NEONATAL MORTALITY AND MORBIDITY REVIEW IN NEW ZEALAND – 2013 REPORT

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NEONATAL SERVICES

PMMRC - JUNE 23, 2015

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CONFLICT OF INTEREST

- No conflict of interest to declare

2013 PMMRC REPORT – OUTLINE

- Data collection and methodology
- Comparison of major outcomes with other mortality and morbidity reports
- Neonatal encephalopathy
- Deaths in infants born at borderline viability

DATA COLLECTION AND METHODOLOGY

- Extensive description on methodology of data collection allows comparison with other data sets and determines integrity of the data
- Use of the PSANZ Perinatal Mortality Classification
  - PSANZ-NDC Neonatal Death Classification
  - PSANZ-PDC Perinatal Data Classification
- Comparison with previous years' data and determination of significance
- Clear and considered recommendations

COMPARISON WITH OTHER COHORTS

- Victoria, Australia
  - Population 5.86 million (September 2014)
  - Livebirths 73,349 (2011)
- New Zealand
  - Population 4.6 million (estimated June 2015)
  - Livebirths 58,717 (2013)

Statistics New Zealand. www.stats.govt.nz/browse_for_stats/population/births/BirthsAndDeaths_HOTPYeDec13.aspx

Consultative Council on Obstetric and Paediatric Mortality and Morbidity (2014): 2010 and 2011, Victoria's Mothers and Babies: Victoria's Maternal, Perinatal, Child and Adolescent Mortality. State Government of Victoria, Melbourne.

COMPARISON WITH VICTORIA

	Victoria 2011	NZ 2013
Fetal deaths	9.5	7.4
Neonatal deaths	3.0	2.6
Perinatal Mortality	12.5	10.0

Consultative Council on Obstetric and Paediatric Mortality and Morbidity (2014): 2010 and 2011, Victoria's Mothers and Babies: Victoria's Maternal, Perinatal, Child and Adolescent Mortality. State Government of Victoria, Melbourne.

CAUSES OF NEONATAL DEATHS
PSANZ PERINATAL DEATH CLASSIFICATION

PSANZ PDC	Victoria 2011	NZ 2013
Congenital abnormality	33.2%	19.1%
Perinatal infection	2.7%	5.3%
Hypertension	1.8%	2.0%
Antepartum haemorrhage	11.2%	16.4%
Maternal conditions	2.7%	5.3%
Specific perinatal conditions	6.7%	9.2%
Hypoxic peripartum death	6.7%	5.3%
Fetal growth restriction	4.5%	1.3%
Spontaneous preterm	28.3%	32.2%
No obstetric antecedent	1.8%	3.9%

CAUSES OF NEONATAL DEATHS
PSANZ NEONATAL DEATH CLASSIFICATION

PSANZ NDC	Victoria 2011	NZ 2013
Congenital Abnormality	31.1%	21.1%
Extreme prematurity	37.4%	40.8%
Cardiorespiratory disease/disorders	6.0%	3.9%
Infection	5.5%	7.9%
Neurological	14.9%	16.4%
Gastrointestinal	3.0%	0.7%
Other	2.1%	9.2%

CONGENITAL MALFORMATIONS

- Lower proportion of Neonatal Death Classifications in New Zealand infants (compared to Victoria)
  - 75 NNDs from congenital abnormality in Victoria in 2011

    38 were terminations of pregnancy
  - 32 NNDs from congenital abnormality in NZ in 2013

    17 did not receive resuscitation at birth

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NEONATAL ENCEPHALOPATHY

NEONATAL ENCEPHALOPATHY 2010-2013

- Neonatal encephalopathy (NE)
  - A clinically-defined syndrome of disturbed neurological function within the first week of life in term (≥37 weeks) infants
  - Difficulty in initiating and maintaining respiration
  - Depression of tone and reflexes
  - Subnormal level of consciousness
  - Seizures are common

- Sarnat Stages 2 and 3 (moderate and severe)

NEONATAL ENCEPHALOPATHY 2010-2013

- Most common identifiable cause is from hypoxia-ischaemia
- Other causes include hypoglycaemia, CNS congenital abnormality, infection, metabolic conditions

NEONATAL ENCEPHALOPATHY 2010-2013

- Cases identified by Paediatric Surveillance Unit and collection of data by paediatricians, LMCs and PMMRC
- Key neonatal clinicians and local PMMRC coordinators since 2012

- Denominator
  - Births at term from the NZ birth registration dataset from BDM

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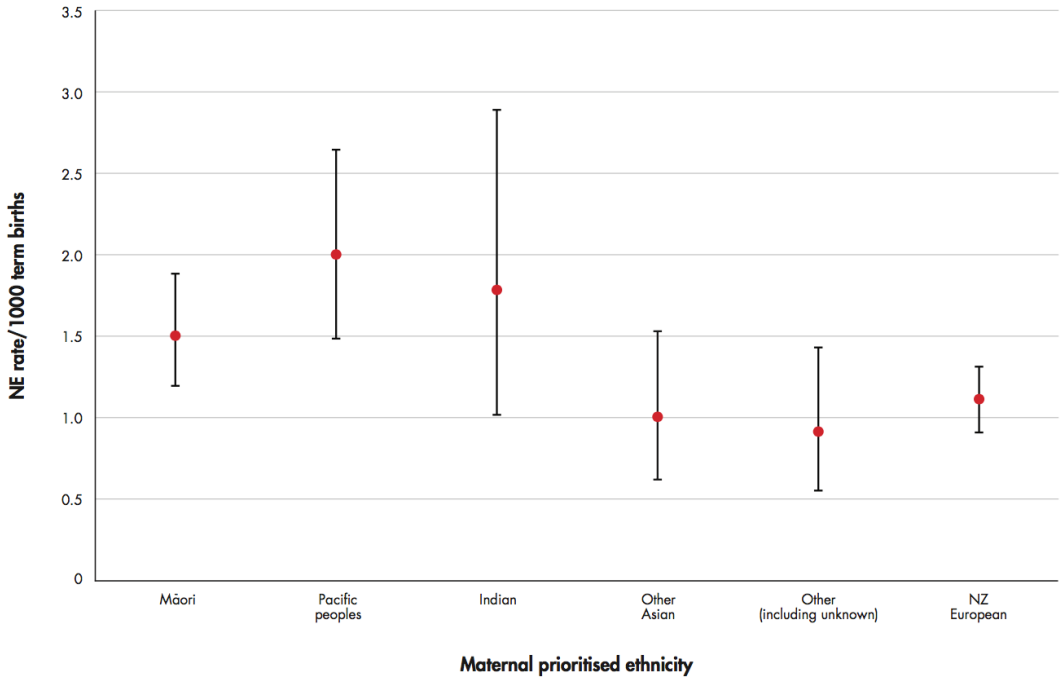
NEONATAL ENCEPHALOPATHY 2010-2013

- Rate of NE in term infants 1.29 per 1000 births (95%CI 1.16-1.45)
- Comparison rates depend on baseline neonatal mortality rates
  - In countries with NMR <5/1000, median NE rate was 1.6/1000 births (range 0.68-3.75)

Lee A, et al. intrapartum-related neonatal encephalopathy incidence an impairment at regional and global levels for 2010 with trends from 1990 Pediatr Res 2013;74(Suppl 1):50-72.

