recent years.[6] Exogenous surfactant and antenatal steroid therapy to enhance lung maturity of preterm infants are thought to be responsible for much of the increased survival.[3,7] Well-equipped, experienced NICUs also have contributed to the increasing survival of VLBW neonates.[8-11]

The decrease in mortality among VLBW infants was initially accompanied by an increase in early life morbidities such as intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), and necrotizing enterocolitis (NEC).[7,12-13] The increases in these morbidities have leveled off in recent years.[14] Results from the first Project cohort showed a decreased mortality rate and an increased incidence of BPD among VLBW infants from the presurfactant to postsurfactant eras.[3] Recently, published work has reported a similar increase in the incidence of BPD.[15]

Characteristics of NICUs, such as annual volume and the presence of a pediatric residency program,

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Table 1. Very Low Birthweight Admissions to Level III Neonatal Intensive Care Units in Wisconsin, 2003-2004

Neonatal Intensive Care Unit	All Admissions N	Outborn Admissions N (%)
St. Joseph's Hospital, Milwaukee	256	19 (7)
Aurora Sinai, Milwaukee	142	8 (6)
St. Joseph's Hospital, Marshfield	129	30 (23)
Meriter Hospital, Madison	115	11 (10)
Children's Hospital of Wisconsin, Milwaukee	110	30 (27)
St. Mary's Hospital, Madison	109	4 (4)
St. Vincent Hospital, Green Bay	109	31 (28)
Columbia-St. Mary's Hospital, Milwaukee	108	3 (3)
St. Luke's Hospital, Racine	71	6 (9)
Children's Hospital of Wisconsin—Fox Valley, Neenah	69	12 (17)
Waukesha Memorial Hospital, Waukesha	56	5 (9)
Aurora Women's Pavilion, West Allis	48	3 (6)
Gunderson Lutheran Hospital, La Crosse	47	5 (11)
Aurora Bay Care, Green Bay	37	0 (0)
St. Elizabeth Hospital, Affinity Health System, Appleton	34	0 (0)
Franciscan Skemp Hospital, La Crosse	23	1 (4)

have been investigated as contributing factors to neonatal outcomes. Higher annual NICU volume has been associated with lower risk for mortality[10,16] and severe IVH,[17] while no association was found between mortality and the presence of a residency program[18] in the 1 study that investigated this relationship.

The authors report on maternal and infant characteristics, NICU practices, and outcomes in the Project. The Project is a population-based cohort of all Wisconsin VLBW infants born during the current era of neonatal care and representing all NICUs. The data includes a range of volume and NICUs with and without residency programs. The objectives of this paper are to (1) describe maternal and infant characteristics, NICU practices, and the incidence of neonatal morbidities in the 16 NICUs in Wisconsin; (2) explore the association between NICU-level variables and the incidence of neonatal morbidities; and (3) compare outcomes in Wisconsin to outcomes of large academic neonatal centers in the National Institute of Child Health and Human Development Neonatal Research Network (Network).

METHODS

The Project is a prospective study of all VLBW infants admitted from January 1, 2003, to December 31, 2004, to the 16 level III NICUs in Wisconsin (Table 1).

Twenty-five designated, trained neonatal nurses at participating centers abstracted deidentified data from each infant's medical record onto standardized forms.[19] Data included pregnancy complications, multiple pregnancy, maternal antenatal steroid therapy to enhance fetal lung maturity, tocolytic therapy to halt premature labor, and outborn status (infant transfer from place of birth to level III NICU). Infant characteristics included birthweight, gestational age, race, sex, and Apgar score for health assessment of the newborn (higher score means better newborn health). Infants who had birthweights ≤1000 grams were classified as extremely low birthweight (ELBW). The Score for Neonatal Acute Physiology II was calculated, and used as an indicator of generic baseline physiologic status in the first 12 hours of life (higher scores indicate worse health).[20] We also collected data on NICU care, such as surfactant therapy, fraction of inspired oxygen at 24 hours of life, ventilation treatment, intubation, postnatal steroid therapy, and length of stay in hospital. The following infant diagnoses were also recorded: IVH, BPD, NEC, patent ductus arteriosus, and retinopathy of prematurity (ROP.)

