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ABSTRACTS

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PRETERM INFANTS ON EARLY SOLID FOODS AND NEURODEVELOPMENTAL OUTCOME: A SECONDARY OUTCOME ANALYSIS OF A RANDOMISED CONTROLLED TRIAL

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Background: Introduction of solid foods in preterm infants is a highly discussed topic and evidence-based recommendations do not exist so far. Aim of this study was to examine whether two different timepoints of introduction of solid foods in preterm infants have an impact on neurodevelopmental outcome in the first 3 years of life.

Methods: This is a secondary outcome analysis of a prospective, randomised, two arm intervention trial of very low birthweight infants randomised to an early (10–12th week corrected age) or a late (16–18th week corrected age) complementary feeding group. Neurodevelopmental outcome was assessed at 1 and 2 years corrected age, and at 3 years, 4 months uncorrected age using the Bayley Scales of Infant-Toddler Development, third edition, German norms.

Results: In total, 177 infants were randomised, 89 to the early group and 88 infants to the late group with a median gestational age of 27 + 1 weeks in both groups. 91%, 89%, and 71% of infants were available for analysis at the three timepoints. To evaluate differences in neurodevelopmental outcome between study groups, a linear mixed effects model was fit through study group, gestational age at birth, sex, nutrition at discharge, highest education of parents, and IVH with a random intercept to adjust for possible correlation between siblings of multiple births. No significant differences in neurodevelopmental outcome between groups were found (Table 1).

Conclusion: The timepoint of introduction of solid foods had no impact on neurodevelopmental outcome at 1 and 2 years corrected age, and at 3 years, 4 months uncorrected age.

Table 1 Bayley-III assessment at one and 2 years corrected age, and at 3 years, 4 months corrected age presented as median (IQR). *P*-values (linear mixed effects model) <0.05 = statistically significant

Conflict of interest: None declared.

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THE DIAMOND TRIAL: DIfferent APPROACHES TO MOderate & LATE PRETERM NUTRITION: DETERMINANTS OF FEED TOLERANCE, BODY COMPOSITION AND DEVELOPMENT

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Background: Moderate-to-late-preterm (32 + 0–36 + 6 weeks' gestation) babies account for >80% of all preterm births. There is a lack of evidence on the optimal nutrition strategy following birth; this has been identified as a research priority by several organisations.

Methods: We undertook a multi-centre, factorial, randomised, controlled trial in babies born 32 + 0–35 + 6 weeks' gestation with intravenous (IV) access whose mothers intended to breastfeed, randomising babies to combinations of three factors until full milk feeds were established: (1) IV amino acid solution versus IV dextrose; (2) milk supplement versus exclusive mother's own milk (MOM), and (3) exposure to taste/smell or not before gastric tube

Bayley III		Early (n=89)	Late (n=88)	p
1 year *corrected age*	Motor	100 (85-103)	92 (85-106)	1
	Cognitive	90 (80-105)	90 (80-105)	.81
	Language	97 (83-103)	97 (84-103)	.54
2 years *corrected age*	Motor	89 (82-100)	89 (76-103)	.67
	Cognitive	85 (75-100)	85 (70-105)	.88
	Language	78 (56-94)	78 (62-96)	.61
3 years 4 months *uncorrected age*	Motor	82 (70-92)	84 (70-89)	.98
	Cognitive	90 (85-100)	95 (80-100)	.48
	Language	84 (72-94)	87 (72-94)	.20

Data presented as median (IQR). P-values (linear mixed effects model) <.05 = statistically significant.

Table 1 Bayley-III assessment at one and 2 years corrected age, and at 3 years, 4 months corrected age presented as median (IQR). *P*-values (linear mixed effects model) <0.05 = statistically significant

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feeds. The primary outcome for factors 1 and 2 was fat mass % at 4 months' corrected age, analysed using linear regression models adjusted for hospital site, gestation and sex, and for factor 3, days to full enteral feeds (defined as 150 mL kg^{-1} day^{-1} or exclusive breastfeeding, whichever occurred first), analysed using Cox proportional hazard models. All analyses were controlled for the non-independence of multiple births using a cluster effect.

Results: 532 (55% boys) babies were recruited. Primary outcomes were assessed in 526 (99%) babies at discharge and 324 (61%) at 4 months' corrected age. % fat mass at 4 months' corrected age was not different between babies given IV amino acids or dextrose (factor 1) (mean (standard deviation, SD) 26.0 (5.4) versus 26.2 (5.2)%, $P = 0.7$) or between babies given milk supplement versus MOM (factor 2) (26.3 (5.3) versus 25.8 (5.4)%, $P = 0.3$). Time to full enteral feeds was not different between babies exposed or not exposed to taste/smell (mean (SD) 5.8 (1.5) versus 5.7 (1.9) days, $P = 0.6$). There also was no difference in the time to full enteral feeds for factor 1 (5.7 (1.7) versus 5.8 (1.8) days, $P = 0.6$) or factor 2 (5.7 (1.7) versus 5.8 (1.7) days, $P = 0.1$). Time to discharge from the neonatal unit was similar between groups (overall 23.0 (12.1)).

Conclusions: Provision of parenteral nutrition or formula in addition to MOM does not affect body composition at 4 months' corrected age. Early nutritional support strategies do not affect time to full enteral feeds or days in hospital. Providing breastmilk only should be the goal for the nutritional management of moderate-to-late-preterm babies.

Conflict of interest: None declared.

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EARLY INTRAVENOUS NUTRITION, HYPOPHOSPHATAEMIA AND REFEEDING SYNDROME IN EXTREMELY LOW BIRTHWEIGHT BABIES: A COHORT STUDY

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Background: In extremely low birthweight babies (ELBW, <1000 g) higher nutritional intakes are associated with hypophosphataemia, refeeding syndrome and increased morbidity and mortality. We investigated whether increased early phosphate intake and enhanced biochemical monitoring are associated with a reduction in these outcomes.

Methods: Prospective cohort study in two Auckland neonatal intensive care units (NICUs) comparing ELBW babies born before (2014–2018; Cohort 1) and after (2020–2021; Cohort 2) intravenous nutrition (IVN) protocol changes to increase phosphate intake and biochemical monitoring. Cohort 1 were participants in a randomised controlled trial of early increased amino acid intake. Cohort 2 were identified prospectively.

Data were retrieved from the trial database or prospectively from electronic medical records. Groups were compared using the χ^2 test, pooled t test and nominal logistic or standard least squares regression analysis. Refeeding syndrome was defined as concurrent hypophosphataemia (serum phosphate <1.4 mmol L^{-1}) and hypercalcaemia (serum calcium >2.8 mmol L^{-1}) and severe hypophosphataemia as serum phosphate <0.9 mmol L^{-1}.

Results: Baseline characteristics were similar in Cohort 1 ($n = 149$) and 2 ($n = 100$). Serum phosphate concentrations were significantly higher in Cohort 2 than Cohort 1 (median (IQR): day 3, 1.9 (0.6) vs. 1.5 (0.7) mmol L^{-1}; $P = 0.0001$; day 5, 1.8 (0.5) vs. 1.4 (0.5) vs. mmol L^{-1}; $P < 0.0001$). The incidence of hypophosphataemia was lower in Cohort 2 than Cohort 1 (day 3, 46% vs. 14% ($P = 0.0003$); day 5, 57% vs. 19% ($P < 0.0001$)). On day 5, in Cohort 2 refeeding syndrome decreased from 16% to 2% ($P = 0.003$) and hypophosphataemia from 12% to zero ($P = 0.0003$) compared with Cohort 1. Hypercalcaemia was similar in the two cohorts. Patent ductus arteriosus (PDA), culture-proven late-onset sepsis (LOS), and probable early- (pEOS) and late- (pLOS) onset sepsis were all significantly decreased in Cohort 2 compared with Cohort 1 (PDA 22% vs. 38%, $P = 0.003$; LOS, 25% vs. 36%, $P = 0.046$; pEOS, 25% vs. 56%, $P < 0.0001$; pLOS 27% vs. 61%, $P < 0.0001$). Other clinical outcomes were similar in the two cohorts.

Conclusion: Revised IVN protocols to increase early phosphate intake and enhance biochemical monitoring are associated with a lower incidence of hypophosphataemia, refeeding syndrome and associated co-morbidities. Whether these associations are causal requires further investigation.

Conflict of interest: None declared.

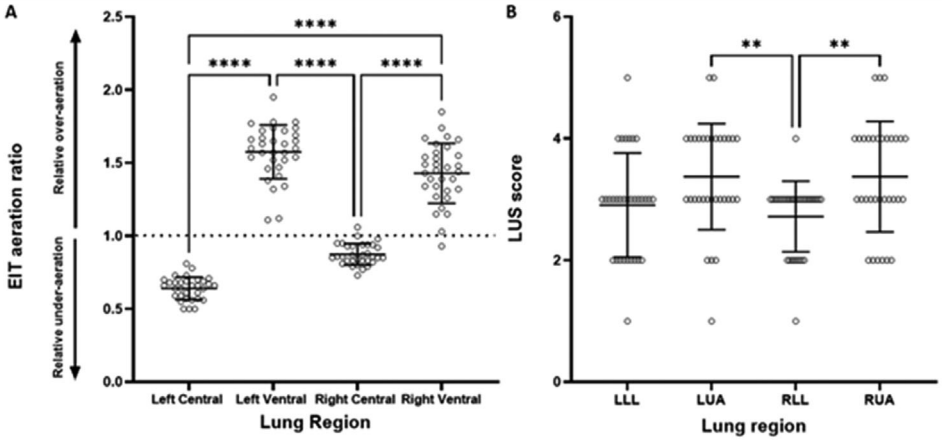


Fig. 1 Regional aeration differences detected by EIT (a) and LUS (b). LLL, left lower lateral; LUA, left upper lateral; RLL, right lower lateral; RUA, right upper lateral.

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LUNG ULTRASOUND DETECTS REGIONAL AERATION INHOMOGENEITY IN VENTILATED PRETERM LAMBS

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Introduction: Preterm infants often develop inhomogeneous lung aeration which may contribute to lung injury. Lung ultrasound (LUS) and electrical impedance tomography (EIT) can non-invasively monitor lung volume in real-time. EIT detects inhomogeneous aeration but is predominantly limited to the research setting. Although more readily available, the ability of LUS to detect inhomogeneous aeration is unknown. The aim of this study was to determine whether LUS detects regional inhomogeneity as detected by EIT in preterm lambs.

Methods: LUS and EIT were simultaneously performed on mechanically ventilated preterm lambs. LUS images from the non-dependent and dependent regions were acquired bilaterally. Ultrasound images were blindly graded. Regional inhomogeneity was determined by calculating the observed to predicted aeration ratio from the EIT reconstructive model. Ultrasound measurements were compared with regional aeration ratios derived from EIT using one-way ANOVA with repeated measures.

Results: LUS was performed in 32 lambs (mean (SD) gestation 125 (1) days). One hundred and twenty-eight images were acquired. LUS scores were greater in the upper anterior compared to lower lateral regions of the left (3.4 vs. 2.9, $P = 0.1$) and right lung (3.4 vs. 2.7, $P < 0.0087$). The left and right upper regions also had greater LUS scores compared to the right lower (3.4 vs. 2.7, $P < 0.0087$) and left lower (3.7 vs. 2.9, $P = 0.1$) regions respectively. These corresponded with regional differences detected by EIT, which demonstrated relative over-expansion of the non-dependent lung compared to dependent regions (Fig. 1).

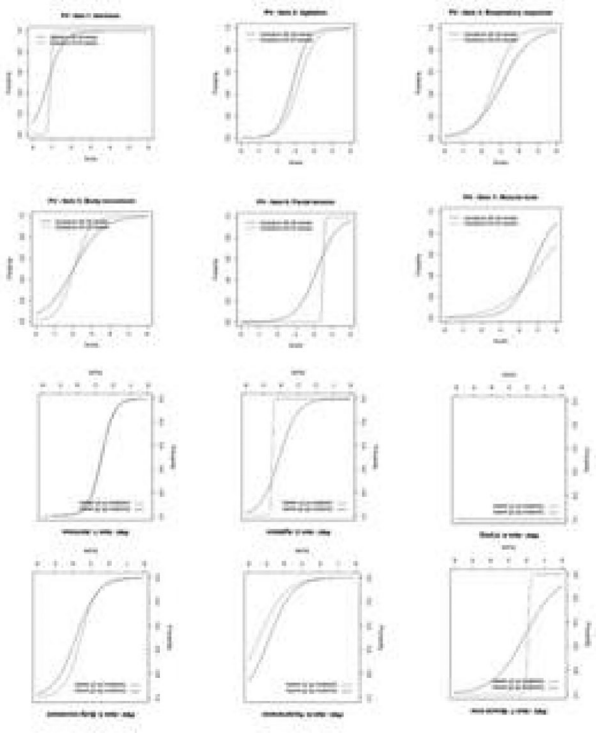


Fig. 1 Differential item function (DIF) plots for (extremely) preterm-born infants, split in (a) ventilated infants; (b) non-ventilated infants. In ventilated infants, sample size for item 4 (Crying) not sufficient for DIF.

Conclusion: LUS may have potential to measure regional aeration, which should be further explored in human studies.

Conflict of interest: None declared.

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THE COMFORT-NEO SCALE: DOES THE SCALE MEASURE DISTRESS IN EXTREMELY PRETERM-BORN INFANTS?

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Introduction: Measuring distress in infants is done using the COMFORT-neo scale. The aim of this study is to determine validity in extremely preterm infants.

Methods: We included 1022 preterm infants admitted to our Neonatal Intensive Care Unit (106 being extremely preterm, gestational age <28 weeks), between 01-01-2018 and 31-12-2022. Using item response theory, we determined (1) validity of the COMFORT-neo scale for preterm, particularly extremely preterm infants; (2) whether distress was measured; (3) whether the score was valid for ventilated and non-ventilated infants.

Results: For ventilated infants, the COMFORT-neo item scale Respiratory Response had a narrow range and category thresholds overlapped with Agitation and Facial Tension. For non-ventilated infants, the COMFORT-neo score adequately covered the latent construct of distress. Uniform and non-uniform differential item functioning was present between the patterns of extremely preterm and other preterm infants (Fig. 1). Ventilated extremely preterm-born infants had higher risks for positive scores on Agitation and Facial Tension (factor 1.09 and 1.79, respectively, although $P > 0.05$). Non-ventilated, extremely preterm infants had a lower risk of scoring positive on Agitation (factor 0.5, $P < 0.05$).

Conclusion: Several COMFORT-Neo scale items, particularly agitation and facial tension, do not contribute to measuring the latent construct of distress. For extremely preterm infants, the latent construct is not well measured at all. The COMFORT-Neo scale therefore warrants further development for this group.

Conflict of interest: None declared.

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GLUCOSE-REGULATORY HORMONES AND GROWTH IN VERY PRETERM INFANTS FED FORTIFIED HUMAN MILK: SECONDARY ANALYSIS OF A RANDOMISED CONTROLLED TRIAL

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Background: Both nutrition and hormones influence metabolism and growth in very preterm infants (VPIs). We investigated if plasma levels of glucose-regulatory hormones during the first weeks after very preterm birth were affected by type of nutrient fortifier, and their association with birthweight (appropriate/small for gestational age, AGA/SGA), post-natal age, enteral nutritional intake, and growth (ΔZ-scores from birth to 35 weeks postmenstrual age).

Methods: A total of 225 very preterm infants (VPIs, 26 + 0 to 30 + 6 weeks of gestation) were randomised to receive intact bovine colostrum (BC) or conventional fortifier (*CF*: PreNAN FM85 based on hydrolysed whey protein). Clinical outcomes were published previously (*Clin. Nutr*. 42:773–783, 2023). Basal hormone concentrations were measured in plasma obtained before the start of fortification and after 1 or 2 weeks of fortification (post-natal age ∼1, 2 and 3 weeks, respectively). Insulin-like growth factor-1 (IGF-1) concentrations were determined using an enzyme-linked immunosorbent assay (Mediagnost) and a metabolic hormone panel by electrochemiluminescence (Meso Scale Diagnostics).

Results: Compared with *CF*, infants who received fortification with BC showed higher glucagon-like peptide-1, gastric inhibitory polypeptide, glucagon, and leptin concentrations after start of fortification ($P < 0.05$), with no significant changes in IGF-1, C-peptide, insulin, pancreatic polypeptide and glucose concentrations. After 1 week of fortification, higher daily enteral milk intake was associated with higher IGF-1, insulin and C-peptide concentrations, while higher total daily protein intake was associated with higher leptin concentration after 2 weeks fortification ($P < 0.05$). Prior to fortification, leptin concentration was negatively associated with weight ΔZ-scores, while during fortification, IGF-1 concentration was positively associated with ΔZ-scores for weight and length ($P < 0.05$). In AGA infants, hormone concentrations generally increased within 1 week of fortification start. Relative to AGA infants, SGA infants showed reduced IGF-1 and leptin concentrations ($P < 0.05$).

Conclusion: Fortification of human milk with BC increased the plasma concentrations of several glucose-regulatory hormones in VPIs. Hormone concentrations also seem to be modified by enteral volume and protein intake, advancing post-natal age and SGA status. Concentrations of IGF-1 were positively, and leptin negatively, associated with growth. However, hormone concentrations were highly variable and only partially accounted for the overall variation in early post-natal growth.

PTS holds a patent related to bovine colostrum for infants (PCT/DK2013/050184) but has declined any share of potential revenue from commercial exploitation. All other authors declare no conflict of interest.

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ASSESSMENT OF HAEMOSTATIC PROFILE OF INTRA-UTERINE GROWTH RESTRICTED NEONATES USING NATEM ASSAY IN CORD BLOOD SAMPLES

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Background: Intra-uterine growth restriction (IUGR) carries severe morbidity during the perinatal period. Although disturbances of the haemostatic system are commonly observed in this population, they are not usually correlated with clinical manifestations. Rotational thromboelastometry (ROTEM) provides a rapid and detailed evaluation of the haemostatic system, though data for neonates are scarce. We aimed at examining the haemostatic profile of IUGR neonates using the non-activated assay (NATEM) in cord blood (CB) samples.

Methods: During a time-period of 18 months NATEM assay was performed in CB samples of 101 IUGR, 19 preterm (gestational age (GA) <37 weeks) and 82 term neonates(GA > 37 weeks), according to manufacturer's guidelines. Additionally, full blood count of the CB was done. One hundred and eighty-nine appropriate for gestational age (AGA) neonates served as controls. Demographic, clinical and laboratory data were documented. NATEM variables documented are: clotting time (CT-seconds), formation time (CFT-seconds), clot amplitude at 5, 10 and 20 min (A5, A10, A20); α-angle (a°), maximum clot firmness (MCF-mm), lysis index at 30 and 60 min (LI30, LI60-%), and maximum clot elasticity (MCE).

Results: IUGR neonates demonstrate a hypocoagulable state, with lower A5, A10, A20, MCF and MCE versus AGA. In multivariate analysis IUGR was established as an independent factor affecting all NATEM parameters (except CT and LI30), portraying a hypocoagulable and hypofibrinolytic profile, as indicated by lower values of A5, A10, A20, MCF, a-angle and MCE and higher values of CFT and LI60. Within the IUGR group, pH is negatively correlated with LI30 and LI60, and GA is positively correlated with LI30 and LI60. Birthweight seems to be weakly positively correlated with LI60. CB platelet count is positively correlated with A5, A10, A20, MCF, alpha-angle and MCE and negatively correlated with CFT. CB haemoglobin is inversely correlated with the same parameters.

