THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

MEDICAL AND HEALTH SCIENCES

Intermittent Hypoxaemia in Late Preterm Babies

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Late preterm babies

- Born 34^{+0} – 36^{+6} weeks gestational age (GA)
- Majority of the preterm population
- “The Great Pretenders”

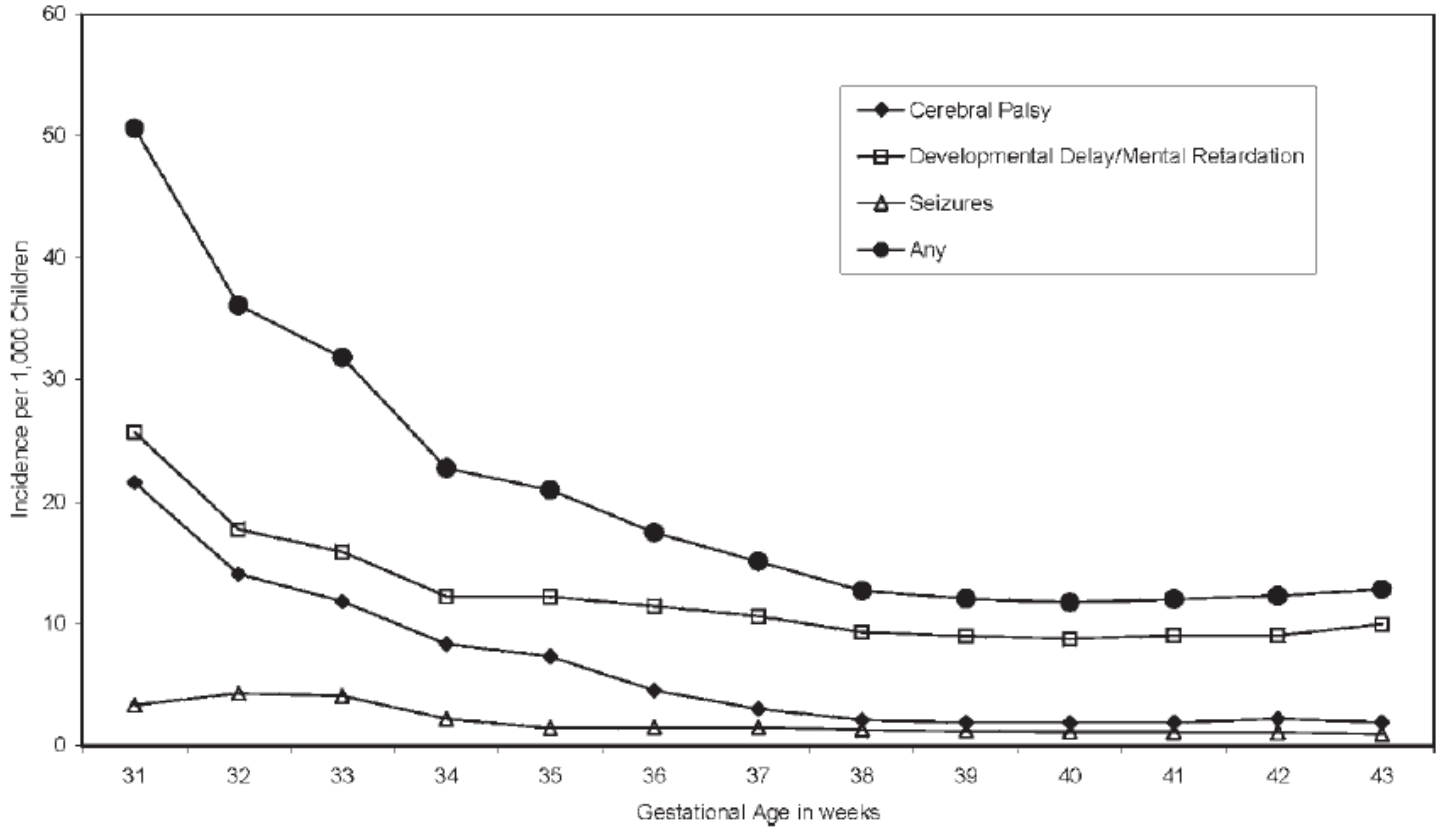


Figure. Incidence of neurodevelopmental outcomes by gestational age (3-week average incidence).

