Outcomes at Age 2 Years of Infants < 28 Weeks' Gestational Age Born in Victoria in 2005

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Objective To determine the survival rates and neurosensory outcomes of infants born at gestational age 22-27 weeks in the state of Victoria in 2005 and compare theses data with those for similar infants born in the 1990s.
Study design This was a population-based study of all extremely preterm (22-27 weeks' gestational age) live births in Victoria in 2005 free of lethal anomalies and randomly selected term controls. Survival and quality-adjusted survival rates at age 2 years were determined relative to the controls, and results were compared with regional extremely preterm cohorts born in 1991-92 and 1997.
Results Of 270 very preterm live births in 2005, 172 (63.7%) survived to 2 years, not significantly different from the survival rate of 69.6% for those born in 1997. Rates of severe developmental delay and severe disability were lower than in the very preterm survivors born in 1997. Quality-adjusted survival rates in the extremely preterm cohorts rose from 42.1% in 1991-92 to 55.1% in 1997, but did not increase in 2005 (53.4%).
Conclusions Survival rates for infants born at 22-27 weeks' gestational age have not increased since the late 1990s, but the neurosensory outcome in survivors has improved. *(J Pediatr 2010;156:49-53)*.

Survival rates for regional cohorts of extremely preterm infants have increased through the 1990s;[1] however, survival rates cannot increase indefinitely, due to limits on the effect of current medical technology on survival rate. Thus, the emphasis of perinatal intensive care must be on reducing the rates of neurosensory disability rates in survivors, which have remained overly high relative to term controls. Moreover, adverse neurosensory outcomes are more prevalent with diminishing maturity, to the extent that some would not offer intensive care to infants born at < 26 weeks' gestation. The rates of neurosensory disability in early childhood have remained stable for very preterm infants born in the 1990s, despite the increased survival of very preterm infants over time.[2] But perinatal practices change constantly, and the increased use of treatments known to improve outcome, such as caffeine therapy,[3] or avoidance of known potentially harmful therapies, such as postnatal corticosteroids,[4] might be expected to improve rates of disability in survivors over time.

The objectives of the present study were to determine the survival and neurosensory disability rates of infants born at < 28 weeks' gestational age and term controls born in the state of Victoria in 2005 and to compare the data with those from earlier cohorts born in the state in the 1990s, details of which have been published previously.[2] It was hypothesized that survival rates would not have increased significantly since the late 1990s, but neurosensory disability rates would have decreased.

Methods

All live-born infants at 22-27 completed weeks of gestation born in the state of Victoria in 2005 were included in this study, except for those live births resulting from termination of pregnancy secondary to lethal anomalies. Multiple data sources (the 4 level-III neonatal intensive care units in the state, the Newborn Emergency Transport Service, and the Victorian Perinatal Data Collection Unit) were cross-checked to verify the number of live births.[5] Gestational age was determined by the best obstetric estimate, based on fetal ultrasound conducted before 20 weeks in most cases. Controls who were both term (> 36 weeks' gestation) and normal birth weight (> 2499 g) were randomly selected from each of the 3 level-III perinatal centers in the state, stratified to balance with preterm survivors for sex, for the mother's health insurance status (as a proxy for social class), and the language spoken primarily in the mother's country of birth (English or other), all variables known to be related to long-term outcome in our cohorts.

CI	Confidence interval
CP	Cerebral palsy
GMFCS	Gross Motor Function Classification System
OR	Odds ratio
SD	Standard deviation

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Survivors were assessed at age 2 years (corrected for prematurity) by pediatricians and psychologists blinded to perinatal details, including prematurity status. Impairments evaluated included cerebral palsy (CP), blindness (visual acuity < 20/200 in the better eye), deafness (hearing loss requiring amplification or worse) and developmental delay. Development was assessed using the Bayley Scales of Infant and Toddler Development,[6] and cognitive and language composite scores were obtained relative to the mean and standard deviation (SD) for the normal birth weight controls on the respective scores. Mild developmental delay was characterized by a score on either scale from -2 SD to < -1 SD; moderate developmental delay, by a score on either scale from -3 SD to < -2 SD; and severe developmental delay, by a score on either scale < -3 SD. A child who was unable to complete psychological testing because of presumed severe developmental delay was assigned a score of -4 SD. The criteria for the diagnosis of CP included abnormal muscle tone and delays in motor control and function.[7] Severe disability comprised severe CP (unlikely ever to walk; Gross Motor Function Classification System[8] [GMFCS] level 4 or 5), blindness, or severe developmental delay; moderate disability comprised moderate CP (not walking at age 2 years but expected to walk eventually; GMFCS level 2 or 3), deafness, or moderate developmental delay; and mild disability comprised mild CP (walking at age 2 years; GMFCS level 1), or mild developmental delay. Neurosensory utilities for survivors were assigned as described previously[9-11] according to the severity of the disability imposed by an impairment; 0.4 for severe, 0.6 for moderate, 0.8 for mild, and 1 for no disability. Utilities were multiplied for children with multiple disabilities; thus, the lowest possible utility for a survivor was 0.0384 for a child with severe CP (0.4), severe developmental delay (0.4), blindness (0.4), and deafness (0.6). Infants who died were assigned a utility of 0. The few infants who survived but were not assessed were assigned a utility equal to the mean utility for survivors assessed for their respective cohort. Utilities were summed and divided by the number of live births to calculate the quality-adjusted survival rate.