Conclusion: IUGR neonates appear with hypocoagulable and hypofibrinolytic profile, lower clot strength and elasticity, prolonged clot kinetics. As this is the first study evaluating NATEM parameters in IUGR neonates, larger studies are needed to validate our results.

Conflict of interest: None declared.

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OBSERVATIONAL COHORT STUDY OF OPIOID USE IN VENTILATED PRETERM INFANTS AND THE ASSOCIATION WITH EVIDENCE OF BRAIN INJURY

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Background: Preterm infants often require mechanical ventilation (MV) which is a painful experience. Opioids such as morphine are used to provide analgesia despite conflicting evidence about their impact on the developing brain. We aimed to quantify the use of opioids during MV in infants born at <32 weeks' gestational age (GA), and to investigate the association between opioid use and evidence of brain injury.

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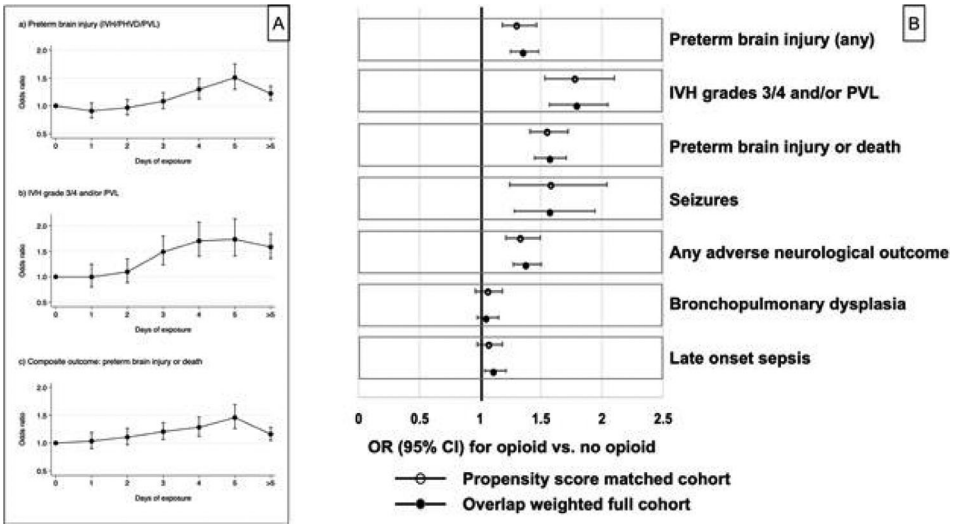


Fig. 1 Outcomes in ventilated infants born at <32 weeks' GA in England&Wales (2012–2020) by (a) the number of days of exposure to opioids and (b) group that did and did not receive opioids.

Methods: Retrospective propensity score matched cohort study using routinely recorded data from the National Neonatal Research Database of infants admitted to neonatal units in England and Wales (2012–2020).

Results: 67% (45 254/67279) of infants were mechanically ventilated for one or more days. Of these, 58% (26 250/45254) received an opioid while ventilated. Opioids were given for a median of 67% of ventilated days (interquartile range (IQR) 43%–92%) and the median (IQR) days of exposure was 4 (2–12). The percentage of mechanically ventilated infants who received opioids while ventilated increased from 52% in 2012 to 60% in 2020 (morphine, 51%–56%; fentanyl, 6%–18%).

In the propensity score matched cohort of 3564 pairs who were ventilated for more than two consecutive days, accounting for differences in infants' characteristics including level of illness, the odds of any preterm brain injury (aOR = 1.21, 95% CI 1.09–1.35), the most severe forms of brain injury, and the composite outcome of death or brain injury were higher in those who received opioids compared to those who did not (Fig. 1b). The adjusted odds of these adverse outcomes increased with increasing number of days of opioid exposure (Fig. 1a).

Conclusion: Use of opioids during mechanical ventilation of preterm infants has increased. Among those ventilated for more than two consecutive days, opioid use is associated with an increased risk of preterm brain injury and the risk increases with longer durations of exposure.

Conflict of interest: None declared.

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FEEDING VERY LOW BIRTHWEIGHT (VLBW) INFANTS WITH PRETERM DONOR MILK AS A SUPPLEMENT TO MOTHER'S OWN MILK HAS A POSITIVE IMPACT ON PROTEIN INTAKE AND GROWTH

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Introduction: Feeding very low birthweight (VLBW) preterm infants with human milk has contributed to increased survival and improved neurodevelopment. When mothers' own milk (MOM) is not available, pasteurised donor milk from human milk banks is the best alternative according to current recommendations. Donor milk is mainly derived from mothers delivering at term (TDM) and is less enriched in protein compared to preterm milk, at least during the first weeks after birth. As adequate protein intake is imperative for growth, we hypothesized that feeding VLBW infants with preterm donor milk (PDM), when MOM is not available or insufficient, may positively influence protein intake and, consequently, the infants' growth. The aim of this study was to evaluate whether MOM supplementation with PDM instead of TDM has any beneficial effects on protein intake and growth in VLBW infants.

Methods: In this randomised, controlled, double-blind study, 120 VLBW infants were allocated into two groups. In Group A ($n = 43$), infants were fed with MOM supplemented with PDM, whereas infants in Group B ($n = 77$) were fed with MOM supplemented with TDM, at least for the first 3 weeks of life (donor milk period). Infants with congenital anomalies, chromosomal disorders, metabolic diseases or fed with formula during the donor milk period were not eligible to participate. A breast milk fortifier was added in human milk when feeds exceeded 50 mL/kg/day. Protein concentration in human milk was measured regularly using a MIRIS Human Milk Analyzer. Infants' growth (body weight, length and head circumference) during the donor milk period and at discharge was also assessed.

Results: Protein intake was higher in Group A than in Group B at initiation of milk fortification ($P = 0.006$), as well as during the 3-week donor milk period ($P = 0.023$) and throughout hospitalisation ($P = 0.014$). Moreover, Group A presented higher Δz-score for body weight ($P = 0.019$) and head circumference

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($P = 0.001$) from birth to the end of donor milk period, and higher mean body weight at discharge ($P = 0.047$), compared to Group B.

Conclusion: When donor milk is required, preterm donor milk has a positive impact on protein intake and growth in VLBW infants.

Conflict of interest: None declared.

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REDUCED LUNG FUNCTION DURING CHILDHOOD AFTER FETAL GROWTH RESTRICTION IN DISCORDANT IDENTICAL TWINS

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Background: Fetal malnutrition can negatively affect lung development, leading to increased respiratory morbidity and reduced lung function later in life. Yet, studies regarding the impact of fetal growth restriction (FGR) on lung function in singletons are subject to genetic, obstetric, and maternal factors potentially influencing the outcomes. Therefore, we aim to investigate childhood lung function in monochorionic (MC) twins with selective FGR (sFGR) eliminating these confounding factors.

Methods: Spirometry was performed in MC twins with sFGR born in our centre between 2002 and 2017. sFGR was defined as birthweight discordance ≥20%. Outcome measures consisted of forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), residual volume (RV), total lung capacity (TLC), and transfer factor for carbon monoxide (TLCO). All outcomes were compared between the smaller and larger twin.

Results: We included 39 twin pairs with sFGR who performed spirometry of sufficient quality. The median gestational age at birth was 34.3 (interquartile range (IQR) 32.1–36.0) weeks with median birthweights of 1500 (IQR 1160–1880) grams for the smaller twin and 2178 (IQR 1675–2720) grams for the larger twin. The median age at spirometry was 11 (IQR 10–14) years, with median study heights of 149.4 (IQR 138.0–164.3) cm and 153.3 (IQR 141.1–167.2) cm for the smaller and larger twin, respectively. Smaller twins had significantly lower z-scores for FEV1 (−0.99 vs. −0.55, $P = 0.001$), FVC (−0.61 vs. −0.09, $P < 0.0001$) and TLCO (−0.47 vs. 0.18, $P < 0.0001$) compared to larger twins. We found no difference in FEV1%FVC, RV, TLC and RV%TLC.

Conclusion: Although being genetically identical, sFGR in MC twins is associated with a reduction in static lung volume with an equivalent decrease in dynamic lung function, suggesting that adverse growth conditions *in utero* negatively affect lung development and function. This can contribute to an increase in respiratory morbidities later in life.

Conflict of interest: None declared.

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DOWNREGULATION OF miR-155-5P AMELIORATES INTESTINAL INJURY IN NECROTIZING ENTEROCOLITIS BY SUPPRESSING FERROPTOSIS AND INFLAMMATION

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Background: Necrotizing enterocolitis (NEC) is an acquired disorder of mucosal damage, especially in premature infants. MicroRNAs (miRNAs) have been found to play an important role in the progression of NEC. Using bioinformatics analysis, we found that the level of miR-155-5p was significantly increased in intestinal tissues from infants with NEC. However, the mechanism of miR-155-5p in the progression of NEC remains unclear.

Methods: Human normal colorectal cells (FHCs) were stimulated with lipopolysaccharide (LPS) to mimic NEC *in vitro*; an NEC rat model was constructed by artificial feeding and hypoxia stimulation for *in vivo* study. Then, the inflammatory cytokine levels, cell viability and apoptosis rate were detected. Biochemical indices, including GSH, SOD, CAT and MDA, were detected by specific detection kits. ROS and MMP in FHC cells were detected by flow cytometry using the corresponding probes. Intracellular iron was detected quantitatively and qualitatively by a kit and probe, respectively. The expression of ferroptosis-related proteins in FHC cells and intestinal tissues of NEC rats was detected by Western blotting. The pathological changes in the intestinal tissues of NEC rats were evaluated by H&E staining.

Results: Downregulation of miR-155-5p increased the viability of LPS-stimulated FHC cells, inhibited cell apoptosis, inflammation and ferroptosis, and alleviated intestinal injury in NEC rats. SLC7A11 was identified as a direct target of miR-155-5p. The miR-155-5p inhibitor inhibited LPS-induced inflammation and ferroptosis in FHC and NEC rats by upregulating SLC7A11, which was manifested as upregulation of the ferroptosis-related proteins FTH1 and GPX4 and downregulation of COX-2 and ACSL4; downregulation of the lipid peroxidation product MDA; downregulation of the antioxidant indices GSH, SOD and CAT; downregulation of the proinflammatory cytokines IL-6 and TNF-α; and inhibition of the IκBα/NF-κB p65 pathway.

Conclusion: Collectively, the downregulation of miR-155-5p was able to ameliorate intestinal injury in NEC by suppressing ferroptosis and inflammation. These findings might provide some theoretical support for exploring new treatments for NEC.

Conflict of interest: None declared.

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BRAIN STATE OF THE NEWBORN (BSN), A FULLY AUTOMATED BEDSIDE TREND, PREDICTS THE CLINICAL OUTCOME AFTER PERINATAL ASPHYXIA

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Background: Long-term EEG monitoring is indicated by many guidelines, but it is hampered by the lack of resources for a continuous EEG review. We have recently developed a robust, deep learning-based algorithm (Brain State in the Newborn, BSN) that makes reliable interpretations and visualisation of the EEG background activity.[1] The BSN is a continuous index that ranges from 0 (inactive) to 100 (fully continuous, age-typical). In this study, we examined the clinical utility of BSN in fully automated interpretation of early EEG background after perinatal asphyxia. Particularly, we evaluated BSN's ability to predict poor clinical outcomes, including death and infantile epilepsy.

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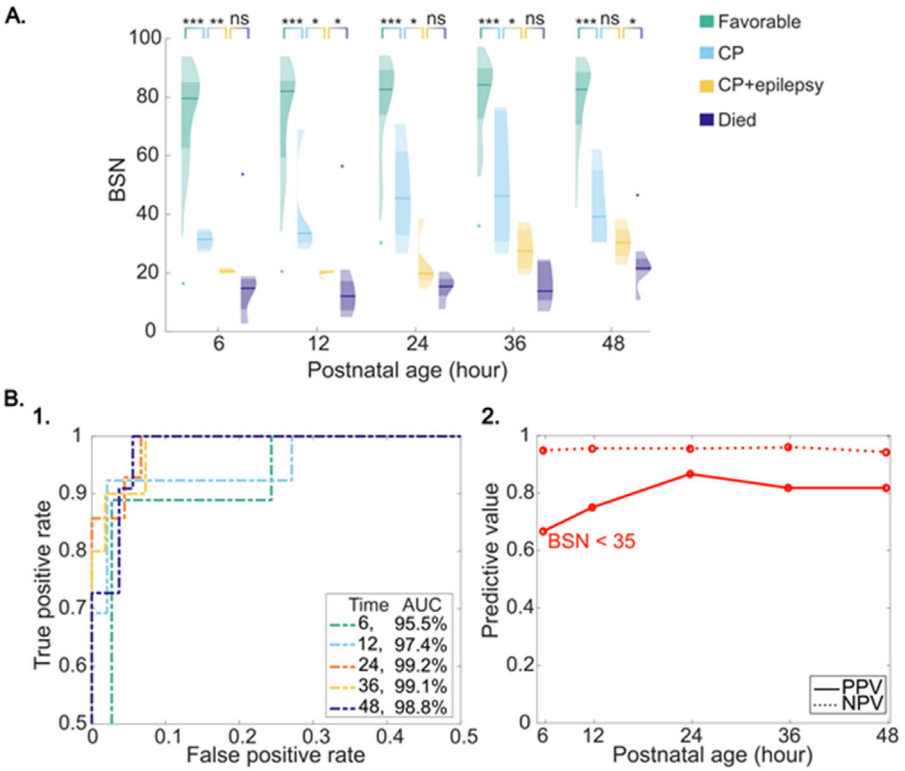


Fig. 1 (a) Distributions of BSN levels in each outcome group. (b1) ROC and AUC. The ROC plot is zoomed in to better visualise the differences. (b2) PPV and NPV time courses.

Methods: The average BSN were calculated for a cohort of $N = 80$ full-term infants with moderate to severe HIE. Clinical outcomes included: death ($N = 11$), epilepsy ($N = 6$), cerebral palsy without epilepsy ($N = 7$), and favourable ($N = 56$).[2] We then calculated the receiver operating characteristic (ROC) curves, area under the curve (AUC) at five time points (6, 12, 24, 36 and 48). Moreover, we inspected temporal changes in positive and negative predictive values (PPV and NPV) when considering a fixed BSN cut-offs (35) selected as optimal operating points at 12 h in the AUC. True positive for poor outcome (death, infantile epilepsy) was defined as a BSN value less than 35. Our cloud server (babacloud.fi) makes the entire BSN algorithm openly available.

Results: Summary distributions at five time points reveal a significant difference in BSN levels between outcome categories (Fig. 1a). From six to 24 h of life, the two worst outcomes – death or infantile epilepsy – were predicted with an AUC value ranging from 95.5% to 99.2%, respectively (Fig. 1b1). Expectedly, the PPV and NPV levels evolve over time (Fig. 1b2).

Conclusion: The present findings show that BSN: (i) Provides an intuitive interpretation of the recovering cortical activity in HIE. (ii) Allows an efficient clinical outcome prediction from early hours of life. Future studies are needed to establish evidence-based, and context-sensitive limits for BSN to provide efficient clinical guidelines for using BSN in the clinical care.

1. Moghadam SM *et al. Lancet Digit. Health*. 2022.
2. Nyman J *et al. Clin. Neurophysiol*. 2022.

Conflict of interest: None declared.

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COMPARISON BETWEEN THREE LUNG ULTRASOUND SCORES USED TO PREDICT THE NEED FOR SURFACTANT REPLACEMENT THERAPY IN PRETERM INFANTS: A RETROSPECTIVE STUDY

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Background: Lung ultrasound scores (LUS) were recently used to quantify the severity of lung disease and to predict the need for surfactant replacement therapy (SRT) in preterm infants with respiratory distress syndrome (RDS). There is no data on the comparison of the three main scores proposed by Brat, Raimondi and Fanjul and there is no evidence available to recommend

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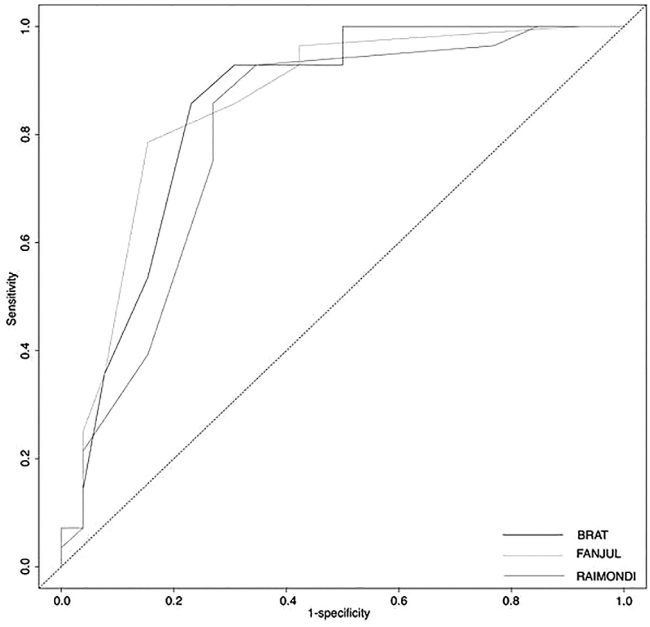


Fig. 1 Receiver operating characteristic (ROC) curve for Brat, Fanjul and Raimondi's scores.

which score and which cut-off should be used to predict the need for SRT. Aim of this study was to compare these three LUS in terms of ability to predict the need for SRT and reproducibility.

Methods: Retrospective, multicenter, national study. Preterm neonates below 32 weeks of gestational age (GA), affected by RDS, on non-invasive ventilation and with a LU performed prior to SRT were included. The centers involved based the surfactant administration decision on the latest European guidelines. LUS were calculated as proposed by Brat, Raimondi and Fanjul between 1 and 3 hours of life. Receiver-operating characteristic (ROC) curve analysis was used to assess the ability to predict SRT need and k-Cohen test was used to assess the intra and inter-observer agreement.

Results: Fifty-four preterm infants with median [IQR] GA of 30+2 [29+1−31+4] and mean ± SD birth weight of 1291± 363 were included in the study. Ability to predict the need for SRT of the LUS by Brat, Raimondi, and Fanjul had the following area under the curve: 0.84 (95%CI 0.74-0.96), 0.85 (95%CI 0.75-0.96) and 0.80 (95% CI 0.68-0.92) respectively. Brat and Raimondi's scores had an optimal cut-off value of 8, while the Fanjul's score of 10. The k-Choen values of intraobserver agreement for Brat, Raimondi and Fanjul's score were 0.896 (0.698-1.000), 1.000 (1.000-1.000) and 0.922 (0.767-1.000) respectively. Instead, the k-Choen values of interobserver agreement were 0.896 (0.698-1.000), 0.911 (0.741-1.000) and 0.833 (0.612-1.000) respectively.

Conclusion: The three studied scores had an excellent ability to predict the need for SRT and an optimal intra and inter-observer agreement. The cut-off value to predict the need for SRT differed according to the score used. The same LUS should be used within the same NICU to uniform the practice among operators.