Petrini et al. J Pediatr 2009;154:169-76

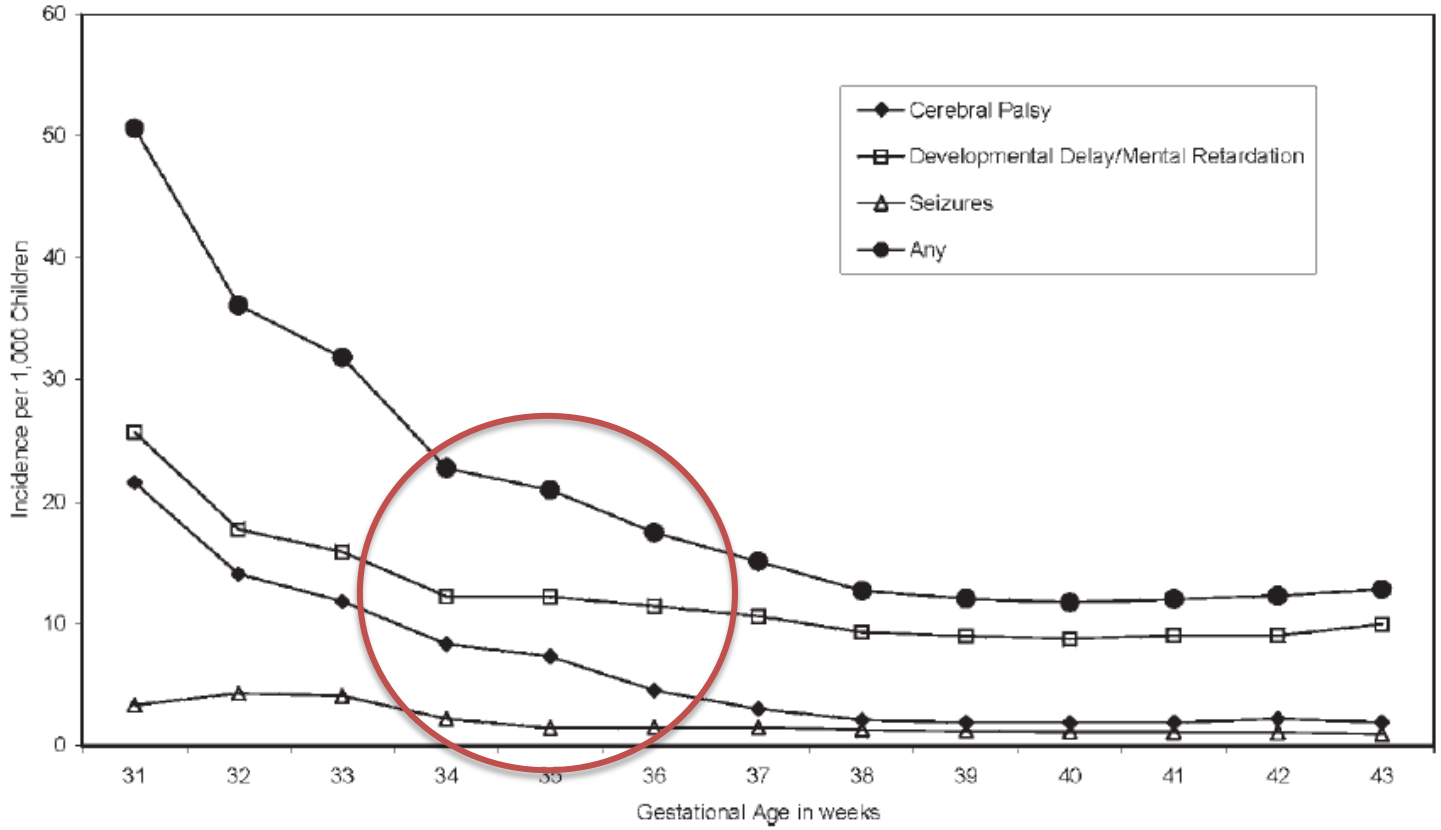
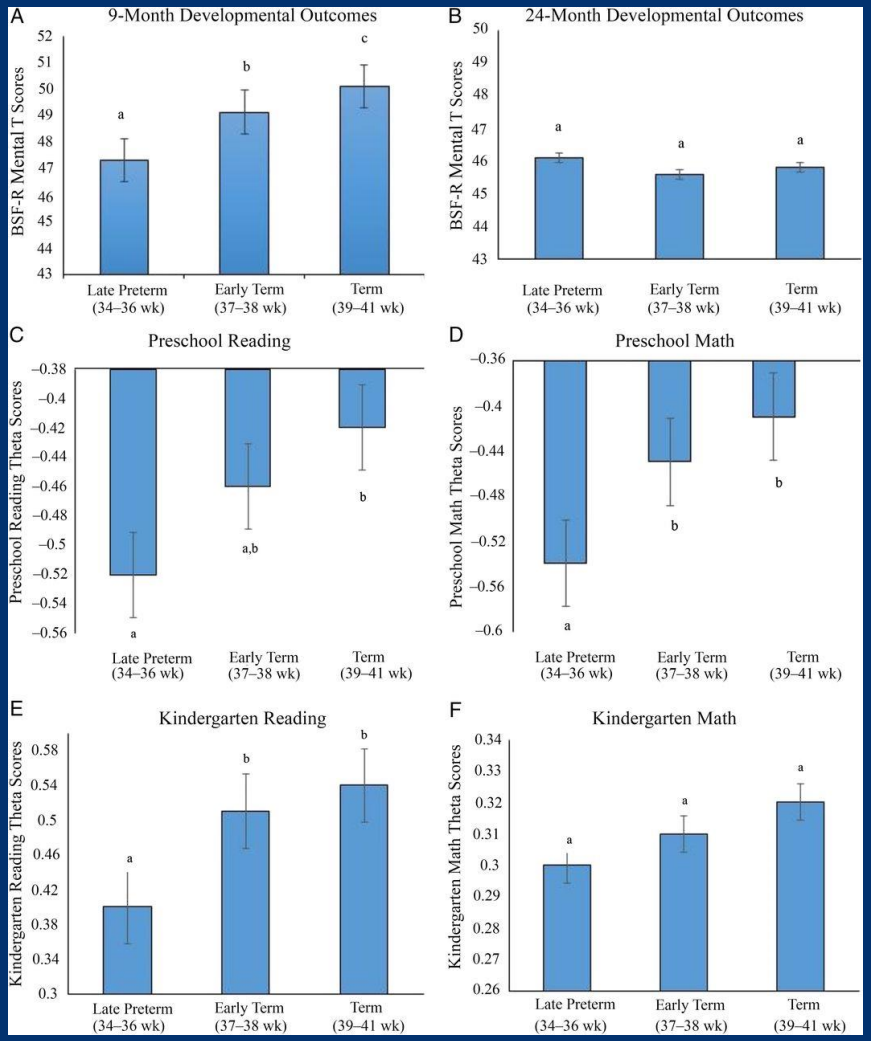


Figure. Incidence of neurodevelopmental outcomes by gestational age (3-week average incidence).

Petrini et al. J Pediatr 2009;154:169-76

Developmental and educational scores in Late Preterm Babies.



Prachi Shah et al. Pediatrics 2016;138:e20153496

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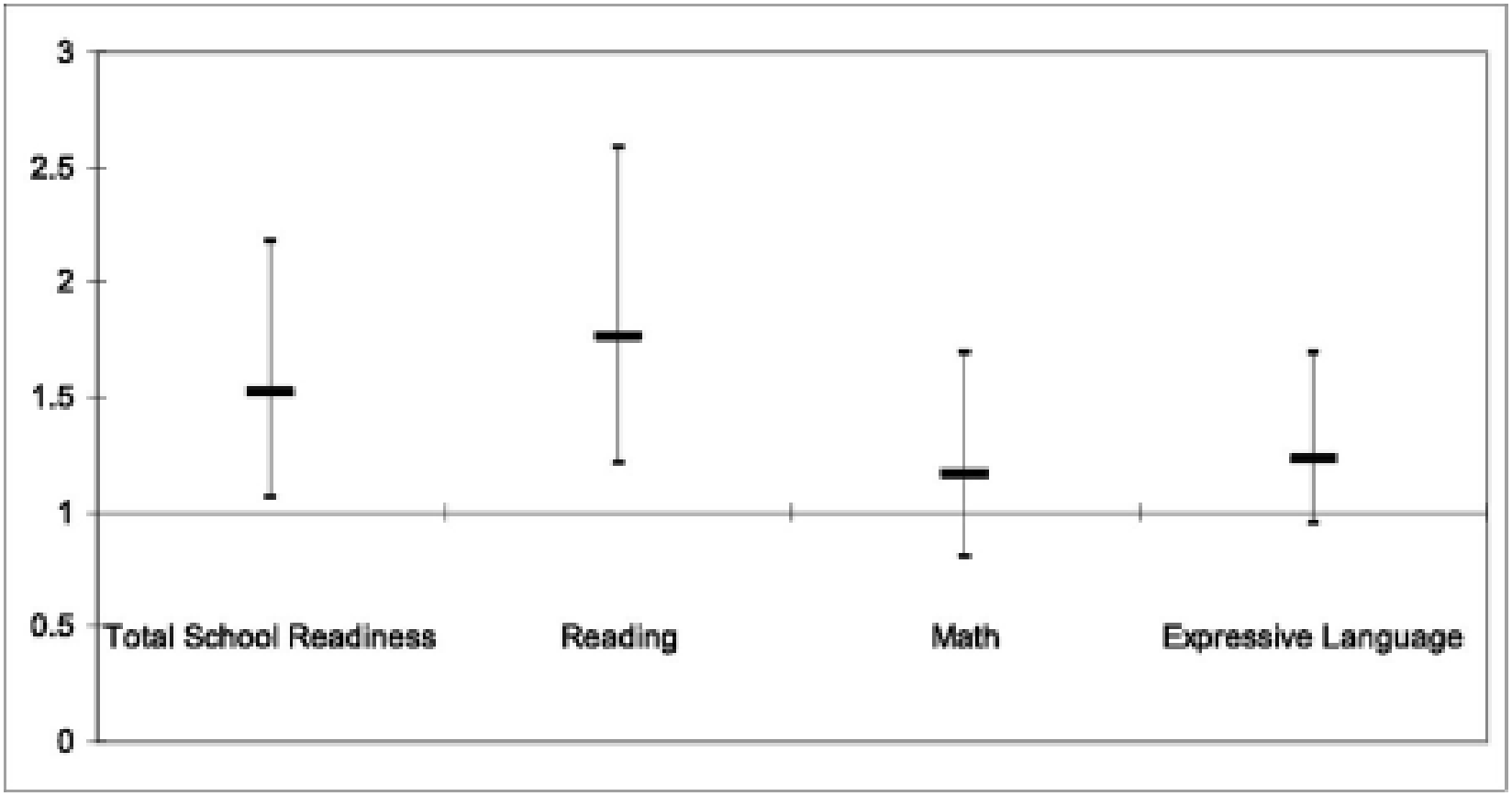
Adjusted odds of direct cognitive scores in the bottom 5th percentile for LPIs compared with FTIs. Adjusted for maternal race, education, marital status, prenatal care, primary language, impoverished household, gender, fetal growth, plurality, delivery type...



