Published in final edited form as:

Early Hum Dev. 2016 April ; 95: 5–8. doi:10.1016/j.earlhumdev.2016.01.015.

Improved Survival and Neurodevelopmental Outcomes Among Extremely Premature Infants Born Near the Limit of Viability

Noelle Younge, MD^a, P. Brian Smith, MD, MPH, MHS^a, Kathryn E. Gustafson, PhD^a, William Malcolm, MD^a, Patricia Ashley, MD, PhD^a, C. Michael Cotten, MD, MHS^a, Ronald N. Goldberg, MD^a, and Ricki F. Goldstein, MD^a

^a

Abstract

Background—Infants born near the limit of viability are at high risk for death or adverse neurodevelopmental outcomes. It is unclear whether these outcomes have improved over the past 15 years.

Aim—Determine if death and neurodevelopmental impairment have declined over the past 15 years in infants born at 22 to 24 weeks' gestation.

Study Design—Retrospective cohort study

Subjects—We identified infants born at 22 to 24 weeks' gestation in our center in two epochs: 1998–2004 (Epoch 1) and 2005–2011 (Epoch 2).

Outcome Measures—The primary outcome, death or neurodevelopmental impairment, was evaluated at 17–25 months' corrected gestational age with neurologic exams and Bayley Scales of Infant Development. Perinatal characteristics, major morbidities, and outcomes were compared between epochs.

Results—Birth weight and gestational age were similar between 170 infants in Epoch 1 and 187 infants in Epoch 2. Mortality was significantly lower in Epoch 2, 55% vs. 42% ($p=0.02$). Among surviving infants, late-onset sepsis ($p<0.01$), bronchopulmonary dysplasia ($p<0.01$), and surgical necrotizing enterocolitis ($p=0.04$) were less common in Epoch 2. Neurodevelopmental impairment among surviving infants declined from 68% in Epoch 1 to 47% in Epoch 2, $p=0.02$. Odds of death or NDI were significantly lower in Epoch 2 vs. Epoch 1, OR=0.31 (95% confidence interval; 0.16, 0.58).

Conclusion—Risk of death or neurodevelopmental impairment decreased over time in infants born at 22 to 24 weeks' gestation.

Address correspondence to Noelle Younge, MD, 2424 Erwin Road, Suite 504, Durham, NC 27710, Noelle.Younge@duke.edu, Phone (919) 681-6024, Fax (919) 681-6065.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflicts of interest:

The authors have no relevant conflicts of interest to disclose.

Keywords

extremely premature infants; mortality; neurodevelopmental outcomes

---

Introduction

Infants born near the limit of viability are at high risk for death or adverse neurodevelopmental outcomes [1–5]. Recent evidence suggests that survival has improved in this population over the past 20 years [5, 6], but there is little evidence that neurodevelopmental outcomes of surviving infants have changed. Two multicenter studies by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network reported that neurodevelopmental outcomes did not improve over consecutive birth epochs in infants born 22–24 weeks' gestation between 1993 and 2004 [1, 4]. The most recent of these studies reported death in 67.6% of these infants in 2002–2004, and neurodevelopmental impairment (NDI) in 58.7% of survivors [4]. A recent study from Japan's Neonatal Research Network described better than previously reported outcomes in this group, with death or NDI seen in 80.0% of infants born at 22 weeks' gestation, 63.7% at 23 weeks' gestation, and 38.9% at 24 weeks' gestation [7]. Current knowledge of outcomes for infants born at these early gestational ages is critical for clinicians and families when making early obstetrical and neonatal care decisions [8].

The objective of this study was to compare death and early childhood neurodevelopmental outcomes for infants born <25 weeks' gestation in our center between two recent birth epochs.