NEONATAL ENCEPHALOPATHY ETHNIC DIFFERENCES

Figure 3.1: Neonatal encephalopathy rates (per 1000 term births) by maternal prioritised ethnicity 2010–2013



- Rates higher in Maori, Pacific and Indian mothers

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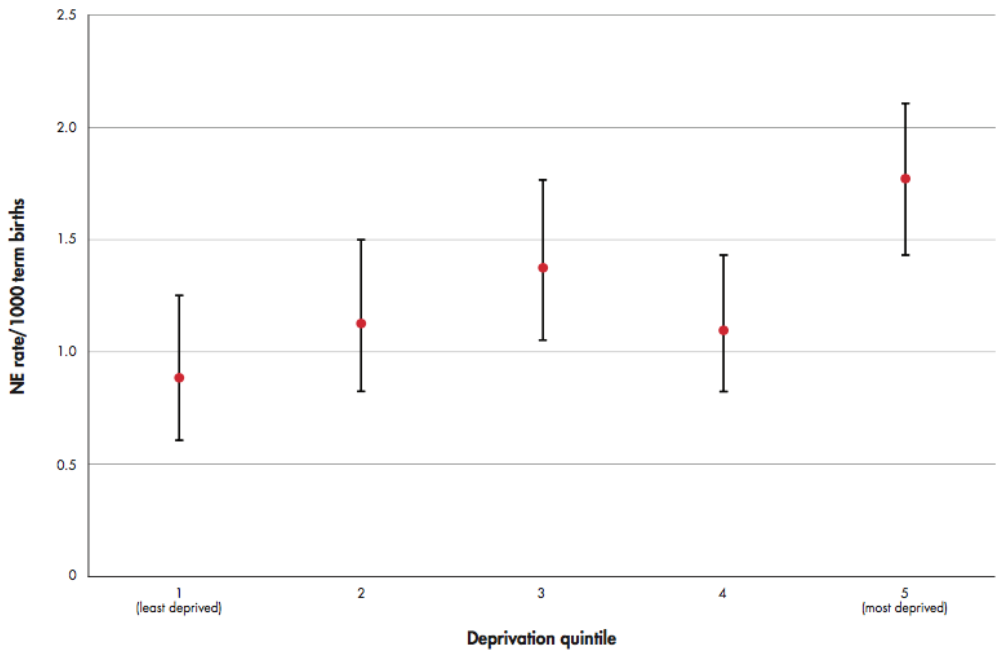
NEONATAL ENCEPHALOPATHY SOCIAL DEPRIVATION

Figure 3.3: Neonatal encephalopathy rates (per 1000 term births) by deprivation quintile 2010–2013



- Risk doubled in infants born to mothers living in the most deprived quintile areas

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NEONATAL ENCEPHALOPATHY
OTHER RISK FACTORS

- Twin deliveries (risk 60% higher), especially the second twin
- Term infants with birthweight <2500g
  - Relative Risk 2.4x higher than term infants 2500-4499g
- Risk is increased at 37 and 41 weeks
- Increasing risk with increasing deprivation quintile
- 20% of NE infants weighed <10th percentile

NEONATAL ENCEPHALOPATHY
NEONATAL CHARACTERISTICS AND CARE

- 80% of infants had an Apgar score <5 at 1 minute
- 78% of infants had an Apgar score <7 at 5 minutes
- 53% of infants had an Apgar score <7 at 10 minutes

- There has been a decline in the proportion of babies without cord gases (28.0% in 2010, 14.3% in 2013 – p=0.03)
- Cord gases were abnormal (pH≤7, BE≤-12, lactate≥6) in 64%

DELIVERY ROOM MANAGEMENT IN INFANTS WITH NEONATAL ENCEPHALOPATHY

- 92% of infants required resuscitation at birth
  - >60% received IPPV with mask
  - 57% were intubated (73% of severe, 50% of moderate)
  - 39% received cardiac massage (60% of severe)
  - 20% received adrenaline (42% of severe)

- 69% of case reviews did not reveal any factors that caused or contributed to unsatisfactory neonatal resuscitation
  - 15% of cases overall identified suboptimal resuscitation

RESUSCITATION OF INFANTS

- 10% of infants will require some form of assistance with breathing
  - 1% require extensive resuscitation

"Although the need for resuscitation of the newborn infant can often be anticipated, and the need for resuscitation in low risk births may be 1% or less, there remain many occasions when it is unexpected. Therefore, a suitable place, equipment and personnel trained to resuscitate a newborn infant must be available at all times, and in all places, where infants are born."

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http://www.nzrc.org.nz/assets/Uploads/Guidelines/guideline-13-1dec10.pdf

NEONATAL ENCEPHALOPATHY THERAPEUTIC HYPOTHERMIA

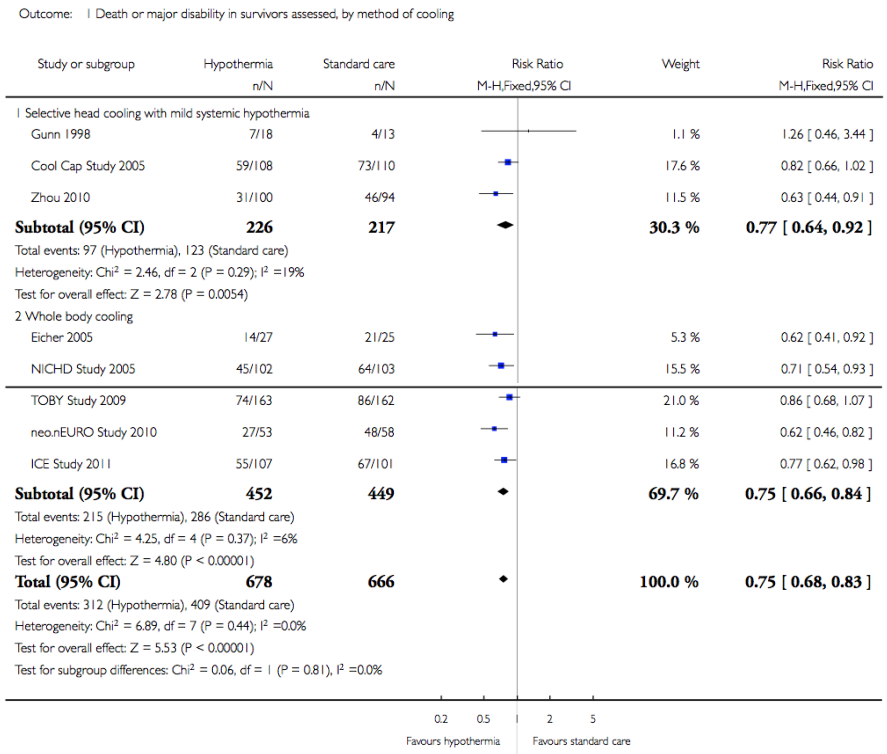
- Therapeutic hypothermia aims to lower the temperature of the vulnerable deep brain structures, the basal ganglia, to 32°C to 34°C
- Two methods have been studied: whole-body cooling and selective head cooling
- Modification of cells programmed for apoptosis
- May also protect by lowering metabolic rate, attenuating release of excitatory amino acids, modify the uptake of glutamate, reduce production of toxic nitric oxide and oxygen free radicals

NEONATAL ENCEPHALOPATHY THERAPEUTIC HYPOTHERMIA

- Effective in reducing mortality and long-term developmental morbidity from neonatal encephalopathy

Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD003311.

NEONATAL ENCEPHALOPATHY THERAPEUTIC HYPOTHERMIA



Outcome: 1 Death or major disability in survivors assessed, by method of cooling

Study or subgroup	Hypothermia n/N	Standard care n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Selective head cooling with mild systemic hypothermia					
Gunn 1998	7/18	4/13		1.1 %	1.26 [0.46, 3.44]
Cool Cap Study 2005	59/108	73/110		17.6 %	0.82 [0.66, 1.02]
Zhou 2010	31/100	46/94		11.5 %	0.63 [0.44, 0.91]
Subtotal (95% CI)	**226**	**217**		**30.3 %**	**0.77 [0.64, 0.92]**
Total events: 97 (Hypothermia), 123 (Standard care)					
Heterogeneity: Chi^2 = 2.46, df = 2 (P = 0.29); I^2 =19%					
Test for overall effect: Z = 2.78 (P = 0.0054)					
2 Whole body cooling					
Eicher 2005	14/27	21/25		5.3 %	0.62 [0.41, 0.92]
NICHD Study 2005	45/102	64/103		15.5 %	0.71 [0.54, 0.93]
TOBY Study 2009	74/163	86/162		21.0 %	0.86 [0.68, 1.07]
neo.nEURO Study 2010	27/53	48/58		11.2 %	0.62 [0.46, 0.82]
ICE Study 2011	55/107	67/101		16.8 %	0.77 [0.62, 0.98]
Subtotal (95% CI)	**452**	**449**		**69.7 %**	**0.75 [0.66, 0.84]**
Total events: 215 (Hypothermia), 286 (Standard care)					
Heterogeneity: Chi^2 = 4.25, df = 4 (P = 0.37); I^2 =6%					
Test for overall effect: Z = 4.80 (P < 0.00001)					
Total (95% CI)	**678**	**666**		**100.0 %**	**0.75 [0.68, 0.83]**
Total events: 312 (Hypothermia), 409 (Standard care)					
Heterogeneity: Chi^2 = 6.89, df = 7 (P = 0.44); I^2 =0.0%					
Test for overall effect: Z = 5.53 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 0.06, df = 1 (P = 0.81), I^2 =0.0%					

0.2 0.5 1 2 5

Favours hypothermia Favours standard care

Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD003311.

