Changing Neurodevelopment at 8 Years in Children Born Extremely Preterm Since the 1990s

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abstract

BACKGROUND AND OBJECTIVE: Survival of extremely preterm (EP; <28 weeks' gestation) infants has increased over the last 2 decades. Equivalent reductions in developmental morbidity in early childhood have not been consistently reported. The aim of this study was to determine trends in neurodevelopmental outcomes at 8 years of age of children born EP (22–27 completed weeks' gestation) over the past 2 decades.

METHODS: Population-based cohorts of all EP survivors born in the state of Victoria, Australia in 1991–1992, 1997, and 2005 were recruited at birth. At 8 years of age, general intelligence (IQ), academic achievement, and neurosensory status were assessed. Major neurosensory disability was defined as any of moderate or severe cerebral palsy, IQ <−2 SD relative to term controls, blindness, or deafness.

RESULTS: Rates of major neurosensory disability were similar in all eras (1991–1992, 18%; 1997, 15%; 2005, 18%), as were rates of IQ <−2 SD, cerebral palsy, blindness, and deafness. Mean *z* scores for IQ were similar across eras, but there was some evidence that scores for academic achievement were lower in 2005 than in 1997, and the odds of having academic problems were higher in 2005 than in both earlier eras. These outcomes were not explained by differences in known perinatal care or sociodemographic variables between eras.

CONCLUSIONS: Contrary to expectations, rates of major neurosensory disability have not improved, and academic performance is poorer at early school age in 2005 than in earlier eras for EP children born in the state of Victoria, Australia.

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WHAT'S KNOWN ON THIS SUBJECT: Despite increases in survival of extremely preterm infants (born at <28 weeks' gestation) with advances in perinatal care, there is no convincing evidence of improved neurodevelopment. There are no studies reporting school-age outcomes over successive eras in recent years.

WHAT THIS STUDY ADDS: Despite improvements in survival rates with advances in perinatal and neonatal intensive care, neurosensory disability, IQ, and academic outcomes at school age are not improving in children born extremely preterm; indeed, academic performance may be deteriorating.

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Survival rates of geographic cohorts of extremely preterm (EP; <28 weeks' gestation) live births increased in the 1990s in Australia, a trend mirrored in other developed countries worldwide.[1,2] These trends were temporally related to the introduction of exogenous surfactant to treat respiratory distress syndrome in the early 1990s[3] and an increased willingness to offer intensive care to more infants.[4] Despite better survival rates, improvements in short-term morbidity and neurodevelopmental outcomes have not been consistently reported.[5–8] Current published studies are mostly limited to reporting neurodevelopmental outcomes in the first few years after birth, before important outcomes, such as general intelligence (IQ) or academic achievement, can be properly assessed.[5–8] Few studies have reported school-age outcomes at repeated intervals from survivors born after the early 1990s. In a previous report from our group comparing children born in 1997 with those born in 1991–1992, the high prevalence of adverse neurodevelopmental outcomes in children born EP compared with term controls at school age had not improved.[9]

Changes in the 2000s that might be expected to improve long-term outcomes of EP survivors include the more frequent use of caffeine as treatment for apnea of prematurity, which improves short-term neurologic outcomes,[10] and a reduction in treatment with postnatal corticosteroids, which are associated with adverse neurologic outcomes in survivors.[11] When we compared outcomes at 2 years of age for EP children born in 2005 with those born in the 1990s, their neurodevelopment seemed to have improved.[2] Rates of severe disability at 2 years of age had decreased to 3.7% for births in 2005 from 15.4% for births in 1997 (relative risk 0.24, 95% confidence interval [CI], 0.10 to 0.57, $P < .001$).[2] Because outcome in early childhood is not a strong predictor of later school-age outcomes,[12,13] it is imperative to reevaluate these children at school age.

The aim of this study was to compare neurodevelopmental outcomes at 8 years in a population-based EP cohort born in 2005 with earlier cohorts recruited in the post surfactant era, in 1991–1992 and 1997, in the state of Victoria, Australia. Based on the improvement observed at 2 years of age in the 2005 cohort, it was hypothesized that neurodevelopmental outcome at school age would be better compared with earlier cohorts at 8 years of age.

