Improved outcome into the 1990s for infants weighing 500–999 g at birth

The Victorian Infant Collaborative Study Group*

Abstract

Aims—To compare the survival and sensorineural disability rates in extremely low birthweight (ELBW) (500–999 g) infants born in 1991–2 with ELBW babies born in 1979–80 and 1985–7, and with normal birthweight infants born in the same time periods.

Methods—ELBW infants born in Victoria in 1991–2 were compared with regional cohorts of ELBW infants born in 1979–80 and 1985–7, and with contemporaneous normal birthweight (>2499 g) controls, and those of birthweight 500–749 g with those of birthweight 750–999 g.

Results—In 1979–80, 25.4% (89/351) ELBW live births survived to 2 years of age, increasing significantly to 37.9% (212/560) in 1985–7, and to 56.2% (241/429) in 1991–2. The rates of severe disability in survivors assessed were 12.4%, 6.6%, and 6.8% in the 1979–80, 1985–7, and 1991–2 ELBW cohorts, respectively. The rate of disability, overall, was significantly lower in the 1985–7 and 1991–2 ELBW cohorts compared with the 1979–80 ELBW cohort, but was significantly higher in 1991–2 ELBW infants than normal birthweight controls. Surviving children with birthweights <750 g had significantly higher rates of sensorineural disability compared with those of birthweight 750–999 g in 1979–80, but not in 1985–7 or 1991–2.

Conclusions—Survival rates for ELBW babies in Victoria have progressively improved since the late 1970s. Sensorineural outcome for survivors born in 1985–7 has also improved compared with those born in 1979–80. However, there is no evidence that further reductions in adverse sensorineural outcomes into the 1990s, and these, as well as disabilities remain higher in ELBW than in normal birthweight babies.

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Keywords: extremely low birthweight; survival; disability

Survivals of extremely low birthweight (ELBW; <1000 g) children have risen progressively through the 1970s and 1980s. However, ELBW children have had lower survivals and higher sensorineural disability rates than normal birthweight (>2499 g) children. As treatments such as antenatal steroids¹ and exogenous surfactant,² which randomised controlled trials show, reduce mortality, have been prescribed more frequently,

it is expected that survival rates will increase further in the 1990s. Although individual hospital reports can provide some data to assess the impact of changes in perinatal care on populations, regional studies are essential.

As survival rates improve, the absolute number of surviving ELBW children must increase, so long term sensorineural outcome assumes greater importance. Moreover, the tiniest survivors, with birthweights <750 g, have been reported to have even higher rates of sensorineural disability³ and may contribute disproportionately to the number of disabled children in the community.

Methods

The ELBW children in this study comprised consecutive live births with birthweights 500–999 g born in the state of Victoria in three distinct eras: (a) 1979–80, n=351; (b) 1985–7, n=560; and (c) 1991–2, n=429. Details of the multiple data sources used to determine the number of live births and their survival in infancy have been reported before.⁴ Survival was determined at 2 years of age; no live births were excluded. The outcome at 2 years for the 1979–80 and 1985–7 ELBW cohorts has already been compared.⁵ The normal birthweight controls for the 1991–2 cohort comprised children with birthweights >2499 g born in each of the three level-III perinatal centres (high risk obstetric hospitals with a neonatal intensive care nursery) in Victoria. The controls were randomly selected from births on the day an ELBW child was due to be born, matched for gender, and the mother's health insurance status and country of origin. There were no normal birthweight controls for the 1979–80 and 1985–7 cohorts.