Data were analyzed by SPSS for Windows version 17.0 (SPSS Inc., Chicago, Illinois). Means were contrasted by mean difference and 95% confidence interval (CI) and by linear regression analysis to adjust for confounding variables, calculating adjusted mean differences and 95% CIs. Proportions were compared by χ^2 analysis, with relative risks and 95% CIs calculated, and by logistic regression analysis, to adjust for confounding variables, with odds ratios (OR) and 95% CIs calculated from the regression coefficients. Differences between ordered categories were compared using the Mann-Whitney U test or the χ^2 test for linear trend. Differences in quality-adjusted survival rates were compared using the Mann-Whitney U test. A P value < .05 was considered statistically significant. Results for the 2005 very preterm cohort were compared with those for the term control group, as well as with those for term and very preterm cohorts born in 1991-1992 and 1997, for which data have been reported previously.[2] Lethal anomalies had been included in the earlier reports but were excluded in this study for comparison of survival rates. The 1991-1992 and 1997 cohorts are the only children selected by gestational age that we assessed at age 2 years, because we lacked the resources necessary to assess all children from all years.

The Research and Ethics Committees at the Royal Women's Hospital, Mercy Hospital for Women, and Monash Medical Centre, Melbourne approved the follow-up studies. Written informed consent was obtained from the parents of term controls. Follow-up was considered routine clinical care for the very preterm infants.

Results

The number of live births at 22-27 weeks' gestational age per year was 32% higher in 2005 (n = 288) compared with 1991-1992 (n = 219) (**Table I**). There were 18 live births from termination of pregnancy for lethal anomalies in 2005, compared with 5 per year in 1991-1992 and 6 in 1997; most terminations were born at 22 weeks' gestation. There were more very immature live births free of lethal anomalies per year in 2005 than in the other 2 eras: 23% were born at 22 or 23 weeks' gestation in 2005, compared with 19% in 1991-1992 and 16% in 1997. There were 220 term controls for the 2005 cohort.

The survival rate to age 2 years was higher at each week of gestation in 1997 compared with 1991-1992, and was significantly higher overall (OR = 2.06; 95% CI = 1.46- 2.92; P < .001) (**Table I**; **Figure 1**). The overall survival rate was lower in 2005 than in 1997, but the overall difference was not statistically significant (OR = 0.77; 95% CI = 0.52-1.12; P = .17), even after adjustment for gestational age (adjusted OR = 0.75; 95% CI = 0.48-1.17; P = .20). The survival rates between 2005 and 1997 varied with individual weeks of gestation, but the largest discrepancy was at 23 weeks.

The follow-up rates were high for both the very preterm and control cohorts born in 2005 (**Table II**). No term control had CP or blindness, but 1 control was deaf at age 2 years, and only the rate of CP was significantly higher in the very preterm children. The means on the cognitive and language composite scales for the term controls were substantially above the normative mean of 100 for both scales and were significantly higher than for the very preterm group. Significantly more very preterm children than controls had developmental delays and neurosensory disabilities.

Rates of CP, blindness, deafness requiring a hearing aid, developmental delay, and neurosensory disability were not significantly different between the preterm cohorts across all eras, although those in 2005 were less likely to have most of these outcomes (**Table III**). However, the 2005 cohort had significantly lower rates of severe developmental delay and severe neurologic disability than the 1997 cohort, who in turn had significantly higher rates of these problems than the 1991-1992 cohort.

Rates of neurosensory disability were similar in each of the term control groups (1991-1992: none, 82%; mild, 15%; moderate, 2%; severe, 2%; 1997: none, 83%; mild, 13%; moderate, 2%; severe, 2%; 2005: none, 79%; mild, 18%;