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NEONATAL ENCEPHALOPATHY THERAPEUTIC HYPOTHERMIA

- Effective in reducing mortality and long-term developmental morbidity from neonatal encephalopathy
  - 25% reduction in death or major neurological deficit
  - Number needed to treat to prevent = 7
  - Low incidence of adverse effects

- Increase in proportion receiving cooling from 68% in 2010 to 83% in 2013 (p=0.03)

Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD003311.

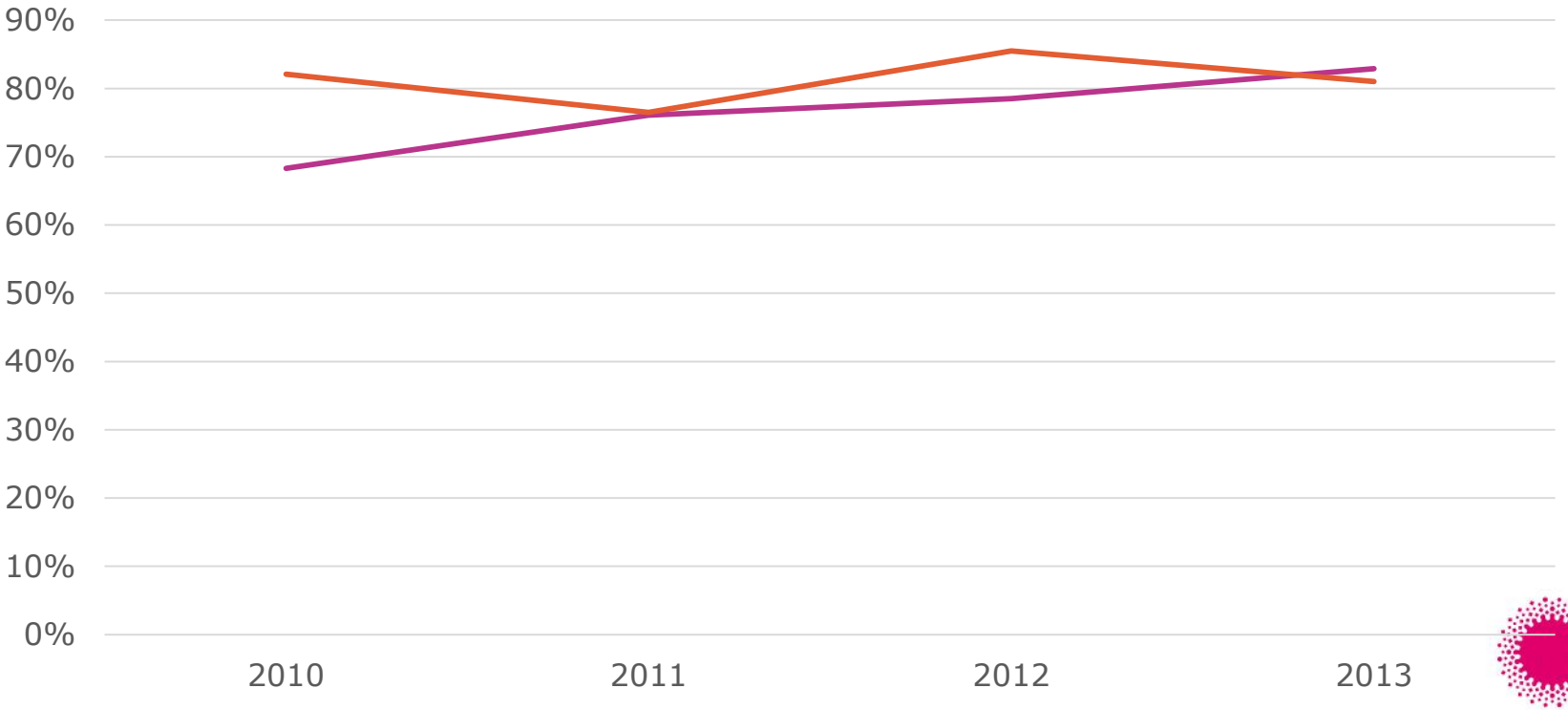
NEONATAL ENCEPHALOPATHY THERAPEUTIC HYPOTHERMIA

- Criteria generally based on infants enrolled in clinical trials showing efficacy
  - Age <6 hours from birth
  - Moderate or severe HIE (or other combination of neurological markers of NE)
  - 35 weeks or more
  - Evidence of perinatal asphyxia, with at least two of:
    - Apgar score 5 or less at 10 minutes
    - Ongoing resuscitation (cardiac massage, ventilation) at 10 minutes
    - Cord arterial pH<7.0 or, if not available, blood gas pH<7 or Base Deficit >12 within 1 hour of birth

NEONATAL ENCEPHALOPATHY THERAPEUTIC HYPOTHERMIA

- Exclusion criteria
  - Birthweight <1800g
  - Major or suspected congenital abnormalities likely to result in death
  - Overt bleeding or severe coagulopathy unresponsive to therapy
  - Imminent/inevitable death

NEONATAL ENCEPHALOPATHY 2010-2013 THERAPEUTIC HYPOTHERMIA PAGE 139



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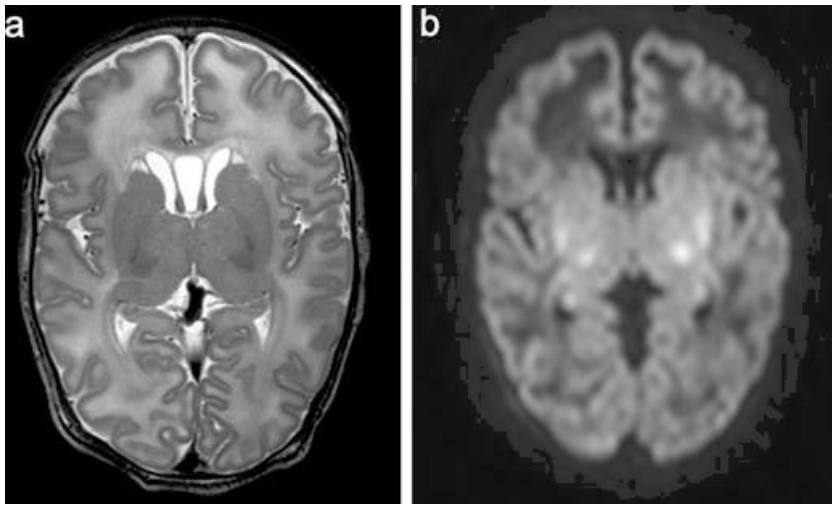
OUTCOMES FOLLOWING NEONATAL ENCEPHALOPATHY

- Outcomes related to severity of NE
- Mortality 34% in infants with Stage 2/3 HIE who did not receive therapeutic hypothermia
  - 23% in Stage 2; 68% in Stage 3
  - Multiorgan failure
  - Withdrawal of intensive care based on prognosis

Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD003311.