Methods

Study Population

We identified all infants born 22 0/7 – 24 6/7 weeks' gestation that were admitted to the Neonatal Intensive Care Unit at Duke University Medical Center from January 1, 1998 to December 31, 2011. Infants admitted from an outside hospital at >48 hours of age were excluded. The study period was divided into two epochs. Epoch 1 included infants born from 1998 to 2004 and Epoch 2 included infants born from 2005 to 2011. Epoch 1 was chosen to overlap with the most recent NICHD Neonatal Research Network study showing no improvement in neurodevelopmental outcomes over time in this population, and Epoch 2 includes the years since this study [4]. Our study was approved by the Duke Institutional Review Board.

Measures

Inpatient charts were reviewed to determine perinatal characteristics and neonatal morbidities. Antenatal steroid use was defined as any steroid exposure in the current pregnancy to accelerate fetal lung maturity. Severe intraventricular hemorrhage (IVH) was defined as unilateral or bilateral grade 3 or 4 hemorrhage [9]. Severe retinopathy of prematurity (ROP) was defined as stage 3 or 4 disease requiring laser therapy. Sepsis was defined as 1 positive blood culture requiring antibiotic treatment. Sepsis was classified as

early-onset if occurring in the first three days of life or late-onset sepsis if occurring after 72 postnatal hours. Necrotizing enterocolitis (NEC) was defined by modified Bell's staging criteria, stage IIA or greater [10]. Bronchopulmonary dysplasia (BPD) was defined by the need for supplemental oxygen at 36 weeks' postmenstrual age. Receipt of postnatal dexamethasone for prevention or treatment of BPD was also noted.

After discharge, infants were followed in the Duke Special Infant Care Clinic. Neurodevelopmental outcomes were assessed at 17–25 months' corrected gestational age (GA) with neurologic examinations performed by a physician trained in neurodevelopmental assessments and Bayley Scales of Infant Development performed by a licensed clinical psychologist. The Bayley II was used from 1998 to 2007 and the Bayley III was used from 2008 to 2011 [11, 12]. Data for infants who received follow-up care at outside clinics or outside of the 17–25 months' corrected GA window were not included in the analysis. Death included in-hospital deaths as well as deaths that occurred from the time of discharge to the follow-up period. Neurodevelopmental impairment (NDI) was defined as any of the following: moderate or severe cerebral palsy (CP), significant cognitive impairment [Mental Developmental Index <70 (Bayley II) or cognitive composite score <85 (Bayley III)], significant motor impairment [Psychomotor Developmental Index <70 (Bayley II) or motor composite score <70 (Bayley III)], or bilateral blindness. We used the higher cognitive composite cut-off score of <85 on the Bayley III for comparison with the Bayley II Mental Developmental Index of <70 to improve consistency based on previous studies showing that the Bayley III overestimates cognitive performance relative to the Bayley II [13–16]. CP was defined as a static neurologic disorder characterized by abnormal muscle tone affecting at least one extremity and interfering with motor function. Those with moderate or severe CP required assistive device(s) for ambulation or were non-ambulatory at the time of follow-up.

Statistical Methods

Our primary outcome was death or NDI, as defined above. Secondary outcomes included death alone and each component of NDI alone in surviving infants who were seen in follow-up. Outcomes, including in-hospital outcomes such as severe IVH and severe ROP, were compared between groups using Fisher's exact test for categorical variables and Wilcoxon ranksum test for continuous data. We also compared outcomes across epochs for subgroups of infants born at 23 weeks and 24 weeks of gestation. We did not include the 22 week infants as a separate subgroup given the low number of survivors at this gestational age. Risk of death or NDI by epoch was compared using logistic regression to control for GA at birth.

For all tests, significance was defined as $P < 0.05$. Statistical analysis was performed using Stata version 12 (College Station, TX).