Conflict of interest: None declared.

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NETwork META-ANALYSIS OF TRIALS OF INITIAL OXYGEN IN PRETERM NEWBORNS (NETMOTION): A SYSTEMATIC REVIEW AND INDIVIDUAL PARTICIPANT DATA NETWORK meta-analysis

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Background: Resuscitation with lower fractional inspired oxygen (FiO_2) reduces mortality in term infants but the impact of this practice on preterm infants is unclear. Network meta-analysis

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Comparison	Overall certainty	Odds Ratio (95% CrI)
Primary Outcome: All-cause mortality to hospital discharge		
High vs Low	⊕⊕⊕◯ Moderate	**0.45 (0.23-0.86)***
High vs Intermediate	⊕⊕◯◯ Low	**0.34 (0.11-0.99)***
Intermediate vs Low	⊕◯◯◯ Very Low	1.33 (0.54-3.15)
Secondary Outcomes:		
Oxygen saturation in target range (80-85%) at five minutes		
High vs Low	⊕◯◯◯ Very Low	0.99 (0.19-6.51)
High vs Intermediate	⊕◯◯◯ Very low	1.43 (0.1-29.23)
Intermediate vs Low	⊕⊕◯◯ Low	0.68 (0.06-6.51)
Severe intraventricular haemorrhage (Grade III-IV)		
High vs Low	⊕◯◯◯ Very low	0.56 (0.10-1.82)
High vs Intermediate	⊕◯◯◯ Very low	0.76 (0.05-6.17)
Intermediate vs Low	⊕◯◯◯ Very low	0.74 (0.12-4.25)
Chronic lung disease		
High vs Low	⊕◯◯◯ Very low	1.17 (0.55-2.52)
High vs Intermediate	⊕◯◯◯ Very low	1.34 (0.38-4.30)
Intermediate vs Low	⊕◯◯◯ Very low	0.86 (0.35-2.39)
Retinopathy of prematurity		
High vs Low	⊕◯◯◯ Very Low	1.17 (0.58-2.20)
High vs Intermediate	⊕◯◯◯ Very low	1.52 (0.51-4.60)
Intermediate vs Low	⊕⊕◯◯ Low	0.77 (0.31-1.77)
Mean difference in oxygen saturation at five minutes		**Mean Difference (95% CrI)**
High vs Low	⊕◯◯◯ Very low	**9.02 (2.08-16.31)***
High vs Intermediate	⊕◯◯◯ Very low	2.55 (-0.13-15.64)
Intermediate vs Low	⊕◯◯◯ Very low	6.39 (-4.04-15.68)

Abbreviations: CrI, credible intervals
**Denotes statistically significant effects*
†Low Oxygen (≤30%), Intermediate Oxygen (50-65%), High Oxygen (≥90%)

Table 1 Summary of relative effect estimates and certainty of evidence for primary and secondary outcomes

(NMA) addresses the limitations of previous pairwise meta-analyses by allowing multiple initial FiO_2 to be compared simultaneously.

Methods: We performed a systematic search for randomised trials (RCT) comparing initial oxygen concentration for resuscitation. We collated individual participant data (IPD) for infants <32 weeks' gestation. Low, intermediate, and high oxygen were defined as FiO_2 <0.3, 0.5–0.65 and >0.9, respectively. The pre-specified primary outcome was all-cause mortality at discharge. Secondary outcomes were morbidities of prematurity and oxygen saturation (SpO_2) at 5 min. We conducted one-stage Bayesian IPD-NMA, adjusting for the covariates of gestational age, mode of delivery and birthweight small for gestational age. Certainty of evidence was graded according to the CINeMA framework.

Results: IPD were provided for 1055 infants from 12 of the 13 eligible studies. Infants resuscitated with high initial FiO_2 had a significantly reduced mortality compared to low (OR 0.45 95% credible interval (CI) 0.23–0.86, moderate certainty) and intermediate FiO_2 (OR 0.34 CI 0.11–0.99, low certainty). High initial FiO_2 had a 97% probability of ranking best to reduce mortality. The effects on other morbidities (Table 1) were inconclusive due to low event rates. Five minute SpO_2 was higher in those given high initial FiO_2 compared to low FiO_2 (mean difference 9.02, 2.1–16.3). Most infants (89%) failed to achieve the 5 min SpO_2 80%–85% target but high FiO_2 had the highest odds of achieving SpO_2 >80% at 5 min.**Conclusion:** We found high initial FiO_2 likely reduces mortality in preterm infants <32 weeks' gestation compared to low (moderate certainty), and that high initial FiO_2 may reduce mortality compared to intermediate (low certainty). Resuscitation with high FiO_2 also led to higher 5 min SpO_2, however, most infants under- or overshot the SpO_2 target regardless of initial FiO_2 received. Importantly, most trials were conducted in settings where oxygen blending and saturation monitoring were available. These findings suggest that high initial FiO_2 may be a reasonable alternative to current standard practice.

Conflict of interest: None declared.

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COMPARING INFLAMMATION PROTEINS BEFORE AND AFTER PLATELET TRANSFUSION IN NICU

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Background: Studies have demonstrated increased morbidity and mortality with platelet transfusions in the neonatal period and at 2 years corrected. Platelets are as important for host immunity and inflammation as for haemostasis. Increased inflammation may explain the dose-associated increase in mortality, bleeding, and lung disease noted after platelet transfusions in the NICU population. Murine neonatal models have demonstrated an increase in inflammation levels after platelet transfusions. This study aims to assess if the there are any changes in inflammatory cytokines post-platelet transfusion in babies in NICU.

Methods: This prospective observational study recruited babies due to receive a non-emergency platelet transfusion. Samples were collected prior to and 2 hours post-platelet transfusion. Samples were processed using multiplex immunoassay to enable analysis of tiny blood volumes in dried bloodspot samples. Statistical analysis was performed using R. Results corrected for multiple pairwise comparisons.

Results: Seventeen babies underwent 26 platelet transfusions across two centres. Median birthweight was 1545 g (535-3960 g) and median birth gestation was 31 weeks and 1 day (23 + 1–40 + 5). Median pre-transfusion platelet count was 19.5×10^9/L.

There was a significant increase in levels of CXCL5 ($P < 0.001$), CD40 ($P = 0.001$), TGF-β ($P = 0.001$) in neonatal blood samples post-platelet transfusion in the study group.

Conclusion: The increase in the pro-inflammatory cytokines CXCL5, CD40 and TGF-β noted in this study after platelet transfusion in babies in NICU could potentiate existing inflammation, NEC, lung, or white matter injury. This is the first time that this has been demonstrated in human neonates. This could potentially explain long-term harm from platelet transfusion in babies.

Conflict of interest: None declared.

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CORRELATION BETWEEN HEART RATE AND REGIONAL CEREBRAL OXYGEN SATURATION IN PRETERM UND TERM NEONATES DURING IMMEDIATE TRANSITION AFTER BIRTH

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Background: Recent publications described an association between heart rate (HR) and cerebral oxygenation in neonates, measured non-invasively using near-infrared spectroscopy (NIRS). An association between cerebral oxygenation and HR may indicate an impairment of cerebral autoregulation, which in turn may increase the risk of cerebral injury, especially in preterm neonates.

Aim of the study was to investigate the correlation between HR and regional cerebral oxygenation saturation (crSO2) during immediate transition after birth in preterm and term neonates.

Methods: A retrospective analysis of secondary outcome parameters of prospective observational studies was performed. Preterm and term neonates, in whom continuous HR and crSO2 measurements during the first 15 min after birth were performed, were eligible. Preterm neonates were included independently of need of medical support and term neonates (control group) were included only without any medical support. HR and arterial oxygen saturation (SpO2) were continuously and non-invasively monitored using pulse oximetry applied on the right hand or wrist. CrSO2 was measured continuously on the left forehead, using the INVOS 5100C (Medtronic, Minneapolis, U.S.A.). Spearman-rank-correlation was used for correlation analysis of HR and crSO2 for every minute in each neonate from minute 10–15 after birth (after the initial increase of HR and SpO2 in the first minutes). Afterwards in preterm and term neonates mean values and standard deviations (SD) of the correlation coefficients were calculated for every minute and preterm and term neonates were compared.

Results: Three hundred and eleven neonates (106 preterm and 205 term neonates) were included. Mean gestational age of the preterm and term neonates was 34.0 ± 2.1 and 38.9 ± 0.8 weeks (P-value <0.001) and mean birthweight was 2012 ± 548 and 3280 ± 493 g (P-value <0.001), respectively. During immediate transition 62 (58%) preterm neonates received non-invasive respiratory support and 4 (4%) received mechanical ventilation. Mean correlation coefficients and SD during minutes 10–15 after birth in preterm and term neonates are presented in Table 1.**Conclusion:** Correlations between HR and crSO2 were predominantly positive in preterm neonates during immediate transition after birth compared to term neonates, with mainly negative correlations. Positive correlations in preterm neonates may indicate immature or impaired cerebral autoregulation.

Conflict of interest: None declared.

Time after birth (minute)	PRETERM NEONATES	TERM NEONATES	p-value
	Correlation coefficient ($HR/crSO_2$)	Correlation coefficient ($HR/crSO_2$)	
10	0.027 ± 0.411	-0.051 ± 0.376	0.132
11	0.045 ± 0.456	-0.101 ± 0.403	0.011
12	0.010 ± 0.412	-0.059 ± 0.364	0.185
13	-0.013 ± 0.471	-0.045 ± 0.386	0.569
14	0.065 ± 0.423	-0.096 ± 0.368	0.003
15	0.000 ± 0.535	-0.036 ± 0.477	0.594

Table 1 Mean correlation coefficients ± standard deviation (SD) of preterm and term neonates during immediate transition after birth. A P-value <0.05 was considered statistically significant

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OBSERVATIONAL COHORT STUDY OF USE OF CAFFEINE IN PRETERM INFANTS AND ASSOCIATION BETWEEN EARLY CAFFEINE USE AND NEONATAL OUTCOMES

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Objective: To quantify trends in caffeine use in infants born at <32 weeks' gestational age (GA), and to investigate the effects of early versus late caffeine on neonatal outcomes.

Study Design: Retrospective propensity score matched cohort study using routinely recorded data from the National Neonatal Research Database of infants born at <32 weeks' GA admitted to neonatal units in England and Wales (2012–2020).

Results: 89% (58 913/66081) of infants received caffeine. In 70%, caffeine was started early (on the day of birth or the day after), increasing from 55% in 2012 to 83% in 2020. Caffeine was given for a median (IQR) of 28 (17–43) days starting on day 2 (1–3) and continued up to 34 (33–34) weeks postmenstrual age.

In the propensity score matched cohort of 13 045 pairs of infants, the odds of preterm brain injury (early caffeine, 2306/13045 (17.7%) vs. late caffeine, 2528/13045 (19.4%), OR = 0.89 (95% CI 0.84 to 0.95)) and bronchopulmonary dysplasia (BPD) (early caffeine, 4020/13045 (32.8%) vs. late caffeine, 4694/13045 (37.7%), OR = 0.81 (95% CI 0.76 to 0.85)) were lower in the group that received early caffeine compared with those who received it later.

Conclusions: Early use of caffeine has increased in England and Wales. This is associated with reduced risks of BPD and preterm brain injury. Randomised trials are needed to find the optimal timing of caffeine use and the groups of infants who will benefit most from early administration of caffeine.

Conflict of interest: None declared.

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PREDICTING FLUID RESPONSIVENESS WITH ULTRASOUND IN A NEONATAL INTENSIVE CARE SETTING

Koert de Waal[1,2], Enrico Petoello[1]

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Background: There are strong and consistent associations between fluid overload and adverse clinical outcomes in intensive care patients, so it is important to assess each patient's fluid status and fluid responsiveness before additional fluid is administered.

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The mini-fluid challenge test uses the Frank-Starling principles to assess dynamic fluid responsiveness based on changes in stroke volume. The aim of this study is to test the feasibility of a standardised mini-fluid challenge in a neonatal intensive care setting and predict fluid responsiveness.

Methods: This prospective observational study included any infant in our neonatal intensive care where a fluid bolus was prescribed for clinical reasons. Cardiac ultrasound was used to measure left ventricular peak velocity of stroke volume before and after a 3 ml/kg fluid bolus was given over 5 min. An increase of more than 15% was considered fluid responsive. The outcome of the mini-fluid challenge was not used to guide additional treatments. Short term clinical outcomes within 4 h after the mini-fluid challenge were collected to detail additional fluid boluses and/or start of inotropes, and an oxygenation index was calculated to describe respiratory support changes as proxy for extravascular lung water changes.

Results: Thus far 11 preterm infants with late onset sepsis and 5 infants with other pathology were studied (Table 1). Four infants (25%) were fluid responsive. Fluid non-responders showed a higher rise in oxygenation index compared to responders (+0.7 versus +0.4). Clinical outcomes and requirement of additional fluid or inotropes in the 4 h after the mini-fluid challenge was not directly associated with fluid responsiveness.

Conclusion: The mini-fluid challenge is feasible in the neonatal intensive care setting and followed the physiological principles of stroke volume and extravascular lung water changes. The mini-fluid test enhanced the clinicians' ability to determine the need for fluid compared to clinical changes alone. Further study will be required to review the optimal bolus volume and definition of fluid responsiveness in preterm and term neonates.

Conflict of interest: None declared.

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RANDOMISED CROSSOVER TRIAL TO COMPARE EFFECT OF DURATION OF SKIN TO SKIN CARE ON PRETERM NEONATAL PAIN CONTROL

Vivek Shukla[2], Pratik Trivedi[1], Jaimin Patel[1], **Archana Nimbalkar**[1], Dipen Patel[1], Ajay Phatak[1], Somashekhar Nimbalkar[1]

[1]Bhaikaka University, [2]University of Alabama

Background: Preterm neonates who receive intensive care undergo multiple painful procedures as a part of their medical management. Skin-to-skin care (SSC) for 30 min before the painful procedure has been shown to provide effective pain control in preterm neonates. We tested the hypothesis that SSC for shorter durations will be as effective as that for 30 min for preterm neonatal pain control.

Methods: Study participants were stratified as per the gestational age into two strata, 28–32 weeks and 33–36 weeks. All neonates requiring heel-stick for glucose monitoring admitted to the study NICU from January 2019 to December 2022 were eligible. Those on the ventilator, haemodynamically unstable, exposed to analgesic/sedative medications within the last 24 h of the procedure, and neurologically impaired were excluded. SSC was given by mothers by crossover design for 10, 15, 20 and 30 min by random sequence allocation generated by a computer-based randomisation software. Blinded PIPP scores assessments at 0, 1 and 5 min of heel-stick were done using video recording. A clinically significant PIPP score difference was defined as a difference of ≥1 in the total PIPP score. The trial was registered at the Clinical Trials Registry of India, registration number: CTRI/2019/05/019428.

Results: A total of 136 neonates (68/stratum) were enrolled. One infant in the 28–32 week strata was excluded as the later 2 heel-stick procedures were not clinically indicated. The male:

Nr	Gestation (weeks)	Indication for prescribing fluid	Main pathophysiology	% change in stroke volume	change in oxygenation index
1	24	Hypotension	LOS	+5	+1.9
2	25	Hypotension	LOS	+17	+1.2
3	25	Hypotension	LOS	+5	+4.9
4	26	Hypotension	LOS	+5	+1.1
5	27	Hypotension	LOS	+9	-0.7
6	25	Hypotension	LOS	+16	-0.1
7	28	Hypotension	LOS	+18	-0.4
8	28	Poor perfusion	LOS	+4	-0.2
9	25	Poor perfusion	LOS	+3	-1.6
10	26	Poor perfusion	LOS	+12	+1.6
11	27	Tachycardia	LOS	+2	+0.1
12	34	Poor perfusion	Gastroschisis	-10	-1.0
13	37	Poor perfusion	Gastroschisis	-1	+0.0
14	32	Poor perfusion	congenital CMV	-14	-1.1
15	41	Tachycardia	Meconium	+7	+3.1
16	36	Hypotension	HIE	+37	+0.8

Table 1 Mini-fluid challenge and outcomes in 16 neonates. LOS, late onset sepsis, HIE, hypoxic ischaemic encephalopathy

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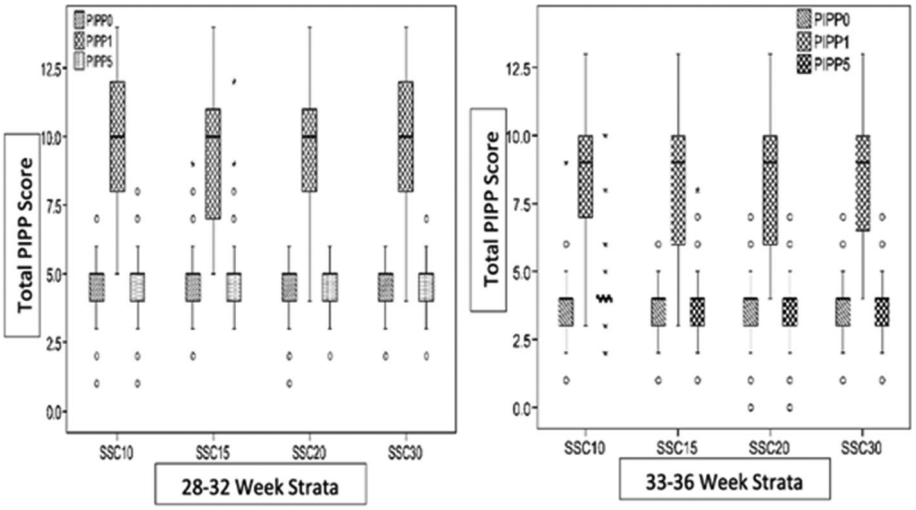


Fig. 1 PIPP score distribution.

female ratio was 1.4:1. The mean (SD) days after birth was 17.6 (11.5) days in the 28–32 and 8.3 (5.8) days in the 33–36 weeks strata. The mean (SD) birthweight was 1.38 (0.33) and 1.68 (0.27) kg in the 28–32 and 33–36 weeks strata, respectively. There was no clinically significant difference between groups for PIPP score at 0.1 and 5 min in both strata (Fig. 1). The PIPP score at 5 min was not significantly different from that at 0 min in all groups in both strata.

Conclusion: Skin-to-skin care for 10, 15 and 20 min were as effective as that for 30 min. The result of this study will help in providing effective pain control in preterm neonates for moderately painful procedures.

Conflict of interest: None Declared.

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THE ROLE OF LUNG ULTRASONOGRAPHY IN THE PERIOPERATIVE EVALUATION OF PULMONARY OEDEMA IN NEWBORNS WITH CRITICAL CONGENITAL HEART DISEASE

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Background: In newborns with critical CHD, pulmonary oedema may be experienced longer and more severely. There are several studies that show that lung ultrasonography detects pulmonary oedema better than chest X-ray. Our aim in this study was to evaluate pulmonary oedema by lung ultrasonography in operated newborns with critical congenital heart disease and to evaluate its effectiveness in the treatment of pulmonary oedema.

Methods: In this prospective observational clinical study, bedside lung ultrasonography was performed for pulmonary oedema in 44 newborns operated for critical CHD. Ultrasonography was performed four times in the perioperative period and the newborns had routine chest Xray and echocardiographic evaluation taken on the day of ultrasonography. The correlation of Lung ultrasonography with radiological imaging and clinical findings of the newborn was examined.