OUTCOMES FOLLOWING NEONATAL ENCEPHALOPATHY

- Basal Ganglia Thalamus pattern
  - Often seen after an acute sentinel event
  - Often severely disabled (cerebral palsy) and not included in follow-up

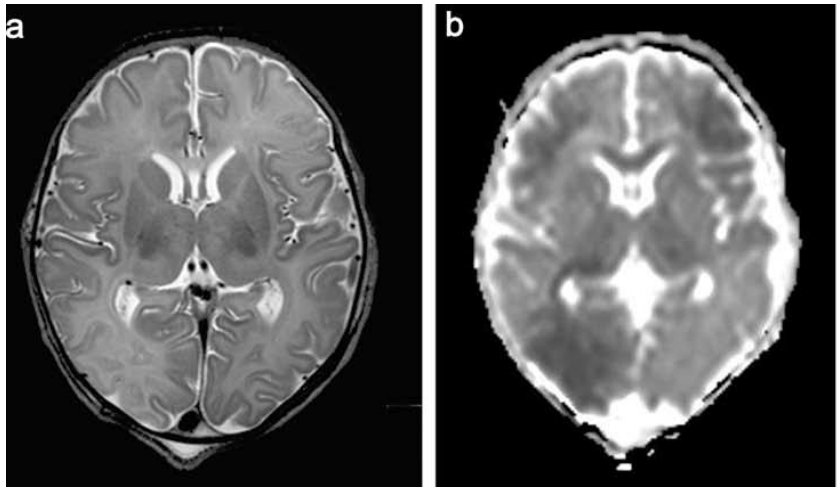


Day 5 MRI

de Vries LS, Jongmans MJ. Long-term outcome after neonatal hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed 2010;95:F220–F224.

OUTCOMES FOLLOWING NEONATAL ENCEPHALOPATHY

- Watershed Injury
  - Follows prolonged partial asphyxia
  - Watershed areas of the anterior-middle cerebral artery and posterior-middle cerebral artery distribution
  - May be seen following infection, hypotension and hypoglycaemia
  - Motor problems less common

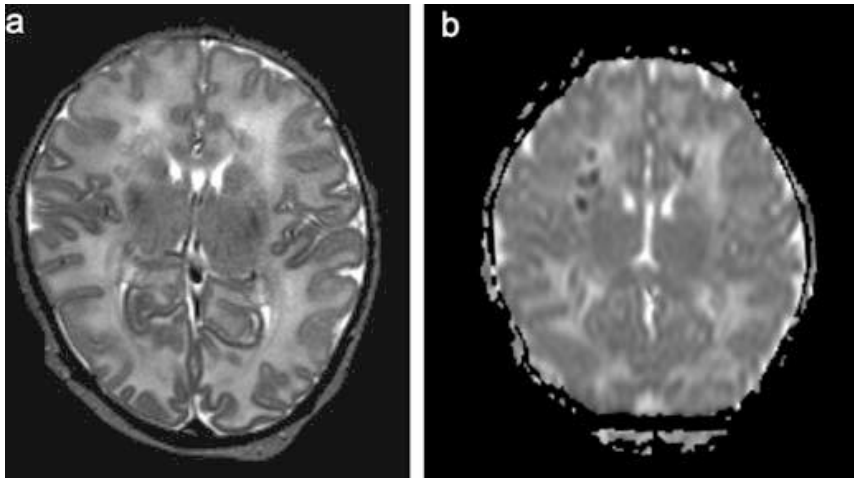


Day 3 MRI

de Vries LS, Jongmans MJ. Long-term outcome after neonatal hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed 2010;95:F220–F224.

OUTCOMES FOLLOWING NEONATAL ENCEPHALOPATHY

- Localised lesions
  - Punctate lesions in white matter
  - Infants often less mature and have a milder clinical course than infants with other patterns



Day 5 MRI

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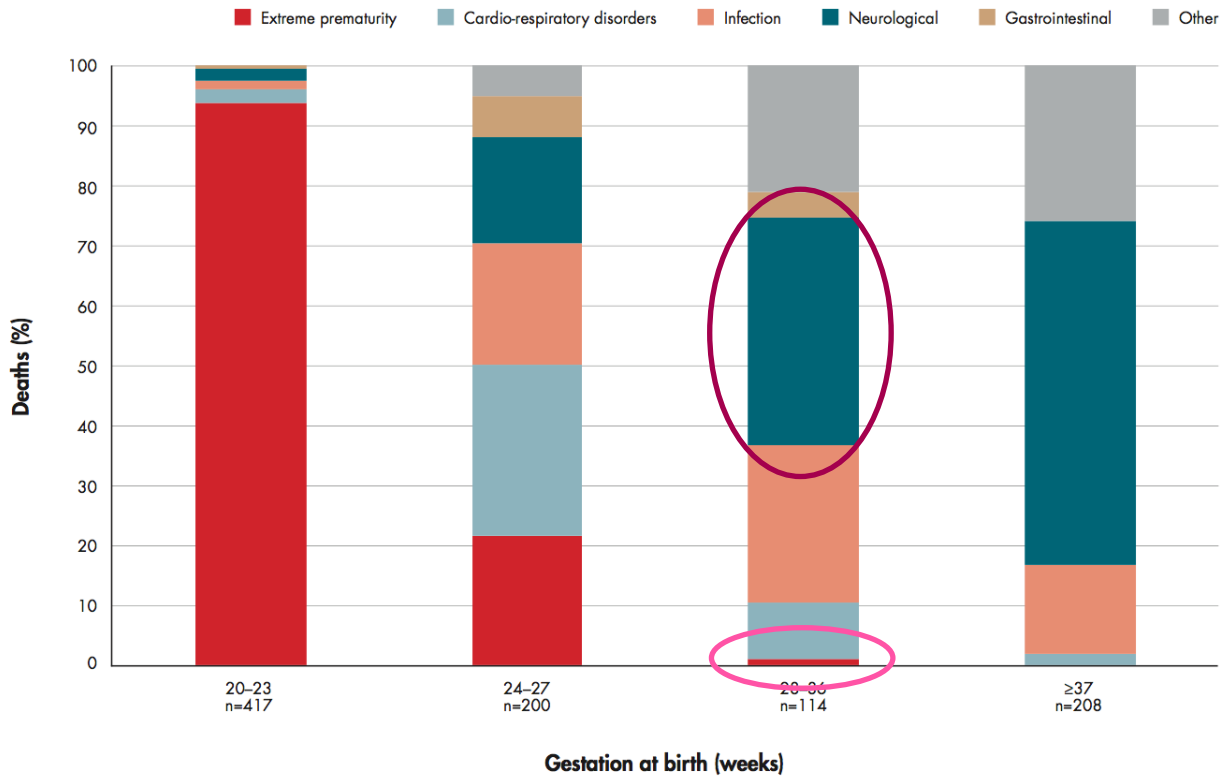
FOLLOW-UP OF INFANTS WITH HIE

- Infants with NE are at high risk of developmental problems
  - A normal MRI is highly predictive of a normal outcome
  - However, increasing evidence that infants with mild NE are less likely to perform as well as unaffected control infants
- 86% of NE infants discharged home were referred for further developmental therapy, home care or outpatient follow-up
  - Likely that the remaining infants were reviewed by local services

DEATHS FROM HIE IN PRETERM INFANTS

- Causes of death (PSANZ-NDC)



