Author/s:
Boland, RA;Bowen, JR

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Boland Rosemarie Anne (Orcid ID: 0000-0002-8127-2133)

**Viewpoint**

**Neonatal Intensive Care at 22-24 weeks' gestation: how low should we go?**

Decisions around provision of care for infants born at 22-24 weeks' gestation provide ethical challenges for clinicians and parents. Central to the decision-making pathway is the need for local, up-to-date data on survival and risks of adverse long-term outcomes of these vulnerable infants, as clinician's perceptions of outcomes may be worse than contemporaneous data (1). Obtaining information about outcomes following active intervention is challenging because of an inconsistent approach to management of births at 22-24 weeks' gestation across Australia and internationally. (2-4) In some centres, infants born at 22 weeks' gestation are being offered neonatal intensive care. (2, 5) Yet in other centres, neonatal intensive care admission is still discouraged below 24 weeks' gestation and provision of intensive care at 24 weeks is considered optional. Such variations in approach result in large variations in reported survival (2, 5-7) and long-term adverse outcome rates, between and within countries. (8)

Sharp and colleagues provide important outcome data for infants born alive at 22 to 24 weeks' gestation in Western Australia (WA). (9) A major strength of this study is the provision of denominators for survival for all livebirths and not just those who received neonatal intensive care. Perinatal services in WA are unique with a single centre, the King Edward Memorial Hospital (KEMH) in Perth, providing centralised tertiary obstetric and neonatal services for a population spread across a vast area of 2.5 million $km^2$. Throughout this study, a pro-active approach to obstetric and neonatal care of periviable infants is evident, with high rates of in-utero transfer and NICU admission at 22-24 weeks' gestation. Overall, only 13% (40/302) livebirths at 22-24 weeks were born outside of KEMH in 2004-2010. This rate is significantly lower than in Victoria, (6) where 23% (41/179) of livebirths at 22-24 weeks' gestation were outborn in 2010-2011, and the United Kingdom, where 48% (447/933) of livebirths at 22-24 weeks' gestation occurred outside of tertiary centres in 2006. (5)

In the WA cohort, outborn infants were less likely to be admitted to NICU compared with inborn infants, with 35% (14/40) outborn versus 79% (208/262) inborn infants admitted. In total, 74% (222/302) of 22-24 week livebirths were admitted to NICU in WA in 2004-2010: a higher overall rate than comparable local and international cohorts. In 2017, Patel and colleagues published a review comparing active management and survival rates of periviable livebirths in developed nations. (4) Table 1 reports NICU admission rates in the Western Australian cohort compared with four population-based cohorts in Patel's review. These data highlight both the wide variation in approach to management of these infants, and the proactive approach to care taken in the WA cohort, with 81% (78/96) of live births admitted to NICU at 23 weeks and 95% (139/146) at 24 weeks' gestation.

**Table 1: NICU admission rates following live birth at 22-24 weeks' gestation**

| | Year of birth | 22 weeks | 23 weeks | 24 weeks |
|---|---|---|---|---|
| Western Australia | 2004-2010 | 8% | 81% | 95% |
| Victoria (6) | 2010-2011 | 5% | 30% | 85% |
| EPICure UK (5) | 2006 | 13% | 64% | 86% |
| EPIPAGE-2 France (7) | 2011 | 3% | 8% | 61% |
| EXPRESS Sweden (2) | 2004-2007 | 38% | 81% | 93% |

**Survival at 22-24 weeks' gestation**

Of the 302 livebirths at 22-24 weeks' gestation in 2004-2010 in WA, 159 (53%) were alive at a median age of 59 months (3-5 years). Overall, 72% of the 222 infants admitted to NICU survived. Comparison of survival rates in the WA cohort with other population-based cohorts is shown in Table 2. At 23 and 24 weeks, WA had higher rates of NICU admission and survival than Victoria, the United Kingdom and France, with similar admission and survival rates to those reported in Sweden.

**Table 2. Survivors after live birth and NICU admission at 22-24 weeks' gestation**

| | Year of birth | 22 weeks | | 23 weeks | | 24 weeks | |
|---|---|---|---|---|---|---|---|
| **Denominator** | | **All LB** | **NICU** | **All LB** | **NICU** | **All LB** | **NICU** |
| Western Australia^ | 2004-2010 | 3/60 (5%) | 3/5 (60%) | 44/96 (46%) | 44/78 (56%) | 112/146 (77%) | 112/139 (81%) |
| Victoria (6) † | 2010-2011 | 0/40 (0%) | 0/2 (0%) | 11/55 (20%) | 11/16 (69%) | 41/84 (49%) | 41/71 (58%) |
| EPICure UK (5) †† | 2006 | 3/152 (2%) | 3/19 (16%) | 66/338 (20%) | 66/217 (30%) | 178/441 (40%) | 178/381 (47%) |
| EPIPAGE-2 France (7) †† | 2011 | 0/58 (0%) | 0/2 (0%) | 1/89 (1%) | 1/7 (14%) | 58/186 (31%) | 58/113 (51%) |
| EXPRESS Sweden (2) † | 2004-2007 | 5/51 (10%) | 5/19 (26%) | 53/101 (52%) | 53/81 (65%) | 96/144 (67%) | 96/132 (73%) |

