### Outcomes for babies born at 23 and 24 weeks gestational age

### Preterm outcomes 23 week infants

Previous external reviewer highlighted low survival of infants born at 23 weeks compared to some ANZNN NICUs

- 5 liveborn infants in 2016
- 4 infants admitted to NICU

(cf 4 infants admitted between 2008 and 2015)

- All received antenatal steroids (only 1 "complete")
- All developed IVH (2 Grade 4, 1 Grade 3, 1 Grade 2)
- Only one survivor; deaths of 3 infants with major IVH on days 3, 3 and 5
- Overall survival since 2007 nearly 60% selection bias previously?

### **Current NZ Practice**

#### **Neonatal Guidelines**





#### **New Zealand Newborn Clinical Network**

New Zealand Consensus Statement on the Care of Mother and Baby(ies) at Periviable Gestations (Draft)

### **Current Practice**

#### New Zealand Newborn Clinical Network Consensus Statement

- Multidisciplinary group
- Recommendations for 23<sup>+0</sup> 24<sup>+6</sup> weeks gestation
- Options for intensive or comfort care
- Interventions from 22<sup>+5</sup> weeks
- Bundle of care
- Shared decision making process

# What is the current practice internationally?

### **EXPRESS Study**

- Extremely Preterm Infants in Sweden Study
- One-Year Survival of Extremely Preterm Infants
  After Active Perinatal Care in Sweden
  - Karel Maršál et al. JAMA. 2009;301(21):2225-2233.
- Intensity of Perinatal Care for Extremely Preterm
  Infants: Outcomes at 2.5 Years
  - Fredrik Serenius et al. Pediatrics. 2015;135:e1163-e1172

### **EXPRESS Study**

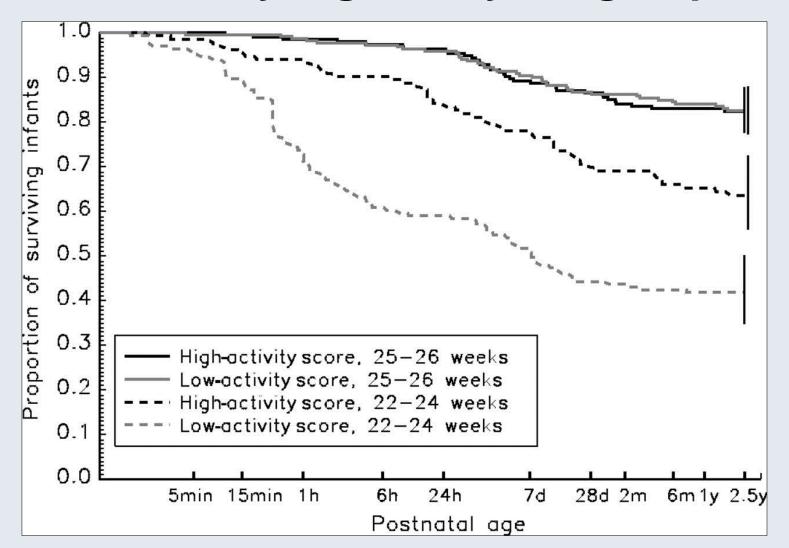
- April 2004 to March 2007
- 844 fetuses alive at presentation
- 707 (84%) born alive; 137 (16%) stillborn
- Perinatal activity score based on intensity of care (interventions) provided
- Scored for each gestational week separately and aggregated for centres
- Primary outcomes 1 year mortality and death or NDI at 2.5 years corrected