METHODS

The setting for this study was the state of Victoria, Australia. All 4 tertiary neonatal units in the state have collaborated with government data collection agencies and the statewide transport service since the late 1970s to obtain population-based data on long-term outcomes for the smallest and most immature survivors in the state, initially for those of birth weight <1000 g, and, from the 1990s, also for those born at <28 weeks' gestation.

Participants

The EP cohorts born in 3 distinct eras of recruitment, 1991–1992 (24 months), 1997 (12 months), and 2005 (12 months), have been described previously.[2] To summarize, all EP live births (22–27 completed weeks' gestation) were recruited at birth. Randomly selected term-born, normal birth weight (≥2500 g) control infants were contemporaneously recruited from each of the 3 main maternity services in the state (Royal Women's Hospital, the Mercy Hospital for Women, Monash Medical Centre) and matched with EP survivors for expected date of birth, sex, the mother's health insurance status (private or public, as a proxy for social class), and the main language spoken in her country of birth (English or other). Outcomes at 2 years of age for these cohorts have been reported.[2] In addition, some 8-year neurodevelopmental outcomes for the 1991–1992[9,14] and 1997[9,13,15] cohorts have been reported.

The studies have been approved by the human research ethics committees at the Royal Women's Hospital, the Mercy Hospital for Women, Monash Medical Centre, and the Royal Children's Hospital, Melbourne. Written informed consent was obtained from the parents of all controls and for the EP cohort born in 2005; follow-up was considered routine clinical care for EP children in the earlier cohorts.

Perinatal Data Collection

Perinatal data (Table 1) were collected at the time of recruitment and prospectively during the course of the study. Gestation at birth was confirmed by obstetric ultrasound before 20 weeks, available for >90% of pregnancies, or by menstrual history in the remainder. Birth weight *z* scores were computed relative to the British Growth Reference.[16] Sociodemographic details collected included maternal age, years of maternal education (dichotomized into lower and higher around the median years of schooling for that era), social class (based on the occupation of the major income earner in the family and categorized as lower [unskilled or unemployed] or higher [semiskilled, skilled, or professional]), and the primary language spoken at home (multilingual versus only English).

Outcomes

At 8 years of age, corrected for prematurity, participants were assessed by pediatricians and psychologists who were unaware of

the participants' group membership or clinical details. Age was corrected for prematurity to avoid a known bias in cognitive test scores, evident even at this age.[17] Cerebral palsy was diagnosed in children with abnormal tone and loss of motor function, and its severity was determined by a functional classification (1991–1992 cohort), or the Gross Motor Function Classification Scale (GMFCS) (1997 and 2005 cohorts). Blindness was defined as having visual acuity <20/200 in the better eye, and deafness was defined as a hearing impairment necessitating amplification or a cochlear implant, or worse. Cognitive ability was assessed via the Wechsler Intelligence Scale for Children, Third Edition[18] for the 1991–1992 cohort, the Fourth Edition[19] for the 1997 cohort, and the Differential Ability Scales, Second Edition[20] for the 2005 cohort. The Global Conceptual Ability score of the Differential Ability Scales, Second Edition is highly correlated with the full-scale IQ score of the Wechsler Intelligence Scale for Children, Fourth Edition (correlation coefficient = 0.84).[20] A few children were assessed with alternative tests of general intelligence because they were evaluated according to protocols required by other studies in which they were participants or because the appropriate test was unavailable or could not be administered because of sensory impairment. To standardize the IQ scores from the different assessments that were administered, *z* scores of general intelligence (IQ) were computed relative to the mean scores (SD 15) for the controls for each cohort. Before this calculation, the mean for the controls was weighted to reflect the distribution of maternal education and social class of the EP groups within each era. Children assessed with alternative tests had *z* scores assigned according to the mean (SD) of the test manual (usually mean 100, SD 15). Children too impaired to complete the cognitive tests were assigned an IQ *z* score of −4 SD. Major neurosensory disability was defined as any of moderate or severe cerebral palsy (unable to walk, or walking with considerable difficulty, with or without appliances, or GMFCS levels 2–5), blindness, deafness, or an IQ <−2 SD.