LB: Livebirths; NICU: Livebirths admitted to a neonatal intensive care unit

^ Survivors at 3-5 years; † Survivors to one year; †† Survivors to discharge

These data support an association between a pro-active approach to perinatal care and neonatal survival. Furthermore, these data serve as a timely reminder that outcomes only reported for infants admitted to NICU are not a true reflection of outcomes of all livebirths at periviable gestations.

**Survival, but at what cost?**

Although survival rates are increasing for neonates at 22-24 weeks' gestation admitted to NICU, there remains uncertainty about long-term outcomes. Studies assessing short-term outcomes have reported increased survival without disability, predominantly due to decreased rates of physical disability, including cerebral palsy, blindness and deafness. However, longer term studies of children

to school age are less reassuring, due to increasing recognition of cognitive or academic problems over time. (8)

In the WA study, 152/159 (96%) survivors were seen in follow-up at a median age of 59 months. (9) Rates of severe physical disability were relatively low, with only three (2%) children experiencing moderate to severe cerebral palsy (GMFCS 111-V) and two (1.3%) children with blindness. In contrast, 27 (18%) children were identified with moderate or severe cognitive disability (IQ more than 2SD below the mean) and 9 (5.9%) children were diagnosed with autism. Overall, 34% of children born at 22-23 weeks gestation and 16% of children born at 24 weeks' gestation were found to have moderate or severe disability. These disability rates are similar at 22-23 weeks and lower for children born at 24 weeks than recent ANZNN data on outcomes for children at 2-3 years (born 2009-2011) which reported moderate-severe functional impairment in 27.2% of children born <24 weeks' gestation and 25.5% of children born at 24 weeks' gestation. (10) Reassuringly, the data from the Western Australia cohort indicate that a proactive approach to neonatal care does not result in a higher proportion of children experiencing adverse neurodevelopmental outcomes.

Some caution should, however, be applied to outcomes reported at 5 years as these may still not provide the full picture of disability for children born extremely preterm, with studies of children at school age demonstrating a higher incidence of academic, psychological and behavioural problems which cannot always be predicted from preschool assessments. For example, recent studies have identified high rates of autism at 10 years (up to 15%) in children born at 23-24 weeks (11) and contrary to expectations, academic problems may be increasing over time, despite improvements in NICU care. (8)

Despite these caveats, the long-term outcomes for the majority of children in the WA study were generally positive. The data provide reassurance that NICU care is likely to be in the best interests of the majority of neonates born at 24 weeks' gestation, with 81% of admitted 24-week infants surviving and 83% of survivors free of moderate or severe disability at 5 years of corrected age. For neonates born at 23 weeks, the study demonstrates that provision of neonatal intensive care is an appropriate option when provided in a Unit with an active approach to obstetric and neonatal care, and expertise in caring for periviable infants. Concerted efforts should be made to transfer in-utero to allow time for appropriate counselling by an experienced neonatologist regarding survival chances and long-term outcomes and to optimise birth conditions. This does not mean neonatal intensive must then be provided. Rather it ensures equitable access to obstetric and neonatal care and high-risk counselling for all women, especially those who would otherwise been disadvantaged by birthing in a non-tertiary hospital.

Ideally parents should be provided with local data on NICU outcomes. For regions in Australia where provision of neonatal intensive care for neonates before 24 weeks' gestation has been actively discouraged, data from this study are important as local survival data may be misleading. However, if intensive care support is to be offered by NICUs with less experience in provision of care at these

very early gestational ages, it will be essential to monitor local outcomes to ensure that they are similar across all neonatal services.

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Rosemarie A Boland,[1,2,3] Jennifer R Bowen[4,5]

[1] Clinical Sciences, Murdoch Children's Research Institute, Parkville, Victoria, Australia. 3052

[2]Department of Obstetrics and Gynecology, University of Melbourne, Royal Women's Hospital, Parkville, Victoria, Australia, 3052.

[3]Paediatric Infant Perinatal Emergency Retrieval, Royal Children's Hospital, Parkville, Victoria, Australia, 3052.

[4]Department of Neonatology, Royal North Shore Hospital, St Leonards, New South Wales, 2065.

[5]Sydney Medical School Northern, University of Sydney, Camperdown, New South Wales, Australia, 2006

Corresponding author:

Dr Rosemarie Anne Boland

Murdoch Children's Research Institute

50 Flemington Road, Parkville, Victoria

E: rose.boland@mcri.edu.au

T: 03 8345 3781