Two NICU-level structure variables were considered. The mean annual volume of infants admitted to the NICU was determined by taking the average of the 2003 and 2004 admissions.[6] The presence of a residency program was defined as having a pediatric residency or a neonatal fellowship program at the hospital.[21]

Statistical Analysis

Statistical analyses were performed using SAS, version 9.1. Means, standard deviations, frequencies, and percentages were used to describe the Project cohort. Logistic regression was used to examine the association between NICU-level characteristics and neonatal outcomes, while adjusting for the following case mix variables: birthweight, gestational age, sex, 1-minute Apgar score, Score for Neonatal Acute Physiology II, and outborn status.

RESULTS

During 2003 and 2004, 1463 VLBW infants were admitted to the 16 level III NICUs in Wisconsin. VLBW admissions to each NICU over this 2-year time period ranged from 23 to 256. The number of infants in the Project cohort was compared to the number of VLBW NICU admissions during 2003 and 2004 reported by the Wisconsin Interactive Statistics on Health.[6] The number of births to Wisconsin residents with birthweight <1500 grams in our cohort was 1385, a close match to the 1386 births reported by Wisconsin Interactive Statistics on Health (1 infant in our dataset had missing data for state of residence). Thus, our

Table 2. Maternal and Infant Characteristics for the Newborn Lung Project Statewide Cohort Study, 2003-2004

	Entire Cohort N=1463	Range Between NICUs
Maternal characteristics		
Maternal age in years, mean (SD)	28.0 (6.1)	24.8-31.5
<18 years	5	0-9
Prenatal care	92	84-100
Pregnancy induced hypertension	28	14-36
Premature rupture of membranes	17	9-35
Chorioamnionitis	8	0-22
Antenatal steroids therapy	69	53-89
Tocolytic therapy[a]	57	51-83
Caesarean delivery[a]	61	54-84
Infant characteristics		
Birth weight in grams, mean (SD)	1049 (298)	960-1192
Gestational age in weeks, mean (SD)	28 (3.0)	27-30
1-minute Apgar score, mean (SD)	5.1 (2.3)	4.2-6.3
SNAP-II[c] score, mean (SD)	17.4 (15.7)	12.9-27.1
FiO_2[d] at 24 hours, mean (SD)	0.27 (0.13)	0.23-0.30
Outborn[b]	12	0-28
Multiple births	27	9-35
Small for gestional age[e]	25	15-33
Male	50	39-65
White race	61	18-94

Note: Numbers shown are percentages, unless otherwise noted. SD=standard deviation.
[a] Available for 1034 infants (71% of cohort) with detailed medical records abstracting after informed consent
[b] Infant born at another hospital and transferred to a study NICU
[c] Score for Neonatal Acute Physiology II
[d] Fraction of inspired oxygen
[e] Weight <10th percentile

cohort contains all VLBW infants born during 2003 and 2004 who survived to admission to all level III NICUs in Wisconsin.

Maternal Characteristics

The mean (standard deviation [SD]) maternal age was 28 (6.1) years, with 5% of mothers <18 years old. Ninety-two percent of mothers received prenatal care. Pregnancy-induced hypertension was diagnosed among 28% of mothers, prolonged rupture of membranes for >24 hours was diagnosed in 17% of mothers, and 8% of mothers were diagnosed with chorioamnionitis (infection of the placenta and amniotic fluid). Antenatal steroids were administered to 69% of mothers before delivery and 57% received tocolytics. Sixty-one percent of mothers had a Caesarean section delivery (Table 2). Maternal characteristics varied between the NICUs. For example, diagnosis of prolonged rupture of membranes ranged from 9% to 34% between NICUs, and diagnosis of chorioamnionitis ranged from 0% to 22%. There were also differences between NICUs in the percentage of mothers who received antenatal steroids (53%-89%) and tocoloytic therapy (51%-83%). The rate of Cesarean section deliveries ranged from 54% to 84%.

Infant Characteristics

Twelve percent of the infants were born at hospitals without level III NICUs and were transferred to participating centers after birth (outborn status). Twenty-seven percent of VLBW infants were multiple births and 25% were small for gestational age. The mean (SD) birthweight was 1049 (298) grams and the mean (SD) gestational age was 28 (3) weeks.

Several infant characteristics varied between study NICUs. The percentage of outborn infants ranged from 0% to 28%; the percentage of infants who were small for gestational age ranged from 15% to 33%; and the percentage of white infants ranged from 18% to 94% between NICUs. Mean birthweight ranged from 960 to 1192 grams and the mean for the Score for Neonatal Acute Physiology II ranged from 12.9 to 27.1, indicating that the illness severity level of the infants varied considerably between NICUs. Table 2 shows birth and early characteristics of the VLBW cohort and the range between NICUs.

