Results

Abstract 169 Table 1

Hospital mortality of infants by SpO ₂ target overall				
	SpO ₂ 85–89%	SpO ₂ 91–95%	Risk Ratio (95% CI)	p value
Hospital mortality	235/1220 (19.3%)	202/1217 (16.6%)	1.16 (0.98–1.38)	0.09

Abstract 169 Table 2

Hospital mortality of infants by SpO₂ target, by old vs new software

Old software				New software			
	SpO ₂ 85–89%	SpO ₂ 91–95%	Risk Ratio (95% CI)	p value	SpO ₂ 85–89%	SpO ₂ 91–95%	Risk Ratio (95% CI)
Hospital mortality*	98/629 (15.6%)	109/630 (17.3%)	0.90 (0.70–1.16)	0.41	137/591 (23.2%)	93/587 (15.8%)	1.46 (1.15–1.85)
							0.0015**

There was no significant mortality difference between SpO₂ targets overall. There was significant heterogeneity between old and new software on mortality (test for interaction $p=0.006$).^{*} Using new software, targeting 91–95% increased hospital survival by 7.4% (from 76.8% to 84.2%) versus targeting 85–89% ($p=0.0015$).^{**}

Conclusions Pending the primary outcome of disability free survival at 2 years it appears wise not to target 85–89%.

References

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170 MATERNAL ALLOPURINOL ADMINISTRATION DURING TERM LABOR IS NEUROPROTECTIVE IN CASE OF FETAL HYPOXIA; A MULTICENTER RANDOMIZED PLACEBO CONTROLLED TRIAL

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Background Hypoxic-ischemic encephalopathy due to perinatal hypoxia-induced free radical formation is an important cause of long-term neurodevelopmental disabilities. Allopurinol reduces the formation of free radicals, which potentially limits hypoxia-induced reperfusion damage. With this trial we aimed to assess whether maternal allopurinol treatment during fetal hypoxia would reduce the release of brain-tissue-specific biomarkers associated with neonatal brain damage.

Methods We performed a randomized double blind placebo controlled multicenter trial (NCT00189007) studying laboring women at term with imminent fetal hypoxia. Fetal distress was suspected in case of an abnormal fetal heart rate trace, ST-wave abnormalities on fetal ECG or fetal scalp pH<7.20. Women were allocated to

receive allopurinol 500 mg IV or placebo immediately prior to delivery. Endpoints were S100B and neuroketal in cord blood, which are brain-tissue-specific biomarkers for brain damage. Because S100B followed a non-normal distribution, we used a poisson regression model with associated RR (95%CI). For neuroketal we report geometric mean differences.

Results We randomized 222 women to allopurinol (n=111) or placebo (n=111). S100B was significantly lower in the allopurinol-group (median 43.4; IQR 20.2–71.5) compared to the placebo-group (median 54.9; IQR 26.8–94.7), RR 0.91 (95%CI 0.88–0.94). Neuroketal did not significantly differ between groups, geometric mean difference –7.57 (95%CI –15.6; 3.57).

Post-hoc analysis showed a marked gender difference in treatment effect in favor of girls for S100B (RR 0.63 (95%CI 0.59–0.68)) and neuroketal (geometric mean difference –16.5 (95%CI –24.6; –1.83)).

Conclusion Maternal treatment with allopurinol during fetal hypoxia reduces damage to neuronal cells as indicated by brain-tissue-specific chemical biomarkers.

171 NIPPV DOES NOT REDUCE BRONCHOPULMONARY DYSPLASIA (BPD) OR DEATH IN EXTREMELY LOW BIRTH WEIGHT INFANTS - A RANDOMISED TRIAL

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Background Standard care of preterm infants includes nCPAP & NIPPV. We compared rates of BPD or death in a randomised trial of NIPPV or nCPAP.

Methods Eligible infants were preterm, birth weight < 1000g; requiring either (i) non-invasive respiratory support within first seven days, “no intubation/early extubation group”, or (ii) were < 28 days at first extubation - “prior intubation”. Central block randomisation to NIPPV or nCPAP was conducted via the web. Primary outcome was a composite of death (prior to 36 weeks' gestational age [GA]) or BPD at 36 weeks' GA: defined as requiring ventilation; FiO₂ > 30%; or positive oxygen reduction test (ORT). Sample size 1000 (β 80%; 2-tailed α 5%) to demonstrate 20% reduction in primary outcome.

Results 36 international sites enrolled 1007 infants. Observed rates of BPD or death were similar in the two groups. BPD outcome,

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in the 21 infants with no ORT, assessed by clinical definition of oxygen at 36 weeks' GA: no alteration in treatment differences.

Abstract 171 Table 1 Outcome data

Outcome	NIPPV	nCPAP	Adjusted OR (95%CI)	p
Primary analysis: death or ORT-BPD n (%)	192/497 (38.6)	179/487 (36.8)	1.09 (0.83, 1.44)	0.53
Supporting analysis: death or imputed BPD	198/504 (39.3)	191/501 (38.1)	1.05 (0.80, 1.38)	0.72
Primary outcome by subgroup				
No intubation/Early extubation n (%)	72/241 (29.9)	72/252 (28.6)	1.1 (0.72, 1.69)	0.64
Prior intubation	120/256 (46.9)	107/235 (45.5)	1.1 (0.73, 1.54)	0.76

Conclusions In infants < 1000g NIPPV does not confer further benefit nor risk for survival free of BPD at 36 weeks' GA compared to nCPAP.

