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Very Low Birth Weight Outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1995 Through December 1996

James A. Lemons, MD*; Charles R. Bauer, MD†; William Oh, MD§; Sheldon B. Korones, MD||; Lu-Ann Papile, MD¶; Barbara J. Stoll, MD#; Joel Verter, PhD**; Marinella Temprosa, MS**;
Linda L. Wright, MD‡‡; Richard A. Ehrenkranz, MD§§; Avroy A. Fanaroff, MB, BCH|||; Ann Stark, MD¶¶;
Waldemar Carlo, MD##; Jon E. Tyson, MD***; Edward F. Donovan, MD‡‡‡; Seetha Shankaran, MD§§§;
and David K. Stevenson, MD||||, for the NICHD Neonatal Research Network

ABSTRACT. *Objectives.* To determine the mortality and morbidity for infants weighing 401 to 1500 g (very low birth weight [VLBW]) at birth by gestational age, birth weight, and gender.

Study Design. Perinatal data were collected prospectively on an inborn cohort from January 1995 through December 1996 by 14 participating centers of the National Institute of Child Health and Human Development Neonatal Research Network and were compared with the corresponding data from previous reports. Sociodemographic factors, perinatal events, and the neonatal course to 120 days of life, discharge, or death were evaluated.

Results. Eighty four percent of 4438 infants weighing 501 to 1500 g at birth survived until discharge to home or to a long-term care facility (compared with 80% in 1991 and 74% in 1988). Survival to discharge was 54% for infants 501 to 750 g at birth, 86% for those 751 to 1000 g, 94% for those 1001 to 1250 g, and 97% for those 1251 to 1500g. The incidence of chronic lung disease (CLD; defined as receiving supplemental oxygen at 36 weeks' postmenstrual age; 23%), proven necrotizing enterocolitis (NEC; 7%), and severe intracranial hemorrhage (ICH; grade III or IV; 11%) remained unchanged between 1991 and 1996. Furthermore, 97% of all VLBW infants and 99% of infants weighing <1000 g at birth had weights less than the 10th percentile at 36 weeks' postmenstrual age.

Mortality for 195 infants weighing 401 to 500 g was 89%, with nearly all survivors developing CLD. Mortality in infants weighing 501 to 600 g was 71%; among survivors, 62% had CLD, 35% had severe ICH, and 15% had proven NEC.

Conclusions. Survival for infants between 501 and 1500 g at birth continued to improve, particularly for infants weighing <1000 g at birth. This improvement in survival was not associated with an increase in major morbidities, because the incidence of CLD, proven NEC, and severe ICH did not change. However, poor postnatal growth remains a major concern, occurring in 99% of infants weighing <1000 g at birth. Mortality and major morbidity (CLD, severe ICH, and NEC) remain high for the smallest infants, particularly those weighing <600 g at birth. *Pediatrics* 2001;107(1). URL: <http://www.pediatrics.org/cgi/content/full/107/1/e1>; *very low birth weight, morbidity, mortality, National Institute of Child Health and Human Development Neonatal Research Network, prematurity, preterm delivery.*

ABBREVIATIONS. NICHD, National Institute of Child Health and Human Development; VLBW, very low birth weight; CLD, chronic lung disease; ICH, intracranial hemorrhage; PDA, patent ductus arteriosus; NEC, necrotizing enterocolitis.

The National Institute of Child Health and Human Development (NICHD) Neonatal Research Network very low birth weight (VLBW) registry was used to assess the mortality and morbidity rates for infants 401 to 500 g and 501 to 1500 g at birth born at the 14 participating centers. Selected morbidities and mortality were evaluated according to birth weight, gestational age, and sex. Additionally, the changing pattern of mortality and morbidity over a 6-year period in the 12 centers that were members of the Network throughout this period (2 additional centers joined the Network in 1996) was evaluated.

POPULATION AND METHOD OF DATA COLLECTION

The study cohort comprised 4438 infants weighing between 501 and 1500 g and 195 infants weighing 401 to 500 g born at the 14 participating centers between January 1, 1995 and December 31, 1996. The NICHD Neonatal Research Network VLBW registry was developed to survey neonatal practice, to assess morbidity and mortality, and to provide information for the planning of randomized clinical trials.

Research nurses at participating centers collected sociodemographic, pregnancy, and delivery data soon after birth on all live-born VLBW infants (401–1500 g), including those who died before admission to the neonatal intensive care unit. Maternal and infant data were collected using common definitions developed

From *Indiana University, Indianapolis, Indiana; †University of Miami, Miami, Florida; §Women and Infants Hospital, Providence, Rhode Island; ||University of Tennessee at Memphis, Memphis, Tennessee; ¶University of New Mexico, Albuquerque, New Mexico; #Emory University, Atlanta, Georgia; **Biostatistics Center, George Washington University, Rockville, Maryland; ‡‡National Institute of Child Health and Human Development, Bethesda, Maryland; §§Yale University, New Haven, Connecticut; |||Case Western Reserve University, Cleveland, Ohio; ¶¶Harvard University, Boston, Massachusetts; ##University of Alabama, Birmingham, Alabama; ***University of Texas Southwestern Medical Center, Dallas, Texas; ‡‡‡University of Cincinnati, Cincinnati, Ohio; §§§Wayne State University, Detroit, Michigan; and ||||Stanford University, Stanford, California.