TABLE 1 Participant Characteristics of EP Cohorts Contrasted Between Eras

Characteristics	1991–1992	1997	2005
Live births free of lethal anomalies, *n*	428	217	270
Survivors to 8 y, *n* (% live births)	225 (53)	151 (70)	170 (63)
Fully assessed at 8 y, *n* (% survivors)	210 (93)	142 (94)	147 (86)
Corrected[a] age at assessment, y, mean (SD)	8.7 (0.3)	8.4 (0.5)	7.7 (0.4)
Perinatal variables (for those fully assessed)			
Outborn,[b] *n* (%)	18 (9)	7 (5)	19 (13)
Antenatal corticosteroids, *n* (%)	149 (71)	126 (89)	125 (85)
Preeclampsia, *n* (%)	25 (12)	16/141 (11)	16 (11)
Multiple birth, *n* (%)	69 (33)	29 (20)	35 (24)
Cesarean delivery, *n* (%)	56 (27)	76 (54)	83 (56)
Gestational age at birth, wks, mean (SD)	25.8 (1.1)	25.6 (1.2)	25.8 (1.2)
Birth weight, g, mean (SD)	887 (175)	820 (173)	867 (193)
Birth weight, *z* score, mean (SD)	−0.28 (0.87)	−0.53 (0.79)	−0.31 (0.84)
Male, *n* (%)	104 (50)	79 (56)	72 (49)
Exogenous surfactant, *n* (%)	88 (42)	120 (85)	127 (86)
Patent ductus arteriosus, *n* (%)	126 (60)	75 (53)	113 (77)
Grade 3 or 4 intraventricular hemorrhage, *n* (%)	17 (8)	5 (4)	13 (9)
Cystic periventricular leukomalacia, *n* (%)	14 (7)	5 (4)	5 (3)
Necrotizing enterocolitis, *n* (%)	15 (7)	8 (6)	16 (11)
Postnatal corticosteroids, *n* (%)	85 (40)	65 (46)	32 (22)
In oxygen at 36 wks postmenstrual age, *n* (%)	98 (47)	59/142 (42)	84 (57)
Surgery in the newborn period, *n* (%)	58 (28)	44 (31)	46 (31)
Social variables (for those fully assessed)			
Mother's age at birth of the child, y, mean (SD)	28.8 (5.7)	29.9 (5.9)	30.6 (5.6)
Lower maternal education, *n* (%)	107/206 (52)	71 (50)	64/144 (44)
Lower social class, *n* (%)	69/206 (33)	37/131 (28)	53 (36)
Multilingual family, *n* (%)	41/208 (20)	31 (22)	22/146 (15)

[a] Corrected for prematurity.

[b] Born outside a tertiary maternity hospital.

Basic academic skills of word reading (single word decoding), spelling, and mathematics were assessed via the relevant subtests from the Wide Range Achievement Test, version 3[21] (1991–1992 and 1997 cohorts) or version 4[22] (2005 cohort). As for IQ, scores from the Wide Range Achievement Test were converted to *z* scores relative to the mean (SD 15) scores for the controls for each cohort, with the mean for the controls weighted to reflect the distribution of social variables of the EP cohorts.

Statistical Analyses

Data were analyzed in Stata version 14.1 (Stata Corp, College Station, TX).[23] To allow for confounding perinatal and sociodemographic variables and for clustering of children of multiple births, data were analyzed with generalized estimating equations. Because there were systematic changes over time in the ages of the mothers and of the children when they were assessed, we included those variables as covariates in all analyses comparing groups. Differences between EP and control groups were also adjusted for social variables (lower maternal education, lower social class, and multilingual households). Within the EP groups alone, differences between eras were adjusted for these social variables, and then for potential confounding perinatal variables (outborn status, antenatal corticosteroids, gestational age at birth, sex, birth weight *z* score, exogenous surfactant, grade 3 or 4 intraventricular hemorrhage, cystic periventricular leukomalacia, postnatal corticosteroids, and