172 THE PROPREMS RANDOMISED TRIAL INVESTIGATING THE EFFECTS OF PROBIOTICS ON LATE ONSET SEPSIS IN VERY PRETERM INFANTS

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Background Late onset sepsis (LOS) frequently complicates prematurity, and is associated with increased mortality and morbidity. Whilst probiotic supplementation in preterm infants reduces mortality and necrotising enterocolitis (NEC), the effect on LOS in the most vulnerable preterms is unknown.

Aim To determine the effects of probiotic supplementation in very preterm infants.

Methods A multi-centred, double-blinded, placebo-controlled, randomised controlled trial in very preterm infants born < 32 weeks' gestation weighing < 1500g, supplemented daily with either a probiotic combination (*Bifidobacterium infantis*, *Streptococcus thermophilus* and *Bifidobacterium lactis* 1 x 10⁹ total organisms) or placebo (multidextrin) from soon after commencement of enteral feeds until discharge home or term corrected age. The primary outcome was the incidence of at least one episode of definite (deep culture positive) late onset sepsis; secondary outcomes included NEC, mortality, duration of primary hospitalisation, number of courses and duration of antibiotics, etc. [Garland et al. *BMC Infectious Diseases*. 2011 Aug 4; 11(1):210].

Results Between October 2007 and November 2011, 1099 very preterm infants were randomised from 10 participating perinatal centres in Australia and New Zealand. Four interim analyses at 100, 200, 350 and 700 recruits confirmed comparable baseline characteristics between groups (for birth weight, gestation, gender, multiple pregnancy, antenatal steroids, caesarean delivery) and recommended trial continuation. Data cleaning is nearing completion prior to unblinding treatment allocation groups and analysis.

Conclusions The ProPrems trial has recruited 1099 very preterm infants; it is the largest randomised trial to date investigating the potential for probiotics to reduce the burden of prematurity.

173 CLUES FOR THE NEURODEVELOPMENTAL PROGNOSIS OF THE HIGH RISK PRETERM AND TERM NEWBORNS

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Premature survivors are at increased risk for impaired neurodevelopmental outcome compared to full terms. These sequelae include cognitive abnormalities, mild fine or gross motor delay, cerebral palsy, vision and hearing losses, impairment increases with decreasing gestational age. Persistence of multiple abnormal neurologic signs in the first 12 to 18 months is ominous. Emergence of other findings (vision impairments, seizures, feeding issues delay of head growth) is associated with poor outcome. MRI is useful in predicting neurodevelopmental outcome at the equivalent of term gestation. Other neonatal complications as; bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity, intraventricular hemorrhage, poor growth, presence of congenital anomalies are associated with an increased risk of poor neurodevelopmental outcome. Premature survivors are more likely to have specific psychological and behavioral problems including attention deficit hyperactivity syndrome, general anxiety, and depression. Individuals with birth weights below 1500 g are at greater risk for poor academic performance than those born with normal birth-weight because of their impaired cognition, neurosensory defects, and behavioral and psychological problems. Neurodevelopmental outcome is assessed more accurately at school age than in early childhood due to the cognitive recovery over time and lack of accurate predictive assessment tools in early childhood.

Survivors of prematures need to be assessed for neurodevelopmental impairment and, if impairment is present, be referred to educational programs and subspecialty care in order to provide the best possible outcome. ELBW infants without evidence of significant neonatal brain injury can recover when exposed to a nurturing home environment and comprehensive early intervention services.

174 OXYTOCIN, VASOPRESSIN AND SOCIAL BONDING: IMPLICATIONS FOR NOVEL THERAPIES FOR AUTISM

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The neuropeptides oxytocin and vasopressin play important roles in several aspects of social cognition and behavior in animal models, including social recognition, maternal nurturing and social bonding. Several studies suggest that these neuropeptides increase the saliency of social stimuli, enhancing the neural processing of social cues. A series of studies in voles demonstrate that variation in oxytocin and vasopressin receptor systems contributes to both species differences and individual variation in social behavior. Oxytocin and vasopressin receptor activation in the mesolimbic dopamine reward pathway plays an important role in social bond formation. We have identified genetic polymorphisms that robustly predict neuropeptide receptor expression in the brain, which in turn predicts social behaviors, including susceptibility to the impact of early social stressors on later life social attachment. There are remarkable parallels between those studies in voles and recent studies in humans which suggest that these mechanisms are highly conserved from rodent to man. In humans, intranasal delivery of oxytocin enhances eye gaze into the eyes of other, the ability to infer the emotions of others from facial cues, empathy, and socially reinforced learning. These observations suggest that the oxytocin system may be a viable target for novel pharmacological strategies for improving social cognition in autism spectrum disorders. Drugs that stimulate endogenous oxytocin release may be useful as an adjunct therapy for behavioral interventions for autism.

175 MATERNAL DIET AND TYPE 2 DIABETES IN THE OFFSPRING

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