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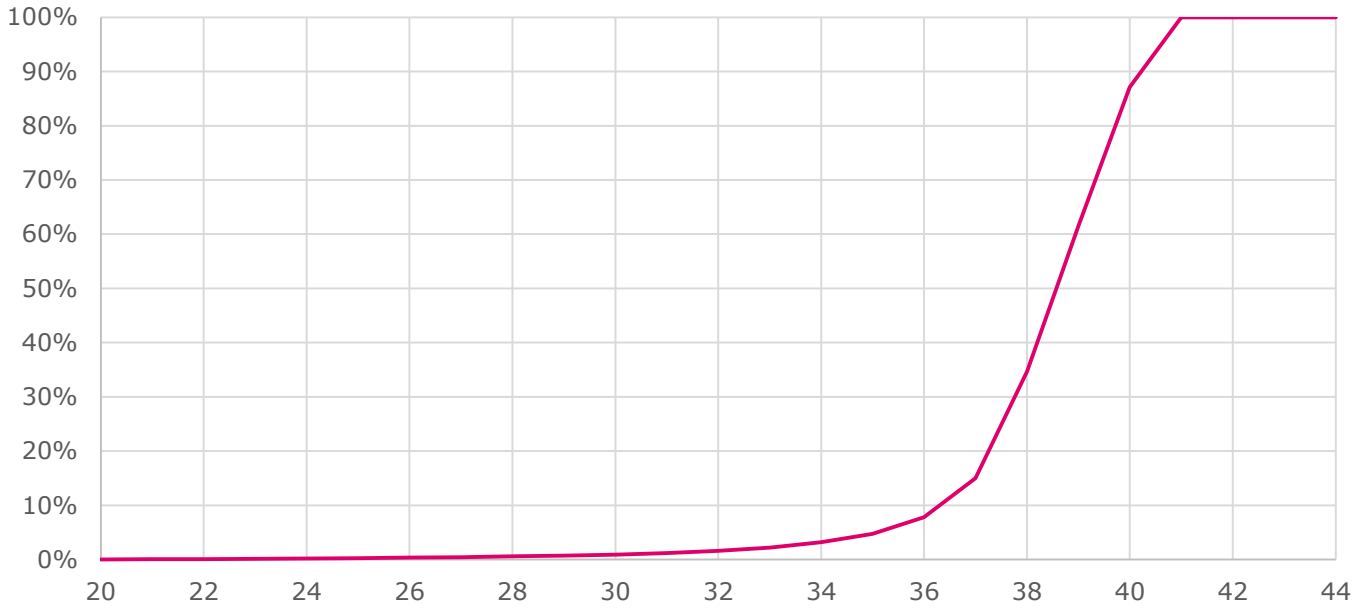
PRACTICE POINT: RECOGNISING THE BABY AT RISK OF NE

- Early recognition and review will facilitate therapeutic cooling
- Practitioners should be aware of factors associated with NE:
  - Abnormal CTG
  - Apgar score ≤7 at 5 minutes
  - Decreased tone or absent primitive reflexes
  - Difficult establishing or maintaining respirations
  - Requiring resuscitation at birth (IPPV or drugs)
  - Slowness in initiating feeds
  - Abnormal level of consciousness
  - Weak or absent cry
  - Seizures

INFANTS BORN AT BORDERLINE VIABILITY

OUTCOMES FOR BABIES BORN AT BORDERLINE VIABILITY

- Prematurity occurs in approximately 8% of births



Li Z, Zeki R, Hilder L & Sullivan EA 2013. Australia's mothers and babies 2011. Perinatal statistics series no. 28. Cat. no. PER 59. Canberra: AIHW National Perinatal Epidemiology and Statistics Unit.

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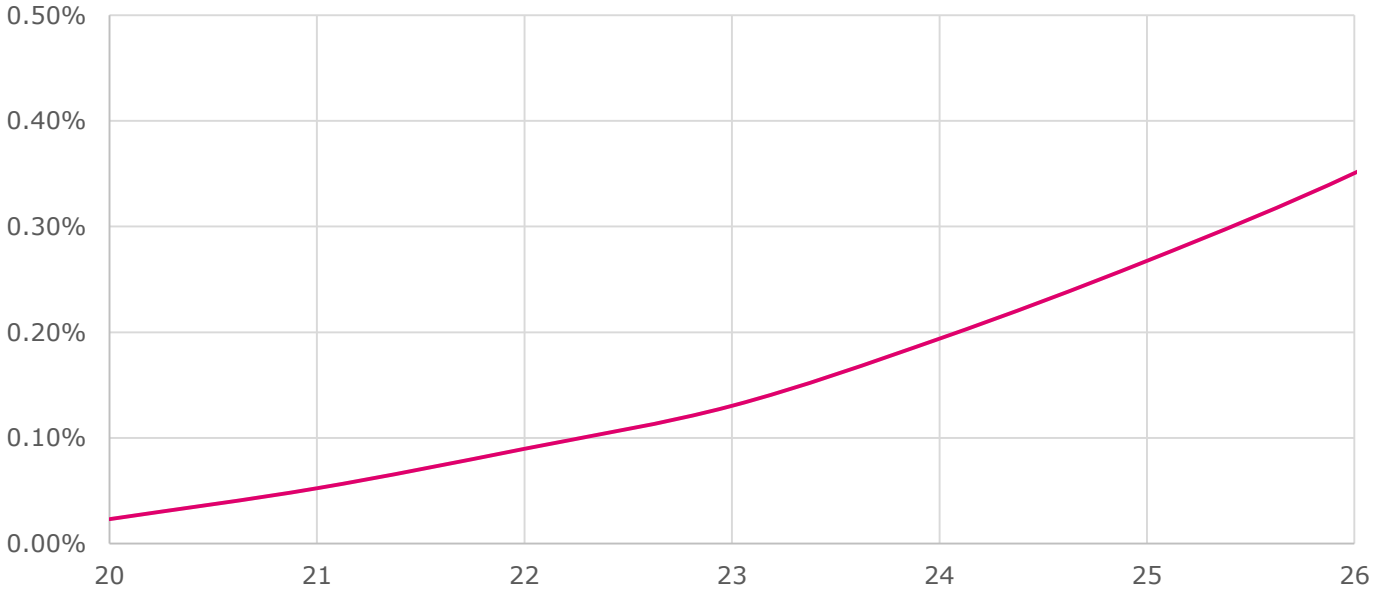
OUTCOMES FOR BABIES BORN AT BORDERLINE VIABILITY

- Only 0.35% of babies are born below 27 weeks' gestation



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OUTCOMES FOR BABIES BORN AT BORDERLINE VIABILITY PAGE 68

	20-23 weeks n=63	24-27 weeks n=19
Resuscitation at birth		
Yes	7 (11%)	18 (95%)
No	56 (89%)	1 (5%)
Outcome of resuscitation		
Resuscitated and transferred	5 (8%)	14 (74%)
Unable to be resuscitated	2 (3%)	4 (21%)

Excludes infants with congenital abnormalities

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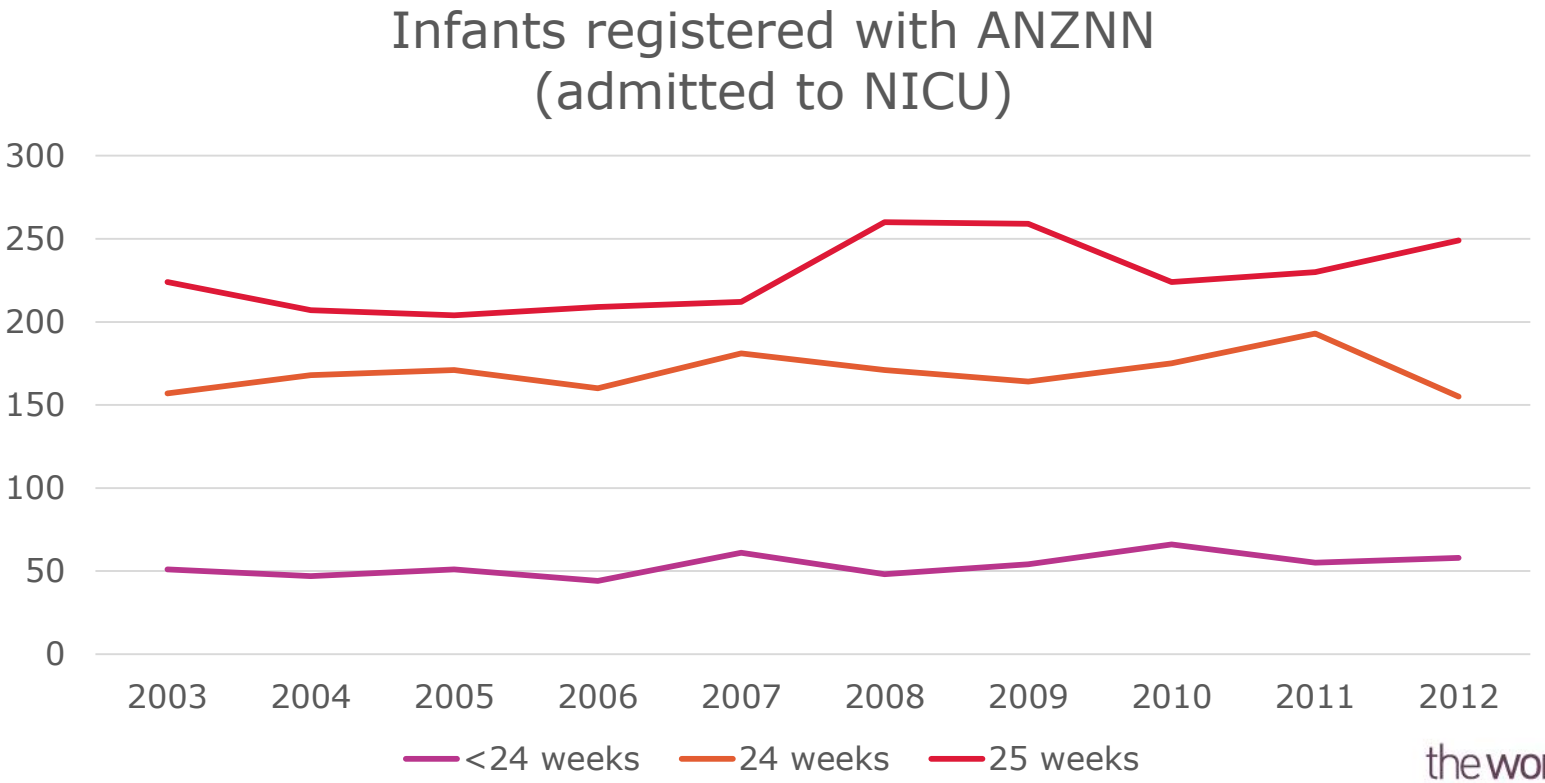
OUTCOMES FOR BABIES BORN AT BORDERLINE VIABILITY PAGE 68