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Reprint requests to (J.A.L.) Department of Pediatrics, Section of Neonatal-Perinatal Medicine, James Whitcomb Riley Hospital for Children, Indiana University Medical Center, 699 W Dr, RR 208, Indianapolis, IN 46202-5119. E-mail: jlemons@iupui.edu

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by the investigators and described in the study *Manual of Operations* and in previous publications.¹⁻⁴ Gestational age in completed weeks was determined by the following obstetric measures: last menstrual period, standard obstetric parameters, and ultrasonography. If there was a 2-week range of gestational age estimates among the various obstetric measures, the lowest estimate was used. If there was a ≥ 3 -week range, the median estimate of gestational age was used. Chronic lung disease (CLD) was defined as receiving supplemental oxygen at 36 weeks' postmenstrual age as determined by the best obstetric estimate of gestational age at birth.

Statistical Analysis

Logistic regression⁵ models of mortality by birth weight and gestational age were developed for inborn singleton infants 501 to 1500 g and < 31 weeks of gestational age at birth. All models included birth weight, gestational age by best obstetric measures, and an interaction term between birth weight and gestational age. Separate models were estimated for male and female infants. Infants > 30 weeks of gestational age were excluded because that group represents a highly skewed and growth restricted population. To avoid extrapolation to subpopulations with small samples, the plots are presented for the cohort of infants > 21 weeks and between the 5th and 95th percentiles of birth weight for each gender at each gestational age.

Tables 1 to 3 present average values for the cohort ($n = 4438$) and the range of values observed among the 14 clinical sites. Figures 4A, B, and C present a comparison of mortality and morbidity over time for the 12 centers that have been Network members since 1991. The 12 centers represent 95% of the 1995 to 1996 cohort.

RESULTS

Forty-two percent of mothers were married, an increase from 35% in our previous report.⁴ Ten percent of mothers were < 18 years old (center range: 4%–16%) and 12% were > 35 years old (center range: 6%–22%). Forty-six percent of mothers were black (3%–81%), 36% were white, and 15% were Hispanic. Nine percent of mothers had no prenatal care.

The prevalences of selected perinatal information are presented in Table 1. Rupture of membranes for ≥ 24 hours preceding delivery occurred in 26% of mothers, while 62% of mothers received antenatal antibiotics. Seventy-one percent of the cohort were exposed to antenatal steroids (range: 49%–95%), an increase from 35% in our previous report.⁴ Forty-

seven percent of the cohort were delivered by vaginal route and 53% were delivered by cesarean section. Multiple births comprised 22% of the study cohort.

Figure 1 presents the logistic estimates of mortality risk for singleton males and females, depicting a decreasing rate of mortality with increasing birth weight and gestational age separately for each gender in the 1995 to 1996 cohort. The limits of the colored area indicate the upper 95th and lower 5th percentiles of birth weight for each gestational age. The curved lines indicate combinations of birth weight and gestational age with the same estimated probability of mortality, ie, 10% to 90%. The gradation of color denotes the change in estimated probability of death: infants of lower gestational age and birth weight who are more likely to die are depicted in red; and infants of higher gestational ages and birth weights who are less likely to die are portrayed in blue. At each gestational age, a lower birth weight carried a higher mortality risk. Large changes in mortality occur for each additional week of gestation and for each 100-g increase in birth weight in the mid and lower gestational age and birth weight ranges. At higher gestational ages, comparable changes in birth weight have relatively smaller impacts on mortality risk. Mortality rates were greater for males than for females when infants of similar gestational ages and birth weights were compared. For example, a 24-week 700-g male had a predicted mortality rate of 51%, whereas a 24-week 700-g female had a predicted mortality rate of 35%.

The birth weight-specific mortality for all inborn infants in 100-g birth weight intervals between 501 and 1500 g is shown in Fig 2. Mortality rate decreased steadily with increasing birth weight between 501 and 1300 g, with some leveling off between 1301 and 1500 g.

The gestational age-specific mortality for all inborn infants is shown in Fig 3. Mortality decreased steadily through a gestational age of 30 weeks, and

TABLE 1. Perinatal Information for Infants Born in the NICHD Neonatal Research Network Between January 1, 1995 and December 31, 1996*

Perinatal Data	501 to 750 Grams $n = 1002$	751 to 1000 Grams $n = 1084$	1001 to 1250 Grams $n = 1053$	1251 to 1500 Grams $n = 1299$	501 to 1500 Grams $n = 4438$
Antenatal steroids	63 (30–92)	76 (52–100)	74 (54–94)	70 (53–93)	71 (49–95)
Antenatal antibiotics	62 (49–82)	65 (54–85)	60 (45–88)	61 (44–79)	62 (52–84)
ROM† > 24 h	27 (17–35)	30 (22–44)	23 (5–30)	24 (13–35)	26 (17–33)
Multiple births	21 (10–36)	19 (10–50)	21 (10–33)	25 (14–50)	22 (13–42)
Small for gestational age‡	16 (11–12)	17 (11–29)	24 (16–41)	29 (17–36)	22 (19–29)
Mode of delivery					
Vaginal vertex	36 (15–45)	34 (23–47)	39 (28–50)	47 (40–55)	40 (31–46)
Vaginal breech	20 (0–35)	6 (0–13)	1 (0–4)	3 (0–6)	7 (1–10)
Cesarean section	44 (27–69)	60 (49–72)	60 (46–72)	50 (43–60)	53 (45–64)
Delivery room resuscitation					
Endotracheal intubation	82 (51–96)	79 (43–97)	54 (19–86)	32 (4–59)	60 (30–79)
Resuscitation medications	15 (2–31)	8 (1–21)	5 (0–17)	3 (0–17)	7 (2–18)
Apgar ≤ 3 at 1 min	57 (29–71)	33 (20–44)	21 (8–28)	13 (2–30)	30 (15–43)
Apgar ≤ 3 at 5 min	27 (0–49)	7 (3–15)	4 (0–11)	3 (0–5)	10 (1–13)

ROM indicates rupture of membranes.