Practices and Outcomes in Wisconsin NICUs

Table 3 shows the variation in NICU practices and outcomes between participating centers. Seventy-seven percent of infants received surfactant, ranging from 41% to 91% between NICUs. Overall, 76% of infants were intubated, with a range of 48%-91% between NICUs. Postnatal steroids were administered to 18% of cohort infants, ranging from 4% to 45% between NICUs. There was a wide range in the median days on supplemental oxygen (medians ranged from 0 to 61 days) and the median days on ventilation (0 to 27 days). As expected, more ELBW infants received surfactant, were intubated, and received postnatal steroids than did VLBW infants. The group of ELBW infants also had a higher median number of days on supplemental oxygen and ventilation than the group of VLBW infants, and had a longer stay in the NICU (Table 3).

Table 3 also shows variation in neonatal diagnoses between the 16 NICUs. The overall incidence of any grade IVH was 23%, with a range of 9%-41% between NICUs. Grade III or higher IVH was diagnosed in 8% of the entire cohort, ranging from 0% to 18% between NICUs. Twenty-four percent of the VLBW cohort was diagnosed as having BPD, with a range of 8%-56% between the 16 NICUs. The incidence of NEC ranged

Table 3. Selected Neonatal Intensive Care Unit Practices and Outcomes of the Newborn Lung Project by Birthweight Category

	VLBW[b] Infants (N=1463)		ELBW[c] Infants (N=626)	
	All VLBW	Range[a]	All ELBW	Range[a]
Received antenatal steroids	70	50-89	76	56-94
Received surfactant	77	41-91	95	79-100
Intubated	76	48-91	90	75-96
Received postnatal steroids	18	4-45	37	6-71
Survival	88	80-96	76	59-90
Any grade intraventricular hemorrhage	23	9-41	33	0-50
≥Grade III intraventricular hemorrhage	8	0-18	13	0-27
Bronchopulmonary dysplasia	24	8-56	42	20-67
Necrotizing enterocolitis	7	0-21	11	0-22
Patent ductus arteriosus	35	21-47	51	29-71
>Grade III retinopathy of prematurity	10	0-35	22	0-61
Discharged home/foster care	85	76-96	73	58-90
Median days on oxygen	61	0-61	73	56-85
Median days on ventilation[d]	4	0-27	29	4-51
Median days in hospital	51	35-62	78	59-95

Note: Numbers shown are percentages, unless otherwise noted.
[a] Range across 16 Wisconsin level III NICUs
[b] Very low birthweight, ≤1500 grams
[c] Extremely low birthweight, ≤1000 grams
[d] Available for 1034 infants (71% of cohort) with detailed medical records abstracting after informed consent

Table 4. Odds Ratios[a] and 95% Confidence Intervals for the Association Between NICU Structure Characteristics and Neonatal Outcomes

	≥ Grade III IVH	BPD	NEC	Death before Discharge
Annual volume (per 10 admissions)	0.94 (0.89, 1.0)	0.98 (0.97, 1.0)	0.99 (0.94, 1.1)	0.97 (0.92, 1.0)
Presence of residency program	0.82 (0.49, 1.4)	2.0 (1.5, 2.5)	1.8 (1.1, 2.9)	1.3 (0.83, 2.2)

Note: IVH=intraventricular hemorrhage, BPD=bronchopulmonary dysplasia, NEC=necrotizing enterocolitis.
[a] Adjusted for birthweight, gestional age, sex, 1-minute Apgar, outborn status, and Score for Neonatal Acute Physiology II

from 0% to 21%; patent ductus arteriosus incidence ranged from 21% to 47%, and grade III or higher ROP ranged from 0% to 35% between NICUs. As expected, the incidence of each of these morbidities was higher among the group of ELBW infants (Table 3).

The mean annual volume for 2003-2004 ranged from 13 VLBW admissions per year to 146 VLBW admissions per year. Three of the NICUs had a pediatric residency program or neonatal fellowship program. There was not a significant association between annual NICU volume and risk for any of the neonatal outcomes examined (Table 4). After adjusting for case mix, infants at NICUs with a residency program tended to have a lower risk for grade III or higher IVH. Infants who were cared for at NICUs with residency programs were at higher risk for BPD and NEC, and showed a trend toward being more likely to die before NICU discharge (Table 4).