	20-23 weeks n=63	24-27 weeks n=19
Place of death		
Home	2 (3%)	2 (11%)
Antenatal ward	1 (2%)	1 (5%)
Delivery suite	45 (71%)	2 (11%)
Neonatal unit	5 (8%)	13 (68%)
Emergency Department	2 (3%)	1 (5%)
Age at death (days)		
0	56 (89%)	9 (47%)
1-6	5 (8%)	5 (26%)
7-13	2 (3%)	3 (16%)
14-20		1 (5%)
21-27		1 (5%)

ANZNN REGISTRANTS AT BORDERLINE VIABILITY – ABSOLUTE NUMBERS



Australian and New Zealand Neonatal Network Annual Reports (2003-12). Available at https://npesu.unsw.edu.au/data-collection/australian-new-zealand-neonatal-network-anznn

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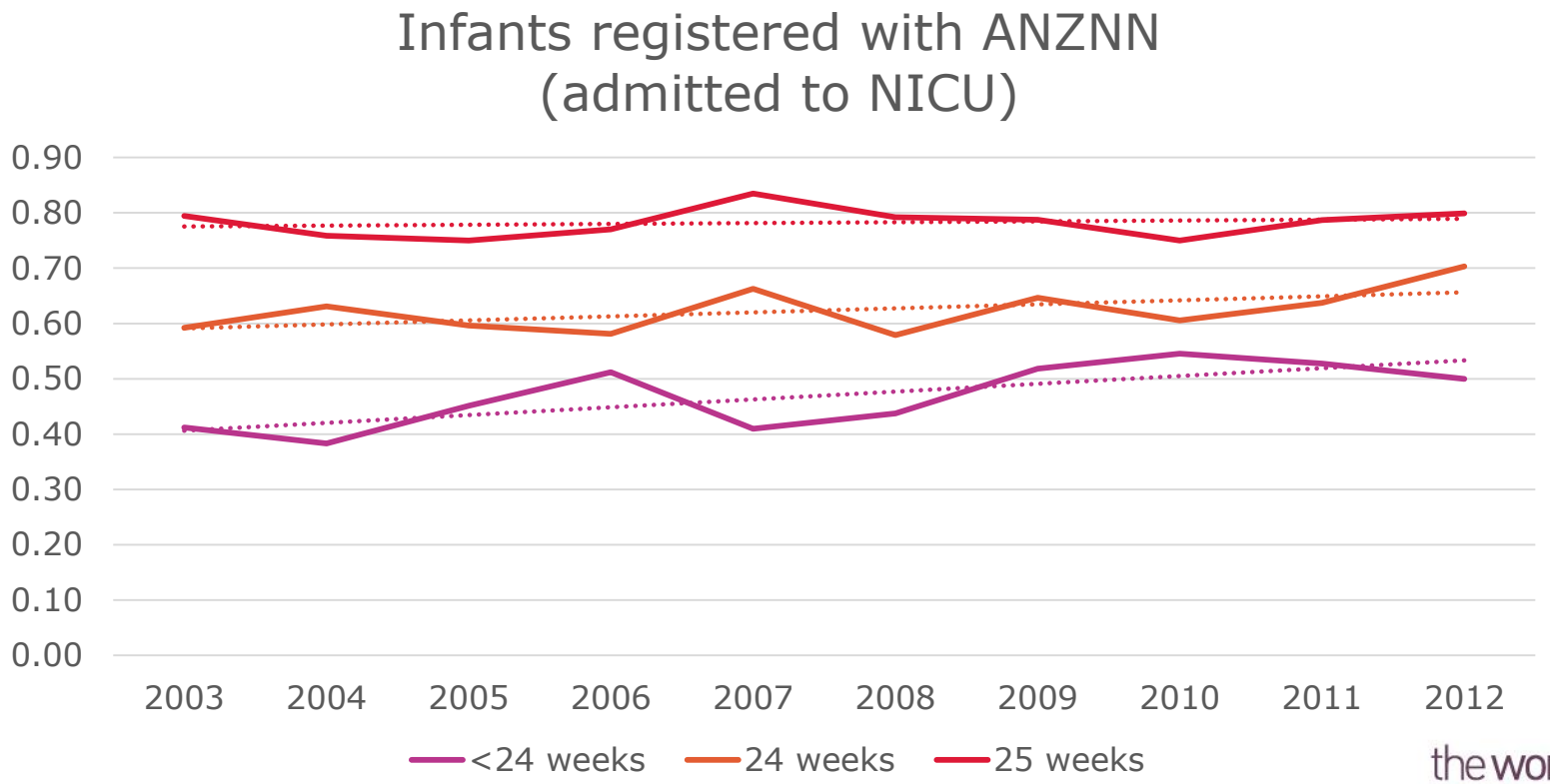
SURVIVAL TO DISCHARGE IN ANZNN REGISTRANTS



Australian and New Zealand Neonatal Network Annual Reports (2003-12). Available at https://npesu.unsw.edu.au/data-collection/australian-new-zealand-neonatal-network-anznn

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SURVIVAL AT THE ROYAL WOMEN'S HOSPITAL 2004-2013

	Admitted	Survival
23 weeks	39	19 (49%)
24 weeks	164	99 (60%)
25 weeks	226	172 (76%)