### One-Year Survival of Extremely Preterm Infants After Active Perinatal Care in Sweden

|                                |                  | No. (%) of Infants by Gestational Age, wk |          |         |                 |             |  |  |
|--------------------------------|------------------|---|----------|---------|-----------------|-------------|--|--|
|                                | ≤22 <sup>a</sup> | 23  | 24       | 25      | 26 <sup>b</sup> | Total <27 w |  |  |
| All infants                    | (n=142)          | (n=183)                                   | (n=191)  | (n=250) | (n=245)         | (N=1011)    |  |  |
| Perinatal death                | 132 (93)         | 121 (66)                                  | 77 (40)  | 68 (27) | 58 (24)         | 456 (45)    |  |  |
| Stillbirth                     | 91 (64)          | 82 (45)                                   | 47 (25)  | 45 (18) | 39 (16)         | 304 (30)    |  |  |
| Intrapartum death              | 40 (28)          | 19 (10)                                   | 2 (1)    | 3 (1.2) | 2 (0.8)         | 66 (6.5)    |  |  |
| Live-born infants              | (n=51)           | (n=101)                                   | (n=144)  | (n=205) | (n=206)         | (N=707)     |  |  |
| Neonatal death                 | 45 (88)          | 46 (46)                                   | 41 (29)  | 29 (14) | 26 (13)         | 187 (26)    |  |  |
| Early neonatal death, 0-6 days | 41 (80)          | 39 (39)                                   | 30 (21)  | 23 (11) | 19 (9.2)        | 152 (22)    |  |  |
| Delivery room death            | 28 (55)          | 16 (16)                                   | 10 (6.9) | 4 (2)   | 0               | 58 (8.2)    |  |  |
| Late neonatal death, 7-27 days | 4 (7.8)          | 7 (6.9)                                   | 11 (7.6) | 6 (2.9) | 7 (3.4)         | 35 (5)      |  |  |
| Infant death, 0-365 days       | 46 (90)          | 48 (48)                                   | 48 (33)  | 38 (19) | 30 (15)         | 210 (30)    |  |  |

<sup>b</sup>Category denotes gestational age of 26 weeks 0 days to 26 weeks 6 days.

### Survival curves from birth to 2.5 years' CA for infants born alive in high- and lowactivity regions by GA group



## Risk of death or NDI at 2.5 years for 3 High-Activity Compared With 4 With Low-Activity Perinatal Care Centres

|  |         |      |         |            | -     |                       |       |                |
|--|---------|------|---------|------------|-------|-----------------------|-------|----------------|
|  | Regiona |      |         |            |       |                       |       |                |
| Outcome  | High    | Low  |         | Unadjusted |       | Adjusted <sup>#</sup> |       |                |
|  | n/N     | %    | n/N     | %          | OR    | 95% CI                | OR    | 95% CI         |
| Alive at mother's admission for delivery ( <i>n</i> = 844) |         |      |         |            |       |                       |       |                |
| Primary composite outcome death or NDI at 2.5 years' CA    |         |      |         |            |       |                       |       |                |
| 22–26 weeks  | 194/358 | 54.2 | 289/451 | 64.1       | 0.66* | 0.50–0.88*            | 0.69* | 0.50–<br>0.96* |
| 22–24 weeks  | 112/158 | 70.9 | 199/232 | 85.8       | 0.40* | 0.24–0.67*            | 0.44* | 0.25–<br>0.77* |
| 25–26 weeks  | 82/200  | 41.0 | 90/219  | 41.2       | 1.00  | 0.68–1.47             | 0.91  | 0.61–1.36      |

<sup>#</sup>Death or NDI was adjusted for GA, multiple birth, gender, Birth weight SD, maternal education, paternal education, ethnicity

### **EXPRESS Study**

- Survival improved after antenatal and neonatal interventions
- Survival better in units with high perinatal activity scores
- Data not shown today:
  - Improved survival did not result in more children with severe NDI

### **Australasian Context**

- Survival and neurodevelopmental outcomes in extremely preterm infants 22–24 weeks of gestation born in Western Australia
  - Mary Sharp et al. J Paeds Child Health.2018;54: 188–193

# Survival and ND in 22–24 weeks gestation infants in Western Australia

- Retrospective collection of survival data from NICU and Health Department records
- All babies born at 22, 23 and 24 weeks gestation between 2004 and 2010
- Neurodevelopment assessed using standardised tests
- Medical examination findings from follow-up records

# Survival for infants born at 22–24 weeks in 2004–2010 in WA

| Gestation                      | 22 weeks              | 23 weeks       | 24 weeks              | All                   |  |
|--------------------------------|-----------------------|----------------|-----------------------|-----------------------|--|
|                                | <i>n</i> (survival %) | n (survival %) | <i>n</i> (survival %) | <i>n</i> (survival %) |  |
| Total survival<br>( <i>n</i> ) | 3                     | 44             | 112                   | 159                   |  |
| All births (LB<br>+ SB)        | 227 (1.3)             | 188 (23)       | 199 (56)              | 614 (24)              |  |
| All live births                | 60 (5)                | 96 (46)        | 146 (77)              | 302 (53)              |  |
| All NICU<br>admissions         | 5 (60)                | 78 (56)        | 139 (81)              | 222 (72)              |  |