Surviving children were assessed at 2 years of age, corrected for prematurity, by a developmental paediatrician and a psychologist. The paediatrician and the psychologist assessed children in the 1991–2 cohort unaware of the birthweight of individual infants, as the normal birthweight cohort was assessed concurrently. Children in the earlier cohorts had been assessed at 2 years of age without concurrent normal birthweight control groups. Details of the 2 year assessments of the 1979–80 and 1985–7 cohorts have been reported.^{5,6} The paediatric assessment included a neurological examination to determine outcomes such as cerebral palsy and blindness. Children had been screened for hearing loss earlier in childhood, but those with suspected deafness or delayed language were referred again for audiological assessment. The psychological

*Participants:

Convener
Lex W Doyle, Royal Women's Hospital
Collaborators (in alphabetical order):
Ellen Bowman, Royal Women's Hospital and the Newborn Emergency Transport Service;
Catherine Callanan, Royal Women's Hospital; Elizabeth Carse, Monash Medical Centre;
Margaret P Charlton, Monash Medical Centre;
John Drew, Mercy Hospital for Women;
Geoffrey Ford, Royal Women's Hospital;
Simon Fraser, Mercy Hospital for Women;
Jane Halliday, Victorian Perinatal Data Collection Unit;
Marie Hayes, Monash Medical Centre;
Elaine Kelly, Royal Women's Hospital and Mercy Hospital for Women;
Peter McDougall, Royal Children's Hospital;
Anne Rickards, Royal Women's Hospital;
Andrew Watkins, Mercy Hospital for Women;
Heather Woods, Mercy Hospital for Women;
Victor Yu, Monash Medical Centre, Melbourne, Australia

Correspondence to:
Associate Professor L W Doyle,
Department of Obstetrics and Gynaecology,
University of Melbourne,
Parkville, Australia, 3052.

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Table 1 Survival rates to 2 years of age for livebirths 500–999 g birthweight born in Victoria during 1979–80, 1985–87 and 1991–92

Years of birth	Birthweight range								
	500–749 g			750–999 g			500–999 g		
	1979–80	1985–87	1991–92	1979–80	1985–87	1991–92	1979–80	1985–87	1991–92
Total livebirths	129	223	169	222	337	260	351	560	429
Survived to 2 years of age (%)	8 (6.2%)	21 (9.4%)	54 (32.0%)	81 (36.5%)	191 (56.7%)	187 (71.9%)	89 (25.4%)	212 (37.9%)	241 (56.2%)

A. Odds ratio (OR) and 95 % confidence interval (CI) for survival between 500–749 g and 750–999 g birthweight subgroups.
 1979–80, OR 4.9, 95% CI 3.0 to 8.1.
 1985–87, OR 7.4, 95% CI 5.2 to 10.5.
 1991–92, OR 5.1, 95% CI, 3.4 to 7.5.

B. OR and 95 % CI for survival between eras.
 500–999 g birthweight:
 1985–87 vs 1979–80, OR 1.76, 95% CI 1.32 to 2.33.
 1991–92 vs 1985–87, OR 2.09, 95% CI 1.62 to 2.69.
 500–749 g birthweight subgroup:
 1985–87 vs 1979–80, OR 1.53, 95% CI 0.70 to 3.36,

not significant.
 1991–92 vs 1985–87, OR 4.28, 95% CI 2.57 to 7.10.
 750–999 g birthweight subgroup:
 1985–87 vs 1979–80, OR 2.24, 95% CI 1.60 to 3.14.
 1991–92 vs 1985–87, OR 1.93, 95% CI 1.38 to 2.69.

assessment included the Mental Developmental Index (MDI) of the Bayley Scales of Infant Development,⁷ or alternative psychological tests if the children were assessed by a psychologist where the Bayley Scales were not available. Psychological test scores were expressed as a standardised normal developmental quotient (DQ) ((test score – mean)/ standard deviation (SD)), using the published mean and SD for the appropriate test. Children unable to complete psychological tests because of other impairments, or who scored less than 50 on the MDI because of severe developmental delay alone, were assigned a DQ of –4 SD.

At the time the psychological assessments began, the revision of the Bayley Scales, which had not been standardised since the 1960s, was unavailable. To compare the 1991–2 ELBW cohort with the NBW cohort, psychological test scores for the 1991–2 children were expressed as DQs recalculated from the mean and SD for the MDI obtained from the normal birthweight controls.