TABLE 2 Cognitive and Academic Outcomes at 8 y for EP and Control Groups

Outcome	1991–1992		1997		2005	
	EP	Control	EP	Control	EP	Control
IQ	94.9 (16.5)	104.7 (14.1)	93.8 (14.7)	105.6 (12.4)	94.7 (15.7)	107.2 (10.9)
	n = 198	*n* = 212	*n* = 133	*n* = 170	*n* = 137	*n* = 189
Mean difference (95% CI)[a]	−9.6 (−12.7 to −6.6)		−11.8 (−14.9 to −8.6)		−12.7 (−15.9 to −9.5)	
Mean difference (95% CI)[b]	−8.0 (−10.9 to −5.1)		−10.5 (−13.8 to −7.1)		−10.2 (−13.3 to −7.1)	
Academic achievement						
Word reading	96.2 (16.4)	103.1 (14.6)	97.1 (16.9)	105.5 (13.8)	94.1 (17.1)	109.4 (14.2)
	n = 200	*n* = 211	*n* = 133	*n* = 168	*n* = 140	*n* = 189
Mean difference (95% CI)[a]	−6.8 (−9.9 to −3.7)		−8.5 (−12.0 to −4.9)		−15.5 (−19.1 to −11.9)	
Mean difference (95% CI)[b]	−5.5 (−8.5 to −2.4)		−8.1 (−11.8 to −4.5)		−12.3 (−16.0 to −8.5)	
Spelling	93.8 (12.9)	99.7 (13.2)	96.4 (16.0)	104.2 (14.5)	93.9 (17.6)	108.6 (15.2)
	n = 199	*n* = 210	*n* = 134	*n* = 168	*n* = 138	*n* = 188
Mean difference (95% CI)[a]	−5.9 (−8.4 to −3.3)		−7.7 (−11.2 to −4.3)		−15.0 (−18.8 to −11.3)	
Mean difference (95% CI)[b]	−4.8 (−7.3 to −2.3)		−7.7 (−11.3 to −4.1)		−12.0 (−15.9 to −8.2)	
Mathematics	88.8 (14.3)	97.9 (13.6)	89.9 (17.5)	99.0 (14.5)	89.4 (18.9)	105.1 (13.4)
	n = 197	*n* = 211	*n* = 131	*n* = 168	*n* = 140	*n* = 188
Mean difference (95% CI)[a]	−9.1 (−11.8 to −6.3)		−9.0 (−12.8 to −5.3)		−16.2 (−20.0 to −12.4)	
Mean difference (95% CI)[b]	−8.3 (−10.9 to −5.6)		−9.1 (−12.9 to −5.3)		−13.1 (−16.9 to −9.2)	

[a] Allowing for clustering for multiple births, age of the child at assessment, and mother's age at birth.
[b] Allowing for clustering for multiple births, age of the child at assessment, and mother's age at birth and adjusted for social variables (multilingual household, lower maternal education, and lower social class).

surgery in the neonatal period). For the multivariable regressions, the 2005 cohort was directly compared with the 1991–1992 and 1997 cohorts. Comparisons are presented primarily as odds ratios (ORs) or mean differences, both with 95% CIs and *P* values.

RESULTS

The numbers of participants in each EP group and their perinatal and sociodemographic characteristics are summarized in Table 1. The proportion of survivors at 8 years of age rose in 1997 compared with 1991–1992 but then fell in 2005. The follow-up rates for all EP cohorts were high. The ages at which children were assessed fell over time. Although outborn births had decreased in 1997 compared with 1991–1992, they more than doubled again in 2005. Antenatal corticosteroids and exogenous surfactant were prescribed more in later cohorts; in contrast, postnatal corticosteroids were used less commonly in 2005 compared with earlier cohorts. Other perinatal events were similar across the 3 eras. Mean maternal age increased by almost 2 years between 1991–1992 and 2005. Other sociodemographic variables were similar between the 3 EP cohorts.

