

Are Neurodevelopmental Outcomes of Infants Born Extremely Preterm Improving Over Time?

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Accurate data on rates of mortality and of neurodevelopmental impairment (NDI) in survivors are critical in decision-making for infants born at 22 to 24 weeks' gestation, the borderline of viability. Despite many studies reporting on mortality and NDI rates, it is concerning that health care professionals continue to overestimate rates of mortality and NDI of infants at the borderline of viability.¹ Because survival rates may have plateaued in recent years,² there is an increasing emphasis on their rates of NDI.

In the current issue of *Pediatrics*, Adams-Chapman et al³ from the Neonatal Research Network (NRN) hypothesized that NDI in children born at <27 completed weeks' gestation would decrease over a 3.75-year period beginning in 2011. The authors reported on neurodevelopmental outcomes at 18 to 26 months' corrected age for 2113 children who had been born and cared for in an NRN center and who were involved in the NRN's follow-up study. NDI comprised any of the following: gross motor impairment as defined by using a Gross Motor Function Classification System⁴ of level 2 or more; a Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III)⁵ cognitive or motor score <70; bilateral blindness; or hearing impairment. The rate of NDI did not change substantially over time, although there was a reduction in the number of children with severe cerebral palsy (Gross Motor Function Classification System level 4 or 5).

There was an increase in the number of infants who survived free of NDI over time; however, complete denominators and numerators for this outcome were not reported.

To determine if rates of survival free of NDI have indeed changed over time, it would be important to know how many live births there were and from what location they were derived to ensure that there were no changes in referral patterns that might be related to different rates of survival or NDI. It would also help to ensure that the proportions of children offered intensive care were similar, that survivors were followed long enough to be certain of any diagnoses made, that the rate of follow-up was high enough to avoid underestimating the rate of NDI,⁶ and that the outcomes being assessed were clinically important, clinically valid, and determined without knowledge of any antecedent events. The latter is best achieved by having contemporaneous control groups of children born at term, with assessors blinded to knowledge of the child's group status.

Of the components of NDI as defined by many investigators, including Adams-Chapman et al,³ the biggest contributor in early childhood is developmental delay; in older children, it is intellectual impairment. Motor impairment, usually caused by cerebral palsy, is next most frequent, whereas substantial hearing and visual impairment are uncommon. Consequently, the assessment of developmental delay or intellectual

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impairment is critical to estimating rates of NDI. In early childhood, the Bayley-III has been the most common assessment tool, which is evident because of its use in multiple publications over the past decade. However, the Bayley-III overestimates developmental performance of many children,⁷ and it is not strongly predictive of later intellectual impairment⁸; the latter problem is only marginally improved by using contemporaneous controls rather than the test manual to identify cut points for delay.⁸

In the study by Adams-Chapman et al,³ because the NRN is large, the sample size of children born at <27 weeks' gestation accumulated rapidly, but the 3.75-year time frame may not have been long enough to detect any real shift in rates of NDI. An alternative would have been to compare rates of NDI in NRN cohorts born in earlier eras. However, switching between different versions of the Bayley Scales makes comparison across eras difficult, particularly in the absence of a normal birth weight or term-born control group whose data could be

used to determine secular trends and compare results.

The age of 18 to 26 months may be too early to be sure if rates of NDI are changing over time. Moreover, many additional cognitive functions important in learning and schooling, such as attention, memory, and executive function, are all better assessed in older children. In a cohort study of all survivors born in 2005 in the state of Victoria at <28 weeks' gestational age, cognitive outcomes at 2 years of age compared with the cognitive outcomes of survivors born in earlier eras seemed to be improving, with fewer children with low developmental scores on the Bayley-III, even after allowing for secular trends by using controls as the basis for comparisons over time.² However, when the children were reassessed at 8 years of age, not only were their IQ scores no better than in survivors born extremely preterm from earlier eras, but their executive function⁹ and their academic performance¹⁰ were worse than in children born extremely preterm in earlier eras.

A definitive answer on whether rates of NDI are improving will need to wait until other cohorts of children born extremely preterm in more recent eras are assessed at school age and are compared with earlier cohorts. Ideally, cognition would be assessed with the same measure; however, with a drift upward in cognitive scores over time, different versions or different tests must sometimes be used. Under such circumstances, it is important to know what is happening to cognitive scores in the general population over the same time, which is best achieved by simultaneously assessing appropriately selected control groups, and where the assessors are blinded to knowledge of group assignment.

ABBREVIATIONS

Bayley-III: Bayley Scales of Infant and Toddler Development, Third Edition

NDI: neurodevelopmental impairment

NRN: Neonatal Research Network

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REFERENCES

1. Boland RA, Davis PG, Dawson JA, Doyle LW. What are we telling the parents of extremely preterm babies? *Aust N Z J Obstet Gynaecol.* 2016;56(3):274–281
2. Doyle LW, Roberts G, Anderson PJ; Victorian Infant Collaborative Study Group. Outcomes at age 2 years of infants < 28 weeks' gestational age born in Victoria in 2005. *J Pediatr.* 2010;156(1):49–53.e1
3. Adams-Chapman I, Heyne RJ, deMauro SB, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Neurodevelopmental impairment among extremely preterm infants in the Neonatal Research Network. *Pediatrics.* 2018;141(5):e20173091
4. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev Med Child Neurol.* 1997;39(4):214–223
5. Bayley N. *Bayley Scales of Infant and Toddler Development.* 3rd ed. San Antonio, TX: Harcourt Assessment Inc; 2006
6. Doyle LW, Anderson PJ, Burnett A, et al. Developmental disability at school age and difficulty obtaining follow-up data. *Pediatrics.* 2018;141(2):e20173102
7. Anderson PJ, De Luca CR, Hutchinson E, Roberts G, Doyle LW; Victorian Infant Collaborative Group. Underestimation of developmental delay by the new Bayley-III Scale. *Arch Pediatr Adolesc Med.* 2010;164(4):352–356
8. Spencer-Smith MM, Spittle AJ, Lee KJ, Doyle LW, Anderson PJ. Bayley-III cognitive and language scales in preterm children. *Pediatrics.* 2015;135(5).

Available at: www.pediatrics.org/cgi/content/full/135/5/e1258

9. Burnett AC, Anderson PJ, Lee KJ, et al. Trends in executive functioning in extremely

preterm children across 3 birth eras. *Pediatrics*. 2017;141(1):e20171958

10. Cheong JLY, Anderson PJ, Burnett AC, et al; Victorian Infant

Collaborative Study Group. Changing neurodevelopment at 8 years in children born extremely preterm since the 1990s. *Pediatrics*. 2017;139(6):e20164086

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