Melissa Woythaler et al. Pediatrics 2015;136:424-431

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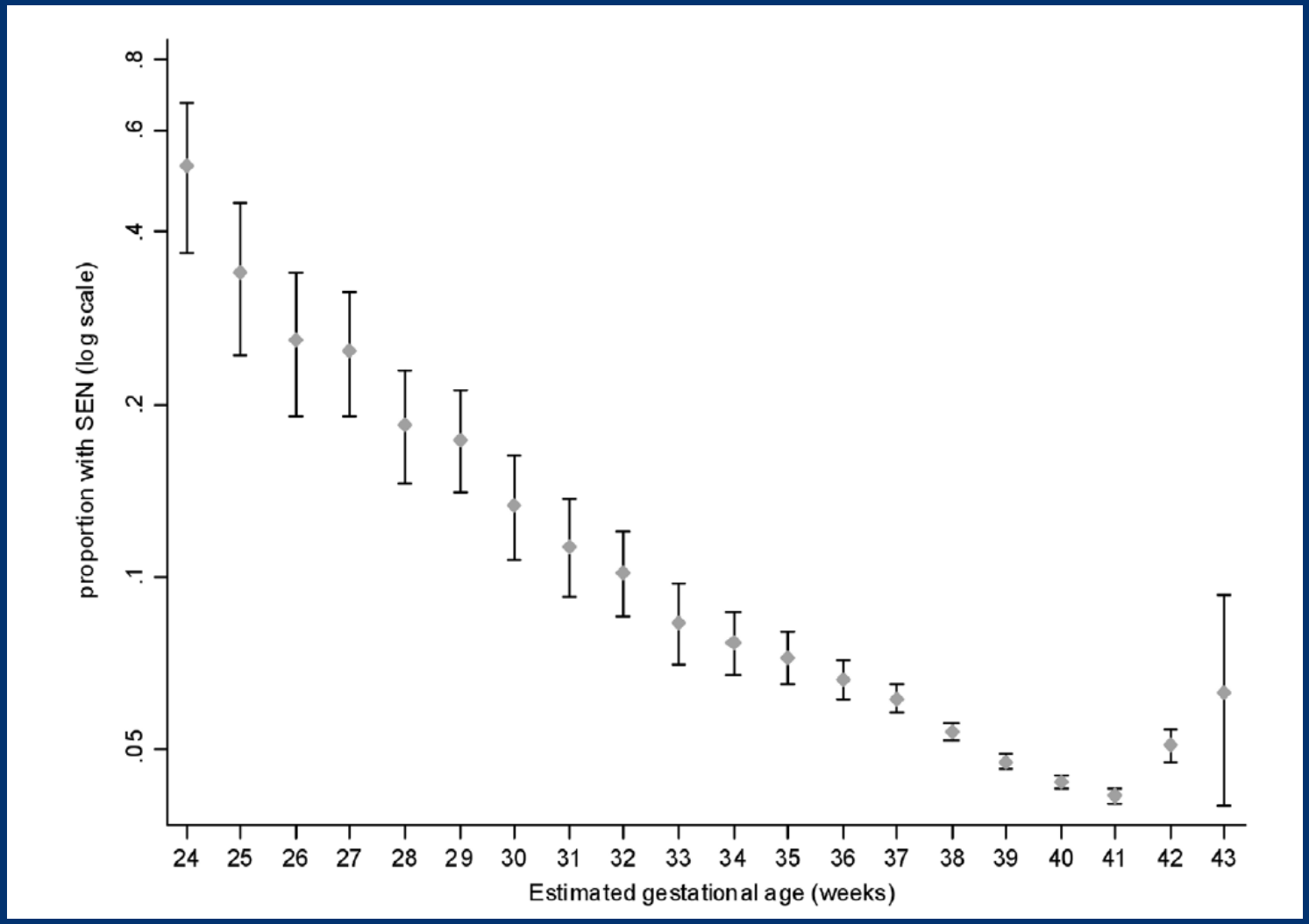
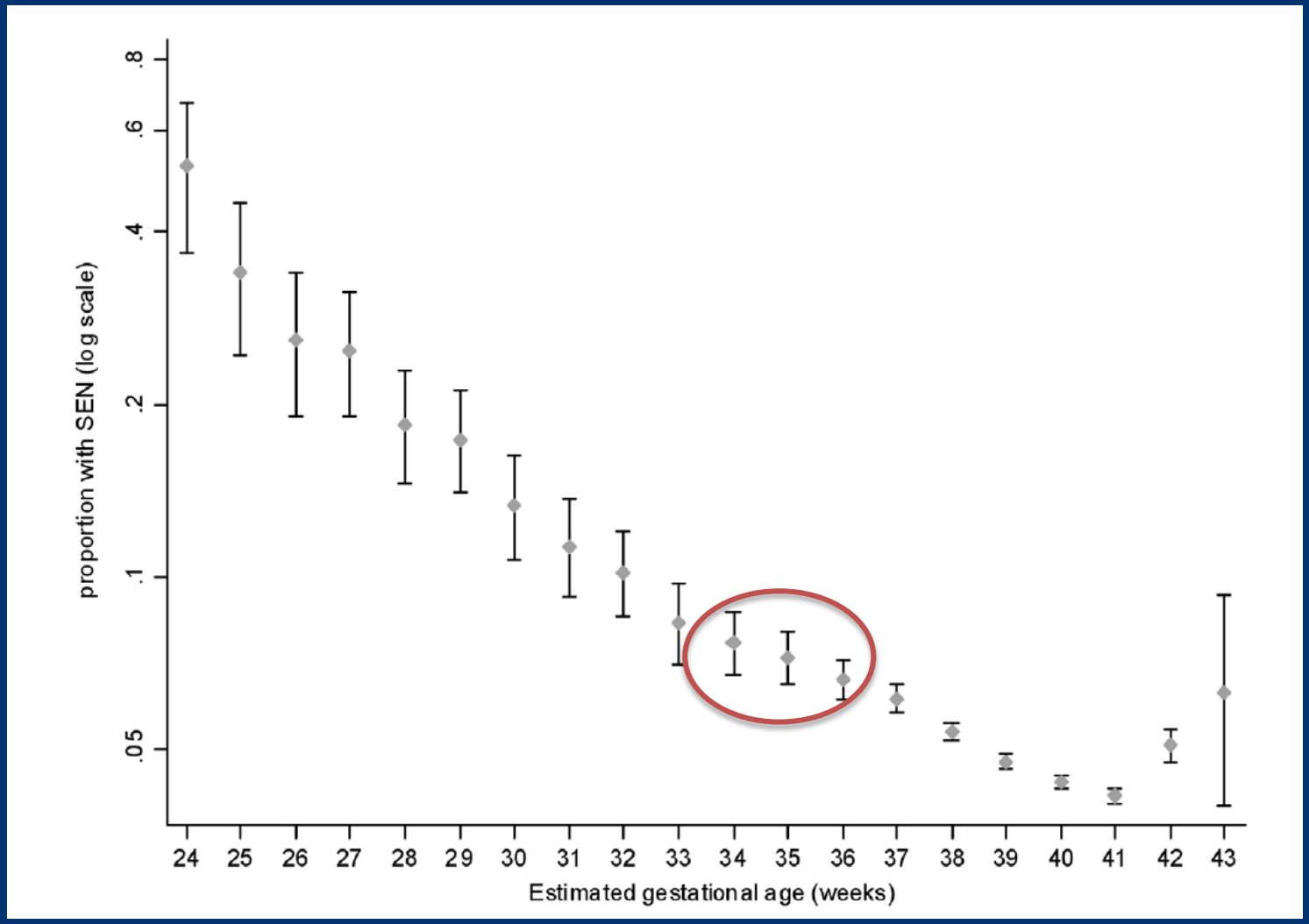
Special Education Needs