Results: Mean gestational age and birthweight were 38.3 ± 1.7 weeks and 3026 ± 432 g, respectively. In the perioperative period, a statistically significant correlation was found between moderate–severe pulmonary oedema on lung ultrasonography, pulmonary oedema findings on chest X-ray and clinical findings of pulmonary oedema in newborns (respectively, $P < 0.001$ and $P < 0.05$). In addition, a significant correlation between the degree of moderate–severe pulmonary oedema in lung ultrasonography and pulmonary hypertension in echocardiographic evaluation was found only in the preoperative period (p:0.04).

Conclusion: Besides the use of ultrasonography in detecting pulmonary oedema and directing the treatment of pulmonary oedema, its secondary contribution is that it can be used effectively in predicting the duration of hospitalisation and mechanical ventilation support.

Conflict of interest: None declared.

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OPTICLAMP: A QUALITY IMPROVEMENT PROJECT INCREASING OPTIMAL CORD MANAGEMENT IN PRETERM BABIES IN A NEONATAL INTENSIVE CARE UNIT (NICU) IN THE UNITED KINGDOM (UK)

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Background: Deferring umbilical cord clamping for >60 s after birth, known as optimal cord management (OCM) is the recommended management for babies <34 weeks in the UK. It is

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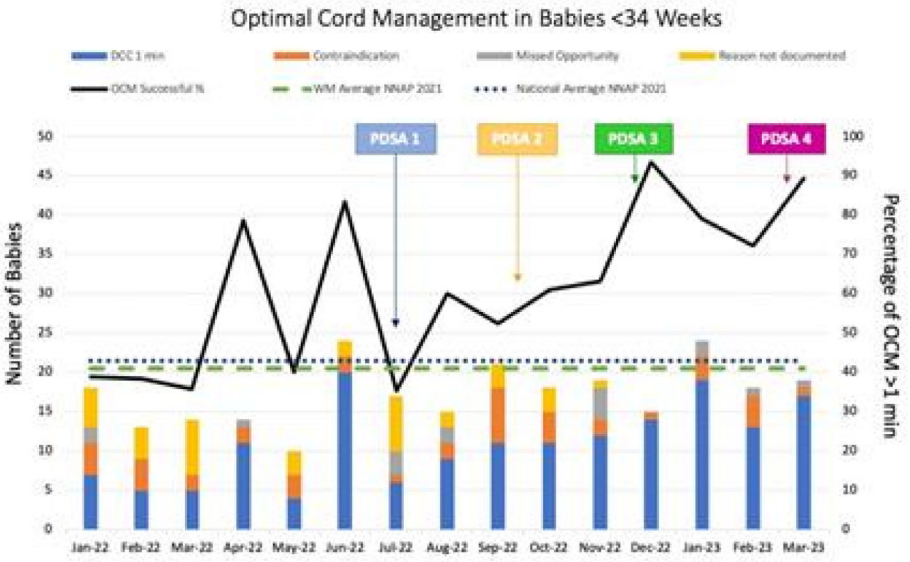


Fig. 1 Optimal Cord Management in Babies older than 34 Weeks.

associated with a 27% reduction in mortality risk, reduction in blood transfusion and need for inotropic support in the preterm population. Our NICU was identified as having a low OCM rate compared to national data in 2021.

Aim: To improve from 20.4% from 2021 National Neonatal Audit Project (NNAP) data, to 80% of babies <34 weeks with OCM over a 12-month period.

Methods: We formed a core team of maternity and neonatal professionals and completed process mapping, cause and effect and driver diagrams. This identified four key target areas: education, environment, equipment and processes.

Results: From February 2022 to February 2023, the percentage of babies <34 weeks receiving >60 s of OCM has improved from 37% to 79% (Fig. 1). It has continued to improve throughout 2023.

The first PDSA cycle was to change our resuscitation documentation to include a section to specifically record this and transfer onto electronic records. The second PDSA cycle was increasing awareness, through safety and champion meetings, labour ward specialty council and an expanded core group to include obstetric and theatre representatives. We performed a staff survey to identify barriers, motivating factors and understanding between PDSA cycles two and three. This identified education as a key factor and the provision of clocks in visible areas. The third PDSA cycle was to change our practice, so a neonatal practitioner was present in theatre during surgical deliveries to facilitate joint decision-making and support maternity colleagues. The fourth PDSA cycle is underway with targeted education sessions being delivered to obstetric, midwifery, neonatal medic and nursing teams. Anaesthetic and theatre staff will also be included. We have monitored admission temperature to ensure OCM does not have an intended negative consequence of increasing rates of hypothermia.**Conclusion:** This demonstrates significant improvement using current staff members and existing equipment. Ongoing work to sustain this improvement includes a clinical guideline, education, simulation sessions and exploring the possibility of stabilisation with the cord intact.

Conflict of interest: None declared.

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ASSOCIATION BETWEEN UMBILICAL CORD pH LEVELS AND NEONATAL MORBIDITY AND MORTALITY: A NATIONAL COHORT STUDY OF 338 720 CHILDREN FROM DENMARK

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Background: Umbilical cord pH (UC-pH) is an important indicator of neonatal well-being, but threshold values for increased risk of morbidity and mortality are unclear. In the clinical setting, a UC-pH < 7.00 is often used as a threshold for pathology, but this may not capture all children at risk.

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Table 1. Outcomes according to UC-pH. Values are numbers (percentages) unless otherwise stated.

	pH <7.00 (n=3510) n (%)	pH 7.00-7.09 (n= 11 920) n (%)	pH 7.10- 7.19 (n=72 531) n (%)	pH 7.20-7.50 (n= 250 741) n (%)	pH <7.00 compared to 7.20-7.40	pH 7.00-7.09 compared to 7.20-7.40	pH 7.10-7.19 compared to 7.20-7.40
					RR (95% CI)	RR (95% CI)	RR (95% CI)
Apgar 0-3/5	103 (2.9)	67 (0.6)	128 (0.2)	222 (0.1)	33.1 (26.3-41.8)	6.4 (4.8-8.3)	2.0 (1.6-2.5)
Apgar 0-6/5	298 (8.5)	324 (2.7)	524 (0.7)	805 (0.3)	26.4 (23.3-30.1)	8.5 (7.5-9.6)	2.3 (2.0–2.5)
CPAP	838 (23.9)	2978 (16.6)	4299 (5.9)	7712 (3.1)	7.8 (7.2-8.2)	5.4 (5.2-5.7)	1.93 (1.9-2.0)
Mechanical ventilation	84 (2.4)	59 (0.5)	134 (0.2)	349 (0.1)	17.2 (13.6-21.8)	3.56 (2.7-4.7)	1.3 (1.1-1.2)
Meconium aspiration	81 (2.3)	151 (1.3)	360 (0.5)	638 (0.3)	9.1 (7.2-11.4)	5.0 (4.2-5.9)	1.95 (1.71-2.22)
iNO	16 (0.5)	13 (0.1)	26 (0.0)	44 (0.0)	26.0 (14.8-46.0)	6.2 (3.4-11.5)	2.0 (1.3-3.3)
Hypoglycemia	481 (13.7)	2407 (20.2)	4876 (6.7)	9870 (3.9)	3.5 (3.2-3.8)	5.1 (4.9-5.3)	1.7 (1.7-1.8)
Convulsions	65 (1.9)	42 (0.4)	142 (0.2)	289 (0.1)	16.1 (12.3-21.0)	3.1 (2.2-4.2)	1.70 (1.39-2.08)
Hypothermia treatment	114 (3.3)	28 (0.2)	38 (0.1)	44 (0.0)	>100	13.4 (8.3-21.5)	3.0 (1.9-4.6)
Neonatal death (0-28 days)	35 (1.0)	11 (0.1)	14 (0.0)	55 (0.0)	40.0 (26.2-60.8)	4.21 (2.20-8.04)	0.9 (0.5-1.6)
Composite neonatal outcome*	186 (5.3)	106 (0.9)	275 (0.4)	622 (0.3)	20.1 (17.1-23.5)	3.4 (2.8-4.1)	1.4 (1.3-1.7)

CPAP= Continuous Positive Airway Pressure; iNO = treatment with inhaled Nitric oxide.

*Composite neonatal outcome: Neonatal death (0–28 days), hypothermia treatment, mechanical ventilation, iNO treatment, or convulsions.

Table 1 Outcomes according to UC-pH. Values are numbers (%) unless otherwise stated

This study aimed to investigate the proportion of children with neonatal complications among those born with UC-pH between 6.00 and 7.50 in a national setting with universal UC-pH measuring.

Methods: This population-based cohort study included live-born singleton term infants born in Denmark from 2012 to 2018. Infants with known malformations of the heart, lungs, or nervous system were excluded. Data on UC-pH, neonatal morbidities and survival were obtained from the national patient register and linked to the civil registration number of the newborn infant. We divided the infants into four groups according to UC-pH levels (<7.00, 7.00–7.09, 7.10–7.19 and 7.20–7.40 as the reference). Multiple imputations were performed for missing UC-pH values (5.9%). We used Poisson regression models and estimated the relative risk ratios with 95% confidence intervals (CI) for morbidities and mortality in the first 28 days after birth.

Results: A total of 338 720 live-born children were included in the study. The proportions of infants with low Apgar scores, respiratory complications, hypoglycaemia, and neurological complications were significantly increased if UC-pH was below 7.20 compared to >7.20 (Table 1). However, there was a steep decline in risk ratios for complication from UC-pH < 7.00–7.20. The risk of neonatal death was increased if UC-pH was <7.10, and there was a tenfold increase in neonatal death if UC-pH was below 7.00 compared to 7.00–7.09.**Conclusion:** This large observational study shows that a threshold of UC-pH <7.00 is associated with the markedly highest risk of death and morbidities compared to higher UC-pH values. However, the rates of other severe neonatal morbidities were also increased at UC-pH values between 7.00 and 7.19 and neonatal mortality was increased if UC-pH was below 7.10. These findings may have important implications for clinical decision-making and the management of neonatal care.

Conflict of interest: None declared.

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PERSISTING EXPOSURE TO ENDOCRINE DISRUPTING PHTHALATES AND ALTERNATIVE PLASTICIZERS IN NEONATAL INTENSIVE CARE UNIT PATIENTS

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Background: Phthalates, plasticizers used to soften plastic materials, can leach from plastic medical devices (PMD) into the human body. Di-(2-ethylhexyl)-phthalate (DEHP) has long been the most popular plasticizer, but its use was restricted in PMDs due to endocrine disrupting properties, being gradually replaced by alternative plasticizers (APs). Premature neonates in the neonatal intensive care unit (NICU) rely on invasive PMDs, and may be exposed to high amounts of plasticizers. This study investigated current phthalate and AP exposure in the NICU using longitudinal urine samples and identified patients at a higher risk.

Methods: This prospective cohort study (NCT05404815) included patients at the Antwerp University Hospital NICU. Throughout hospitalisation, 840 urine samples were collected from 100 preterm (gestational age (GA) 24–31 weeks) and

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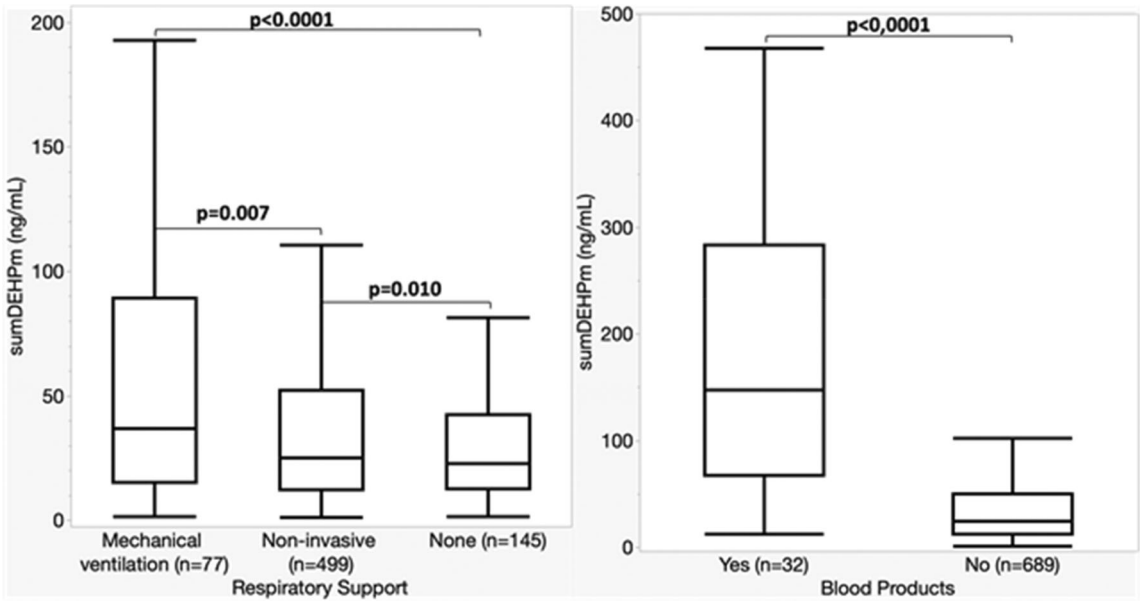


Fig. 1 DEHP metabolite concentrations (sumDEHPm) in neonatal urine samples after different medical equipment exposure. *P*-values are derived from the Mann–Whitney *U* test when comparing two groups, the Kruskal–Wallis for more groups.

20 control neonates, and analysed for phthalate and AP metabolites by LC–MS/MS. Birth characteristics, sampling time, and PMD exposure (defined in a 2-day window before each urine collection) were analysed as predictors for urinary metabolites using univariate non-parametric tests.

Results: Phthalate metabolites were detected in ≥90% of neonatal samples, AP metabolites in ±50%. Median urinary phthalate metabolite concentrations were lower compared to previous NICU studies (2005–2019). DEHP-metabolites were significantly higher in preterm than in control neonates ($P = 0.0497$) and compared to NICU/control mothers ($P < 0.0001$). Within the preterm group, DEHP-metabolites were negatively correlated with GA (rho = −0.37) and birthweight (rho = −0.26). DEHP-metabolite concentrations gradually increased after birth until week three post-natal age, then decreased until discharge. Concerning parenteral nutrition and a central catheter, no significant differences were observed in exposed compared to unexposed preterms. Respiratory support ($P = 0.0003$) and blood products ($P < 0.0001$) were associated with significantly higher urinary DEHP-metabolites. Post hoc analysis showed higher concentrations with invasive ($P < 0.0001$) and non-invasive ventilation ($P = 0.010$) than without respiratory support. After blood transfusion, ±50% had an estimated daily intake of DEHP above the tolerable daily intake (36 µg/kg/d).**Conclusions:** This study shows persisting NICU exposure of premature neonates to endocrine disrupting phthalates, despite changing legislation (MDR 2017/745). We are the first to map neonatal exposure to APs. More immature children, especially with respiratory support and/or receiving blood products are at increased risk of phthalate exposure above reference levels.

Conflict of interest: None declared.

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INTERMITTENT SIGH BREATHS DURING HIGH-FREQUENCY OSCILLATORY VENTILATION ARE ASSOCIATED WITH IMPROVED VENTILATION DISTRIBUTION IN PRETERM INFANTS

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Background and Aims: Recruitment manoeuvres during high frequency oscillatory ventilation (HFOV) are used to open collapsed alveoli. However, the increase in mean airway pressure could also lead to hyperinflation and volutrauma incurring further lung damage. Using intermittent sigh breaths during HFOV has been proposed as an alternative. The aim of this study was to determine if HFOV with intermittent sigh breaths, compared to HFOV alone, could improve ventilation distribution and oxygenation, in preterm infants with hypoxic respiratory failure (HRF).

Methods: In this prospective interventional cross-over study, ventilated preterm infants <30 weeks gestational age randomly received HFOV with sigh breaths followed by HFOV-only for alternating 2 h periods. Sigh breaths were delivered with an inspiratory time of 1 s, a peak inspiratory pressure (PIP) of 30 cmH_2O and a frequency of 3 breaths/min. During sigh breath periods the set-mean airway pressure (MAP) was reduced in proportion to the difference between PIP and set-MAP to keep the mean airway pressure constant. Electrical impedance tomography (EIT) measured ventilation distribution (end-expiratory lung volume (EELV),