Results

During the study period, a total of 357 infants were born at 22–24 weeks' gestation. Of these infants, 170 (48%) were born in Epoch 1 and 187 (52%) were born in Epoch 2. Epoch 1 and 2 infants did not differ significantly in birth weight, GA, inborn status, gender, multiple

gestations, or receipt of antenatal steroids (Table 1). The proportion of infants born by Cesarean delivery was higher in Epoch 2. Among surviving infants, incidence of severe IVH, periventricular leukomalacia, post-hemorrhagic hydrocephalus requiring ventricular shunt, severe ROP, medical NEC, early-onset sepsis, and PDA requiring surgical ligation was similar between Epochs. Incidence of BPD and use of postnatal dexamethasone were significantly lower in Epoch 2. Surgical NEC and late-onset sepsis were also less common among infants born in Epoch 2.

Data on the primary outcome was available for 140/170 (82%) of infants in Epoch 1 and 166/187 (89%) of infants in Epoch 2, $p=0.10$. Post-discharge follow-up among surviving infants was 75% across the entire study period. Follow-up was significantly higher in Epoch 2, with 49 infants (64% of survivors) in Epoch 1 and 91 infants (83% of survivors) in Epoch 2 having follow-up at 17–25 months' corrected GA, $p<0.01$. Infants with and without follow-up had similar median (range) birth weight [647.5 (410–916) g versus 640 (450–900) g, $p=0.60$] and birth GA [24 (22–24) versus 24 (22–24) weeks, $p=0.15$]. The proportion of infants with severe IVH was greater among infants with follow-up than those lost to follow-up [35/140 (25%) versus 3/46 (7%), $p<0.01$]. Incidence of other major morbidities was similar between infants with and without follow-up, including periventricular leukomalacia, posthemorrhagic hydrocephalus requiring ventricular shunt, severe ROP, PDA ligation, NEC, sepsis, and BPD (data not shown). Of the infants with follow-up data, corrected GA at the time of follow-up was higher in Epoch 1, with a median (range) of 20 (17–25) months in Epoch 1 versus 19 (17–25) months in Epoch 2, $p=0.03$.

Overall, death occurred in 171 of 357 infants (48%). Mortality was significantly lower in Epoch 2 compared to Epoch 1 (Table 2). The primary outcome, the composite of death or NDI, was also lower in Epoch 2. NDI among surviving infants decreased in Epoch 2. Odds of death or NDI, adjusted for birth GA, were significantly lower in Epoch 2, OR=0.31 (95% CI; 0.16, 0.58). Incidence of the components of NDI, moderate or severe CP, significant cognitive impairment, significant motor impairment, and blindness, was similar between Epochs. When divided by birth GA, risk of death or NDI was lower in Epoch 2 among infants born at 24 weeks' gestation, but did not change significantly in infants born at 23 weeks' gestation (Table 2). For infants born at 23 weeks' gestation, neither death alone nor NDI among survivors changed significantly. Among the 24 week infants, risk of death alone did not change significantly, but NDI among survivors decreased. Blindness decreased among the 24 week infants, while there was no significant change in other individual components of NDI.

Discussion

In our center, survival of infants born 22–24 weeks' GA has improved over the past 15 years. In fact, we observed decreased mortality as well as decreased NDI among survivors. When the cohort was divided by birth GA, we saw a decrease in NDI in infants born at 24 weeks' gestation, but no improvement in outcomes among the infants born at 23 weeks' gestation. While these results are limited by the small number of surviving infants born at 23 weeks' gestation in our cohort, it suggests that the trend in improved outcomes seen in the 24 week infants did not extend to the less mature infants.

The factors underlying the improved outcomes in our study are unclear, but there are a number of possible contributing factors. The increased proportion of Cesarean deliveries in Epoch 2 suggests a more proactive perinatal care approach, which has been associated with better outcomes at these early gestational ages [18]. Lower proportions of infants in Epoch 2 had late-onset sepsis, surgical NEC, receipt of dexamethasone, and BPD, each of which has been associated with adverse neurologic outcomes [19–24]. There were a number of quality improvement efforts and practice changes in our unit over the study period that may have contributed to the improved outcomes. In 2001, we introduced an educational campaign to prevent lung injury and established written guidelines to promote a consistent approach to caring for extremely premature infants. In 2007, we initiated an infection control program that resulted in a significant reduction in bloodstream infections [25]. In 2008, we began using donor breast milk in place of preterm formula when mother's milk was unavailable. In 2010, we introduced the use of early oropharyngeal colostrum in extremely low birth weight infants [26].