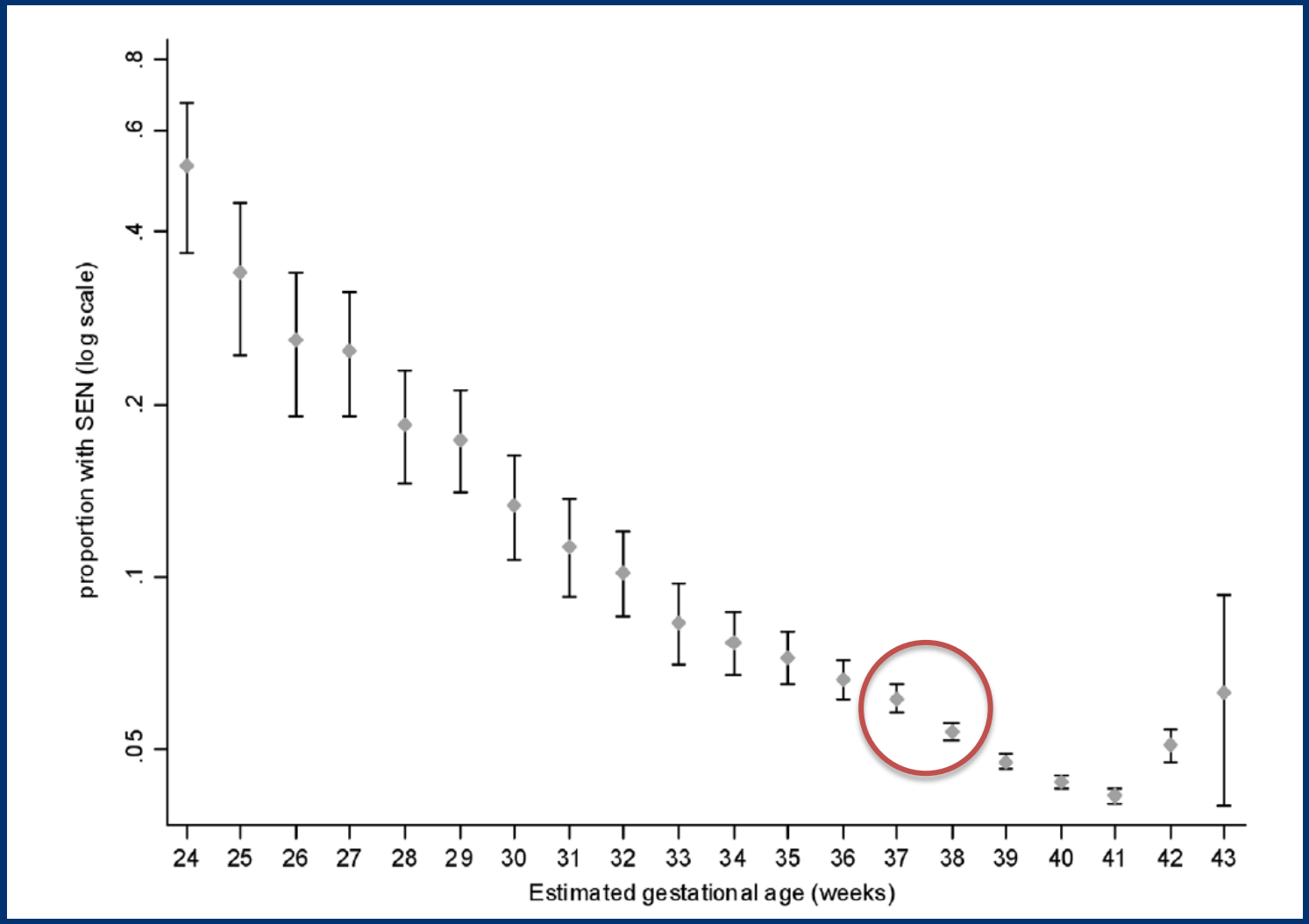
Mackay. DF. et al. *PLOS*. 2010; 7(6)

Special Education Needs



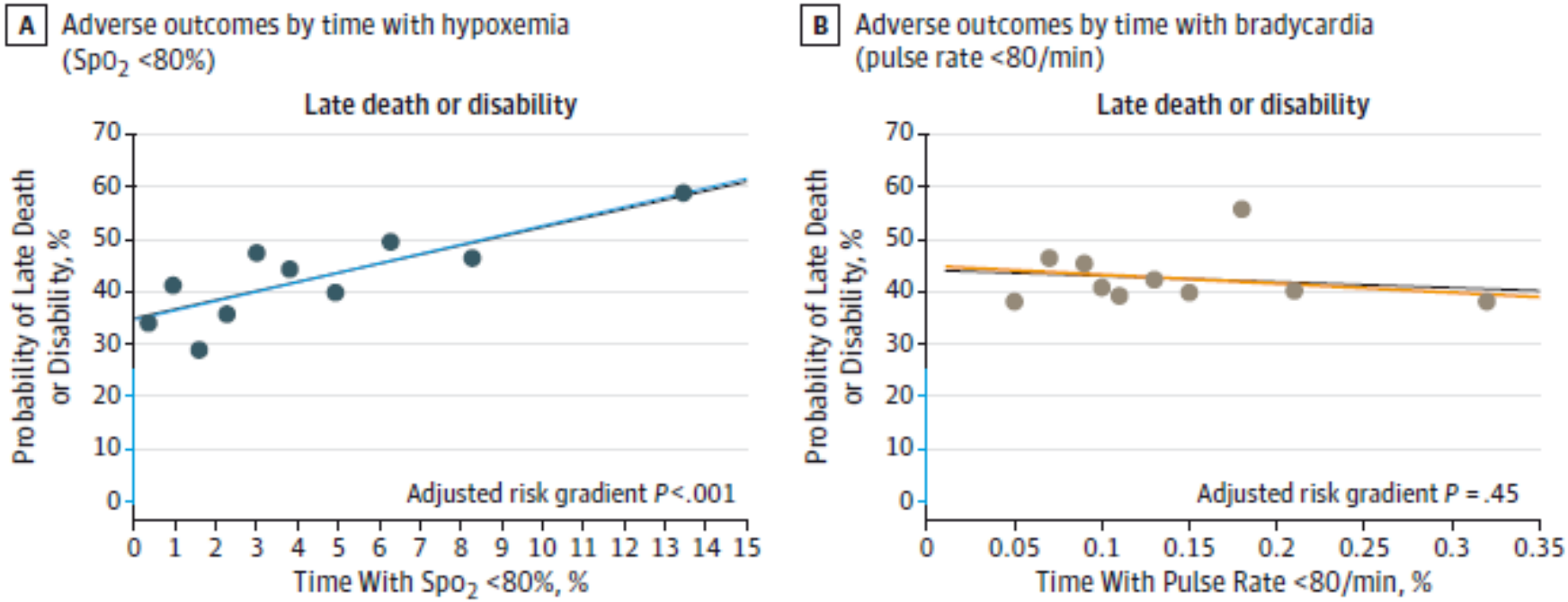
Mackay. DF. et al. *PLOS*. 2010; 7(6)