* Data expressed as percent with center ranges in parentheses.

† Time between rupture of membranes and delivery.

‡ Small for gestational age as weight < 10 th percentile at birth.

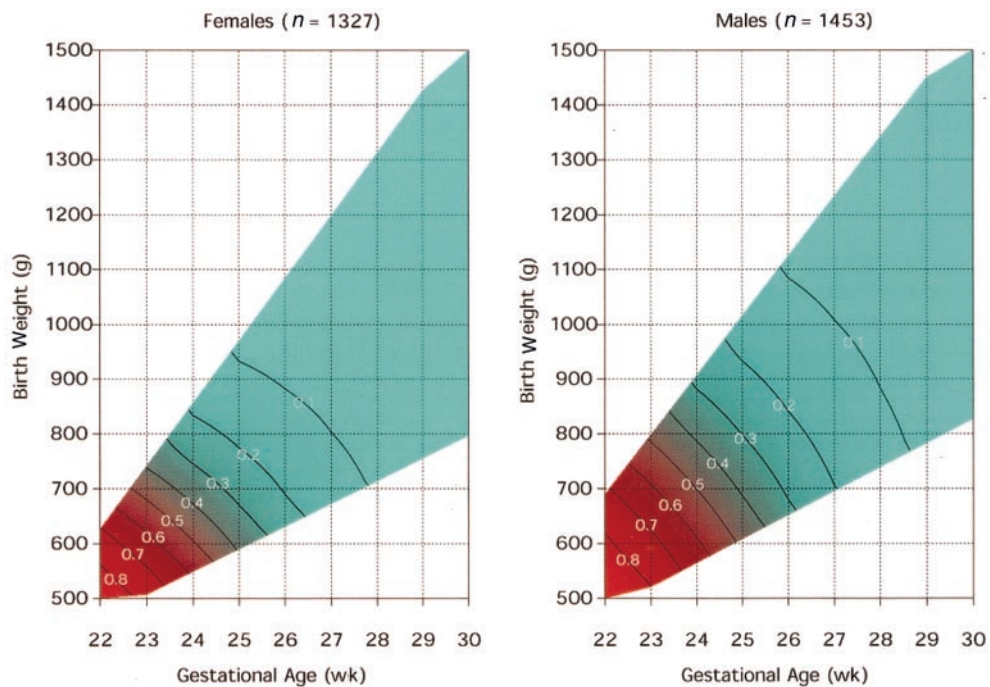


Fig 1. Estimated mortality risk by birth weight and gestational age based on singleton infants born in NICHD Neonatal Research Network Centers between January 1, 1995 and December 31, 1996.