LB, live births; NICU, neonatal intensive care unit; SB, stillbirths

#### Neurodevelopmental Outcomes for infants born at 22–24 weeks in 2004– 2010 in WA

| Gestational age   | 22 weeks    | 23 weeks   | 24 weeks   | All        |
|---|-------------|------------|------------|------------|
| Survivors, n  | 3           | 44         | 112        | 159        |
| Overall outcome, n (%)  |             |            |            |            |
| Outcome assessed in FU Program                                      | 3 (100)     | 41 (85)    | 103 (92)   | 147 (93)   |
| Outcome known<br>assessed elsewhere                                 | 0           | 3          | 2          | 5          |
| Outcome unknown   | 0           | 0          | 7          | 7          |
| Corrected median age<br>at last assessment,<br>months, median (IQR) | 59 (57–122) | 58 (39–62) | 59 (56–61) | 59 (55–62) |
| Overall<br>disability, <i>n</i> (%)                                 |             |            |            |            |
| Mild  | 1 (33)      | 11 (25)    | 21 (19)    | 32 (20)    |
| Moderate  | 2 (67)      | 5 (11)     | 5 (5)      | 12 (8)     |
| Severe  | 0           | 9 (21)     | 12 (11)    | 21 (13)    |
| Free of<br>moderate/severe<br>disability                            | 1 (33)      | 30 (68)    | 84 (83)    | 118 (78)   |

# Survival and ND in 22–24 weeks gestation infants in Western Australia

#### Babies born <25 weeks gestation 2004 - 2010

- 53% survived if born alive
- 72% of NICU admissions survived
- 78% of the survivors were free of moderate to severe disability i.e. normal development or mild NDI

### **North America**

- Survival and Neurodevelopmental Outcomes among Periviable Infants
  - Noelle Younge et al., for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. N Engl J Med 2017; 376:617-628.

### Survival and Neurodevelopmental Outcomes among Periviable Infants

- Survival and neurodevelopment at 18-22 months for infants born at 22-24 weeks
- Three epochs:

Epoch 1 - 2000 – 2004, Epoch 2 - 2004 – 2007, Epoch 3 - 2008 – 2011

- Primary outcome (3 level)
  - Survival without neurodevelopmental impairment
  - Survival with neurodevelopmental impairment
  - Death

### Survival and Neurodevelopmental Outcomes among Periviable Infants

- Data available on 4274 out of 4458 (96%) babies
- 11 centres in National Institute of Child Health and Human Development Neonatal Research Network

| Outcome   | Adjusted Relati                                | ve Risk (9 <del>5% CI)*</del>                  |
|---|--|--|
|   | Epoch 3 (2008–2011) vs.<br>Epoch 2 (2004–2007) | Epoch 3 (2008–2011) vs.<br>Epoch 1 (2000–2003) |
| All infants†  |  |  |
| Survived without neurodevelopmental impairment vs. died   | 1.52 (1.22-1.88)                               | 1.59 (1.28-1.99)                               |
| Survived with neurodevelopmental impairment vs. died  | 1.43 (1.14–1.79)                               | 1.27 (1.01–1.59)                               |
| Survived without neurodevelopmental impairment vs. survived with neurode-<br>velopmental impairment | 1.08 (0.83–1.40)                               | 1.27 (0.99–1.65)                               |
| Survived without neurosensory impairment vs. died   | 1.39 (1.15–1.68)                               | 1.44 (1.18-1.75)                               |
| Survived with neurosensory impairment vs. died  | 1.93 (1.38–2.70)                               | 1.54 (1.11–2.15)                               |
| Survived without neurosensory impairment vs. survived with neurosensory<br>impairment               | 0.72 (0.51–1.02)                               | 0.93 (0.66–1.32)                               |
| Infants born at 22 wk‡  |  |  |
| Survived without neurodevelopmental impairment vs. died   | 0.74 (0.16-3.47)                               | 1.30 (0.21-8.08)                               |
| Survived with neurodevelopmental impairment vs. died  | 0.63 (0.20-1.97)                               | 1.30 (0.34-5.02)                               |
| Survived without neurodevelopmental impairment vs. survived with neurode-<br>velopmental impairment | 1.13 (0.17–7.41)                               | 0.99 (0.11–9.34)                               |
| Infants born at 23 wk∬  |  |  |
| Survived without neurodevelopmental impairment vs. died   | 1.29 (0.86-1.94)                               | 2.31 (1.46-3.66)                               |
| Survived with neurodevelopmental impairment vs. died  | 1.53 (0.98-2.40)                               | 1.07 (0.71-1.62)                               |
| Survived without neurodevelopmental impairment vs. survived with neurode-<br>velopmental impairment | 0.86 (0.49–1.50)                               | 2.17 (1.23–3.83)                               |
| Infants born at 24 wk¶  |  |  |
| Survived without neurodevelopmental impairment vs. died   | 1.63 (1.26-2.11)                               | 1.46 (1.12–1.90)                               |
| Survived with neurodevelopmental impairment vs. died  | 1.46 (1.11-1.92)                               | 1.34 (1.01-1.78)                               |
| Survived without neurodevelopmental impairment vs. survived with neurode-<br>velopmental impairment | 1.12 (0.83–1.51)                               | 1.08 (0.79–1.47)                               |
| Infants receiving active treatment  |  |  |
| Survived without neurodevelopmental impairment vs. died   | 1.55 (1.24–1.93)                               | 1.64 (1.30-2.06)                               |
| Survived with neurodevelopmental impairment vs. died  | 1.44 (1.14-1.81)                               | 1.30 (1.03–1.64)                               |
| Survived without neurodevelopmental impairment vs. survived with neurode-<br>velopmental impairment | 1.08 (0.83–1.40)                               | 1.26 (0.97–1.65)                               |