Sensorineural impairments included cerebral palsy, blindness, deafness requiring hearing aids, or a DQ score more than 1 SD below the mean. The severity of the sensorineural disability imposed by the impairment was graded as follows: severe = bilateral blindness, cerebral palsy with the child unlikely ever to walk, or a DQ score <–3 SD; moderate = bilateral sensorineural deafness requiring hearing aids, cerebral palsy in children not walking at 2 but expected to walk, or a DQ score from –3 SD to <–2 SD; mild = cerebral palsy but walking at 2, or a DQ score from –2 SD to <–1 SD. The remaining children were considered to

have no sensorineural disability. As the criteria for sensorineural disabilities for the 1979–80⁶ and 1985–7⁵ cohorts were slightly different, their 2 year sensorineural outcome was re-coded to match the 1991–2 cohort. For the 1991–2 ELBW and normal birthweight cohorts, sensorineural disabilities were recalculated using the mean and SD for psychological test scores for the normal birthweight cohort.

Data from all children were entered on to a computer for editing and analysis using SPSS for windows programs. Differences between groups in proportions were contrasted by computing odds ratios (OR) and 95% confidence intervals (CI).⁸ Differences between two groups in ordered categories were contrasted using the Mann-Whitney U test,⁹ or for continuous variables using Student's *t* test.

Results

During 1991–2 there were 429 consecutive live births with birthweights 500–999 g, of whom 242 (56.4%) survived their primary hospital stay. One child subsequently died before 2 years of age following genitourinary surgery at 1 year of age. Survival to 2 years of age was therefore 56.2%, a 48% relative increase compared with those in 1985–7 (37.9%), which in turn was a 49% relative increase compared with those in 1979–80 (25.4%), all differences being significant (table 1). Survival was significantly higher in heavier infants in each era (table 1). The larger increase in survival between 1979–80 and 1985–7 was in infants of birthweight 750–999 g; the small increase in survival in infants of birthweight 500–749 g was not significant. Survival increased significantly in both birthweight subgroups in 1991–2 compared with 1985–7, but the larger increase was in infants of birthweight 500–749 g (table 1).

Of the 265 normal birthweight controls for the 1991–2 cohort, two died before 2 years of age, three emigrated, the families of four refused the two year assessment, and 14 were lost to follow up. Of the 242 normal birthweight children assessed at 2 years of age, four had alternative psychological tests and four had severe developmental delay and scored < 50 on the MDI. The MDI for the remaining 234 normal birthweight controls was 115 (SD 20). Of the 242 normal birthweight controls assessed at 2 years of age, none had cerebral palsy, blindness or deafness; disability in the

Table 2 Sensorineural impairments at 2 years of age for ELBW children for each era

	Years of birth		
	1979–80	1985–87	1991–92
Survivors	89	212	241
Survivors assessed	89	211	237
Impairment:			
Cerebral palsy (% assessed)	12 (13.5)	14 (6.6)	22 (9.3)
Blind (% assessed)	6 (6.7)	9 (4.3)	5 (2.1)*
Deaf (% assessed)	3 (3.4)	1 (0.5)	2 (0.8)
Impaired development (% assessed)†			
Psychological test <–3 SD	7 (7.9)	13 (6.2)	14 (5.9)
Psychological test –3 SD to <–2 SD	6 (6.7)	9 (4.3)	15 (6.3)
Psychological test –2 SD to <–1 SD	21 (23.6)	30 (14.2)	33 (13.9)
Psychological test >= –1 SD	55 (61.8)	159 (75.4)	174‡ (73.4)

* 1992–92 vs 1979–80 odds ratio 0.24, 95% confidence interval 0.06 to 0.93.

† Mann-Whitney U test for ordered categories, 1979–80 vs 1985–87 *z* = –2.25, *P* < 0.025; 1979–80 vs 1991–92, *z* = –1.93, not significant (NS), 1985–87 vs 1991–92 *z* = 0.4, NS.

‡ Excludes one child difficult to assess, but probably normal.