Perinatal characteristics between EP subjects who were assessed and those not assessed at 8 years were similar, except that those assessed were more likely to be from multiple pregnancies (OR 2.44; 95% CI, 1.01 to 5.89) and were less mature at birth (mean difference −0.4 weeks, 95% CI, −0.8 to −0.1) (Supplemental Table 4).

The numbers of controls recruited, who survived to 8 years of age, and who were assessed at that age are shown in Supplemental Table 5. Birth weight and birth weight *z* score increased, and age at 8 years fell over time. Mothers were older, and fewer had lower education and lower social class over time (Supplemental Table 5).

Cognitive and Academic Achievement Scores in EP and Control Groups

As expected, IQ and academic achievement scores were much higher in controls than in EP children in all cohorts (Table 2). Although different versions of the tests were used, mean scores for IQ and academic achievement were similar between the EP cohorts from different eras. In contrast, scores for controls increased over time in all areas, and consequently the gap between the EP children and controls widened over time.

Neurodevelopmental Outcomes Contrasted Between Eras Among EP Cohorts

Major neurosensory disability rates were similar across eras, as were rates of cerebral palsy, blindness, and deafness (Table 3). Mean differences in *z* scores for IQ were not substantially different comparing 2005 with both earlier eras; adjustment for perinatal variables had little effect (Fig 1A). Word reading, spelling, and mathematics scores were all lower in 2005 than in 1997, before and after adjustment for perinatal variable (Fig 1A). The proportions with *z* scores <−2 SD for IQ were similar across eras (Fig 1B). The odds of having problems in word reading, spelling, and mathematics were higher in 2005 than in both earlier eras, although the strength of the evidence was stronger for some comparisons and weaker for others (Fig 1B).

In the multivariable analyses among EP groups from all 3 epochs combined, grade 3 or 4 intraventricular hemorrhage, cystic periventricular leukomalacia, postnatal corticosteroids, and

TABLE 3 Neurodevelopmental Outcomes at 8 y Contrasted Between Eras

Outcome	1991–1992	1997	2005
	n = 210	*n* = 142	*n* = 147
Neurosensory			
Major neurosensory disability,[a] *n* (%)	38 (18)	22 (15)	26 (18)
Any cerebral palsy, *n* (%)	27 (13)	15 (11)	20 (14)
Moderate or severe[b]	13 (6)	9 (6)	11 (7)
Blindness, *n* (%)	2 (1)	3 (2)	0 (0)
Deafness, *n* (%)	3 (1)	3 (2)	5 (3)
IQ *z* score, mean (SD)	−0.70 (1.26)	−0.80 (1.11)	−0.74 (1.22)
IQ *z* score −2 SD to <−1 SD, *n* (%)	39 (19)	47 (33)	29 (20)
IQ *z* score <−2 SD, *n* (%)	30 (14)	14 (10)	20 (14)
Academic achievement			
Word reading *z* score, mean (SD); *n*	−0.39 (1.10); 200	−0.51 (1.12); 132	−0.87 (1.14); 140
<−2 SD, *n* (%)	19 (10)	11 (8)	23 (16)
Spelling *z* score, mean (SD); *n*	−0.34 (0.86); 199	−0.50 (1.07); 134	−0.87 (1.18); 138
<−2 SD, *n* (%)	6 (3)	7 (5)	20 (14)
Mathematics *z* score, mean (SD); *n*	−0.57 (0.96); 197	−0.53 (1.16); 131	−0.94 (1.26); 140
<−2 SD, *n* (%)	12 (6)	13 (10)	32 (23)

Major neurosensory disability; 2005 compared with 1991–1992: OR 0.80, 95% CI, 0.34 to 1.92, $P = .62$; 2005 compared with 1997: OR 0.99, 95% CI, 0.44 to 2.23, $P = .99$. Moderate or severe cerebral palsy; 2005 compared with 1991–1992: OR 1.23, 95% CI, 0.53 to 2.83, $P = .63$; 2005 compared with 1997: OR 1.18, 95% CI, 0.47 to 2.96, $P = .72$. OR and 95% CIs not calculated for blindness or deafness because rates were too low.

[a] Any of moderate or severe cerebral palsy, blindness, deafness, or an IQ *z* score <−2 SD.