Special Education Needs



Mackay. DF. et al. *PLOS*. 2010; 7(6)

Figure 1. Adverse Outcome Rates by Deciles of Percentage of Time With Hypoxemia or Bradycardia



Poets et al. JAMA. 2015; 314(6): 595-603

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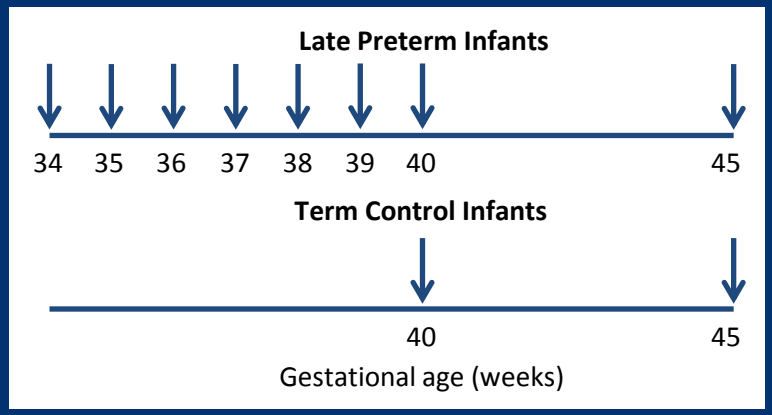
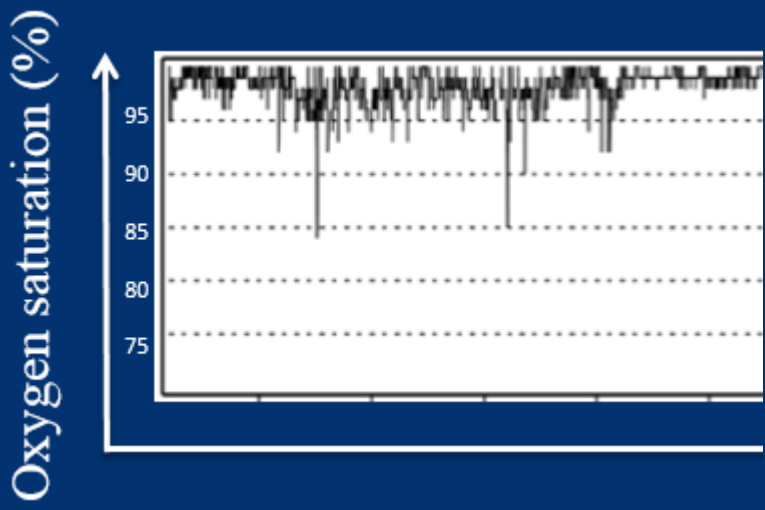
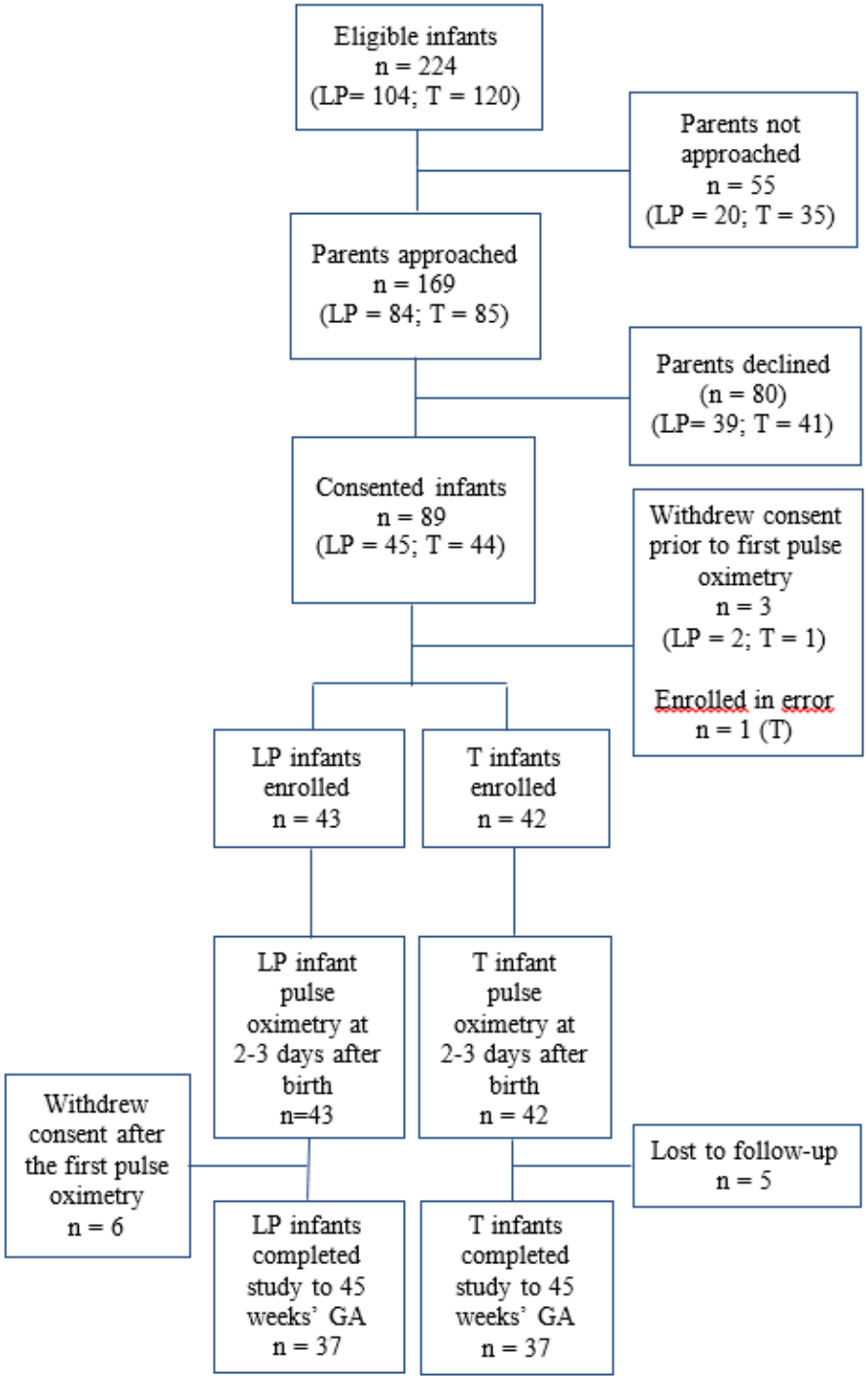
LaP Study





When a desaturation was defined as a decrease of:	10%
Total number of events less than 3 minutes:	414
Number of events excluded due to artifact:	0
Number of events over 3 minutes duration:	3
Mean high event saturation:	97.7
Mean low event saturation:	83.7


Eligible infants
n = 224
(LP= 104; T = 120)
Parents not approached
n = 55
(LP = 20; T = 35)
Parents approached
n = 169
(LP = 84; T = 85)
Parents declined
(n = 80)
(LP= 39; T = 41)
Consented infants
n = 89
(LP = 45; T = 44)
Withdrew consent prior to first pulse oximetry
n = 3
(LP = 2; T = 1)
Enrolled in error
n = 1 (T)
LP infants enrolled
n = 43
T infants enrolled
n = 42
LP infant pulse oximetry at 2-3 days after birth
n=43
T infant pulse oximetry at 2-3 days after birth
n = 42
Withdrew consent after the first pulse oximetry
n = 6
Lost to follow-up
n = 5
LP infants completed study to 45 weeks' GA
n = 37
T infants completed study to 45 weeks' GA
n = 37