Our study did not include data on the number of infants in each epoch in whom delivery room resuscitation was not attempted. While our results may be reflective of changes in these practices over time, our general approach to delivery room resuscitation at the limits of viability did not change over the study period. We do not routinely attempt resuscitation in the delivery room for infants born <23 0/7ths weeks' gestation. The majority of infants born 23–24 weeks' gestation are resuscitated, except when a decision has been made in conjunction with the infant's family to not attempt resuscitation or when other poor prognostic factors are present, such as congenital anomalies or extremely small size (<400 g birth weight). Resuscitation is often limited for infants who do not respond to intubation and positive pressure ventilation. This practice has also not changed over the study period.

Our results are contrary to previous multicenter studies of extremely premature infants showing no improvement in neurodevelopmental outcomes over time [1, 4]. One potential explanation for this divergence is the single-center nature of our study. Previous studies have shown that regional and center differences are significant determinants of outcome [27–29]. Center differences in outcomes are most pronounced in the least mature infants [28, 30]. In multicenter studies, improving outcomes in certain centers may be offset by other centers that have stable or worsening outcomes. Exploration of factors associated with improving outcomes at individual centers, including demographic factors, perinatal and neonatal care practices, and approach to extremely premature infants is critical.

One limitation of our study was the number of infants lost to follow-up, with a greater number and percentage of infants receiving follow-up care in Epoch 2. Previous studies have shown that infants who are seen in follow-up may have different outcomes than those who are lost to follow-up [17, 31]. In our study, infants with and without follow-up were similar in terms of baseline characteristics and major morbidities, with the exception that severe IVH was more common among infants with follow-up. Nonetheless, we found that neurodevelopmental outcomes improved as follow-up rates improved in Epoch 2, supporting our conclusion of improved outcomes over time.

Another limitation of our study was the use of different versions of the Bayley over the study period. Previous studies have shown that compared with the Bayley II, the Bayley III overestimates cognitive performance, raising caution about making direct comparisons between the two versions of the test [13–16, 32]. An MDI<70, which is two standard deviations below the mean on the Bayley II, correlates more closely with a cognitive composite score of 80–85 on the Bayley III, or one standard deviation below the mean [13–15]. To address this limitation, we raised the cut-off for significant cognitive impairment to the more conservative cut-off cognitive composite score of <85 on the Bayley III.

Conclusions

In our center, the incidence of death or NDI decreased over time in infants born 22–24 weeks' gestation. In particular, NDI significantly decreased in infants born at 24 weeks' gestation. While these results are encouraging, the rates of death or NDI remain very high and clinicians should continue to counsel parents of the significant risks at these early gestational ages. Further research is needed to identify and implement practices associated with improving outcomes in this vulnerable population.

Acknowledgments

Dr. Younge received support from National Institutes of Health (5T32HD043728-10). Dr. Smith received support from the National Institutes of Health and the National Center for Advancing Translational Sciences (HHSN267200700051C, HHSN275201000003I and UL1TR001117); he also receives research support from industry for neonatal and pediatric drug development (www.dcri.duke.edu/research/coi.jsp). Dr. Cotten received support from National Institutes of Health (5U10 HD040492-10).