[b] Cerebral palsy severity defined by either functional classification (1991–1992 cohort) or the GMFCS (1997 and 2005 cohorts); moderate (walking with considerable difficulty, with or without appliances, GMFCS level 2 or 3), or severe (unable to walk, GMFCS level 4 or 5).

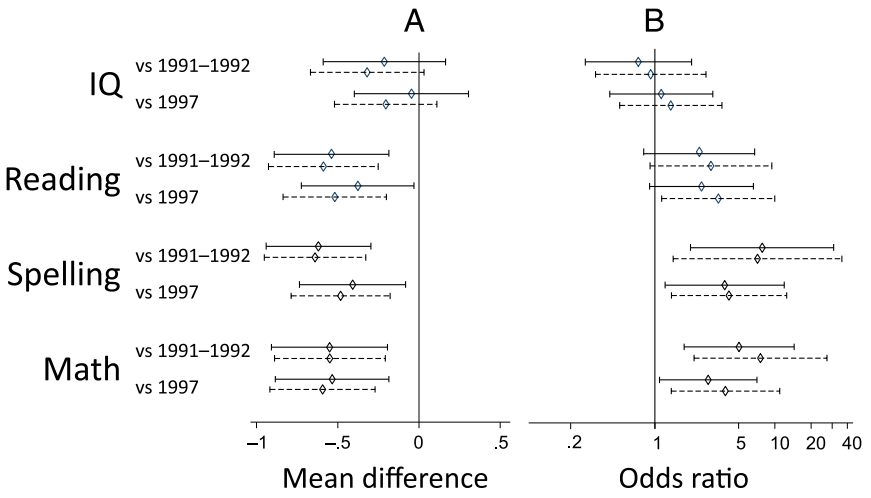

FIGURE 1
Differences on standardized cognitive and academic scores comparing 2005 cohort with both earlier eras. A, Continuous scores. B, Dichotomous scores <−2 SD vs ≥−2 SD. Solid line is adjusted for age at assessment, age of mother, and sociodemographic variables; dashed line is adjusted for age at assessment, age of mother, sociodemographic variables, and perinatal variables.

surgery in the newborn period were adversely associated with most outcomes, as were lower social class and lower maternal education, whereas increasing gestational age and birth weight *z* scores were associated with better outcomes. Age at assessment and mother's age had little effect on most outcomes, except that mother's age was positively related to better academic achievement in all areas.

DISCUSSION

Because rates of severe developmental delay at 2 years of age were lower in 2005 compared with the earlier cohorts,[2] and because cognitive impairment is the most common reason for overall neurosensory disability, we expected rates of cognitive impairment, and hence rates of major disability, in EP survivors at school age to decrease in our geographic cohort born in 2005 compared with earlier cohorts born in 1991–1992 and 1997. However, the results from our study were contrary to expectations. Moreover, academic achievement in EP children was poorer in 2005 compared with earlier eras. The current study highlights the importance of long-term assessment of neurodevelopment, because developmental assessments in early childhood are only moderately predictive of later cognitive outcomes and may provide false reassurance. Of note, developmental delay for the 2005 cohort was assessed via the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III),[24] and there have been reports of significant concerns about assessing cognitive development with this measure.[8,25,26]

We could find no other reports where school-age outcomes have been contrasted in different eras from geographic cohorts of EP children born since the 1990s. However, there is 1 report of outcomes in preschool-age children from geographic cohorts born since the 1990s. Moore et al[27] reported outcomes at 2½ to 3 years of age of 2 EP cohorts born in the United Kingdom, 1 in 1995 and the other in 2006. There were no differences in rates of severe disability for 1995 births (18%) compared with 2006 births (19%). Similar to our study, when our children were 2 years of age they used the Bayley-III at 3 years of age to assess cognitive outcomes for the 2006 cohort. However, developmental assessments other than the Bayley-III, such as the Bayley-II, in early childhood are also only moderately related to cognitive outcome at school age.[12,13] Thus,

we would caution against assuming there are no differences in more important longer-term outcomes in more recent survivors until such cohorts have been reevaluated at school age.