Comparison of NICU Practices and Outcomes in Wisconsin with National Data

Wisconsin infant characteristics and NICU practices were compared to those in the Network for infants born between 1997 and 2002 (Table 5). The mean birthweight of infants in the Project was similar to the mean birthweight of infants in the Network (mean [SD], 1049 [298] and 1033 [289] grams, respectively). The percentage of infants from multiple-birth pregnancies was similar in the 2 cohorts, with 27% in the Project and 26% in the Network, while the percentage of infants who were small for gestational age was slightly higher in the Project (25%) than in the Network (21%).

NICU practices differed somewhat between the Project and the Network. Fewer mothers of infants in the Project received antenatal steroids than in the Network (69% versus 79%) and more infants in the Project received surfactant (77% versus 58%). There were slightly more Caesarean deliveries among infants in the Project than the Network (61% versus 58%). The administration of postnatal steroids was similar across the 2 cohorts (18% in the Project and 17% in the Network).

The incidence of major neonatal morbidities was

Table 5. Selected Patient Characteristics, Neonatal Intensive Care Unit Practices, and Outcomes of Wisconsin Very Low Birthweight Infants and the National Institute of Child Health and Human Development Neonatal Research Network

	Newborn Lung Project N=1463		Neonatal Research Network N=18,153	
	Overall	Range[a]	Overall	Range[b]
Birth weight in grams, mean	1049	960-1192	1033	998-1066
Standand deviation	298	219-321	289	273-295
Multiple births	27	9-57	26	18-40
Small for gestational age[c]	25	15-32	21	17-26
Antenatal steroid therapy	69	53-90	79	47-90
Received surfactant	77	41-91	58	42-74
Caesarean delivery[d]	61	53-84	58	50-69
Received postnatal steroids	18	6-48	17	4-29
Premature rupture of membranes	17	9-35	24	16-28
Bronchopulmonary dysplasia	24	8-56	22	10-50
Intraventricular hemorrhage > grade III	8	0-18	12	6-19
Necrotizing enterocolitis	7	0-21	7	4-11
Survival	88	80-96	85	79-93

Note: Numbers shown are percentages, unless otherwise noted.
[a] Range across 16 Wisconsin level III NICUs
[b] Range across Neonatal Research Network centers
[c] Weight <10th percentile
[d] Available for 1034 Wisconsin infants with detailed medical records abstracting after informed consent

similar among the 2 cohorts. The incidence of BPD was slightly higher among Project infants than Network infants (24% versus 22%), while the incidence of grade III or higher IVH was somewhat lower among Project infants than Network infants (8% versus 12%). The incidence of NEC was 7% in each of the cohorts. Slightly more infants in the Project survived to discharge (88%) than in the Network (85%).

DISCUSSION

This report summarizes infant and maternal characteristics, survival and the incidence of major neonatal morbidities, and NICU care practices for a Wisconsin cohort of VLBW infants born over 2 years and receiving recent neonatal care. We also compared characteristics, survival and morbidities, and NICU care among the 16 NICUs in Wisconsin and compared outcomes in Wisconsin to those in a cohort of infants cared for in major academic NICUs.

In the first cohort of the Project (1988-1991 births), we evaluated mortality and neonatal morbidities, as well as the receipt of perinatal therapies.[3] Survival was higher and the incidence of major morbidities, such as IVH and BPD, was lower for infants in the more recent cohort than for those in the first cohort. Additionally, the use of both surfactant and antenatal steroids has increased.

Results from the most recent Project show a rather wide variation in the survival rate of infants, the incidence of major neonatal morbidities, and NICU care practices between the 16 level III NICUs in Wisconsin. In order to investigate whether NICU-level characteristics help explain some of the variation between NICUs, we investigated whether annual volume and the presence of a pediatric residency program were associated with neonatal outcomes, as these have been identified as important factors in the literature. Our results suggest that while annual volume seemed to have little association with neonatal outcomes, the presence of a residency program may be associated with higher risk for BPD and NEC, and lower risk for at least grade III IVH and for death before NICU discharge.

Results from other studies that have evaluated the effect of NICU volume have been mixed. A study of NICUs in California found that infants born at level III NICUs with low volume were at higher risk for death than infants born at level III NICUs with high volume.[10] Annual volume was not associated with neonatal mortality among infants born during 1992-1993 at NICUs participating in the Vermont Oxford Network,[18] but analysis of Vermont Oxford Network infants born between 1995 and 2000 found a threshold effect, such that higher volume was associated with lower mortality risk ≤50 admissions per year, and higher mortality >50 admissions per year.[16] Among infants in the Canadian Neonatal Network, larger NICU volume was associated with lower risk for severe IVH (grade III or higher).[17] To our knowledge, the relationship between

NICU volume and other neonatal morbidities has not been evaluated in other studies.