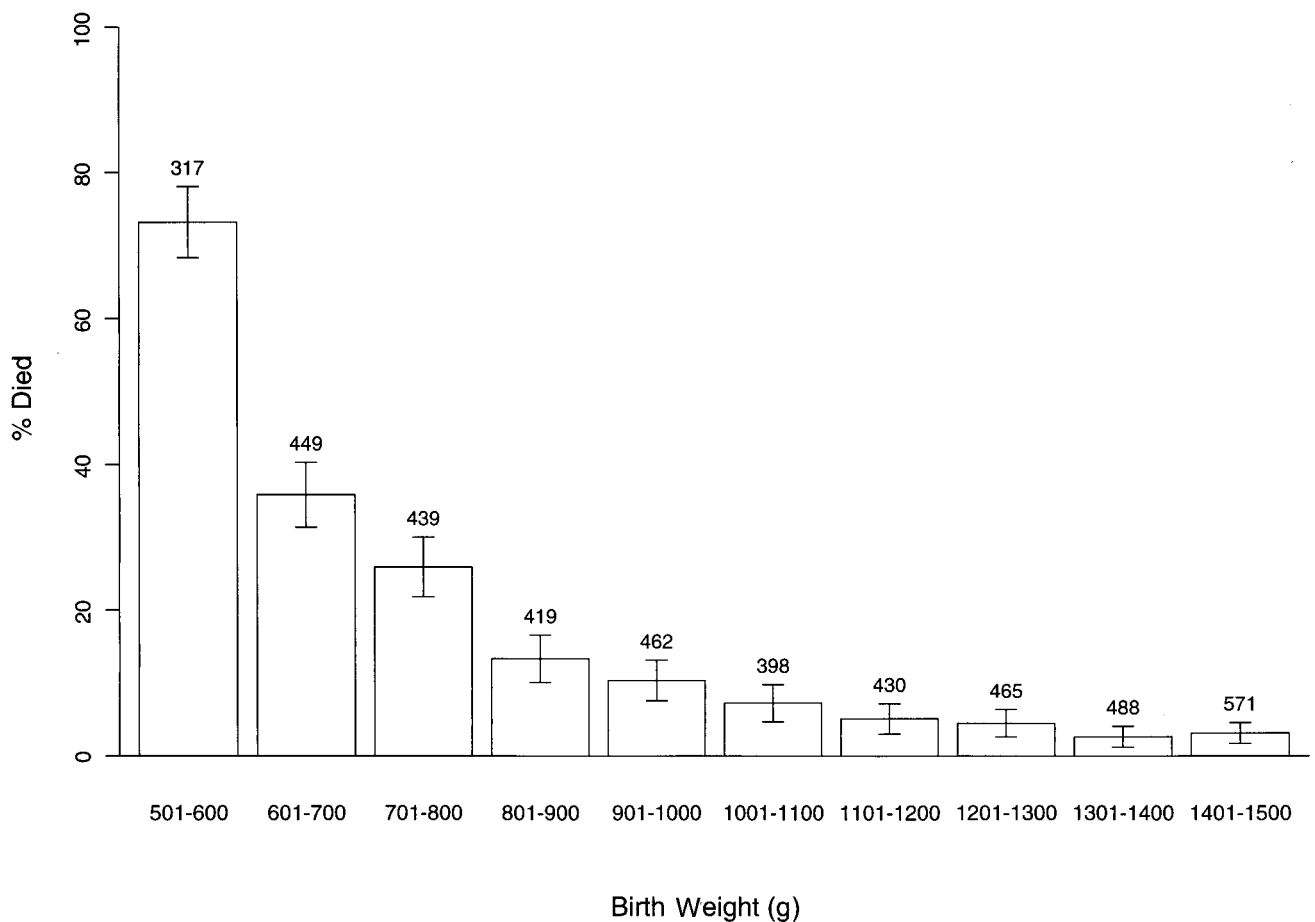


Fig 2. Mortality before discharge by birth weight among infants born in NICHD Neonatal Research Network Centers between January 1, 1995 and December 31, 1996. Data expressed as percentage died and 95% confidence intervals for each 100-g birth weight interval.

then rose slightly for infants between 31 and 42 weeks. The increase in mortality apparent at later

gestational ages reflects the greater incidence of growth restriction and congenital malformations in

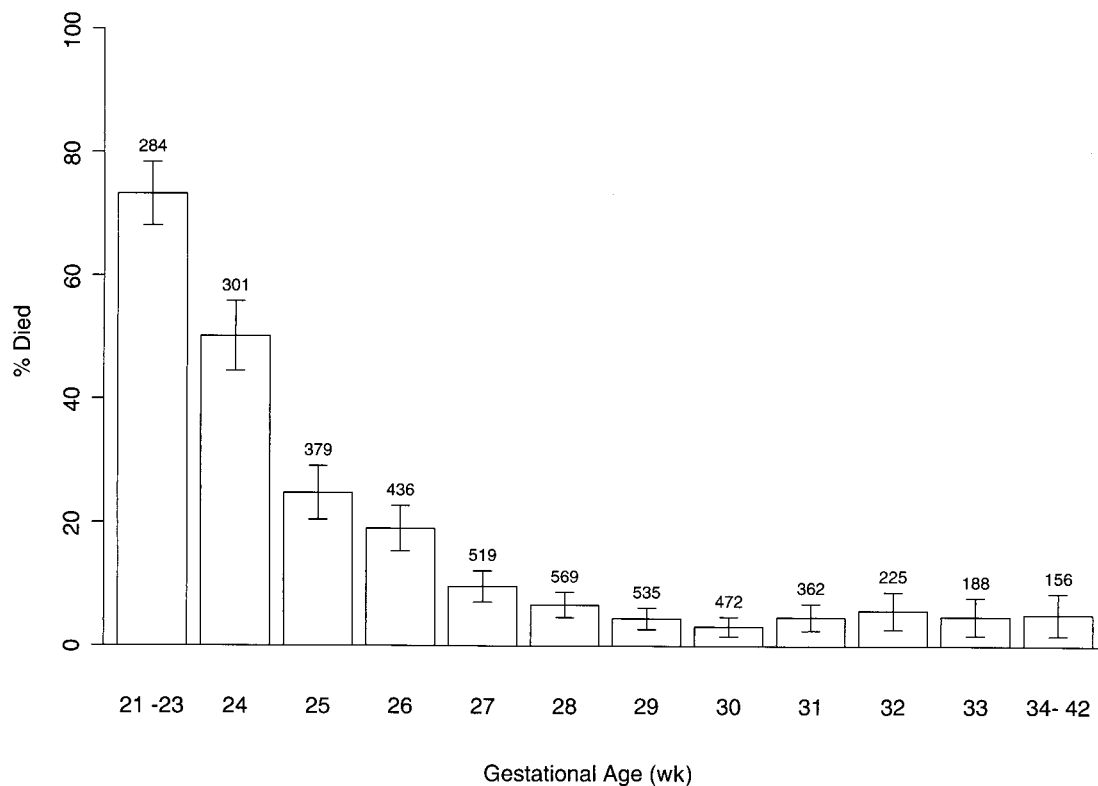


Fig 3. Mortality before discharge by gestational age as estimated by best obstetrical estimate among infants born in NICHD Neonatal Research Network Centers between January 1, 1995 and December 31, 1996. Data expressed as percentage died and 95% confidence intervals for each gestational age group.

this group, which by protocol could not exceed 1500 g at birth. At the lowest gestational ages, there were 12 infants at 21 weeks with 100% mortality, 56 infants at 22 weeks with 79% mortality, and 216 infants at 23 weeks with 70% mortality.

The length of stay and incidences of selected morbidities for the VLBW population are presented in Table 2. Of the 4438 VLBW infants, 84% survived until transfer or discharge to home. The average length of hospitalization for survivors was 68 days and was inversely related to birth weight. The average length of stay for surviving infants 501 to 750 g was 116 days, compared with an average length of stay of 40 days for surviving infants 1251 to 1500 g. Among infants who died, the average length of stay was 18 days. For infants 501 to 750 g who died, the length of stay was 16 days; for those who received mechanical ventilation and died, length of stay was 21 days. Fifty-seven percent of deaths occurred in the first 3 postnatal days.

Respiratory distress syndrome was the most frequent acute pulmonary disease (50% of all VLBW infants), diagnosed in 78% of infants 501 to 750 g and 26% of infants 1251 to 1500 g. Fifty-two percent of the cohort were treated with surfactant therapy. Postnatal corticosteroids were given to 23% of VLBW infants, ranging from 53% of infants 501 to 750 g to only 2% of infants 1251 to 1500 g. CLD affected 23% of all infants (center range: 3%–43%). CLD was diagnosed in 52% of infants 501 to 750 g and 7% of infants 1251 to 1500 g. Four hundred thirty-eight infants (10%) were discharged to home receiving supplemental oxygen.