Abbreviations

BPD	Bronchopulmonary dysplasia
CP	Cerebral palsy
GA	Gestational age
IVH	Intraventricular hemorrhage
NEC	Necrotizing enterocolitis
NDI	Neurodevelopmental impairment
PDA	Patent ductus arteriosus
ROP	Retinopathy of prematurity

References

1. Hintz SR, Kendrick DE, Vohr BR, Poole WK, Higgins RD. Changes in neurodevelopmental outcomes at 18 to 22 months' corrected age among infants of less than 25 weeks' gestational age born in 1993–1999. *Pediatrics*. 2005; 115:1645–1651. [PubMed: 15930228]
2. Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. *Pediatrics*. 2010; 126:443–456. [PubMed: 20732945]

3. Mercier CE, Dunn MS, Ferrelli KR, Howard DB, Soll RF. Neurodevelopmental outcome of extremely low birth weight infants from the Vermont Oxford network: 1998–2003. *Neonatology*. 2010; 97:329–338. [PubMed: 19940516]
4. Hintz SR, Kendrick DE, Wilson-Costello DE, Das A, Bell EF, Vohr BR, et al. Early-childhood neurodevelopmental outcomes are not improving for infants born at <25 weeks' gestational age. *Pediatrics*. 2011; 127:62–70. [PubMed: 21187312]
5. Stoll BJ, Hansen NI, Bell EF, Walsh MC, Carlo WA, Shankaran S, et al. Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993–2012. *JAMA*. 2015; 314:1039–1051. [PubMed: 26348753]
6. Patel RM, Kandefer S, Walsh MC, Bell EF, Carlo WA, Laptook AR, et al. Causes and timing of death in extremely premature infants from 2000 through 2011. *N Engl J Med*. 2015; 372:331–340. [PubMed: 25607427]
7. Ishii N, Kono Y, Yonemoto N, Kusuda S, Fujimura M. Outcomes of infants born at 22 and 23 weeks' gestation. *Pediatrics*. 2013; 132:62–71. [PubMed: 23733804]
8. Raju TN, Mercer BM, Burchfield DJ, Joseph GF. Periviable birth: executive summary of a Joint Workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Academy of Pediatrics, and American College of Obstetricians and Gynecologists. *J Perinatol*. 2014; 34:333–342. [PubMed: 24722647]
9. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. *J Pediatr*. 1978; 92:529–534. [PubMed: 305471]
10. Walsh MC, Kliegman RM. Necrotizing enterocolitis: treatment based on staging criteria. *Pediatr Clin North Am*. 1986; 33:179–201. [PubMed: 3081865]
11. Bayley, N. Bayley Scales of Infant Development. San Antonio, TX: The Psychological Corporation; 1993.
12. Bayley, N. Bayley Scales of Infant Development. San Antonio, TX: The Psychological Corporation; 2006.
13. Vohr BR, Stephens BE, Higgins RD, Bann CM, Hintz SR, Das A, et al. Are outcomes of extremely preterm infants improving? Impact of Bayley assessment on outcomes. *J Pediatr*. 2012; 161:222 e3–228 e3. [PubMed: 22421261]
14. Moore T, Johnson S, Haider S, Hennessy E, Marlow N. Relationship between test scores using the second and third editions of the Bayley Scales in extremely preterm children. *J Pediatr*. 2012; 160:553–558. [PubMed: 22048046]
15. Jary S, Whitelaw A, Walloe L, Thoresen M. Comparison of Bayley-2 and Bayley-3 scores at 18 months in term infants following neonatal encephalopathy and therapeutic hypothermia. *Dev Med Child Neurol*. 2013
16. Anderson PJ, De Luca CR, Hutchinson E, Roberts G, Doyle LW. Underestimation of developmental delay by the new Bayley-III Scale. *Arch Pediatr Adolesc Med*. 2010; 164:352–356. [PubMed: 20368488]
17. Guillen U, DeMauro S, Ma L, Zupancic J, Roberts R, Schmidt B, et al. Relationship between attrition and neurodevelopmental impairment rates in extremely preterm infants at 18 to 24 months: a systematic review. *Arch Pediatr Adolesc Med*. 2012; 166:178–184. [PubMed: 22312176]
18. Serenius F, Blennow M, Marsal K, Sjors G, Kallen K. Intensity of perinatal care for extremely preterm infants: outcomes at 2.5 years. *Pediatrics*. 2015; 135:e1163–e1172. [PubMed: 25896833]
19. Short EJ, Klein NK, Lewis BA, Fulton S, Eisengart S, Kercsmar C, et al. Cognitive and academic consequences of bronchopulmonary dysplasia and very low birth weight: 8-year-old outcomes. *Pediatrics*. 2003; 112:e359. [PubMed: 14595077]
20. Jeng SF, Hsu CH, Tsao PN, Chou HC, Lee WT, Kao HA, et al. Bronchopulmonary dysplasia predicts adverse developmental and clinical outcomes in very-low-birthweight infants. *Dev Med Child Neurol*. 2008; 50:51–57. [PubMed: 18173631]