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	No Sigh	Sigh	Sigh p-value	Baseline	30 min	60 min	Time p-value
	Mean ± SE (95% CI)			Mean ± SE (95% CI)			
EIT							
Amp - Global	0.01 ± 0.002 (0.01-0.02)	0.02 ± 0.01 (0.01-0.03)	0,26	0.01 ± 0.002 (0.004-0.01)	0.01 ± 0.002 (0.01-0.02)	0.02 ± 0.01 (0.01-0.03)	0,05
Amp - R	0.02 ± 0.003 (0.01-0.02)	0.03 ± 0.007 (0.02-0.04)	0,24	0.01 ± 0.003 (0.01-0.02)	0.02 ± 0.004 (0.01-0.03)	0.02 ± 0.007 (0.01-0.04)	0,08
Amp - L	0.01 ± 0.002 (0.01-0.02)	0.01 ± 0.002 (0.01-0.02)	0,07	0.01 ± 0.002 (0.01-0.01)	0.01 ± 0.002 (0.01-0.02)	0.01 ± 0.002 (0.01-0.02)	0,16
Amp - A	0.01 ± 0.003 (0.01-0.02)	0.02 ± 0.004 (0.01-0.03)	0,16	0.02 ± 0.004 (0.01-0.02)	0.02 ± 0.003 (0.01-0.02)	0.02 ± 0.003 (0.01-0.02)	0,63
AMP - P	0.02 ± 0.003 (0.01-0.02)	0.03 ± 0.01 (0.01-0.04)	0,18	0.01 ± 0.004 (0.005-0.02)	0.02 ± 0.003 (0.01-0.02)	0.03 ± 0.007 (0.01-0.04)	0,18
EELV - Global	0.05 ± 0.02 (0.01-0.10)	0.12 ± 0.03 (0.05-0.18)	0.04*	0.00 ± 0.002 (-0.01 - -0.001)	0.08 ± 0.03 (0.02-0.14)	0.11 ± 0.04 (0.04-0.19)	0.03*
EELV - R	0.06 ± 0.03 (0.01-0.12)	0.14 ± 0.05 (0.05-0.24)	0,08	0.00 ± 0.001 (-0.01 - -0.004)	0.10 ± 0.04 (0.02-0.19)	0.14 ± 0.05 (0.05-0.23)	0.02*
EELV - L	0.04 ± 0.02 (-0.01-0.08)	0.09 ± 0.03 (0.03-0.16)	0.01*	0.001 ± 0.001 (-0.004-0.002)	0.06 ± 0.03 (0.01-0.12)	0.09 ±0.04 (0.01-0.16)	0.04*
EELV - A	0.06 ± 0.04 (-0.01-0.14)	0.12 ± 0.05 (0.02-0.22)	0,23	0.00 ± 0.003 (-0.01 - -0.002)	0.09 ± 0.04 (0.01-0.17)	0.13 ± 0.06 (0.001-0.26)	0,18
EELV - P	0.04 ± 0.02 (-0.003-0.08)	0.10 ± 0.04 (0.03-0.18)	0.04*	0.00 ± 0.002 (-0.01 - -0.002)	0.07 ± 0.03 (0.01-0.14)	0.08 ± 0.04 (0.02-0.16)	0,14
Avg GI Index	0.51 ± 0.01 (0.48-0.54)	0.49 ± 0.14 (0.46-0.51)	0,52	0.54 ± 0.03 (0.49-0.59)	0.49 ± 0.01 (0.46-0.51)	0.49 ± 0.01 (0.46-0.52)	0.04*
Physiological							
SpO2	92.16 ± 0.49 (91.19-93.012)	95.02 ± 0.56 (93.93-96.11)	0.00*	93.06 ± 0.74 (91.60-94,51)	93.51 ± 0.54 (92.46-94.56)	93.22 ± 0.53 (92.18-94.26)	0,26
SpO2/FiO2	249.58 ± 26.57 (197.51-301.65)	291.12 ± 25.51 (241.13-341.12)	0,17	251.12 ± 23.54 (204.98-297.27)	262.74 ± 23.21 (217.25-308.22)	277.19 ± 22.30 (233.49-320.90)	0,20
HR	157.58 ± 3.60 (150.53-164.64)	157.01 ± 3.35 (150.45-163.57)	0,80	160.30 ± 4.81 (150.86-169.73)	156.60 ± 3.04 (150.64-162.57)	156.63 ± 3.06 (150.62-162.64)	0,49
SBP	69.33 ± 3.40 (62.68-75.99)	66.07 ± 3.47 (59.27-72.86)	0,24	67.86 ± 3.43 (61.14-74.58)		67.54 ± 3.37 (60.93-74.15)	0,90
DBP	34.89 ± 1.70 (31.56-38.23)	34.66 ± 2.56 (29.65-39.67)	0,91	34.75 ± 2.31 (30.22-39.28)		34.80 ± 1.99 (30.90-38.70)	0,98
Mean BP	49.75 ± 2.46 (44.93-54.58)	48.25 ± 3.31 (41.76-54.74)	0,44	49.22 ± 3.27 (42.81-5564)		48.78 ± 2.68 (43.52-54.05)	0,85
Ventilator settings							
FiO2	40.18 ± 3.29 (33.73-46.63)	37.07 ± 2.85 (31.49-42.65)	0.05*	38.92 ± 2.92 (33.19-44.64)	39.22 ± 3.06 (33.23-45.21)	38.66 ± 3.20 (32.40-44.93)	0,19
MAP-measured	12.72 ± 0.65 (11.44-14.00)	12.50 ± 0.58 (11.36-13.64)	0,41	12.72 ± 0.66 (11.42-14.01)	12.58 ± 0.61 (11.38-13.77)	12.65 ± 0.60 (11.47-13.82)	0,80
MAP-set	12.85 ± 0.62 (11.64-14.06)	11.91 ± 0.60 (10.72-13.08)	0.00*	12.41 ± 0.61 (11.22-13.60)	12.36 ± 0.61 (11.16-13.56)	12.36 ± 0.61 (11.16-13.56)	0,79
Amplitude	18.82 ± 1.02 (16.83-2081)	19.26 ± 0.95 (17.39-21.12)	0,26	18.58 ± 1.09 (16.44-20.72)	18.89 ± 1.00 (16.94-20.84)	19.30 ± 0.95 (17.43-21.17)	0,32
MV	1.27 ± 0.09 (1.11-1.45)	1.32 ± 0.11 (1.11-1.53)	0,63	1.26 ± 0.08 (1.09-1.42)	1.26 ± 0.10 (1.06-1.46)	1.33 ± 0.11 (1.12-1.55)	0,33
DCO2	48.87 ± 5.34 (38.40-59.34)	53.40 ± 7.58 (38.53-68.26)	0,47	46.58 ± 4.96 (36.86-56.30)	50.41 ± 6.62 (37.43-63.40)	53.01 ± 6.86 (39.56-66.45)	0,54
Leak	1.69 ± 1.64 (-1.54-4.91)	0.69 ± 0.67 (-0.62-2.00)	0,31	2.37 ± 2.30 (-2.12-6.87)	1.11 ± 1.09 (-1.02-3.25)	0.92 ± 0.90 (-0.85-2.69)	0,57
Vosc	2.39 ± 0.24 (1.92-2.86)	3.02 ± 0.52 (1.99-4.04)	0,31	2.30 ± 0.17 (1.96-2.63)	2.87 ± 0.53 (1.84-3.90)	2.58 ± 0.33 (1.93-3.23)	0,82
Freq	10,69	10,69	0,00	10,69	10,69		0,00
Hz	10,69	10,69	0,00	10,69	10,69	10,69	0,00
PIP		30,00	0,00		24,00	24,00	
SD GI Index	0.04 ± 0.004 (0.03-0.05)	0.0409 ± 0.004 (0.03-0.05)	0,95	0.0382 ± 0.004 (0.03-0.05)	0.0401 ± 0.004 (0.03-0.05)	0.0419 ± 0.005 (0.03-0.05)	0,62
GC – xGlobal	17.44 ± 0.33 (16.81-18.08)	17.13 ± 0.34 (16.45-17.80)	0,87	18.15 ± 0.67 (16.83-19.47)	17.18 ± 0.28 (16.64-17.72)	17.04 ± 0.36 (16.32-17.75)	0,29
GC – yGlobal	17.44 ± 0.34 (16.76-18.11)	17.65 ± 0.37 16.93-18.37	0,59	17.28 ± 0.53 16.24-18.33	17.54 ± 0.35 16.85-18.23	17.62 ± 0.37 16.90-18.34	0,88

Table 1 AMP, EELV, Avg GI: EIT measures. EELV = end expiratory lung volume. SpO2 and FiO_2: pulse oximetry and fraction of inspired oxygen. MAP, PIP = mean airway an peak inspiratory pressure

global inhomogeneity (GI), and amplitude), and physiological variables were recorded to monitor oxygenation (Table 1).

Results: Sixteen infants (10 males, 6 females) were included in the study with a median (range) gestational age of 25.5 weeks (23–31), weight of 950 g (660–1920), and post-natal age of 25 days (3–49). EIT identified that the addition of sigh breaths resulted in a significantly higher EELV ($P = 0.04$;). This was primarily due to an increase in ventilation in the posterior (dependent) lung.

SpO2 was improved and FiO_2 lower ($P < 0.05$) during sigh breaths, and $SpO2/FiO_2$ accordingly higher although not statistically significant (291 ± 26 vs. 250 ± 27, $P = 0.17$).

Conclusion: This is the first study to use EIT during HFOV-sigh breaths to assess distribution of ventilation. Intermittent sigh breaths during HFOV were associated with improved distribution of ventilation and lower oxygen requirement in preterm infants with HRF.

Conflict of interest: None declared.

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TRANSPLANTATION OF VIABLE FAECAL VIROME IS NECESSARY AND SUFFICIENT FOR REDUCING NECROTIZING ENTEROCOLITIS SEVERITY

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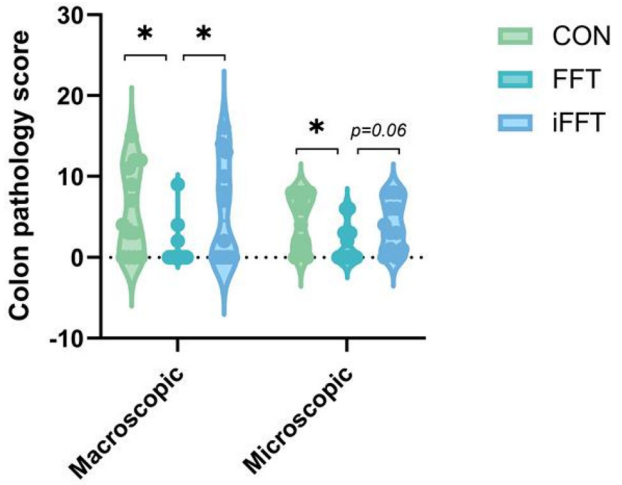


Fig. 1 Colon pathology scores. *$P < 0.05$. Statistical analysis: Kruskal–Wallis non-parametric test followed by post hoc pairwise comparison by Dunn test with Benjamin Hochberg *P*-value adjustment.

Background: Necrotizing enterocolitis (NEC) is a severe gastrointestinal disease affecting premature infants, usually preceded by gut dysbiosis and increased relative abundance of Proteobacteria. We recently found that transferring donor faecal filtrate (FFT), where bacteria were removed by filtration, could prevent NEC and reduce the relative abundance of mucosa-associated Proteobacteria. We propose that this is due to bacteriophages infecting intestinal bacteria in a host-specific manner, but we cannot exclude the potential effect of faecal metabolites. In this study we compared the NEC-preventive capacity of native FFT versus inactivated FFT, and provide evidence that intact faecal bacteriophages are necessary for NEC prevention.

Methods: Colon content from four healthy 10-day-old suckling piglets was filtered at 0.45 μm to remove bacteria (FFT). An aliquot of FFT was exposed to UV-irradiation at 265 nm to target nucleic acids and inactivate faecal viruses (iFFT). Premature caesarean-born piglets were fed increasing volumes of formula for NEC induction, and were orally administered saline (CON), FFT or iFFT during the first 2 days of life. The animals were closely monitored, and clinical and faecal assessments were performed twice daily. Animals were euthanized on day 5 or when presenting clinical signs of NEC. Macroscopic NEC-like lesions were graded in a blinded fashion, and organs were collected for analysis and microscopic scoring of intestinal pathology.

Results: Reduced colon pathology score was observed in animals receiving FFT ($P < 0.05$) relative to controls, whereas no reduction was seen in the iFFT group (Fig. 1). The iFFT group displayed an increased stomach pathology score relative to FFT ($P < 0.05$) and controls ($P = 0.06$). No differences were found for small intestinal pathology scores. Additionally, earlier onset of diarrhoea was observed in the FFT group but not in the iFFT group ($P < 0.05$).

Conclusion: We demonstrated that the NEC preventive effect of FFT requires viable donor faecal viruses. Moreover, when the FFT is UV-irradiated, inactivating viruses, the residual faecal metabolites appear incapable of preventing NEC. Paradoxically, the earlier onset of diarrhoea occurring in the FFT group is likely a result of donor-derived porcine viruses also susceptible to UV-irradiation. Further refinement is necessary to develop an effective and safe virome-based treatment against NEC.

Conflict of interest: None declared.

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SOCIAL AND NEONATAL RISK PROFILES IN EXTREMELY AND VERY PRETERM BORN CHILDREN: THE IMPACT ON DEVELOPMENTAL OUTCOMES AND SUPPORT AT 5.5 YEARS

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Background: Outcomes after extremely (EP) and very preterm (VP) birth have mostly been studied from a biomedical perspective with little attention for social/environmental factors. Lack of improvements in developmental outcomes and long-term effects of interventions mark the importance of narrowing this knowledge gap. This study aimed to describe the EP/VP population in terms of social and neonatal risk exposure, and to study associations between risk and intelligence, motor skills, behaviour, and use of specialised care and education at 5.5 years.

Methods: Samples included 553 EP (<28 weeks' gestation) and 1497 VP (28–31 weeks) born children from the French population-based EPIPAGE-2 cohort. Ten social/environmental factors measuring five aspects of the environment (socio-professional status, education level, minority status, family composition and neighbourhood) and six neonatal factors were used to compose social and neonatal cumulative risk indices and to identify latent profiles. Regression models were used to test associations of cumulative risk and risk profiles with outcomes.

Results: A higher socio-economic status (SES) subgroup was distinguished from two lower SES subgroups that mainly differed in country of birth of parent(s). Neonatal risk profiles were characterised by lower, intermediate, and high morbidity. Cumulative risk was associated with worse outcomes. Lower SES subgroups showed poorer outcomes, particularly for intelligence. Children with parent(s) born in non-European countries or French overseas departments had the poorest outcomes but received the least specialised care and education. Boys received more specialised support than girls, irrespective of neurodevelopmental impairments (Fig. 1).

Conclusion: The important role of social factors in developmental outcomes and social and sex disparities in support suggest that a considerable proportion of EP/VP children does not reach their full potential. The largest gains are to be made in lower SES groups. Social factors should be considered in identifying high-risk infants and increased efforts must be made to reach children from disadvantaged backgrounds for monitoring and support. The environment provides ample opportunities to intervene,

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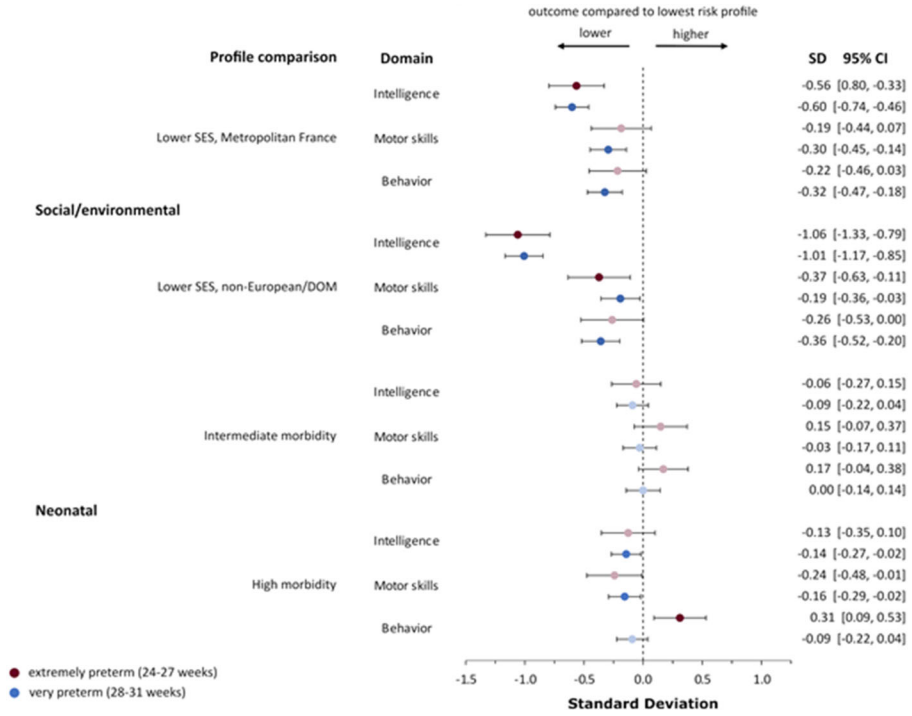


Fig. 1 Associations of social/environmental and neonatal risk profiles with intelligence, motor skills, and behaviour in the extremely and very preterm sample. For all domains, lower SD indicates worse functioning.

particularly on modifiable factors and mechanisms that link social factors with children's outcomes. However, this research is still in its infancy. Thus, opportunities are far from being exploited, which offers hope for the future.

Conflict of interest: None declared.

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EXTRACELLULAR VESICLES FROM IMMORTALISED AND CLONALLY EXPANDED MESENCHYMAL STROMAL CELLS AS ADJUNCT THERAPY TO THERAPEUTIC HYPOTHERMIA FOR NEONATAL HYPOXIC–ISCHAEMIC BRAIN INJURY

Nicole Labusek[1], Yanis Mouloud[2], Parnian Ghari[1], Christian Köster[1], Urusla Felderhoff-Müser[1], Ivo Bendix[1], Bernd Giebel[2], Josephine Herz[1]

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Background: Neonatal encephalopathy (NE) caused by hypoxia–ischaemia (HI) is a leading cause for childhood morbidity and mortality. The only available but obligatory therapy is hypothermia (HT), which is, however, limited due to a short therapeutic window. Despite tremendous research, an adjuvant therapy overcoming limitations of HT is still missing. Extracellular vesicles (EVs) from mesenchymal stromal cells (MSCs) showed promising effects in different neonatal and adult brain injury models. According to issues associated with MSC heterogeneity and senescence, we recently demonstrated a high therapeutic efficiency of EVs from immortalised and clonally expanded MSCs (ciMSCs). In the present study we investigated, whether an intranasal ciMSC-EV therapy overcomes limitations of HT.

Methods: Nine-day-old C57BL/6 mice were exposed to HI through ligation of the right common carotid artery and 1 h hypoxia (10% oxygen) followed by 4 h hypothermia or normothermia. ciMSC-EVs were administered intranasally at day 1, 3 and 5 after HI. Analyses of brain tissues were performed *via* immunohistochemistry, western blot and real time PCR at day 7 post HI. Long-term functional outcome was assessed by neurobehavioral testing 35 days after HI.

Results: Confirming previous reports, therapeutic effects of HT were limited with regard to protection in the striatum and improvement of myelination deficits. Furthermore, long-term functional outcome was only partially improved. Compared to a HT single therapy, the combined treatment with ciMSC-EVs resulted in an increased protection from HI-induced neuronal loss, astro- and microgliosis and myelination deficits, accompanied by an increased neurotrophic growth factor expression. These short-term effects translated into long-term improvement of cognitive deficits and amelioration of HI-induced alterations in risk assessment behaviour.

Conclusion: The availability of ciMSCs provides new avenues for the standardised and scaled manufacturing of clinical grade EV products. Importantly, the present findings demonstrate that intranasal administration of ciMSC-EVs improve the outcome of HT therapy. Therefore, ciMSC-EV application appears a

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promising adjuvant therapy, overcoming current limitations of the obligate clinical care for the treatment of NE caused by HI.

Conflict of interest: None declared.

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IMPACT OF INSULIN-LIKE GROWTH FACTOR 1 AND PRETERM BIRTH ON KIDNEY DEVELOPMENT IN NECROTIZING ENTEROCOLITIS-SENSITIVE PIGS

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Background: Preterm birth can affect normal prenatal renal development, leading to increased risk of post-natal kidney injury and failure. Preterm infants are deficient in insulin-like growth factor 1 (IGF-1), a critical growth factor that stimulates tissue perfusion and development. Using necrotizing enterocolitis (NEC)-sensitive preterm pigs as a model for preterm infants, we investigated whether exogenous IGF-1 supplementation would improve kidney maturation and ameliorate preterm birth related renal impairments.