After adjusting for patient level characteristics, the presence of a pediatric residency program was not associated with neonatal mortality among infants in the Vermont Oxford Network.[18] Among infants in the Project, being cared for at a NICU with a residency program showed a trend toward being associated with increased mortality, and was significantly associated with higher risk for BPD and NEC, while it was associated with lower risk for grade III or higher IVH. Infants at 2 of the 3 NICUs in the Project that have residency programs were less healthy shortly after birth than infants at the NICUs without residency programs, with higher mean values on the Score for Neonatal Acute Physiology II. Each of these NICUs also had a rather high percentage of patients who were born elsewhere and transferred in for care. It could be that the NICUs with residency programs are serving different populations of infants than NICUs without residency programs, and that our adjustment for case mix to take into account baseline illness severity was not adequate to account for these differences. It is not clear what differentiates NICUs with and without residency programs, and further investigation is warranted to determine what is contributing to the poor outcomes with respect to mortality, some of the neonatal morbidities, and how outcomes may be improved.

The National Institute of Child Health and Human Development Neonatal Research Network is a network of NICUs at academic research hospitals that report on neonatal outcomes for infants weighing 500-1500 grams.[7] These centers generally represent cutting edge neonatal care in the United States. Their recent report of neonatal outcomes combines data from their 1997-1998, 1999-2000, and 2001-2002 data collection periods as there was very little difference in any of their parameters across these years.[14]

Compared to the national Network data, our Wisconsin cohort of VLBW infants had similar incidence rates for major neonatal morbidities, but NICU care practices were somewhat different in Wisconsin and the Network. For example, fewer Wisconsin mothers received antenatal steroids (69%) than mothers of infants in the Network (79%) and more Wisconsin infants received surfactant (77%) than those in the Network (58%). While variation in outcomes and NICU practices was more substantial between NICUs in the Project than the Network, there was quite a bit of variation in outcomes and practices between NICUs in the Network as well. Ranges in practices and outcomes reported from the Canadian NICU Network, another population-based cohort of VLBW infants, were also quite large.[22] It is likely that the smaller amount of variation seen for Network NICUs is due to the much larger sample size for these NICUs arising from more years of follow-up.

The Project and Network cohorts differ in some significant ways. First, the Project is a population-based cohort that includes all VLBW admissions in Wisconsin. As the cohort includes infants born at all the level III NICUs in Wisconsin, NICUs with and without residency programs are included, and a wide range of annual admissions is represented among cohort NICUs. In contrast, each of the NICUs in the Network is at a large research university hospital and the cohort is not population-based. The Network evaluated outcomes for infants who weighed 500-1500 grams, while the Project included all VLBW NICU admissions (≤1500 grams). However, birthweight was similar across the 2 cohorts, as only 40 infants (3%) had a birthweight <500 grams in the Project, and the mean [SD] birthweight in each cohort was very similar (1049 [298] grams for the Project and 1033 [289] grams in the Network).

Despite the differences between the Wisconsin and national cohorts, the groups of infants in each are rather similar, as the incidence rates of most major neonatal morbidities are quite comparable. The difference in care practices between the Project and the Network could be indicative of differences in physician habits in university and non-university settings.

CONCLUSION

The incidence of mortality and neonatal morbidities, in addition to NICU care practices, vary widely between NICUs in Wisconsin. Neonatal care and outcomes in Wisconsin are similar to care and outcomes reported in the National Institute of Child Health and Human Development Neonatal Research Network. These similarities indicate that Wisconsin is doing well compared to some of the leading NICUs in the United States.

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Appendix: Neonatal Diagnoses

Bronchopulmonary dysplasia (BPD): Chronic lung disease of prematurity. Defined as receiving supplemental oxygen at 36 weeks postmenstrual age (gestational age plus chronological age).[23-24]

Intraventricular hemorrhage (IVH): A bleeding inside or around the ventricles, the spaces in the brain containing cerebral spinal fluid. Graded on a scale of I-IV, with IV being the most severe.[25]

Necrotizing enterocolitis (NEC): Gastrointestinal disease that mostly affects premature infants.

Patent ductus arteriosus (PDA): A type of congenital heart defect in which a blood vessel that is supposed to be shut soon after birth remains open.

Retinopathy of prematurity (ROP): A disease that affects immature vasculature in the eyes of premature babies. Graded on a scale of I to IV, with IV being the worst.

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