21. Natarajan G, Pappas A, Shankaran S, Kendrick DE, Das A, Higgins RD, et al. Outcomes of extremely low birth weight infants with bronchopulmonary dysplasia: impact of the physiologic definition. *Early Hum Dev.* 2012; 88:509–515. [PubMed: 22236557]
22. Stoll BJ, Hansen NI, Adams-Chapman I, Fanaroff AA, Hintz SR, Vohr B, et al. Neurodevelopmental and growth impairment among extremely low-birth-weight infants with neonatal infection. *JAMA.* 2004; 292:2357–2365. [PubMed: 15547163]
23. Yeh TF, Lin YJ, Lin HC, Huang CC, Hsieh WS, Lin CH, et al. Outcomes at school age after postnatal dexamethasone therapy for lung disease of prematurity. *N Engl J Med.* 2004; 350:1304–1313. [PubMed: 15044641]
24. Wadhawan R, Oh W, Hintz SR, Blakely ML, Das A, Bell EF, et al. Neurodevelopmental outcomes of extremely low birth weight infants with spontaneous intestinal perforation or surgical necrotizing enterocolitis. *J Perinatol.* 2014; 34:64–70. [PubMed: 24135709]
25. Neill S, Haithcock S, Smith PB, Goldberg R, Bidegain M, Tanaka D, et al. Sustained Reduction in Bloodstream Infections in Infants at a Large Tertiary Care Neonatal Intensive Care Unit. *Adv Neonatal Care.* 2015
26. Seigel JK, Smith PB, Ashley PL, Cotten CM, Herbert CC, King BA, et al. Early administration of oropharyngeal colostrum to extremely low birth weight infants. *Breastfeed Med.* 2013; 8:491–495. [PubMed: 23805944]
27. Vohr BR, Wright LL, Dusick AM, Perritt R, Poole WK, Tyson JE, et al. Center differences and outcomes of extremely low birth weight infants. *Pediatrics.* 2004; 113:781–789. [PubMed: 15060228]
28. Lee SK, McMillan DD, Ohlsson A, Pendray M, Synnes A, Whyte R, et al. Variations in practice and outcomes in the Canadian NICU network: 1996–1997. *Pediatrics.* 2000; 106:1070–1079. [PubMed: 11061777]
29. Serenius F, Sjors G, Blennow M, Fellman V, Holmstrom G, Marsal K, et al. EXPRESS study shows significant regional differences in 1-year outcome of extremely preterm infants in Sweden. *Acta Paediatr.* 2014; 103:27–37. [PubMed: 24053771]
30. Rysavy MA, Li L, Bell EF, Das A, Hintz SR, Stoll BJ, et al. Between-hospital variation in treatment and outcomes in extremely preterm infants. *N Engl J Med.* 2015; 372:1801–1811. [PubMed: 25946279]
31. Castro L, Yolton K, Haberman B, Roberto N, Hansen NI, Ambalavanan N, et al. Bias in reported neurodevelopmental outcomes among extremely low birth weight survivors. *Pediatrics.* 2004; 114:404–410. [PubMed: 15286223]
32. Serenius F, Kallen K, Blennow M, Ewald U, Fellman V, Holmstrom G, et al. Neurodevelopmental outcome in extremely preterm infants at 2.5 years after active perinatal care in Sweden. *JAMA.* 2013; 309:1810–1820. [PubMed: 23632725]