Methods: Caesarean-delivered preterm pigs (90% gestation) received vehicle or recombinant human IGF-1 with binding protein 3 (rhIGF-1/IGFBP-3, systemically) for 5, 9 or 19 days. Postnatal age-matched term pigs served as references to preterm pigs. At the end of each experiment, blood and urine samples were collected for biochemical analysis. Kidney tissue was collected for histological, protein and gene expression analyses

Results: Preterm pigs showed delayed kidney maturation and kidney impairments, as indicated by reduced average glomerular

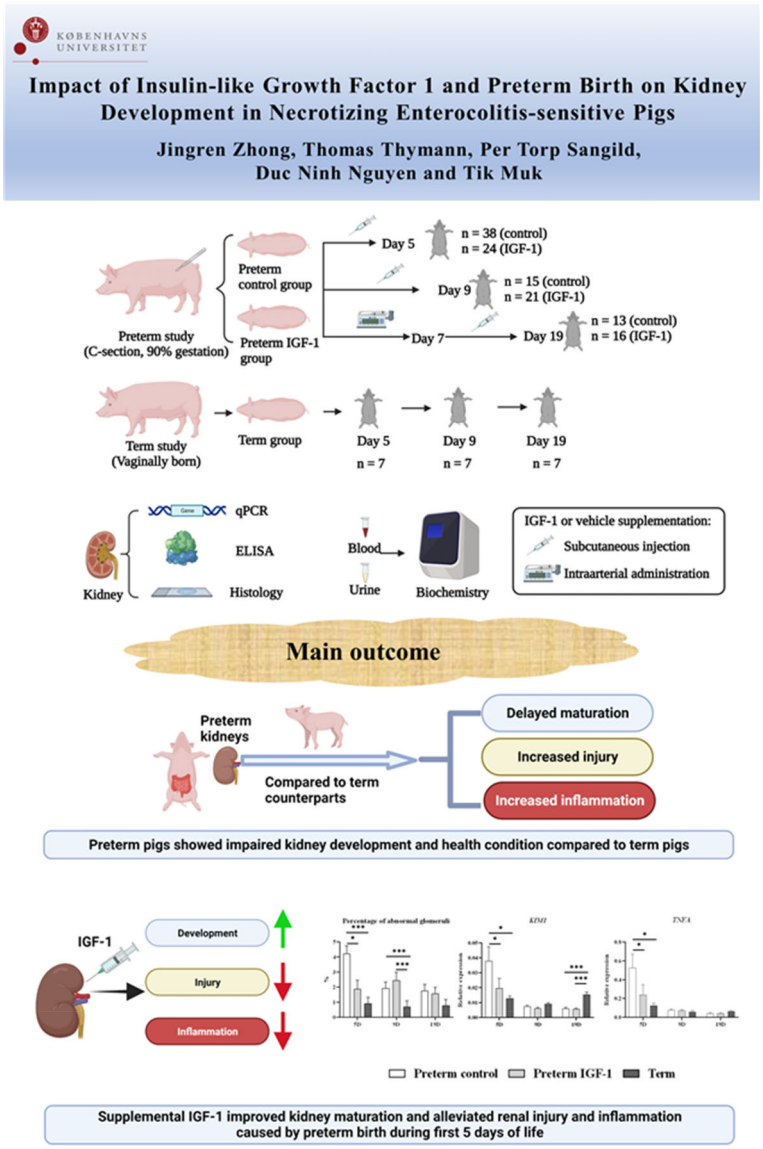


Fig. 1 IGF-1 supplementation promotes kidney maturation and alleviates kidney insults in preterm piglets: Study design and main outcome.

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area, increased abnormal glomeruli percentage, altered expression of renal development related genes, and increased markers of renal injury and inflammation, when compared with term pigs. Especially by day 5, IGF-1 supplementation reduced the abnormal glomeruli percentage, renal injury and inflammation related markers, together with up-regulation of selected maturation-related genes. There was limited effect of mild NEC-like lesions on kidney insults (Fig. 1).

Conclusion: Preterm birth induced impaired kidney development in pigs. Supplementation of IGF-1, especially in the first week of post-natal life, supports kidney maturation and alleviates kidney insults after preterm birth. How supplemental IGF-1 may affect kidney development in preterm infants should be investigated.

Conflict of interest: Author Per Torp Sangild, Thomas Thymann, Duc Ninh Nguyen, and Tik Muk are currently involved in a patent application directed to use of rhIGF-1 for preterm infants.

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LARYNGEAL CLOSURE IN PRETERM INFANTS CAUSES OBSTRUCTION DURING NEONATAL TRANSITION AFTER BIRTH: AN OBSERVATIONAL STUDY

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Background: Lung aeration is necessary to achieve optimal transition after birth. Preterm infants receive respiratory support and non-invasive ventilation with continuous positive airway pressure (CPAP) and/or intermittent positive pressure ventilation (IPPV). However, recent animal data showed that the larynx is predominantly closed during apnoea after birth, negating the effect of non-invasive ventilation. We hypothesized that laryngeal closure also occurs in preterm infants. The aim of this study was to visualise the position/movement of the vocal cords during non-invasive respiratory support of preterm infants at birth.

Methods: In this observational study, vocal cords were visualised using ultrasonography, of infants <30 weeks gestation directly after birth and at 1 h after birth. To determine the percentage of time the vocal cords were closed, position of the vocal cords was reviewed by 15 frames per second and compared with the breathing patterns of the respiratory function monitor.

Results: Twenty infants were included (GA of 27 + 5 (26 + 2–291) weeks), of which 60% (12/20) were initially breathing and 40% (8/20) were apnoeic at birth. In infants breathing at birth, vocal cords were closed in between breaths and during breath holds, resulting in a closed position for 55% (45–64) in the minutes that CPAP was given. In infants who were apnoeic at birth, vocal cords were closed 100% of time during apnoea, obstructing positive pressure ventilation. The vocal cords opened only during a spontaneous breath, resulting in a closed position for 93% (80–99) of the time during PPV (Fig. 1).

Conclusion: In preterm infants at birth, vocal cords are closed during apnoea, in between breaths and during breath holds, negating the effectiveness of ventilatory support.

Conflict of interest: None declared.

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ANTIBIOTIC EXPOSURE FOR PRESUMED CULTURE-NEGATIVE EARLY-ONSET SEPSIS IS PREDOMINANT IN EUROPE, NORTH AMERICA AND AUSTRALIA

Varvara Dimopoulou[1], Claus Klingenberg[2,3], Lars Navér[4], Viveka Nordberg[4], Alberto Berardi[5], Salhab El Helou[6], Gerhard Fusch[6], Joseph M. Bliss[7], Dirk Lehnick[8], Nicholas Guerina[7], Joanna Seliga-Siwecka[9], Pierre Maton[10], Donatienne Lagae[11], Judit Mari[12], Jan Janota[13,14,15], Philipp KA Agyeman[16], Riccardo Pfister[17], Giuseppe Latorre[18], Gianfranco Maffei[19], Nicola Laforgia[20], Enikő Mózes[21], Ketil Størdal[22], Tobias Strunk[23], Martin Stocker[24], Eric Giannoni[1]

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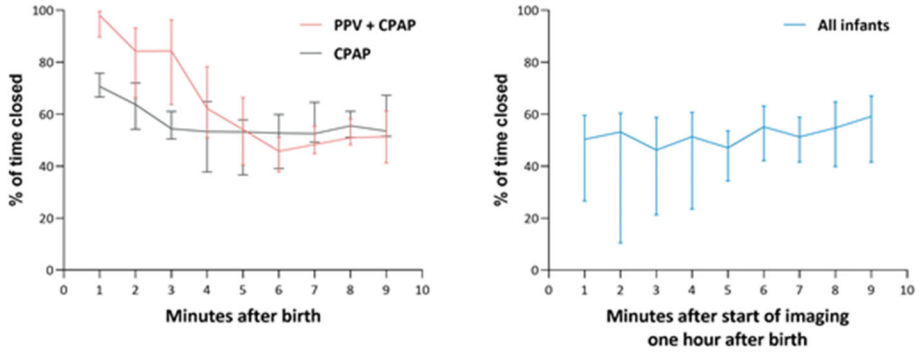


Fig. 1 The percentage of time the vocal cords are in a closed position. Data are presented as median (IQR).

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Background: Due to the potentially fulminant nature of neonatal early-onset sepsis (EOS), there is a low threshold to initiate empirical antibiotics. Predominantly, blood cultures remain negative, allowing antibiotics to be discontinued within 48 h. As the sensitivity of blood cultures is not 100%, a subset of patients are given prolonged antibiotic treatment for presumed 'culture negative EOS' (CN-EOS). Our goal was to determine the incidence of presumed CN-EOS and related antibiotic exposure during the first post-natal week.

Methods: We conducted a secondary analysis of a retrospective study of late-preterm and term infants born between January 2014 and December 2018 in 13 networks from 11 countries in Europe, North America and Australia. Culture-proven EOS (CP-EOS) was defined as positive blood and/or cerebrospinal fluid culture and antibiotic treatment for ≥5 days. In the absence of positive cultures, newborns were considered as having a presumed CN-EOS when treated with antibiotics for ≥5 days, and considered as having culture-negative ruled-out sepsis (CN-ROS) when treated <5 days. We determined the incidence of CP-EOS, CN-EOS and CN-ROS and related antibiotic exposure.

Results: Among 757 979 late-preterm and term infants born in the participating networks during the study period, 21 703 were treated with antibiotics (2.86%, 95% CI 2.83%–2.90%). The number of infants classified as CN-EOS, CP-EOS and CN-ROS was 7996 (36.8%), 375 (1.7%) and 13 330 (61.4%). The incidence of CN-EOS, CP-EOS and CN-ROS was 10.55 (95% CI 10.32–10.78), 0.49 (95% CI 0.44–0.54) and 17.58 (95% CI 17.29–18.88) cases per 1000 livebirths. The median (IQR) duration of treatment for CN-EOS, CP-EOS and CN-ROS was 6 (5–8), 9 (7–14) and 3 (3–4) days. The median (IQR) number of antibiotic days (per 1000 livebirths) administered for CN-EOS, CP-EOS and CN-ROS was 77 (76–78), 5 (5–5.5) and 53 (52–53). There was a positive correlation between the incidence of CP-EOS and CN-EOS in each network ($R = 0.79$, 95% CI 0.43–0.94).

Conclusions: Presumed CN-EOS was responsible for over half of the total number of antibiotic days administered to late-preterm and term newborns. Implementing restrictive diagnostic criteria for CN-EOS may lead to a more targeted and reduced use of antibiotics in early life.

Conflict of interest: None declared.

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FINDING BALANCE BETWEEN DELIBERATION AND INTUITION IN DECISION-MAKING AT THE LIMIT OF VIABILITY: A QUALITATIVE DUTCH INTERVIEW STUDY

Angret De Boer[1,2], Lien De Proost[3,4], Marieke de Vries[5], Marije Hogeveen[2], Martine C. de Vries[4,6], E. Joanne Verweij[1], Rosa Geurtzen[2]

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Background and Aim: When extremely premature birth is imminent, a complex decision must be made regarding the infant's treatment directly after birth. A shared decision-making approach exploring parental values is recommended. Next to more rational deliberation, intuition and feelings play an important role. Therefore, this study aims to gain further insight into (I) whether parents base their decision on intuition and feelings, rational deliberation, or both (II) which values are important for parents in decision-making at the limit of viability and (III) how to best clarify those values during prenatal counselling.

Methods: A semi-structured qualitative interview study was conducted with experienced parents. They were invited through purposive sampling to include perspectives of parents with different experiences and backgrounds. Interviews were recorded, transcribed and a thematic analysis was performed by two researchers.

Results: Between September 2022 and April 2023, 19 interviews were performed. All experienced an imminent extremely preterm birth (23–26 weeks GA) in the period 2009–2022, both palliative comfort care and intensive care treatment decisions were made and the outcomes varied. Some did eventually not deliver extremely preterm but >26 weeks.

Initial analysis showed variation in themes on what was considered important in decision-making, such as 'giving a chance', 'potential disabilities', 'our own happiness' and 'quality of life'. Most parents based their decision mostly on intuition and feelings instead of deliberating their values. They indicated that emotions and intuition were inevitable in a challenging situation like imminent extremely premature birth, which did not negatively influence their decision-making. Lastly, parents provided suggestions for value clarification during counselling, such as 'just ask parents

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about what they value in life' and 'include social work in counselling'.

Conclusion: Parents discussed various values and acknowledged a significant role for emotions and intuition in their decision-making at the limit of viability. Gaining a deeper understanding of parental considerations and feelings during this decision, and how to clarify what is important to them, may lead to improvement of prenatal counselling.

Conflict of interest: None declared.

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CHARACTERISATION OF THE PATHO-IMMUNOLOGY OF NECROTIZING ENTEROCOLITIS REVEALS NOVEL THERAPEUTIC OPPORTUNITIES

Steven X Cho[1,2], Ina Rudloff[1,2], Jason Chun Lao[1,2], Andrew M Ellisdon[3], James C Whisstock[3], Marcel F Nold[1,2], Doris Fischer[4], Alex Veldman[4], **Claudia Nold-Petry**[1,2]

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Background: Necrotising enterocolitis (NEC) is a severe, insidious intestinal disease of preterm infants. Despite its pivotal pathogenetic role in NEC, the excessive inflammation that drives NEC remains poorly characterised; consequently, no targeted therapy exists. The interleukin (IL)1 family cytokine IL-37 is one of the rare anti-inflammatory interleukins with broad and powerful properties in inhibiting inflammation.

Methods: NEC was induced in newborn C57BL/6J and interleukin (IL-) 37-transgenic mouse pups by 3-hourly formula feeding, 12-hourly asphyxia and cold stress. Dam-fed littermates served as controls. Intestinal tissues in were collected 1. in mice at the experimental endpoint (up to 72 h), 2. from human infants with NEC and appropriate controls, for analysis by either histology, immunohistochemistry, multiplex ELISA, real-time PCR and flow cytometry.

Results: Here we show that human and murine NEC intestines exhibit an unexpected predominance of type 3/TH17 polarisation over types 1, 2 and Treg. In murine NEC, pro-inflammatory type 3 NKp46-RORγt+Tbet+ innate lymphoid cells (ILC3) are 7-fold increased, whereas ILC1 and protective NKp46 + RORγt+ ILC3 are obliterated. IL-36β/γ:IL-36Ra ratios are increased in human NEC, and both species exhibit dysregulation of intestinal TLR repertoires (TLRs4&8 increased, TLRs5-7&9–12 reduced). The anti-inflammatory cytokine IL-37 protects from intestinal injury, modestly when injected, but potently when transgenically expressed; only the transgene dramatically reduces mortality (−84%). Mechanistically, IL-37 ameliorates imbalances in innate and adaptive immunity, favourably modulates TLR repertoires, and preserves microbial diversity. Importantly, IL-37 and its receptor IL-1R8 are 51% reduced in human NEC epithelia; and at 2 weeks, when NEC frequently occurs, IL-37 is 78% lower in monocytes from blood of infants with NEC and/or lower birthweight.

Conclusions: By advancing knowledge on NEC pathomechanisms, we reveal the therapeutic potential of IL-37, type 3 cytokines, TLRs and IL-36, whose exploitation may relieve our young patients' suffering.

Conflict of interest: Monash University, Hudson Institute (J.C. W., M.F.N., C.A.N.-P., and A.M.E.) hold patents on IL-37, PCT/AU2016/050495, PCT/ EP2020/08703. There are no other conflicts of interest to declare.

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NORMAL VALUES FOR VENOUS, ARTERIAL, AND CAPILLARY POTASSIUM: STATEMENTS ON THE DISPENSABILITY OF CONTROLS THROUGH EVALUATION OF 166 604 BLOOD GAS ANALYSES

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Background: In neonatal intensive care units (NICU), potassium is frequently determined in blood gas analyses (BGA). If it does not fall within classical normal values, controls are ordered because complications of hyperkalaemia are feared. Separate references for capillary, venous and arterial samples are lacking.

Methods: From over 200 000 patient days of electronic patient records 166 604 BGA were extracted and annotated with gestational age (GA), day of life (DOL), and weight at the time of sampling, diuretic administration up to 4 h, and potassium substitution up to 24 h before sampling. As a surrogate for impaired general condition (GC), we considered administration of certain medications (inotropes, buffers, doxapram, etc.) up to 12 h, $FiO_2 > 0.4$ up to 1 h, urine production <0.5 mL/kg/h up to 24 h, and central-peripheral temperature difference >2°C up to 4 h before sampling. Values are median (P2.5;P97.5).

Results: Annotation was successful in 97.8% of the BGAs. Of these, 99.8% had credible potassium (1.5–10 mM). Hence, 162 722 values from 8994 patients (GA 36.3 (25.6; 41.4) weeks, 55.2% male, 9 (1; 107) BGA/patient) are considered. Arterial samples were 11%, venous 21%, and capillary 68%; samples were taken on the 7th (1–104) DOL; weight was 2.08 (0.66; 4.41) kg. In a multivariate model, diuretics, DOL, GC, and postmenstrual age – unlike weight and potassium substitution – were significant. Distributions of all values after excluding samples taken under impaired GC and diuretics are presented in the table. Comparing capillary samples with values from other sites within ±2 h ($n = 4635$), showed a

	all ages		after 14th day of life	
sample site	n	K^+ [mM]	n	K^+ [mM]
capillary	38863	4.4 [3;6.5]	13371	4.3 [3;6.1]
arterial	2585	3.7 [2.8;5.3]	112	4.1 [2.6;5.7]
venous	8019	3.7 [2.5;5.4]	1495	3.9 [2.6;5.5]

Table 1 Potassium values from all blood gas analyses in our neonatal intensive care unit after exclusion of samples drawn during impaired general condition and diuretics. Values are median (P2.5;P97.5)

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difference of 0.7 (−1.0; 3.6) mM ($P < 0.00001$). This difference is smaller under the interval (3.5; 6.1) formulated here than above it (0 (−1.6; 0.9) vs. 2.4 (0; 5.1) mM, $P < 0.00001$) (Table 1).

Conclusion: This is the most extensive analysis of BGAs in NICU patients to date. We recommend new thresholds for capillary potassium: 3.5–6.1 mM. Potassium is 0.7 mM higher in capillary samples than in other sites; this difference is greater in hyperkalaemia. To avoid overdiagnosis, we suggest very restrictive control of capillary potassium under 6.1 mM in a stable clinical situation. Incorporating these recommendations into routine practice can prevent many unnecessary and painful blood draws.

Conflict of interest: None declared.

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CHARACTERISATION OF CELL DEATH AFTER PERIVENTRICULAR HAEMORRHAGIC INFARCTION IN PRETERM INFANTS

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Background: Periventricular haemorrhagic infarction (PVHI) occurs in 5%–10% of very preterm newborns (VPT, <28 weeks) in the first week of life and carries substantial neurological morbidity To date no study has systematically investigated the different types of cell death and which cell type is affected in the context of PVHI. Understanding the way cells are damaged is crucial to design brain protective and/or repair strategies.

Methods: Human brain tissues were obtained from 23 VPT (Institute of Pathology, Lausanne) with ethical approval. The studied population of VPT born <28 0/7 gestational age (GA) was selected retrospectively from death reports of the Clinic of Neonatology (CHUV, Lausanne) from 2005 to 2015. Cases with PVHI (ultrasonographic and pathological diagnosis, $n = 12$) were compared to controls without significant brain injuries according to the autopsy reports ($n = 11$). Newborns with cerebral malformations and known genetic anomalies were excluded. Haematoxylin–eosin (HE) and immunohistochemistry (IHC) stainings were performed with cell type and cell death markers in five different regions of interest (ROIs) (see Fig. 1).

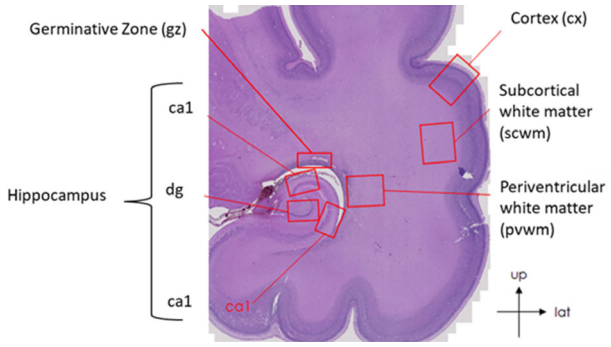


Fig. 1 Haematoxyline-Eosine and Immunohistochemistry stainings.