	Late Preterm (n = 43)	Term (n = 42)	p value
Sex (female)	15 (35)	20 (48)	0.23
Gestational age (weeks)	35.4 (0.1)	40.1 (0.1)	<0.0001
Birthweight			
Grams	2571 (66)	3685 (78)	<0.0001
z score	0.0 (0.2)	0.5 (0.2)	0.06
Admission to NICU	22 (58)	0(0)	<0.0001
Respiratory Support	8(22)	0(0)	<0.0005

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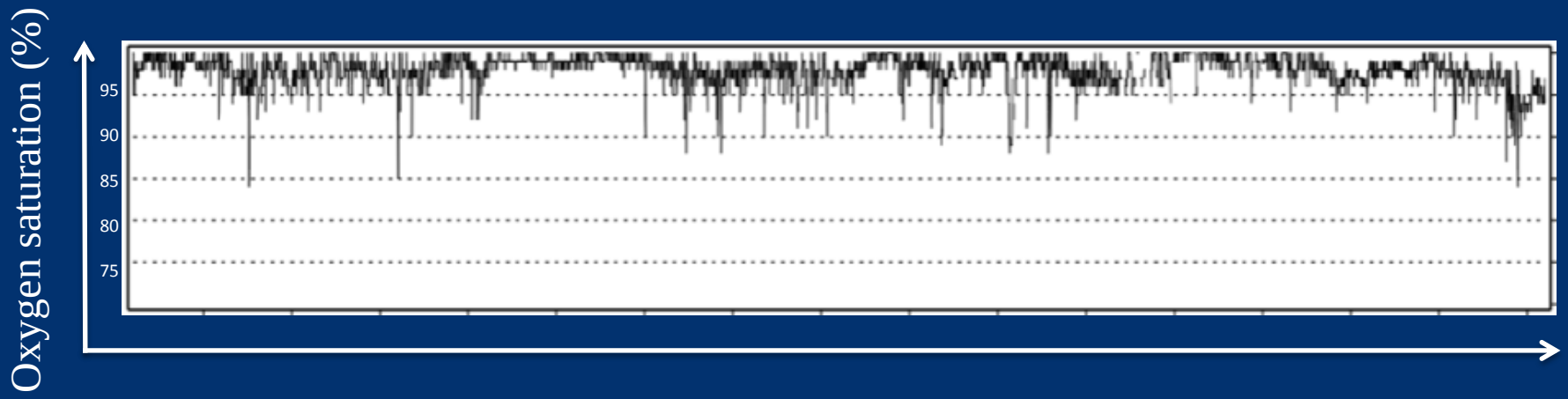
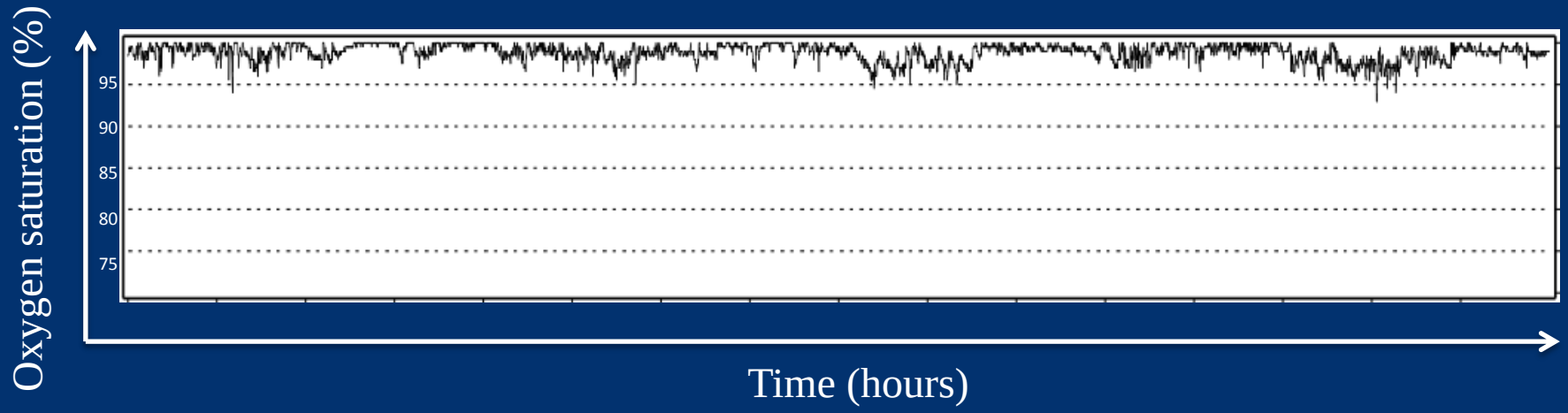
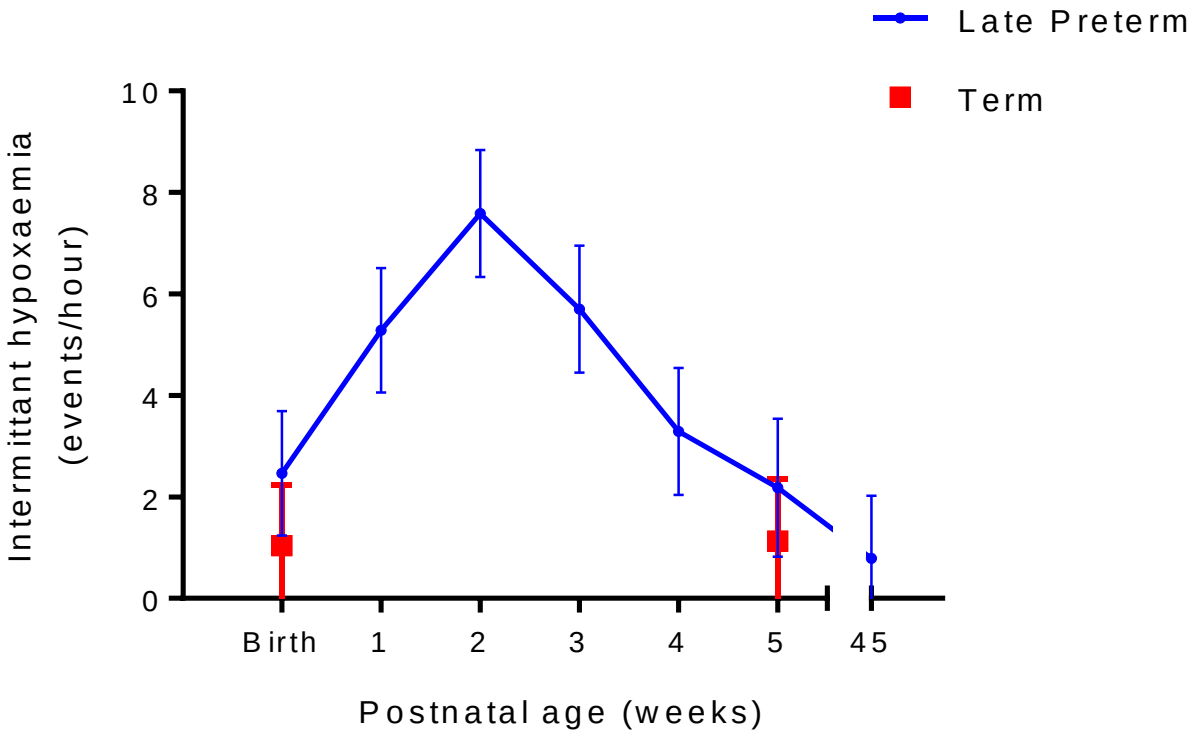
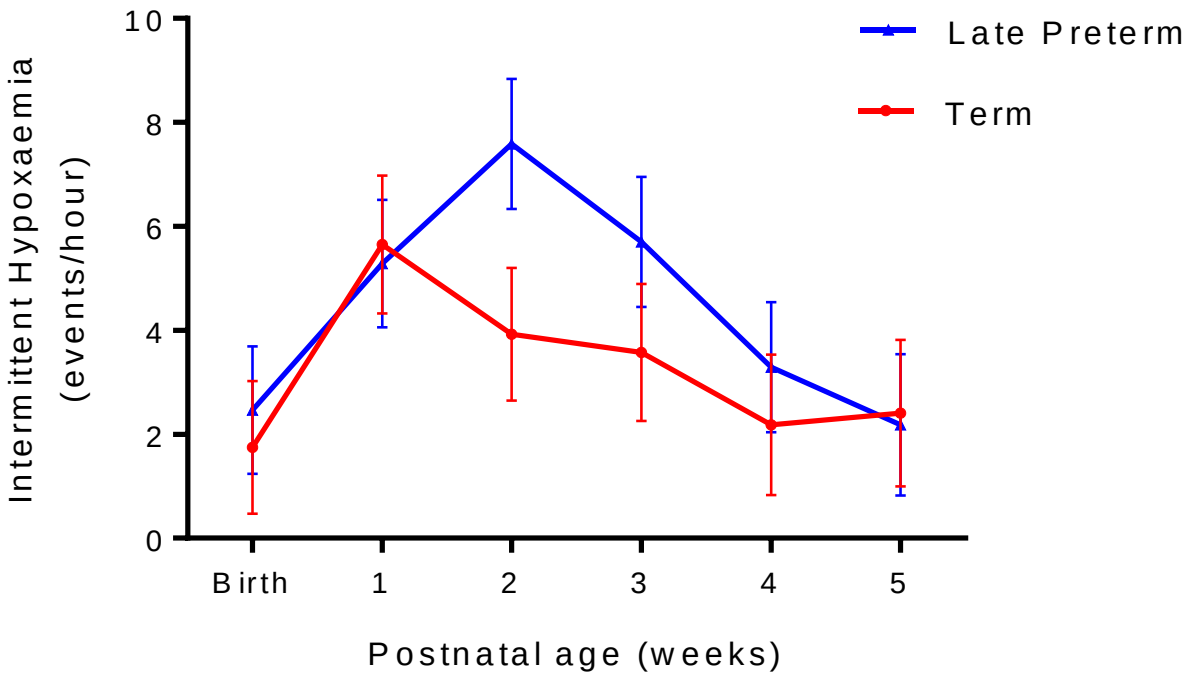
Late preterm baby