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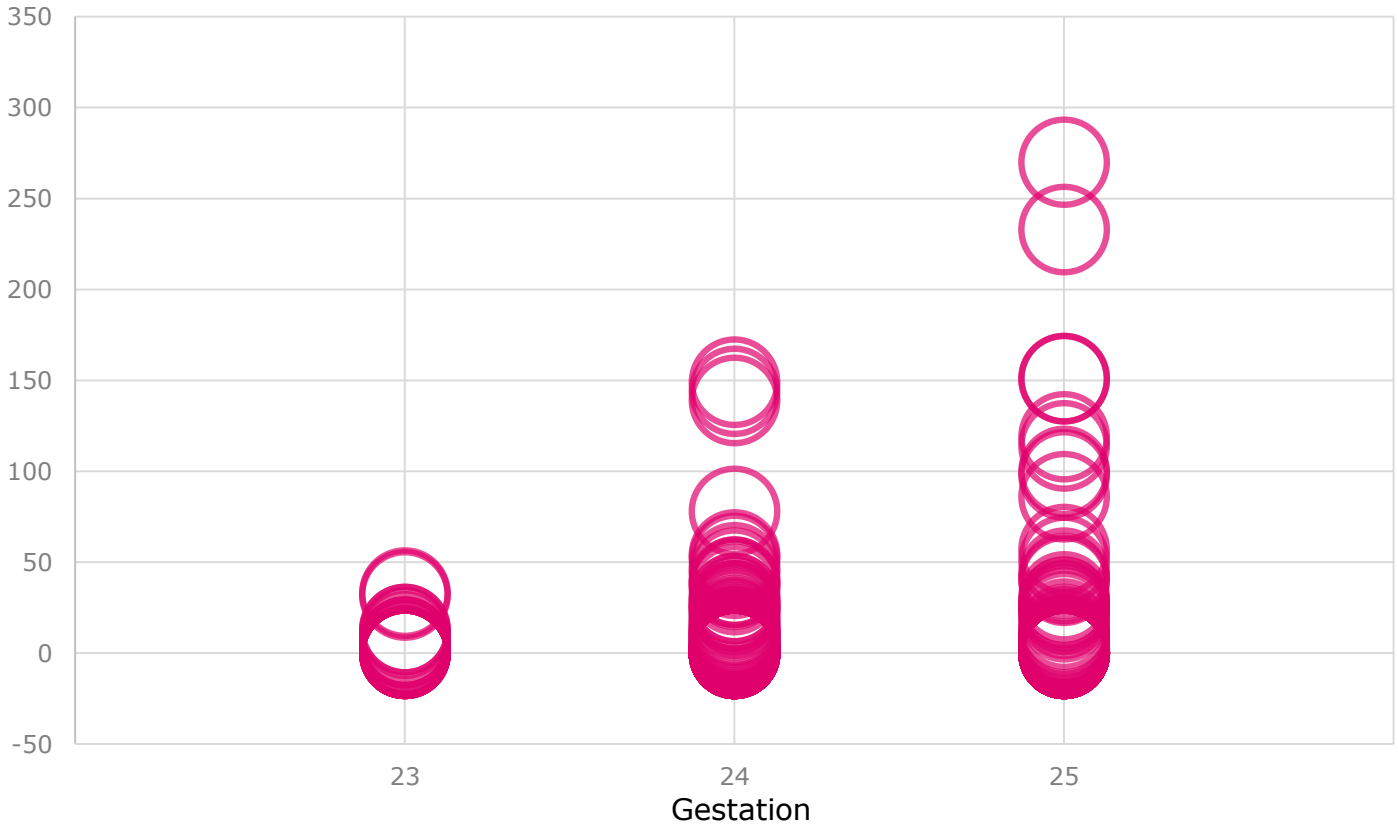
AGE AT DEATH IN BABIES BORN AT BORDERLINE VIABILITY RWH DATA 2004-13



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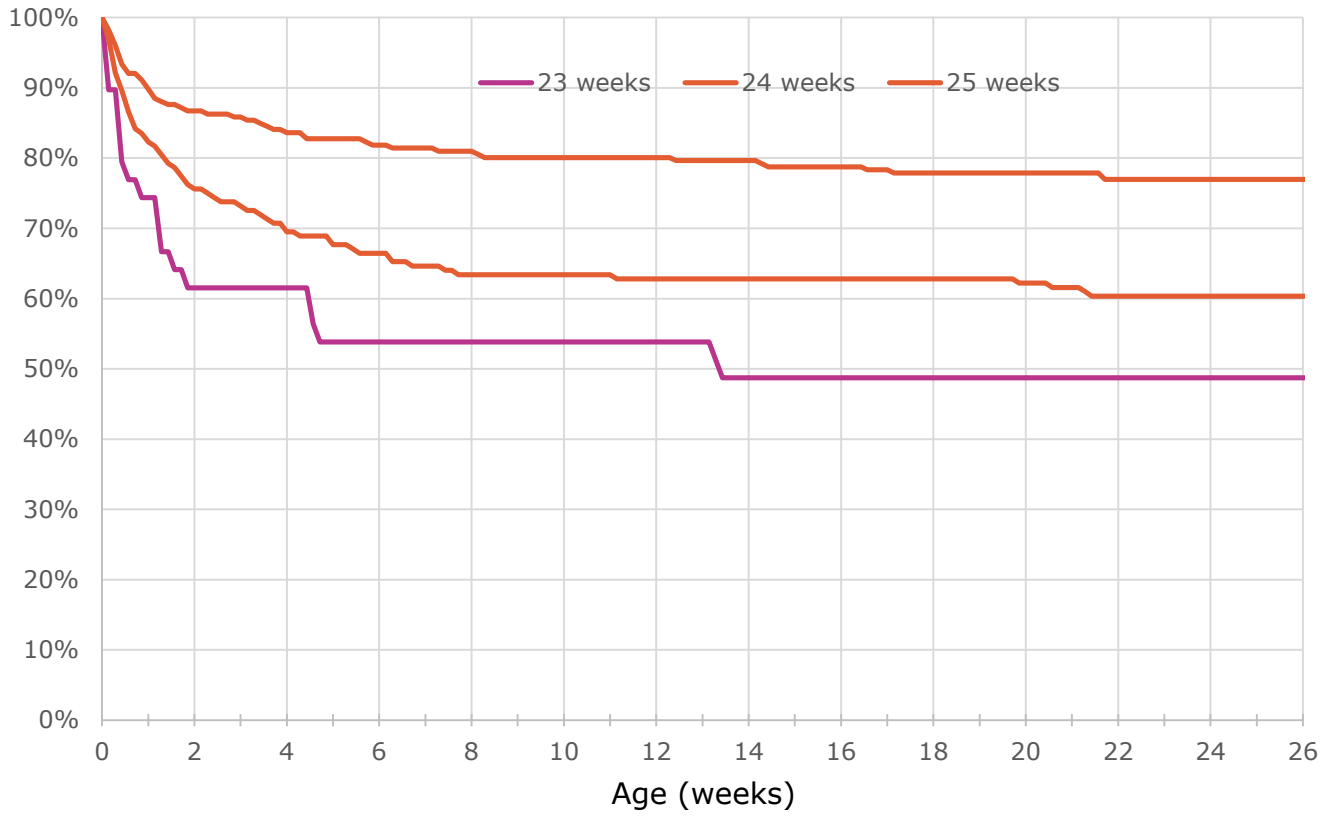

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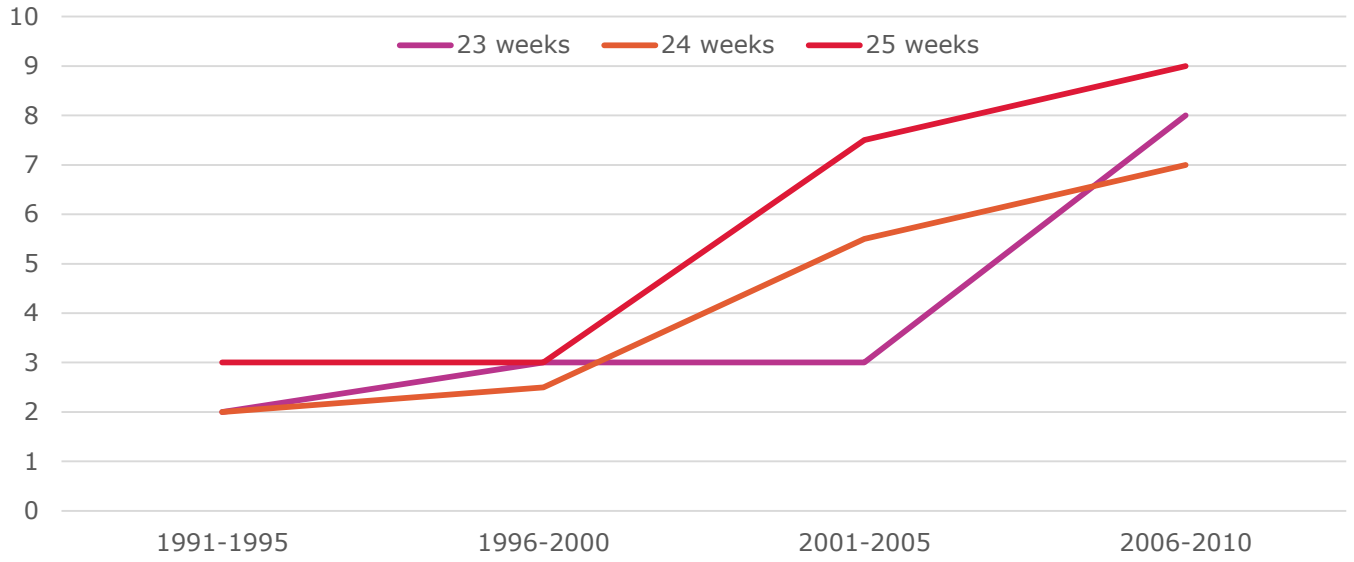
USE OF INTENSIVE CARE IN INFANTS BORN AT BORDERLINE VIABILITY

- Median number of days of NICU care in non-surviving infants



Seaton SE, et al. Babies born at the threshold of viability: changes in survival and workload over 20 years. Arch Dis Child Fetal Neonatal Ed 2013;98:F15-20.