Poor in-hospital growth was the most frequent morbidity seen in the VLBW population. Using the reference fetal growth curve described by Alexander et al,⁶ growth restriction at birth (<10th percentile for gestational age) was present in 22% of the cohort. Growth restriction was evident in 16% of infants 501 to 750 g, 17% of infants 751 to 1000 g, 23% of infants 1001 to 1250 g, and 29% of infants 1251 to 1500 g. Poor in-hospital growth, defined as weight <10th percentile for anticipated weights at 36 weeks postmenstrual age, was present in 97% of the VLBW infants. Poor in-hospital growth occurred in 100% of infants born at 501 to 750 g, 98% of infants born at 751 to 1000 g, 97% of infants born at 1001 to 1250 g, and 95% of infants born at 1251 to 1500 g.

Cranial sonograms were obtained in 89% of the infants. Thirty percent of these infants had intracranial hemorrhage (ICH), and 11% were diagnosed as severe ICH (grade III or IV⁷). Of infants 501 to 750 g who had cranial ultrasonography, severe ICH was present in 26%, compared with 3% of infants 1251 to 1500 g. Among VLBW infants who had cranial ultrasonography after 2 weeks (69%), periventricular leukomalacia was noted in 5%.

The diagnosis of patent ductus arteriosus (PDA) was made in 30% of infants. Among those with a diagnosis of PDA, indomethacin was administered to 75% (center range: 44%–85%) and surgical closure was performed in 15% (range: 0%–27%).

The incidences of both late-onset sepsis and necrotizing enterocolitis (NEC) were inversely related to birth weight. Late-onset sepsis occurred in 24% of the cohort; it was diagnosed in 48% of infants weighing

TABLE 2. Morbidity and Length of Stay for Infants Born in the NICHD Neonatal Research Network Between January 1, 1995 and December 31, 1996*

	501 to 750 Grams <i>n</i> = 1002	751 to 1000 Grams <i>n</i> = 1084	1001 to 1250 Grams <i>n</i> = 1053	1251 to 1500 Grams <i>n</i> = 1299	501 to 1500 Grams <i>n</i> = 4438
Morbidity (%)					
Respiratory distress syndrome	78 (54–97)	63 (23–81)	44 (23–63)	26 (9–45)	50 (27–66)
Surfactant therapy	70 (40–96)	68 (48–94)	47 (31–64)	28 (19–41)	52 (40–63)
Oxygen at 28 d	81 (64–92)	59 (33–74)	25 (4–40)	7 (2–28)	36 (25–44)
Postnatal steroids	29 (6–46)	29 (4–61)	14 (2–33)	6 (0–23)	19 (3–35)
CLD†	52 (8–86)	34 (4–69)	15 (2–35)	7 (0–23)	23 (3–43)
Growth failure‡	100 (92–100)	98 (90–100)	97 (83–100)	95 (90–36)	97 (93–100)
Discharged home on oxygen	34 (5–65)	22 (4–62)	10 (0–30)	4 (0–21)	15 (2–36)
Discharged home on monitors	40 (10–95)	32 (5–91)	23 (2–69)	17 (2–45)	26 (7–70)
Sonogram performed (%)§	77 (50–100)	95 (91–100)	95 (81–100)	88 (75–99)	89 (80–97)
Grade I	12 (0–26)	15 (3–32)	15 (7–34)	14 (7–30)	14 (7–30)
Grade II	10 (0–19)	7 (1–18)	4 (0–13)	3 (0–11)	5 (2–13)
Grade III	13 (6–29)	6 (3–15)	5 (0–13)	2 (0–5)	6 (3–13)
Grade IV	13 (3–26)	6 (0–14)	3 (0–10)	1 (0–3)	5 (2–11)
Sonogram after 2 wk	86 (65–100)	80 (54–98)	68 (40–96)	51 (19–81)	69 (46–91)
Periventricular leukomalacia	7 (2–30)	7 (0–18)	4 (0–11)	3 (0–10)	5 (2–13)
NEC ≥stage II	14 (9–38)	9 (3–22)	5 (0–8)	3 (0–9)	7 (4–13)
Late septicemia	48 (30–64)	33 (16–51)	18 (6–39)	7 (0–17)	24 (12–38)
PDA	51 (19–76)	39 (13–73)	25 (8–55)	13 (0–31)	30 (10–54)
Indomethacin for PDA	79 (33–91)	76 (50–93)	70 (40–86)	65 (22–82)	75 (44–85)
Surgery for PDA	23 (0–42)	17 (0–38)	8 (0–26)	4 (0–17)	15 (0–27)
Length of stay (mean d)					
Survivors	116 (97–138)	86 (66–108)	58 (46–70)	40 (34–49)	68 (58–82)
Deaths	16 (7–39)	24 (8–59)	17 (2–59)	24 (1–87)	18 (10–36)
Deaths + intensive care¶	21 (9–43)	25 (7–58)	18 (1–115)	27 (1–86)	22 (11–41)
Mortality					
By d 3	26 (8–55)	6 (0–11)	3 (0–9)	2 (0–4)	8 (3–14)
By d 7	30 (8–57)	7 (0–11)	4 (0–10)	2 (0–7)	10 (3–15)
By d 14	35 (17–64)	8 (3–14)	5 (0–12)	2 (0–7)	12 (5–17)
By d 28	40 (21–67)	11 (7–20)	5 (2–12)	3 (0–7)	14 (7–20)

* Data expressed as percent affected among all VLBW births with center ranges in parentheses.