Results: The mean GA at birth was 26 in both groups, without significant difference in birthweight or gender. In HE staining, we found a significant decrease in cortical thickness after PVHI, but no difference in global cellular density. In IHC, we found a significant increase in GFAP (astroglia), cCASP3 and TUNEL (apoptosis), pMLKL (necroptosis) and Iba1 (microglia) in the white and grey matter after PVHI. We also found a significant increase in LC3 positive dots (autophagosomes), CathD positive dots and dots mean area (autolysosomes) in the ipsilateral white and grey matter after PVHI, suggesting an increased autophagic flux.

Conclusions: A strong astrogliosis occurs in the overall brain of VPT after PVHI, and apoptotic and necroptotic markers are significantly increased. There is also an increased inflammation and indications of enhanced autophagy, suggesting its possible role in cell death after PVHI. We are now using markers of other types of cell death (ferroptosis, pyroptosis) as well as performing co-labelling analysis of cell death and cell type markers to characterise the type of dying cells in every brain region after PVHI in immature brains.

Conflict of interest: None declared.

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REPRODUCIBILITY OF THE EL-KHUFFASH PDA SEVERITY SCORE AND PDA DIAMETER MEASUREMENTS IN EXTREMELY PRETERM INFANTS

Aisling Smith[1], Rachel Mullaly[1], Orla Franklin[2], Afif EL-Khuffash[1]

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Introduction: Almost all randomised controlled trials use a Patent Ductus Arteriosus (PDA) diameter ≥1.5 mm as the primary criterion to ascribe haemodynamic significance to the PDA despite strong evidence that PDA diameter in isolation is a very poor predictor of adverse outcome in preterm infants. Our group have developed a PDA Severity Score (PDAsc). We hypothesized that the calculation of the PDAsc possesses superior intra- and inter-rater reproducibility when compared with the measurement of PDA diameter alone.

Methods: This cross sectional study assessed echocardiograms performed on infants <30 weeks gestation at 36–72 h of age between July 2020 and December 2022 to calculate the PDAsc. Intra-observer reproducibility of the PDAsc were assessed by blinded repeated measurements performed by one investigator (AS) 4 weeks apart. One set of those measurements was compared with blinded measurements by another investigator (RM) to assess inter-rater reliability.

Results: Echocardiograms from one 150 infants were examined. Their mean ± SD gestation and birthweights were 26.5 ± 1.7 weeks and 903 ± 249 g, respectively. The PDAsc has superior intra- and inter-reproducibility values when compared with PDA diameter measurements alone, with near perfect agreement values as demonstrated by a low bias and LOA, ICC values >0.98 and COV values <1.5% (Table 1). PDA diameter and LVO measurements demonstrated the poorest reproducibility values. The PDAsc demonstrated near perfect agreement both

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	Intra-Rater Reproducibility			Inter-Rater Reproducibility		
	Bias (95% LOA)	ICC (95% CI)	COV (%)	Bias (95% LOA)	ICC (95% CI)	COV (%)
PDA Score	0.1 (-0.9 – 1.0)	0.99 (0.98 – 0.99)	1.4%	0.0 (-1.1 – 1.2)	0.98 (0.97 – 0.98)	0.8%
PDA Diameter	0.1 (-0.7 – 0.9)	0.85 (0.80 – 0.89)	3.0%	0.1 (-0.9 – 1.2)	0.76 (0.67 – 0.83)	5.4%
PDA Max Velocity	0.0 (-0.4 – 0.5)	0.94 (0.92 – 0.96)	2.1%	0.0 (-0.5 – 0.5)	0.93 (0.91 – 0.95)	1.0%
LVO	3 (-46 – 52)	0.92 (0.89 – 0.94)	1.5%	-17 (-102 – 68)	0.76 (0.64 – 0.84)	8.4%
LV a`	-0.1 (-1.0 – 0.9)	0.94 (0.92 – 0.96)	1.6%	-0.2 (-1.5 – 1.1)	0.90 (0.86 – 0.93)	4.0%

LOA: Limits of agreement; ICC: Intraclass correlation coefficient; COV: Coefficient of variation; PDA: Patent Ductus arteriosus; LVO: Left ventricular output.

Table 1 Reproducibility analysis of the echocardiography parameters

within raters (Cohen's Kappa 0.97, $P < 0.01$) and between raters (Cohen's Kappa 0.94, $P < 0.01$) with regards to the threshold for treatment (a cut off ≥5.0). The PDA diameter threshold only demonstrated moderate agreement within raters (Kappa 0.57, $P < 0.01$) and between raters (Kappa 0.54, $P < 0.01$). In this cohort, 31% of infants with a low risk PDAsc (<5.0) also had a PDA diameter greater than 1.5 mm.

Conclusion: In this study, we demonstrated excellent intra- and inter-rater reproducibility of the EL-Khuffash PDA Severity Score. Conversely, measurement of the PDA diameter illustrated much poorer intra- and inter-rater agreement. Future RCTs for PDA treatment should strongly consider abandoning the use of PDA diameter in isolation as a criterion for recruitment into clinical trials.

Conflict of interest: None declared.

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ASSESSMENT OF MYOCARDIAL FUNCTION IN INFANTS OF MOTHERS WITH GESTATIONAL DIABETES MELLITUS USING DEFORMATION IMAGING OVER THE FIRST YEAR OF AGE

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Introduction: An increasing number of studies have highlighted impaired biventricular myocardial function and altered pulmonary haemodynamics during the early newborn period in infants

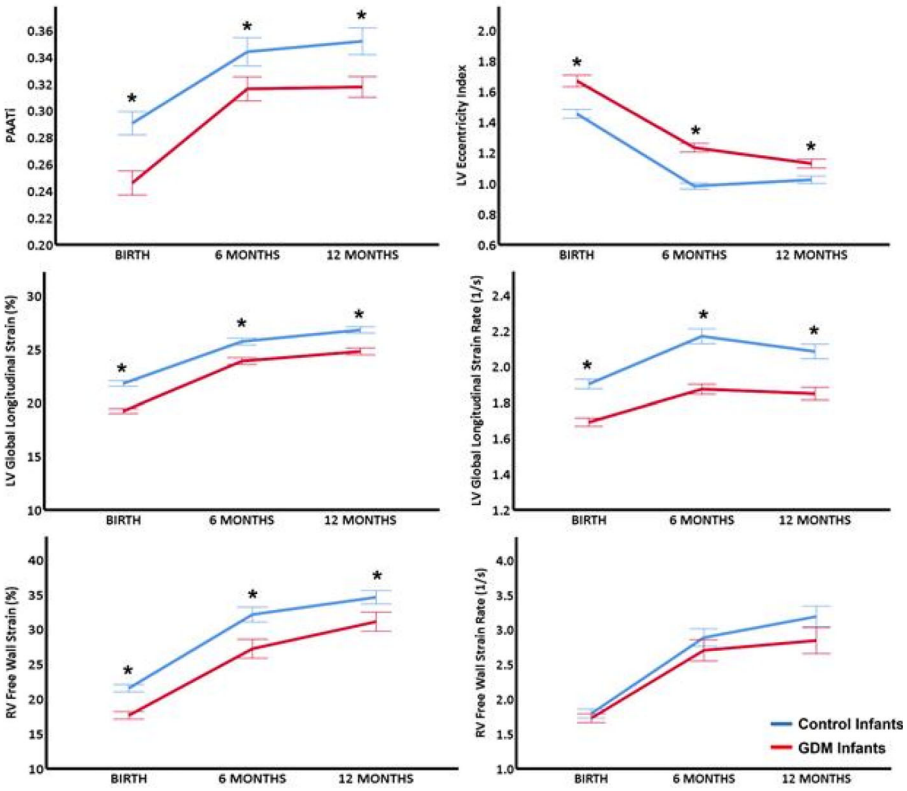


Fig. 1 Pulmonary haemodynamics and biventricular myocardial function over the first year of age in the GDM and control cohorts.

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of mothers with gestational diabetes mellitus (GDM). The aim of this study was to serially assess myocardial performance and pulmonary vascular resistance (PVR) in infants of mothers with GDM over the first year of age and to compare them to a group of controls.

Methods: This was a prospective, observational study. Echocardiography was performed at birth, 6 months and 1 year of age. Pulmonary artery acceleration time (PAAT) and left ventricular (LV) eccentricity index (LVEI) provided measurements of PVR. Biventricular function was assessed using deformation analysis.

Results: Fifty infants of mothers with GDM were compared to 50 controls with no difference in gestation (38.9 ± 0.8 vs. 39.3 ± 0.9 weeks, $P = 0.05$) or birthweight (3.55 ± 0.49 vs. 3.56 ± 0.41 Kg, $P = 0.95$). Mothers with GDM had a higher BMI (31 ± 6 vs. 25 ± 5, $P < 0.01$). At 1 year of age PAAT was lower (70 ± 11 vs. 79 ± 10, $P = 0.01$) and LVEI higher (1.1 ± 0.2 vs. 1.0 ± 0.1, $P < 0.01$) in the GDM group. LV global longitudinal strain (24.7 ± 1.9 vs. $28.8 \pm 1.8\%$, $P < 0.01$), LV systolic strain rate (1.8 ± 0.2 vs. 2.1 ± 0.3 1/s, $P < 0.01$) (Fig. 1), and RV free wall strain (31.1 ± 4.8 vs. $34.6 \pm 3.9\%$, $P < 0.01$) were lower in the GDM cohort at 1 year of age (all P values adjusted for gestation, mode of delivery and maternal BMI).

Conclusion: Our findings demonstrate sustained abnormal elevation of pulmonary pressures and impaired biventricular performance in infants of mothers with GDM in comparison to controls that do not normalise by 1 year of age. At present data is limited to explain the biological underpinnings of the findings described in our study. Overall there is a now a growing body of evidence suggesting that GDM is a significant neonatal cardiovascular risk factor and greater surveillance of infants of mothers with GDM with increasing age may be warranted.

Conflict of interest: None declared.

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POST-NATAL COLLAGEN VI EXPRESSION IN THE DEVELOPING HUMAN LUNG

Laszlo Markasz[1], Hamid Mobini-Far[1], Richard Sindelar[2]
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Background: Collagen VI (COL6) is primarily localised to the basement membrane (BM) and required for the alveolar structure and maintenance of pulmonary epithelial function. COL6 promotes lung epithelial cell spreading and wound closure. The COL6 network may have a crucial role in alveolar septation since COL6 −/− mice have simplified alveolar structure. Less is known about its role in human lung development. Our aim was to study COL6 expression in preterm infants with different lung maturational and clinical features.

Methods: COL6 expression was studied in 115 lung samples from newborn infants (21–41 weeks' gestational age (wGA); 0–228 days' post-natal age (dPNA)), and from adult and school child controls, by immunohistochemistry and digital image analysis. The percent of high intensity area in the stained area (HI%) was calculated.

Results: Patients were categorised into groups depending on their GA (21–26; 27–35; >35wGA) and PNA (0–1; 2–7;

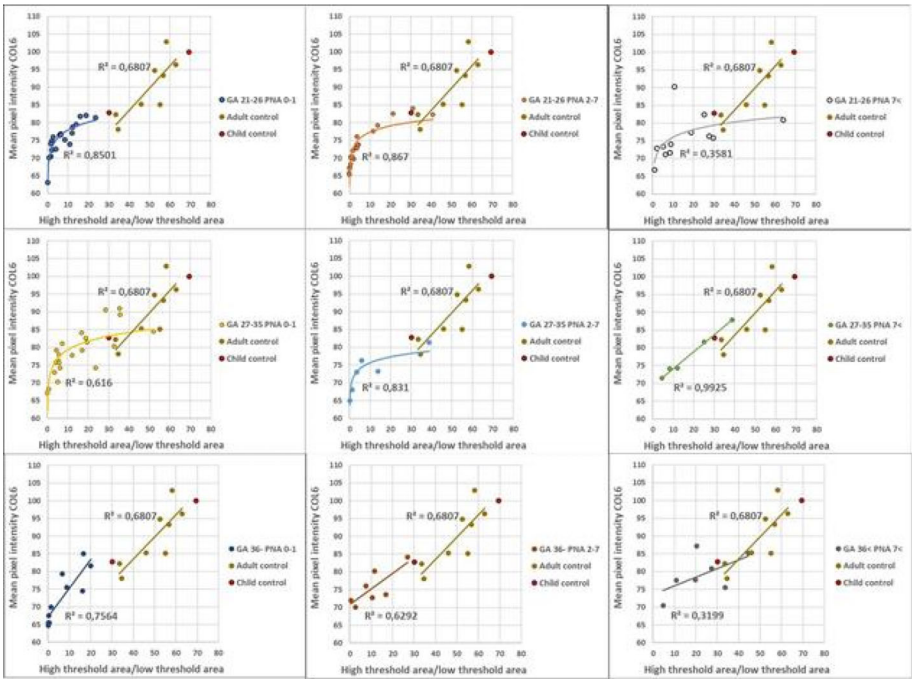


Fig. 1 Categorization of the patients depending on their GA and PNA.

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>7dPNA; Fig. 1). The general expression level (mean pixel intensity, MPI) of COL6 varied in all groups. Adults and school children had the highest MPI with a linear correlation to HI%. A levelled logarithmic correlation was found between MPI and HI% in <35wG. The linear correlation corresponded to homogenously increased COL6 expression in the stained area whereas logarithmic correlation described focal increase of the high intensity areas in the less stained areas. The distribution of COL6 in lung tissue was homogenous in adults, school children and >35wGA, while COL6 expression appeared condensed around air spaces in infants born between 21 and 26 wGA, but only during 0-7dPNA. After 1 week of age the distribution became homogenous.

Conclusions: The distribution of COL6 changes during different lung developmental stages and during post-natal life. COL6 seems to be concentrated to epithelial cells at birth during the canalicular stage, with a post-natal spreading into the surrounding mesenchyme. The post-natal reorganising of COL6 network in the BM of preterms might destabilise the interaction between the epithelium and the extracellular matrix, thereby promoting lung developmental arrest.

Conflict of interest: None declared.

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EARLY PHENOBARBITONE TREATMENT REDUCES SEIZURES INDUCED INCREASE IN CEREBRAL PERFUSION IN NEWBORN BRAIN

Alan Bainbridge[1], Magdalena Sokolska[1], Francisco Toarrealdea[1], Alexiane Touze[2], Kelly Harvey-Jones[3], Vinita Verma[3], Chris Meehan[3], Alison Mintoft[3], Ellie Campbell[3], Katie Tucker[3], Frederic Lange[4], Ilias Tachtsidis[4], Xavier Golay[2], Geraldine Boylan[5], Nicola Robertson[3], **Subhabrata Mitra**[3]

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Background: Seizures induce changes in cerebral metabolism and perfusion. MR imaging and proton MR spectroscopy (1H MRS) are standard MR modalities used for clinical assessment. Arterial spin labelling (ASL) MRI and phosphorus (31P) MRS are other useful tools for the assessment of cerebral oxidative metabolism and perfusion. The objective of this study was to comprehensively assess the impact of neonatal seizures on brain perfusion and metabolism using MR imaging, ASL MRI, 1H MRS, and 31P MRS in a preclinical model.

Methods: Ten healthy male newborn piglets underwent seizure induction with bicuculine 4 mg/kg IV over two time points 4 h apart. Another seven piglets had similar seizure induction and treatment with phenobarbitone 20 mg/kg IV after 10 min of continuous electrographic seizures, after each induction.

Piglets were sedated and anaesthetised throughout the experiment and underwent EEG and systemic monitoring. Imaging data were acquired in a 3 T scanner. Each animal had a scan at the start of the study and a repeat scan after 10 h. ASL was performed using pseudo-continuous labelling (pCASL). Cerebral blood flow (mL/100 g/min) maps were computed and mean CBF within regions was quantified using an automated atlas segmentation approach. Chemical shift imaging (CSI) was acquired for 1H MRS. 31P MRS was acquired with Image-Selected *In vivo* Spectroscopy (ISIS), adapted to include the whole brain.

Results: Generalised tonic clinic seizures with corresponding electrographic changes were noted immediately after bicuculine administration. Significant differences were noted between the pre-ictal and post-ictal period in the whole brain ($P = 0.007$) and cortical ($P = 0.004$) cerebral blood flow (CBF) (Fig. 1a,b). Following phenobarbitone treatment, CBF reduced significantly in the post-ictal period in the whole brain ($P = 0.0072$), cortex ($P = 0.0146$) and DGM ($P = 0.0342$) (Fig. 1a,c).

A trend towards an increase in intracellular pH (pHi) was noted in the post-ictal period (7.13 ± 0.07 vs. 7.18 ± 0.08), with a reduction in brain high energy phosphates (NTP/epp). No significant differences were noted following treatment. Deep grey matter Lac/NAA (lactate/N acetyl aspartate ratio) did not differ between the groups.

Conclusion: Increased whole brain and cortical perfusion persisted even 6 h after the seizures (untreated). Early

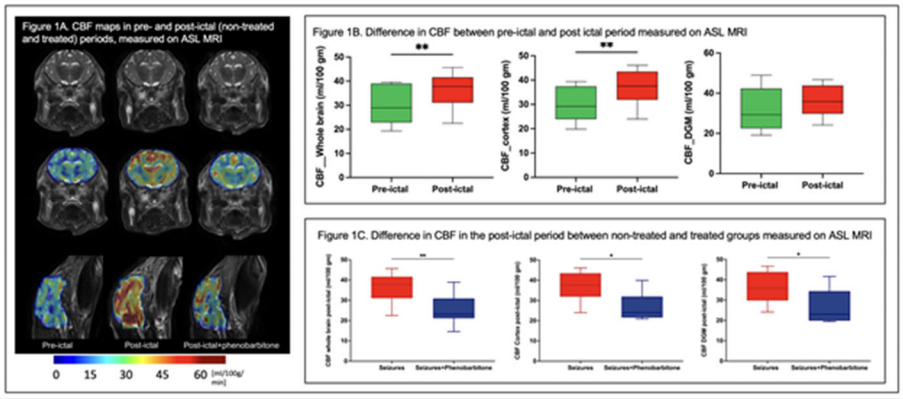


Fig. 1 Increased whole brain ($P = 0.007$) and cortical ($P = 0.004$) perfusion were noted following seizures (a and b). Early phenobarbitone reduced CBF in the whole brain ($P = 0.0072$), cortex ($P = 0.0146$) and DGM ($P = 0.0342$).

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phenobarbitone treatment had a significant impact in reducing the seizure-induced increased perfusion.

Conflict of interest: None declared.

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SOUND(A)SLEEP: A PILOT STUDY INVESTIGATING THE ACOUSTIC LANDSCAPE ON NICU AND ITS EFFECTS ON SLEEP WAKE CYCLING IN PRETERM NEONATES

Magdalena Smolkova[1], Topun Austin[2], Andrea Edwards[2], Lynn Thompson[3], Katherine Beardsall[3], Alex Grafton[4]

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Background: Impaired sleep–wake cycling has been shown to affect the functional connectivity of the neonatal brain. Preterm infants display impaired functional brain connectivity and disturbance of sleep–wake cycling may further exacerbate it. Evidence suggests that neonates physiologically respond to sound stimuli, and that sound protection devices and 'quiet time' may increase the proportion of time infants spend asleep. We hypothesized that the native acoustic landscape on NICU would alter sleep behaviour in premature neonates and developed a method to measure this effect.