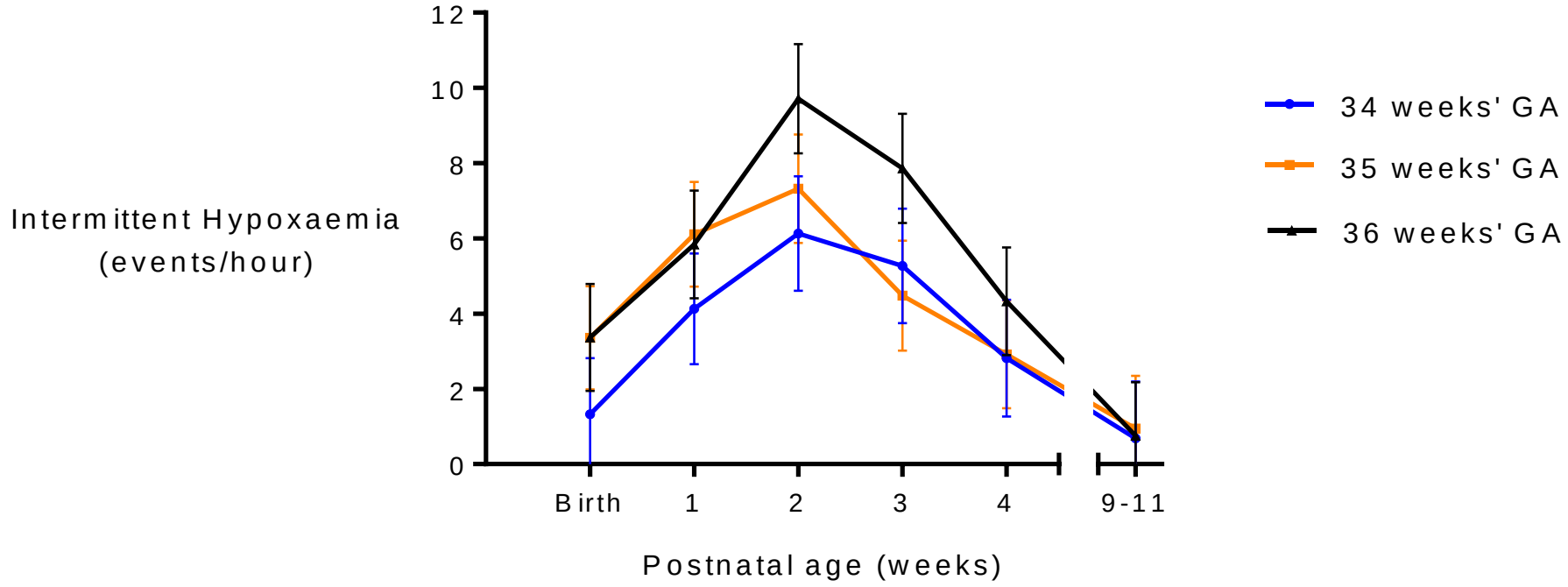


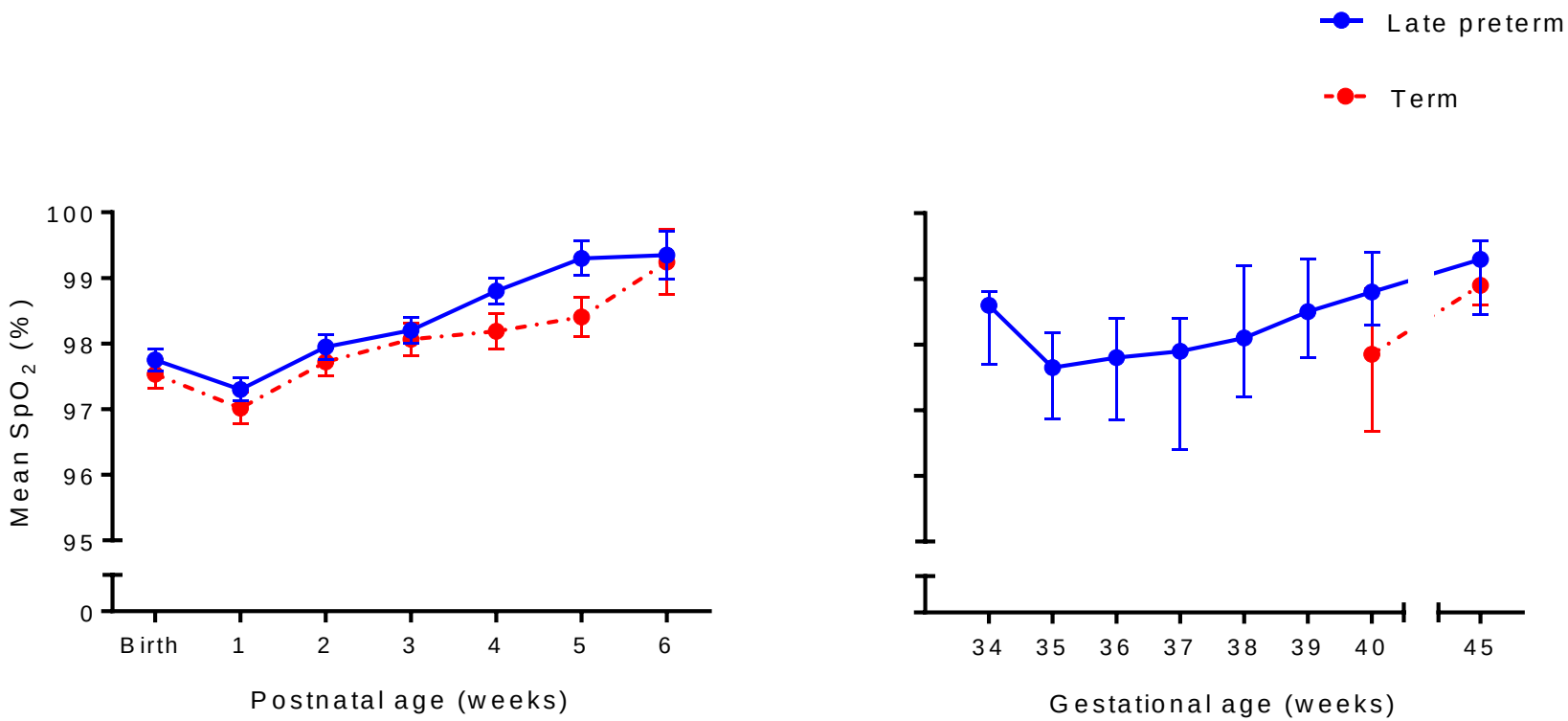
Term baby




Late Preterm
Term
Intermittant hypoxaemia (events/hour)
10
8
6
4
2
0
Birth
1
2
3
4
5
45
Postnatal age (weeks)


Late Preterm
Term
Intermittent Hypoxaemia (events/hour)
10
8
6
4
2
0
Birth
1
2
3
4
5
Postnatal age (weeks)


Intermittent Hypoxaemia (events/hour)
12
10
8
6
4
2
0
Birth
1
2
3
4
9-11
Postnatal age (weeks)
34 weeks' GA
35 weeks' GA
36 weeks' GA


Late preterm
Term
Mean SpO2 (%)
100
99
98
97
96
95
0
Birth
1
2
3
4
5
6
Postnatal age (weeks)
34
35
36
37
38
39
40
45
Gestational age (weeks)

Conclusions

- Late preterm babies have more intermittent hypoxemia than babies born at term.
- Intermittent hypoxaemia is more frequent several weeks after birth.

Latte Dosage Trial

Caffeine in very preterm babies

- reduces apnoea of prematurity
- reduces bronchopulmonary dysplasia
- improves neurodevelopmental outcome at 2 years of age
- reduces intermittent hypoxaemia

Aim:

To determine the most effective dose of caffeine citrate to reduce intermittent hypoxaemia in late preterm babies.

Study design

- Multi-centre, double blind, dosage, randomised controlled trial

Setting

NICUs and postnatal wards in Auckland NZ

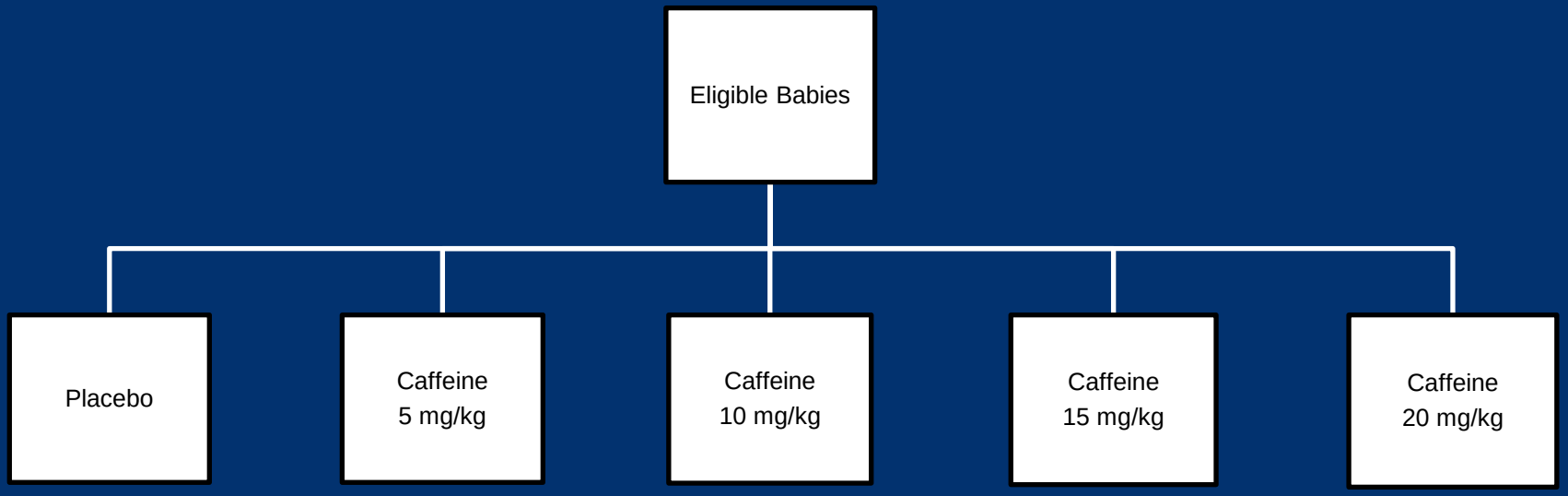
Population

- Infants born between 34^{+0} – 36^{+6} weeks' GA

Exclusion criteria

- Major congenital abnormality
- Minor congenital abnormality likely to affect respiration, growth or development