† CLD as 2 at 36 weeks' postmenstrual age.

‡ Growth failure as weight <10th percentile at 36 weeks' postmenstrual age.

§ Most severe grade⁷ in infants who had an ultrasound (*n* = 3941).

|| Of infants who had an ultrasound after 2 weeks of age (*n* = 2597).

¶ Infants who received mechanical ventilation.

501 to 750 g, but in only 7% of those infants weighing 1251 to 1500 g at birth. Of infants with late-onset sepsis, 60% had blood cultures positive for coagulase-negative staphylococcus (center range: 6%–88%). The incidence of NEC (Bell's stage: ≥II)⁸ was 7% (range: 4%–13%). It occurred in 14% of infants weighing 501 to 750 g versus 3% of infants weighing 1251 to 1500 g.

Percent survival with and without selected neonatal morbidity is shown in Table 3. Survival to dis-

charge was 54% at birth weights of 501 to 750 g, 86% at 751 to 1000 g, 94% at 1001 to 1250 g, and 97% at 1251 to 1500 g. The incidence of major morbidity was greater among surviving infants in the 501- to 750-g group, with 63% of these infants experiencing one or more major morbidity (CLD, severe ICH, and/or proven NEC). In contrast, 42% of the 751- to 1000-g group, 23% of the 1001- to 1250-g group, and 10% of the 1251- to 1500-g group had major morbidity.

TABLE 3. Birth Weight-Specific Survival and Selected Neonatal Morbidity Among Survivors Born in the NICHD Neonatal Research Network Between January 1, 1995 and December 31, 1996*

	501 to 750 Grams <i>n</i> = 1002	751 to 1000 Grams <i>n</i> = 1084	1001 to 1250 Grams <i>n</i> = 1053	1251 to 1500 Grams <i>n</i> = 1299	501 to 1500 Grams <i>n</i> = 4438
Survivors	540 (53.9)	935 (86.3)	992 (94.2)	1257 (96.8)	3724 (83.9)
Survived without morbidity	199 (36.9)	540 (57.8)	766 (77.2)	1132 (90.1)	2637 (70.8)
Survived with morbidity	341 (63.1)	395 (42.2)	226 (22.8)	125 (9.9)	1087 (29.2)
CLD†	189 (35.0)	245 (26.2)	121 (12.2)	71 (5.6)	626 (16.8)
Severe ICH‡	33 (6.1)	47 (5.0)	46 (4.6)	22 (1.8)	148 (4.0)
NEC§	22 (4.1)	30 (3.2)	32 (3.2)	23 (1.8)	107 (2.9)
CLD/severe ICH	56 (10.4)	39 (4.2)	19 (1.9)	6 (0.5)	120 (3.2)
CLD/NEC	25 (4.6)	26 (2.8)	6 (0.6)	3 (0.2)	60 (1.6)
NEC/severe ICH	9 (1.7)	5 (0.5)	2 (0.2)	0 (0.0)	16 (0.4)
CLD/severe ICH/NEC	7 (1.3)	3 (0.3)	0 (0.0)	0 (0.0)	10 (0.3)

* Data expressed as number of infants with percentages in parentheses.

† CLD as 2 at 36 weeks' postmenstrual age.

‡ Grade III to IV ICH.

§ NEC (Bell's classification stage ≥2).

Mortality and selected morbidities were analyzed for 195 infants weighing 401 to 500 g born at the 14 centers. Of the 11% who survived to 36 weeks or to discharge, 86% had CLD. Cranial ultrasound was performed in only 30% of the cohort, with one half of these (or 15% of the entire group) demonstrating grade III/IV ICH (most likely a significant underestimation of the true incidence). NEC was documented in 15% of the 401- to 500-g cohort.

There were 317 infants who weighed 501 to 600 g at birth with a 29% survival rate; 62% had CLD. Cranial ultrasound was performed in 53% of this cohort and severe ICH was documented in 35% of the entire cohort. NEC was again documented in 15%.

Mortality and selected morbidities among VLBW infants were compared for the years 1991 and 1996 for the 12 centers that were Network participants during both years. Mortality for the entire cohort decreased from 20.2% in 1991 to 17.0% in 1996. Figure 4A plots birth weight and percent mortality by 250-g birth weight groups. For the lowest birth weight group, mortality decreased from 59.3% in 1991 to 48.0% in 1996, a relative decline of 19%. For infants whose birth weights were 751 to 1000 g, mortality decreased from 19.1% to 14.6%, a relative decline of 24%. Among the 1001- to 1250-g group, mortality decreased from 7.7% to 6.0%, a relative decline of 16%; among the heaviest group (1251–1500 g), mortality decreased from 4.2% to 3.5%, a relative decline of 16%.

Figure 4B depicts the incidence of major morbidity among all VLBW infants (surviving and nonsurviving infants) cared for at the 12 centers by 250-g birth weight groups. Associated with the decline in mortality, there was an increase in major morbidity over the 6-year interval (27% in 1991 and 30% in 1996), because of an increase in the incidence of CLD.

Figure 4C presents the data for major morbidity among surviving infants during the 2 periods. There was an increase in major morbidities among survivors in the VLBW cohort as a whole. This was primarily attributable to an increase in CLD in all survivors from 19% in 1991 to 23% in 1996. The largest increase occurred in infants 501 to 750 g, from 41% in 1991 to 56% in 1996. No change in severe ICH or NEC was apparent (8.4% and 4.5%, respectively).

DISCUSSION

This report summarizes the mortality and morbidity among VLBW infants born at the 14 NICHD Neonatal Research Network Centers in 1995–1996. During these years, 84% of inborn VLBW infants survived to discharge, ranging from 11% of infants weighing 401 to 500 g at birth, to 52% of infants weighing 501 to 750 g at birth, to 97% of infants weighing 1250 to 1500 g at birth.