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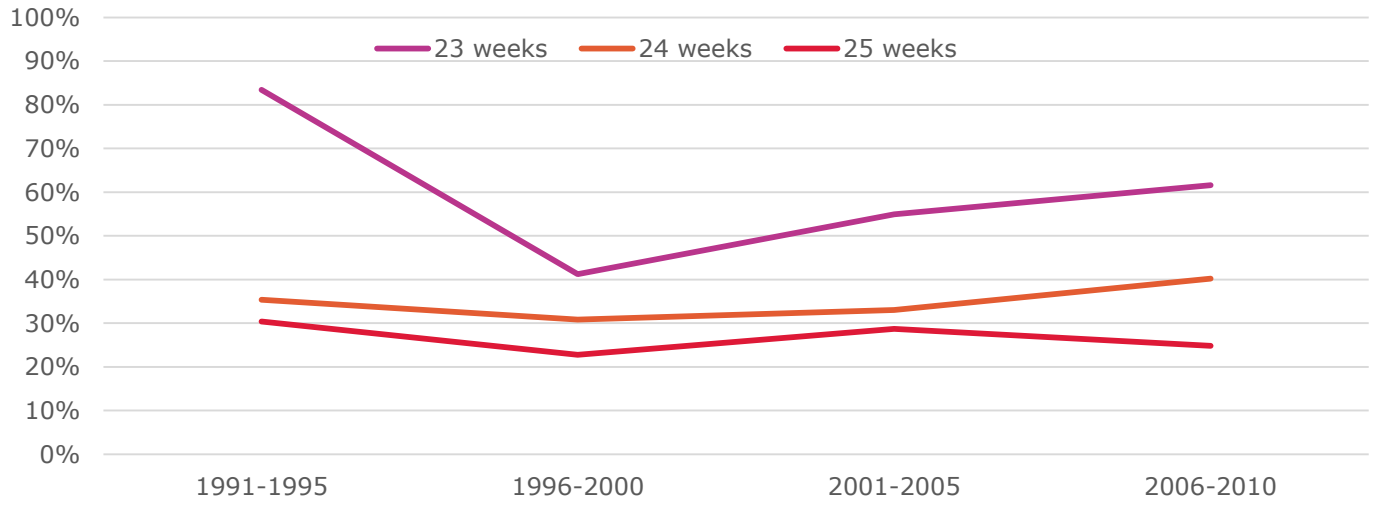
USE OF INTENSIVE CARE IN INFANTS BORN AT BORDERLINE VIABILITY

- Total number of ventilation days in non-survivors (as a proportion of hours for all infants for that gestational age group)



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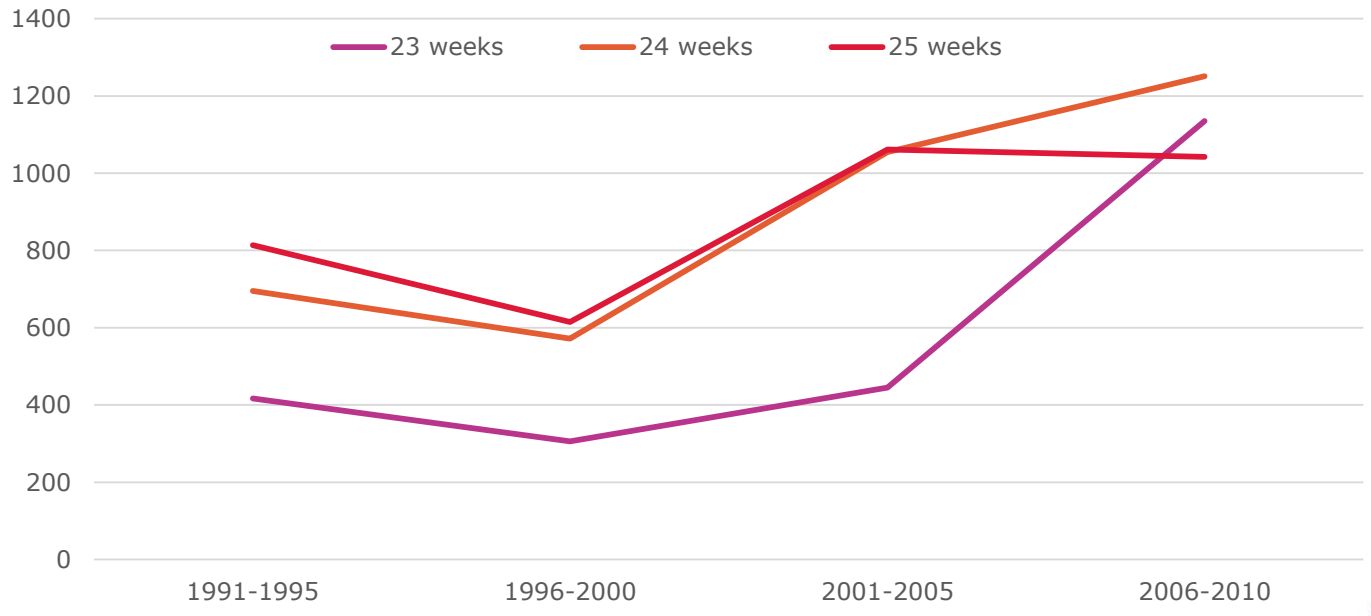
USE OF INTENSIVE CARE IN INFANTS BORN AT BORDERLINE VIABILITY

- Absolute number of ventilation days in non-survivors



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LONG-TERM OUTCOMES FOR BABIES BORN AT BORDERLINE VIABILITY

- Multitude of reports from different jurisdictions

Gestation	No disability	Mild	Moderate	Severe
23 weeks	30%	19%	30%	21%
24 weeks	34%	33%	21%	13%
25 weeks	44%	29%	17%	10%

- Mild — BSID 1-2 SD<mean, mild CP
  Moderate — BSID 2-3 SD<mean, moderate CP, moderate visual or hearing impairment
  Severe — BSID composite score 3+SD <mean, severe CP, or bilateral blindness or deafness

Serenius F, et al. Neurodevelopmental Outcome in Extremely Preterm Infants at 2.5 Years After Active Perinatal Care in Sweden. JAMA. 2013;309(17):1810-1820

LONG-TERM OUTCOMES FOR BABIES BORN AT BORDERLINE VIABILITY

- Estimate of disability in survivors
  - 23 weeks 1 in 2
  - 24 weeks 1 in 3
  - 25 weeks 1 in 4
  - 26 weeks 1 in 5
  - 27 weeks 1 in 6
  - 28 and 29 weeks 1 in 10

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SUMMARY

- Excellent report
- Data are presented in a format that is (relatively) easy to follow
- Strengthened by the report on Neonatal Encephalopathy, with population-based mortality and morbidity data
- Recommendations are specific and relevant

SUGGESTIONS?

- Infants born at 23 weeks – if admitted to a NICU – have around 50% survival to discharge. Should these be separated from the 20-23 week outcomes?
  Should data on infant deaths (beyond 28 days) in preterm infants be presented?
- The NEWG has looked only at infants 37 weeks or greater.
  Consideration should be given to including infants at lower gestation (especially where cooling is applied)

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