Younge N et al. N Engl J Med 2017;376:617-628.

### Summary

- Significant increase in the rate of survival at 18 to 22 months of age in babies born between 22 and 24 weeks
- Rates of death, NDI and other adverse outcomes remains high
- Despite the improved survival, the rates of neurodevelopmental impairment hasn't increased

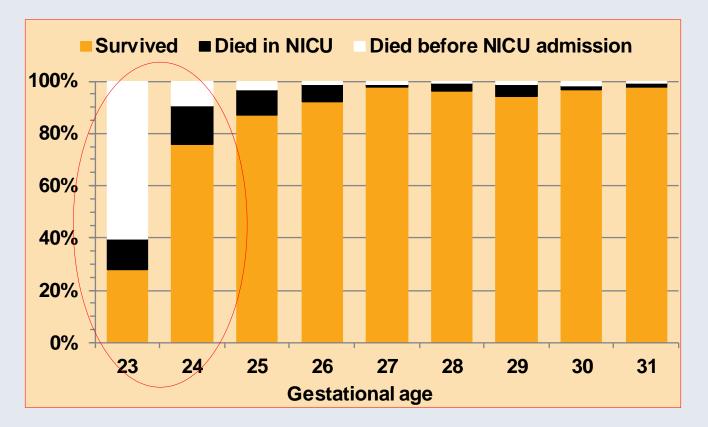
### **Newborn Outcomes (1)**

Admissions of *inborn* babies to NICU by gestational age 2008-2017

| Gestation<br>(weeks) | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
|----------------------|------|------|------|------|------|------|------|------|------|------|
|                      |      |      |      |      |      |      |      | (    |      |      |
| 23                   | 0    | 1    | 0    | 2    | 0    | 1    | 0    | 0    | 4    | 3    |
|                      |      |      |      |      |      |      |      |      |      |      |
| 24                   | 8    | 9    | 13   | 8    | 7    | 7    | 12   | 6    | 11   | 8    |
|                      |      |      |      |      |      |      |      |      |      |      |
| 25                   | 16   | 12   | 15   | 8    | 13   | 10   | 7    | 9    | 9    | 10   |
|                      |      |      |      |      |      |      |      |      |      |      |
| 26                   | 17   | 15   | 10   | 14   | 7    | 13   | 14   | 14   | 10   | 11   |

### **Newborn Outcomes (3)**

Survival of live inborn babies 23-31 weeks 2008-2017 (n=1481)



### **Newborn Outcomes (4)**

Survival of live inborn babies admitted to NICU 2008-2017 (n=1426)



### Newborn Outcomes – long term

| Outcome of children <1500g born in 2015<br>(corrected) by gestational age groups  | at 2 years             |
|---|------------------------|
| Outcome Category  | 23 - 28 weeks<br>n= 48 |
|   | n (%)                  |
| I (Severe disability – deafness, blindness, severe CP, developmental delay – Bayley cognitive score >2 SD below mean)   | 1 (2)                  |
| II (impaired vision requiring glasses, deafness corrected with hearing aid, mild – mod CP without developmental delay, Bayley cognitive score 1-2SD below mean) | 3 (6)                  |
| III (Presence of tone disorder or motor delay without cognitive impairment)   | 0 (0)                  |
| IV (normal development)   | 44 (92)                |

74% follow-up rate for all children <1500 g at birth

# Outcomes for babies born at 23 and 24 weeks' gestation

- Outcomes for babies born at 23 and 24 weeks gestation has improved over the years
- Outcomes improve with provision of antenatal and neonatal care
- Higher rates of mortality and short & long term morbidity compared to babies born > 24 weeks' gestation
- Improved survival  $\neq$  more survivors with NDI