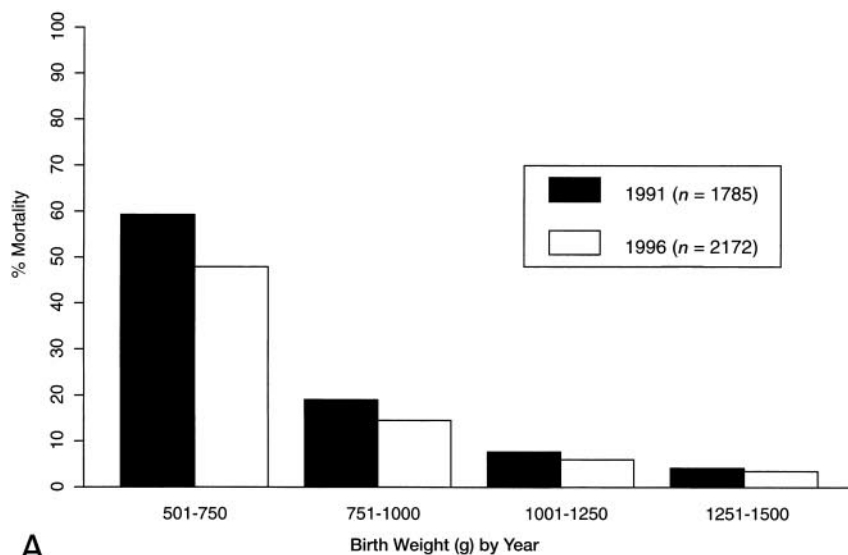
Among all VLBW infants cared for at network centers in 1996 compared with 1991, mortality decreased, especially for infants weighing <1000 g at birth. Respiratory distress syndrome remained the most common acute pulmonary disease, although there was a relative decrease of nearly 20% in the frequency of the diagnosis, compared with the 1991

cohort. We propose that a marked increase in antenatal steroid use from ~20% in 1991 to 71% in 1996 may, in part, explain the reduced mortality and lower incidence of respiratory distress syndrome. Further, there was no change in the incidence of severe ICH or proven NEC. Other changes in practice may also have had an effect on outcomes, including increased surfactant use (1991, 46% and 1996, 52%).

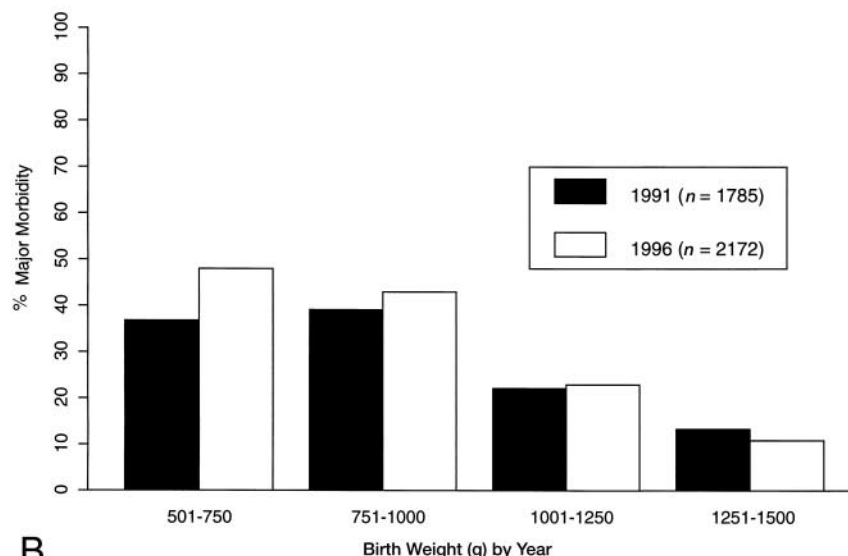
Although survival rates improved, the incidence of most major morbidities remained unchanged. However, the incidence of CLD increased from 19% in 1991 to 23% in 1996 (19%), despite a change in the Network's method of gestational age assessment that would have expected to decrease the frequency of diagnosis of CLD. Before 1995, the estimate of 36 weeks' postmenstrual age (used in the definition of CLD) was based on the Ballard estimate of gestational age at birth. For this report, the definition of CLD used a gestational age based on the best obstetric estimate. The Network recently completed a comparative study of gestational assessment determined by best obstetric estimate and Ballard in infants 24 ≤ 27 weeks of gestational age.^{9,10} The results indicated that the Ballard consistently estimates a higher gestational age (by ~10 days) at birth than does the best obstetric estimate. Therefore, using best obstetric estimate of gestational age would result in the cohort reaching 36 weeks' postmenstrual age ~10 days later than when postmenstrual age was based on the Ballard. This would be expected to result in a lower percentage of infants remaining on oxygen at 36 weeks, thereby decreasing the frequency of diagnosis of CLD. The fact that the incidence increased may reflect, in part, the improved survival rate of the VLBW infants, particularly those weighing <1000 g. In contrast, it may simply reflect changing practice and the more liberal use of supplemental oxygen in a population of poorly growing VLBW infants.

Another major morbidity in the VLBW population is poor postnatal growth. In 1996 growth failure, defined as weight less than the 10th percentile expected at 36 weeks' postmenstrual age, was present in 99% of infants who weighed ≤1000 g at birth (similar to 98% in 1991). Growth curves constructed from 1660 infants with gestational age <30 weeks who were cared for within the Neonatal Research Network Centers have previously confirmed poor in-hospital growth.¹¹ Optimizing nutritional support of the VLBW infant remains a difficult challenge, in part, because of the severity of illness and extreme organ immaturity encountered in this population. However, lack of current information and different attitudes toward nutritional management of these small infants may also contribute to the problem of poor growth. Additional research regarding new strategies for providing better parenteral and enteral nutrition is needed.