Table 3 Sensorineural disabilities at 2 years of age for ELBW children for each era

Years of birth	Birthweight subgroup								
	500-749 g			750-999 g			500-999 g		
	1979-80	1985-87	1991-92	1979-80	1985-87	1991-92	1979-80	1985-87	1991-92
Survivors assessed	8	21	54	81	190	183	89	211	237
Disability:									
Nil	1 (12.5%)	18 (85.7%)	33 (61.1%)	46 (56.8%)	133 (70.0%)	136 (74.3%)	47 (52.8%)	151 (71.6%)	169 (71.3%)
Mild	4 (50.0%)	1 (4.8%)	11 (20.4%)	19 (23.5%)	32 (16.8%)	24 (13.1%)	23 (25.8%)	33 (15.6%)	35 (14.8%)
Moderate	1 (12.5%)	1 (4.8%)	5 (9.3%)	7 (8.6%)	12 (6.3%)	12 (6.6%)	8 (9.0%)	13 (6.2%)	17 (7.2%)
Severe	2 (25.0%)	1 (4.8%)	5 (9.3%)	9 (11.1%)	13 (6.8%)	11 (6.0%)	11 (12.4%)	14 (6.6%)	16 (6.8%)

Data are number of infants (% survivors assessed).

Mann-Whitney U test for disability in 1979-80 vs 1985-87, $z = 3.1$, $P < 0.01$; 1979-80 vs 1991-92, $z = 3.0$, $P < 0.01$; 1985-87 vs 1991-92, $z = 0.1$, not significant (NS).

Mann-Whitney U test for disability in subgroup 500-749 g vs subgroup 750-999 g, 1979-80, $z = 2.24$, $P = 0.025$; 1985-87, $z = -1.4$, NS; 1991-92, $z = 1.84$, NS.

controls was therefore assessed solely on the basis of psychological tests.

Of the 241 ELBW survivors in 1991-2, 237 (98.3%) were assessed at 2 years of age, corrected for prematurity. Of the remaining four children, two emigrated, the families of one refused the two year assessment, and one was lost to follow up. Twenty two (9.3%) of the 237 survivors assessed had some form of cerebral palsy, predominantly quadriplegia (table 2). The disability imposed by the cerebral palsy was severe in nine children, moderate in four, and mild in nine. Five (2.1%) children were blind, three from retinopathy of prematurity and two from cortical blindness, both of whom had severe quadriplegia. Two (0.8%) children required hearing aids for sensorineural deafness, one of whom also had a DQ of -4 SD. The rates of cerebral palsy and deafness were not significantly lower than in children in the 1979-80⁶ and 1985-7⁵ cohorts assessed at 2 years of age, but the rate of blindness was significantly lower in 1991-2 compared with 1979-80 (table 2). Fourteen (5.9%) children, all of whom were unable to complete the MDI because of blindness, severe cerebral palsy, or severe developmental delay, had DQ scores <-3 SD, 15 (6.3%) children had DQ scores from -3 SD to <-2 SD, 33 (13.9%) had DQ scores from -2 SD to <-1 SD, and 174 (73.4%) had DQ scores >-1 SD. One child in a non-English speaking family could not complete the MDI because of extreme shyness but was considered by the testing psychologist to be probably normal, although no standardised DQ score was assigned. As the child was free of other impairments, she was considered to have no disability; she has been fully assessed subsequently and is free of disability at 5 years of age. For ELBW children born in 1991-2 able to complete psychological tests, the mean MDI was 99 (SD 20, $n = 220$), significantly higher than for the children able to be tested in the 1979-80 cohort (mean MDI 91; SD 17, $n = 74$) ($t = 3.1$, $P < 0.01$), but not significantly different from the 1985-7 cohort (mean MDI 99; SD 18, $n = 183$). For the 1991-2 cohort, overall, sensorineural disability was severe in 16 (6.8%); nine (3.8%) children had multiple severe disabilities. Compared with the 1979-80 ELBW cohort, the overall rate of disability was significantly lower in the 1985-7 and 1991-2 ELBW cohorts; the rates of disability were not significantly different in the 1991-2 and

Table 4 Sensorineural disabilities at 2 years of age for children born in 1991-92: disability for ELBW and NBW children reclassified on mean (SD) for psychological test scores for NBW children

	Birthweight subgroup	
	ELBW (500-999 g)	NBW (> 2499 g)
Survivors assessed	237	242
Disability:		
Nil	133 (56.1%)	198 (81.8%)
Mild	59 (24.9%)	36 (14.9%)
Moderate	29 (12.2%)	4 (1.7%)
Severe	16 (6.8%)	4 (1.7%)

Data are numbers of infants (% survivors assessed).