- Previous caffeine treatment
- Renal or hepatic impairment
- Tachyarrhythmia
- Seizures

Randomisation



- Randomised, stratified by site and GA (34/35/36 weeks)
- <72 hours after birth to 40 weeks GA
- Multiples randomised to same group
- Loading 2 ml/kg, then daily 1 ml/kg

Outcomes

- Primary outcome: Intermittent Hypoxaemia (10% below baseline) at 2 weeks after randomisation
- Secondary outcomes:
  - **Intermittent hypoxaemia at term equivalent age**
  - **Salivary caffeine concentration**
  - **Breastmilk caffeine concentration**
  - **Growth**
  - **Tachycardia**
  - **Feed intolerance**
  - **Sleeping**
  - **Maternal Depression**

Sample Size

- To detect a 50% reduction of 3.5 episodes per hour, and allowing a 10% drop out rate and 90% power we will require 23 babies in each arm x 5 arms = 120 babies, with two sided alpha of 0.05.

Conclusions:

- Late preterm babies are at increased risk of IH, for weeks after birth
- Caffeine improves IH and neurodevelopment in very preterm babies
- The Latte dosage trial will determine if caffeine reduces intermittent hypoxaemia in late preterm babies, and which dose is the most effective.

Acknowledgments

- Logan Williams
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- Chris McKinlay
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hrc Health Research Council of New Zealand

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