Highlights

- Death or neurodevelopmental impairment among surviving infants decreased among infants born 22 to 24 weeks' gestational age from 1998–2011.
- Incidence of several major morbidities, including late-onset sepsis, surgical necrotizing enterocolitis, and bronchopulmonary dysplasia also declined.

Table 1

Perinatal Characteristics and In-Hospital Morbidities

	Epoch 1 (n=170)	Epoch 2 (n=187)	P
Baseline characteristics			
Birth weight (g), median (range)	600 (350–916)	620 (330–904)	0.05
Birth gestational age, %			0.69
22 weeks	3	2	
23 weeks	36	35	
24 weeks	61	63	
Inborn, %	88	82	0.14
Male, %	55	55	>0.99
Multiple birth, %	28	27	0.91
Cesarean delivery, %	38	49	0.04
Antenatal steroid use, %	83	84	0.87
In-hospital morbidities and treatments*			
Severe IVH, %	18	22	0.58
PVL, %	9	9	>0.99
Shunt for hydrocephalus, %	5	2	0.23
Severe ROP, %	36	35	0.88
Medical NEC, %	17	9	0.17
Surgical NEC, %	16	6	0.04
Early-onset sepsis, %	1	4	0.41
Late-onset sepsis, %	75	55	<0.01
PDA ligation, %	34	39	0.54
Postnatal dexamethasone, %	55	17	<0.01
BPD, %	79	39	<0.01

* Percentages calculated from the number of infants who survived.

IVH, Intraventricular Hemorrhage; PVL, Periventricular Leukomalacia; ROP, Retinopathy of Prematurity; NEC, Necrotizing Enterocolitis; PDA, Patent Ductus Arteriosus; BPD, Bronchopulmonary Dysplasia

Table 2

Death and Neurodevelopmental Outcomes at 17–25 months' Corrected Gestational Age

	22–24 weeks			23 weeks			24 weeks		
	Epoch 1 (n=170)	Epoch 2 (n=187)	P	Epoch h 1 (n=61)	Epoch h 2 (n=66)	P	Epoch h 1 (n=104)	Epoch h 2 (n=118)	P
Death, n (%)	93/170 (55)	78/187 (42)	0.02	43/61 (70)	39/66 (59)	0.20	46/104 (44)	38/118 (32)	0.07
Death or NDI, n (%) *	125/140 (89)	119/166 (72)	<0.01	52/57 (91)	53/61 (87)	0.56	69/79 (87)	63/102 (62)	<0.01
NDI, n (%) *	32/47 (68)	41/88 (47)	0.02	9/14 (64)	14/22 (64)	>0.99	23/33 (70)	25/64 (39)	<0.01
Moderate/Severe CP, n (%) *	8/49 (16)	17/91 (19)	0.82	1/15 (7)	3/23 (13)	>0.99	7/34 (21)	12/66 (18)	0.79
Motor impairment, n (%) *	17/44 (39)	29/85 (34)	0.70	4/13 (31)	8/21 (38)	0.73	13/31 (42)	21/64 (33)	0.49
Cognitive impairment, n (%) *	24/43 (56)	33/89 (37)	0.06	7/13 (54)	9/22 (41)	0.50	17/30 (57)	23/66 (35)	0.07
Blindness, n (%) *	4/49 (8)	3/91 (3)	0.24	1/15 (7)	2/23 (9)	>0.99	3/34 (9)	0/66 (0)	0.04

* Percentages calculated from the number of infants who survived and had the corresponding follow-up assessment.

NDI, Neurodevelopmental Impairment; CP, Cerebral Palsy