Mann-Whitney U test for disability in ELBW cohort vs NBW cohort; $z = 6.4$, $P < 0.0001$.

ELBW = extremely low birthweight; NBW = normal birthweight.

1985-7 ELBW cohorts (table 3). For the 1979-80 cohort, the overall sensorineural disability rate was significantly worse in survivors of birthweight 500-749 g compared with those of birthweight 750-999 g, but there was no significant difference between the birthweight subgroups for the 1985-7 and 1991-2 cohorts (table 3).

For the 1991-2 ELBW cohort compared with the normal birthweight controls, the overall rate of disability was significantly higher in ELBW survivors (Mann-Whitney U test, $z = 6.4$, $P < 0.0001$) (table 4).

Discussion

The survival rates for ELBW infants in Victoria have risen progressively since the late 1970s, through the 1980s, and now into the 1990s. Survival rates rose more for larger infants, with birthweights 750-999 g, into the 1980s, but more for the smaller infants, with birthweights 500-749 g, into the 1990s. Improvements in perinatal care, such as antenatal steroids and exogenous surfactant (first used in Victoria in 1991) have been partly responsible, but recognition of rising survival rates and an increasing willingness and ability to treat tiny babies have also probably contributed.

As well as a higher survival, sensorineural outcome improved for survivors born in 1985-7 compared with those born in 1979-80.⁵ However, despite an improvement in survival, there is no indication of a further reduction in the rates of adverse sensorineural outcome in survivors from the 1980s into the 1990s. Moreover, the rates of sensorineural

impairments and disabilities in ELBW infants born in the 1990s remain higher than for normal birthweight infants.

The different categorisation of disability for ELBW infants in 1991–2 based on psychological test scores for the normal birthweight controls highlights the importance of control groups. However, the number of ELBW and normal birthweight children born in 1991–2 surviving with severe disability was not affected by the reclassification. It would have been desirable to recruit control groups for the 1979–80 and 1985–7 ELBW cohorts to permit a more appropriate classification of disability for these groups.

The sensorineural outcome for the tiniest survivors of birthweight 500–749 g was significantly worse than for the larger infants of birthweight 750–999 g in only one of our three cohorts. In other regional studies Hack *et al*⁹ reported higher rates of adverse sensorineural outcome for children of birthweight < 750 g compared with those of birthweight 750–1499 g, and French *et al*¹⁰ described higher sensorineural disability rates in children of birthweight 500–799 g compared with those of 800–999 g. However, it is important to realise that most of the survivors of 500–749 g birthweight in our study were not severely disabled, and the absolute numbers of children with disabilities of all severities were fewer for those of birthweight 500–749 g compared with those of birthweight 750–999 g in each era.

A comparison of the absolute number of ELBW and NBW children expected to survive per year might help to reduce anxiety that the improving survival rates for the tiniest babies will result in large numbers of severely disabled children in the community. Using the definitions of disability in our study, if the rate of severe disability of 1.7% in our normal birthweight control group truly reflects the rate for all such children born in Victoria, as the number of normal birthweight children born in Victoria 1991–2 was 123 100^{11 12} we would expect about 1000 normal birthweight children to have severe disability every year, compared with only eight children with severe disability per year in the 1991–2 ELBW cohort.

Although ELBW survivors are few, the number with adverse sensorineural outcome

should be reduced if possible. Several treatments offer promise, such as antenatal magnesium sulphate¹³ and postnatal indomethacin,¹⁴ and are currently being evaluated in large multicentre randomised controlled trials, with the major endpoint being to reduce adverse sensorineural disabilities. Trials such as these should be strongly promoted and supported.

In conclusion, survivals of ELBW infants in this regional cohort have improved further in the early 1990s. However, rates of sensorineural disability in ELBW survivors have not improved since the mid-1980s and remain too high.

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