In contrast to evaluations at school age from serial geographically determined cohorts of EP children born since the 1990s, there have been several reports from single EP cohorts at school age. Serenius et al[28] reported outcomes at 6.5 years of children born <27 weeks' gestation in 2004–2007 in Sweden. Using criteria for disability that were similar to those used in our study, they reported rates of major disability of 34%, higher than the 18% rate for the 2005 cohort in our study, possibly because their cohort did not include children born at 27 weeks, who have lower rates of disability than those born at earlier gestations. Overall they had more children with IQ scores <−2 SD (30%) but fewer with cerebral palsy (10%) than in our study. Larroque et al[29] reported rates of cerebral palsy of 15% in a cohort of 5-year-old children born at <28 weeks in France in 1997, similar to the rates of cerebral palsy in our study. The rate of IQ scores <−2 SD was 18% in the children born at <28 weeks in their study, which was higher than the rates in our study. In another study of children born at <26 weeks' gestational age in the United Kingdom in 1995, Marlow et al[30] reported that 15% (35/241) had cerebral palsy at 6 years of age, again similar to the rates in our study. They reported that 41% (98/241) had IQ scores <−2 SD relative to controls, much higher than the rates observed in our cohorts, but their cohort did not include children born at 26 or 27 weeks' gestation. In addition, they did not correct for degree of prematurity, which may have led to lower IQ scores and higher rates of intellectual impairment than if they had corrected for prematurity.[17]

The lack of improvement in rates of neurodevelopmental disability and the poorer academic functioning at 8 years in the 2005 EP cohort compared with earlier cohorts is concerning. Although we adjusted for confounding variables, such as postnatal corticosteroids, intraventricular hemorrhage grade 3 or 4, cystic periventricular leukomalacia, surgery in the newborn period, and sociodemographic variables, known to be associated with adverse outcomes,[31] birth in 2005 remained independently predictive of adverse academic outcomes at 8 years. We would have expected the 2005 cohort to have better neurodevelopment compared with earlier cohorts because of known clinical practice changes. Caffeine, which was unavailable in the 1990s, was frequently prescribed in 2005 and is known to improve some neurodevelopmental outcomes.[10,32] Postnatal corticosteroids, which are associated with adverse neurodevelopment,[33,34] were prescribed less in 2005 than in earlier eras.[11] Variables such as parenting practices and mental health, nutrition, and epigenetics are areas worthy of future research, as are attentional, executive, and behavioral difficulties, to help explain the discrepancy in outcomes over time.

The strengths of our study include the prospective population-based cohorts comprising all births within discrete periods of time, with high follow-up rates at 8 years. Data for comparison were available from contemporaneously recruited term or normal birth weight controls, selected to match well with the EP cohorts on sociodemographic variables, reducing bias arising from comparisons with published normative data that may not truly reflect the norms of the population being studied. The study period encompasses the era when exogenous surfactant was available for clinical use, and thus the results are relevant when counseling families today. Limitations include the use of different assessments for cognitive ability for each cohort, although we have tried to address this limitation by generating standardized IQ scores relative to contemporary term controls. Although we selected controls at birth to be similar on sociodemographic characteristics to the EP group, by the time the groups were assessed at 8 years, the control groups were advantaged on sociodemographic characteristics. To counteract this imbalance we corrected for the sociodemographic variables before calculating *z* scores.

CONCLUSIONS

Previously observed trends of improved survival in early childhood since the early 1990s are reflected at school age as well. However, a similar trend was not observed for neurodevelopmental outcome. This study highlights the need to identify potentially modifiable factors contributing to cognitive and academic impairment in EP survivors and to develop better treatments before, during, and after birth to improve their long-term outcome. Future cohorts of EP children must be recruited and followed until at least school age to ensure there are no other unexpected harms from the continuing evolution of intensive perinatal and neonatal care.

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ABBREVIATIONS

Bayley-III: Bayley Scales of Infant and Toddler Development, Third Edition
CI: confidence interval
EP: extremely preterm
GMFCS: Gross Motor Function Classification Scale
OR: odds ratio

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