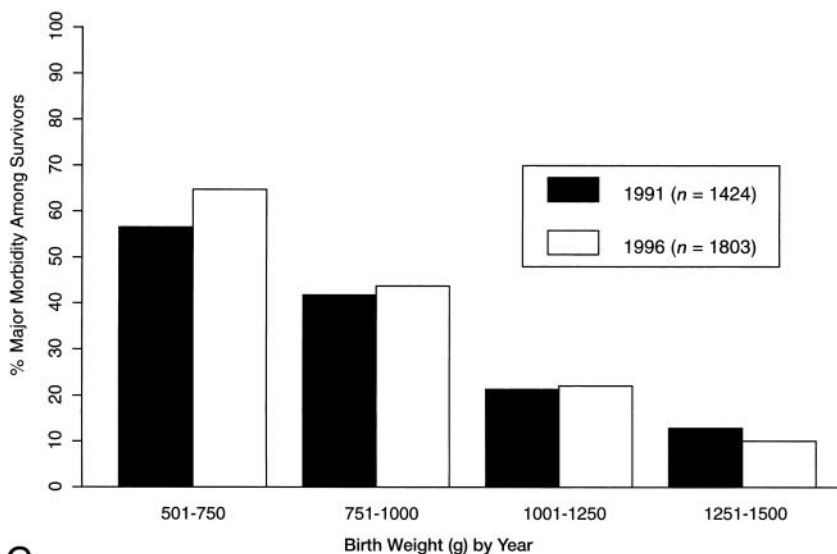
Mortality and morbidity for the smallest infants remain high: only 11% of infants weighing 401 to 500 g at birth survived to discharge, compared with 29% of infants weighing 501 to 600 g at birth. Of infants weighing 401 to 500 g, 60% were not resuscitated in the delivery room; 33% of infants weighing



A



B



C

Fig 4. A, Mortality in VLBW infants cared for in NICHD Neonatal Research Network Centers ($n = 12$) in 1991 and 1996 by 250-g birth weight intervals. B, Major morbidity for all VLBW infants cared for in NICHD Neonatal Research Network Centers ($n = 12$) in 1991 and 1996 by 250-g birth weight intervals, including severe ICH, CLD, and proven NEC. C, Major morbidity among VLBW survivors cared for in the NICHD Neonatal Research Network ($n = 12$) in 1991 and 1996 by 250-g birth weight intervals, including severe ICH, CLD, and proven NEC.

501 to 600 g were not resuscitated. Furthermore, it is important to note that mortality risk at the lowest

birth weights and gestational ages (Fig 1) is dramatically influenced by gender and intrauterine growth

rate.^{3,4,12} For example, a birth weight of 600 g is associated with a mortality risk ranging from ~85% for a 22-week male to 35% for a 25-week female. Similarly, at 23 weeks of gestation, mortality risk ranges from ~80% for a 520-g male to 40% for a 740-g female.

Infants with birth weights between 401 and 1500 g continue to contribute disproportionately to perinatal mortality and morbidity despite accounting for ~1.5% of deliveries. For the current VLBW cohort, we speculate that the increased use of antenatal corticosteroids and surfactant has played an important role in the improvement in survival, compared with the 1991 cohort. However, the high incidence of poor growth remains of major concern and requires additional investigation.

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*Principal Investigator.

REFERENCES

1. Hack M, Horbar JD, Malloy MH, et al. Very low birth weight outcomes of the National Institute of Child Health and Human Developmental Neonatal Network. *Pediatrics*. 1991;87:587-597
2. Hack M, Wright LL, Shankaran S, et al. Very-low-birth-weight outcomes of the National Institute of Child Health and Human Developmental Neonatal Network, November 1989 to October 1990. *Am J Obstet Gynecol*. 1995;172:457-464
3. Fanaroff A, Wright L, Stevenson D, et al. Very-low-birth-weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, May 1991 through December 1992. *Am J Obstet Gynecol*. 1995;173:1423-1431
4. Stevenson D, Wright L, Lemons J, et al. Very-low-birth-weight (VLBW) outcomes of the NICHD Neonatal Research Network, January 1993 through December 1994. *Am J Obstet Gynecol*. 1998;179:1632-1639
5. Walker SH, Duncan DB. Estimation of the probability of an event as a function of several independent variables. *Biometrika*. 1967;54:167-179
6. Alexander GR, Himes JH, Kaufman RB, et al. A United States national reference for fetal growth. *Am J Obstet Gynecol*. 1996;87:163-168
7. Papile L, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1500. *J Pediatr*. 1978;92:529-534
8. Walsh MC, Kliegman RM. Necrotizing enterocolitis: treatment based on staging criteria. *Pediatr Clin North Am*. 1986;33:179-201
9. Donovan EF, Tyson JE, Ehrenkranz RA, et al. Inaccuracy of Ballard scores before 28 weeks' gestation. *J Pediatr*. 1999;135:147-152
10. Ballard JL, Khoury JC, Wedig K, et al. New Ballard score: expanded to include extremely premature infants. *J Pediatr*. 1991;119:417-423
11. Ehrenkranz RA, Younes N, Lemons JA, et al. Longitudinal growth of hospitalized very low birth weight infants. *Pediatrics*. 1999;104:280-289
12. Tyson JE, Younes N, Verter J, Wright LL. Viability, morbidity and resource use among newborns of 501-800 g birth weight. *JAMA*. 1996; 276:1645-1651

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