Methods: A prospective pilot study of six preterm infants on NICU was carried out following informed parental consent. Infants were observed for 3 h each and their behaviour was recorded using an iPad app interface recording each behaviour and its exact timing. This was based on the Behavioural Sleep Stage classification for Preterm Infants (BeSSPI). Sound level was recorded by two sound meters in the cot and the environment at a constant distance from the cot. Physiological data were extracted from the monitoring device. Data were analysed on a second-by-second basis using generalised linear modelling for the increased occurrence of gross body movement (GBM) in response to increased sound level of different frequencies. Frequencies used for analysis, 2, 4 and 8 kHz, were shown to best correlate with physiological responses through preliminary analysis of 24-h recordings.

Results: In three infants, the probability of GBM increased significantly with increasing environmental and cot sound. In two infants, one of whom was in a sound-proof incubator, this relationship was only significant for cot sound. One infant, who was ventilated and sedated at the time of observation, did not show any relationship. 5/6 infants showed a steeper relationship with A-weighted sound, which assigns greater weight to sound audible to the human ear, as opposed to the flat *Z*-weighted trace. Furthermore, the proportion of time spent performing GBM seemed to increase with A-weighted peak sound pressure level (ns) (Fig. 1).

Conclusion: This pilot data suggests the native NICU acoustic landscape alters the sleep behaviour of preterm neonates, and a larger prospective study is planned to relate sleep behaviour and the development of functional connectivity.

Conflict of interest: None declared.

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SHORT AND MID-TERM NEONATAL OUTCOMES IN HIGH-RISK PRETERM AND TERM INFANTS UNDERGOING FICARE: A CASE CONTROL STUDY

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Background: FICare model reports mainly on stable preterm infants. We have recently published on FICare feasibility at a complex level IIIC NICU, scaling the model to two implementation levels (basic and advanced), making it suitable to the whole spectrum of care of high-risk neonates.[1]

Aims: We report on the short- (hospital discharge) and mid-term (first 6 months) outcomes of infants enrolled in a pilot on FICare implementation at our NICU.

Methods: From July 2018 to October 2022 families were invited to join the programme if their newborn's admission required neonatal specialised care for at least 3 weeks. Family caregivers were trained according to the programme's curricula. Each case was matched by a control infant, admitted at the same time (contemporary control, CC), plus 2 infants (historical control, HC) born within the 3 years pre-FICare site implementation.

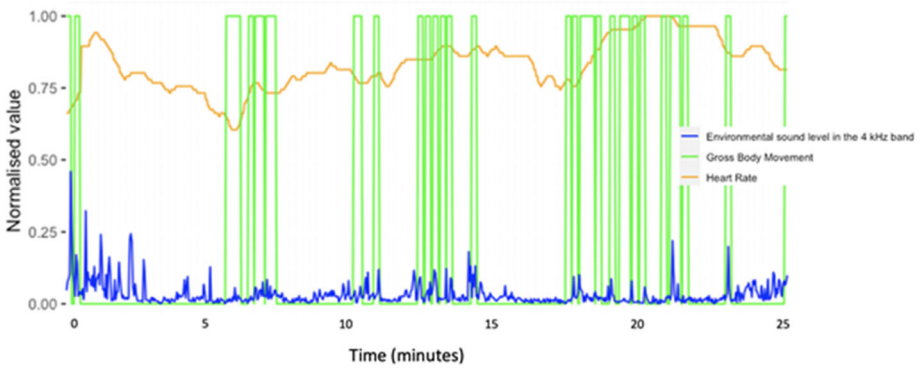


Fig. 1 Example trace showing behaviour-sound correlations. GBM is recorded as either 1 (present) or 0 (absent) with vertical lines representing change. Heart rate and sound level are plotted as normalised values.

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Results: Infant-family dyads of 134 preterm (median GA 284wk (265–310); median BW 1151 g (855–1403)) and 52 term-infants entered the FICare programme at a median post-natal age of 8 days. The CC was compound of 134 preterm (median GA 284wk (264–310) and BW 1105 g (890–1349)) and 52 term infants; finally the HC consisted on 268 preterm (median GA 284wk (264–310) and BW 1076 (813–1441)) and 104 term-infants. Rates of breastmilk on admission (preterm cohort $P = 0.017$; term cohort $P < 0.001$) and at discharge (preterm and term cohorts, $P < 0.001$) were higher in the FICare compared to CC and HC groups; whereas intermediate care length of stay (preterm cohort $P = 0.019$; term cohort $P < 0.001$), or mid-term use of emergency services (preterm and term cohorts $P < 0.001$) were lower. In addition, infants on FICare shorter total hospital length of stay(term cohort $P = 0.029$), than their corresponding CC and HC groups.

Conclusions: This is the first report on the mid-term impact of FICare implementation on health outcomes and family empowerment in a broader highly-vulnerable neonatal population. The positive results apply to both the high-risk preterm but also to the sick full-term newborn, reflecting the strengths and feasibility of the model in more complex healthcare neonatal services.

1. Moreno-Sanz B *et al*. https://doi.org/10.3389/fped.2021.682097.

Conflict of interest: None declared.

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TO DETERMINE WHETHER PREGNANT WOMEN WITH A HISTORY OF GENITAL HERPES SIMPLEX VIRUS (HSV) AND THEIR INFANTS ARE MANAGED ACCORDING TO BEST PRACTICE RECOMMENDATIONS

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Introduction: Herpes simplex virus (HSV) is a double stranded deoxyribonucleic acid (DNA) virus with 2 serotypes, HSV-1 and HSV-2. Neonatal HSV disease is classified as: (1) disease limited to the skin, eyes, or mouth; (2) central nervous system disease, with or without skin lesions and (3) disseminated disease involving multiple visceral organs. Neonatal HSV infection and disease is largely uncommon due to evidence-based interventions for pregnancy, delivery and the newborn. The aim of the study was to determine whether pregnant women with a history of genital HSV and their newborn are managed according to best practice recommendations.

Methods: Four-year retrospective chart review of pregnancies 01/01/2018–31/12/2021 at a large tertiary maternity unit in Dublin Ireland with over 9000 deliveries per year. Inclusion criteria were women with genital HSV first diagnosed pre-pregnancy or the current pregnancy; women with recurrent lesions in pregnancy and/or women with positive HSV diagnostics.

Results: Two hundred and thirty-four women with 261 pregnancies were identified. The prevalence of genital HSV in this population was 0.007%, incidence 0.003%. Mean maternal age was 32 years (SD = −5.2). One hundred and ten (42%) pregnancies had visible lesions, 135 (52%) had no lesions, 15 (6%) had a history of HSV but did not declare whether they had any recurrence or not. Two (0.07%) had primary HSV diagnosed within 6 weeks of delivery. Eleven (4.2%) had lesions at labour onset representing recurrence, 7 of these had received prophylaxis. One hundred and seventy-eight (68%) pregnancies had Aciclovir prophylaxis indicated and prescribed from 32 weeks; prophylaxis was not prescribed in 69 (26%) pregnancies based on low risk category or treatment declined. Fourteen (5%) infants were identified as high risk and evaluated post-delivery. One with a positive nasal swab was treated for 10 days with acyclovir.

Conclusion: Rate of primary genital HSV infection within 6 weeks of delivery was low, there were no cases of primary infection at labour onset. Rate of recurrent lesions in pregnancy was less than 50% with only 4.2% at labour onset. Requirement for infant evaluation was low (5%). There was one case of neonatal infection and no cases of disease identified.

Conflict of interest: None declared.

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THE MAGNITUDE OF RISK FOR EARLY ONSET SEPSIS IN NEONATES BORN AFTER RUPTURE OF MEMBRANE ≥18 H IN IBADAN NIGERIA

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Background: Prolonged rupture of membranes (PROM) is a recognised risk factor for early onset sepsis, which often necessitates institution of empiric antibiotics in many babies born following PROM especially in resource constrained settings where laboratory support is limited. However, only a proportion of babies born after PROM actually develop sepsis. This study was carried out to determine the magnitude of risk for early onset sepsis in neonates born after rupture of membrane of 18 h or more.

Methods: This was a cross sectional study of 164 consecutive neonates born to mothers with PROM of 18 h or more. The neonates were screened for sepsis and monitored for clinical features of neonatal sepsis for 72 h while placenta histology was carried out for evidence of chorioamnionitis.

Results: Nine (5.5%) mothers had features of clinical chorioamnionitis while 88(53.7%) had histologic chorioamnionitis. Thirty-seven (22.6%) neonates had clinical features of sepsis, mainly respiratory symptoms. Only 8 (4.9%) neonates had culture proven sepsis. The majority of the symptoms were observed within 24 h of life. There was a minimal increase in the odds of having culture proven sepsis with PROM ≥18 h by a factor of 1.04 ($P = 0.020$, OR 1.04 CI 1.01, 1.08). In addition, mothers with rupture of the membranes more than 3 days were 11.8 times more likely to have culture proven sepsis compared with mothers with rupture of the membranes less than 3 days ($P = 0.010$, OR = 11.8, CI = 1.799–77.839).

Conclusion: The incidence of culture proven sepsis was low among neonates delivered following >18 h of PROM only as a

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risk factor. Most of the babies exposed to histologic chorioamnionitis were neither symptomatic nor had culture proven sepsis. It is recommended that PROM >18 h alone should not be an absolute indication for empiric antibiotic therapy in otherwise well neonates in order to stem the tide of emergence of antibiotic resistance.

Keywords: Chorioamnionitis, EOS, PROM.

Conflict of interest: None declared

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POST-NATAL CORTICOSTEROID TREATMENT OF EXTREMELY PRETERM INFANTS IN A TERTIARY PERINATAL CENTRE

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Background: Bronchopulmonary dysplasia (BPD) is a form of chronic respiratory illness of the very preterm infant associated with increased mortality and morbidity, including worse neurodevelopmental outcomes and respiratory health in childhood. Post-natal systemic corticosteroids are effective in reducing the risk of BPD, but unfortunately associated with short- and long-term side effects, most importantly an increased risk of cerebral palsy. Several post-natal steroid regimens have been proposed over the last 30 years in an attempt to find the optimal balance between benefits and side-effects. The objective of this study was to describe the pattern of use of post-natal dexamethasone for the prevention of BPD in a large perinatal centre in the current era.

Methods: A retrospective cohort study of extremely preterm infants (gestational age < 28 weeks) born at the Royal Women's Hospital, Melbourne (RWH) between January 2017 and December 2019. Data regarding cumulative dexamethasone dose and duration, ventilation requirements, BPD and death were recorded.

Results: A total of 252 infants were included, of whom 38% received post-natal dexamethasone to prevent BPD. Infants in the steroid-exposed group were more immature than those in the no-steroid group, median (IQR) gestation of 25 (24–26) weeks and 27 (26–27) weeks respectively. In the steroid-exposed group 29% of infants received one standard 10-day dexamethasone course, cumulative dose 0.89 mg/kg, as per the regimen used in the Dexamethasone: A Randomised Trial (DART), remaining infants received either further 'DART' courses, the 'Cumming's' regimen (a 42-day weaning course, total cumulative dexamethasone dose of 8.86 mg/kg) or an 'individualised' course. Overall, the median (IQR) cumulative dexamethasone dose given was 1.89 (0.89–3.90) mg/kg with a duration of 20 (10–40) days. A diagnosis of BPD was more common in the steroid-exposed group compared to the no-steroid group (94% vs. 52%) and survival at discharge was lower in the steroid-exposed group (86% vs. 97%).

Conclusion: Approximately one third of extremely preterm infants at RWH receive post-natal steroids. As the coordinating centre of the original DART trial, 13 years later, we find that most infants do not receive the standard 10-day DART regimen, rather receiving on average twice the standard total dose.

Conflict of interest: BM is a co-author on recently updated Cochrane Reviews of 'early' and 'late' post-natal corticosteroids for preterm infants.

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ANTIBIOTIC USE IN SWEDISH NEONATAL UNITS: A NATIONWIDE POPULATION-BASED COHORT

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Background: Antibiotic use varies between neonatal units. The magnitude of this variation, and its relation to outcome, have not been studied in Sweden.

Methods: All hospital live births from 34 weeks' gestation ($n = 1\,025\,515$) during 2012–2020 were included in this nationwide population-based cohort. Data were collected from the Swedish Neonatal Quality Register and the Swedish Medical Birth Register. The primary outcome was the usage of systematic antibiotics in the first week of life. Secondary outcomes were the duration of antibiotic treatment, the incidence of culture-proven EOS, and EOS-associated mortality.

Results: A total of 19 286 (1.9%; 95% CI: 1.85%–1.91%) newborns (7686 girls (39.9%), median (IQR) gestational age 40 (38–41) weeks, median (IQR) birthweight 3610 (3140–4030) g) received antibiotics during the first week of life with a range between different neonatal units from 0.9% to 4.3% ($P < 0.001$). Antibiotic use was lower in level I units (1.6%) than in level II and level III units (1.9% and 1.9%, respectively, $P < 0.001$) and the duration of antibiotic treatment was 102 days per 1000 live births in level I, 114 days in level II and 113 days per 1000 live births in level III units. In contrast, the incidence of EOS was higher in level I (1.1 newborns per 1000 live births) than at level II (0.71) and III hospitals (0.39 newborns per 1000 live births). The majority of EOS was caused by group B streptococci (0.34

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per 1000 live births). Mortality associated with EOS was 1.39% (9 of 647 newborns). For each infant with EOS, 30 infants were started on antibiotics and 179 antibiotic days were administered. The median (IQR) duration of antibiotic treatment in infants without EOS was 5 (3–7) days, with a range between neonatal units from 3 (2–6) to 7 (3–10) days.

Conclusions: To our knowledge, this large study report the lowest rate of antibiotic use among late preterm and term newborns in a nationwide population. The incidence of culture-proven EOS was in line with other international reports and the mortality rate associated with EOS was low.

Conflict of interest: None declared.

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TWELVE-YEAR NEONATAL OUTCOMES OF VERY LOW BIRTHWEIGHT INFANTS FROM THE SOUTH AMERICAN NEOCOSUR NEONATAL NETWORK

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Background: NEOCOSUR is a nonprofit collaborative neonatal network that continuously evaluates VLBW infant's outcomes in the region. The participant centres are university-affiliated and represent both public and private institutions whose primary mission is the improvement of neonatal care and outcome in this region.

Objective: To describe main outcomes in perinatal care, mortality, morbidities and survival without major morbidities of VLBW infants admitted in 20-selected level III NICUs, from five South American countries: Argentina, Chile, Paraguay, Peru and Uruguay throughout 12 years.

Patients: All inborn infants with birthweight (BW) 500–1500 g and gestational age (GA) 230–336 weeks in the participating centres. Bio-demographic data were collected online from 01/01/2010 to 12/31/2021, with predefined diagnostic criteria and analysed by a central database unit.

Design: Retrospective analysis of prospectively collected data. Descriptive analysis, mean and standard deviation values were used for numerical variables, whereas frequency and proportion values were used for categorical variables. The former were compared using Student's t test and the latter, using the χ^2 test. Significance was defined with P-values <0.05. SPSS version 17 software (IBM Corp, Armonk, NY, USA) was used for statistical analysis. The Research Ethics Committees of all the participating centres approved the data collection protocol.

Results: 14833 VLBW infants were enrolled during the study period. Mean BW was 1086 g (±277), mean GA 28.6 weeks ±2.7. Death in the delivery room was 4% ($n = 600$) and mortality after admission 19.9% ($n = 2.942$). Results for main outcomes are presented in Table 1.

Condition	Global n=14.833	2010-2013 n=5.243	2014-2017 n=5.411	2018-2021 n=4.179	p-value
Global Mortality	24.1%	25.2%	22.8%	23.8%	0.007 *
n	3542	1283	1561	938	
Death in Delivery room	4.0%	4.1%	4.0%	4.8%	--
n	600	217	214	169	
Death after admission	19.9%	21.0%	21.2%	17.8%	--
n	2942	1046	1147	749	
Maternal Age mean (SD)	28.9 ± 7	28.4 ± 7	28.5 ± 7	29.6 ± 7	0.000 *
Pregnancy control	93.0%	96.8%	98.7%	89.1%	0.058
Multiple Gestation	22.0%	28.9%	22.6%	22.5%	0.145
Prenatal steroids	83.7%	83.2%	84.8%	86.3%	0.000 *
C-section	76.2%	74.8%	78.4%	77.8%	0.000 *
Major congenital anomalies	4.7%	5.3%	4.6%	4.1%	0.021 *
Male gender	53%	52.2%	52.2%	54.8%	0.066 *
Gestational Age mean (SD)	28.8 ± 2.7	28.8 ± 2.7	28.6 ± 2.8	28.6 ± 2.7	0.415
Birth Weight mean (SD)	1086 ± 277	1085 ± 279	1084 ± 277	1089 ± 276	0.733
Surfactant use	59.6%	58.7%	58.7%	60.5%	0.011 *
Mechanical ventilation Mean days	63.3% 5	63.3% 4	63.8% 5	62.7% 5	0.582
CPAP Mean days	66.8% 5	64.7% 5	65.6% 5	71.8% 6	0.000 *
Early onset Sepsis	2.6%	2.2%	2.8%	2.8%	0.050
Late onset Sepsis	19.3%	21.1%	19.8%	17.5%	0.000 *
O; 36 weeks	25.5%	24.8%	23.3%	23.3%	0.482
HIC G III – IV	9.6%	9.6%	9.5 %	9.1%	1.88
Global ROP	19.1%	20.9%	17.8%	19.4%	0.291
NEC	11.1%	11.8%	10.9%	10.5%	0.039 *

O; 36 weeks and ROP calculated over survivors > 28 days

Table 1 Perinatal results in 20 NEOCOSOR centres

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Conclusions: Twelve-year outcomes in the NEOCOSUR's network show important progress in obstetrical and neonatal care and especially significative reduction in global mortality. There was a significant change in survival without major morbidities throughout the study period. There is a high variability among centres for main outcomes.

Conflict of interest: None declared.

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EFFECT OF SKIN-TO-SKIN CONTACT AT BIRTH FOR VERY PRETERM INFANTS ON QUALITY OF MOTHER–INFANT INTERACTION AT 4 MONTHS: A SECONDARY OUTCOME FROM THE IMMEDIATE PARENT–INFANT SKIN-TO-SKIN STUDY (IPISTOSS)

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Background: Good quality of mother–infant interaction has protective effects on the infant's socio-emotional and behavioural development. It is especially critical to the very preterm infant with a risk of vulnerabilities related to immaturity early in life. Skin-to-skin contact (SSC) in general has been found to improve mother–preterm infant interaction, but little evidence exists regarding benefits when initiated immediately at birth. Thus, the objective was to determine the impact of immediate SSC at birth for very preterm infants on mother–infant interaction at 4 months of corrected age.

Methods: This study is part of the Immediate Parent–Infant Skin-TO-Skin Study (IPISTOSS), a randomised clinical trial. IPISTOSS was conducted in three neonatal units in Sweden and Norway from 04/2018 to 06/2021 and included very preterm infants and their parents. The intervention was SSC initiated at birth and continued throughout the first 6 h post-birth with either parent versus standard care in incubator. One of the secondary outcomes was the quality of mother–infant interaction as measured with the Parent–Child Early Relational Assessment (PCERA), based on a five-minute free play situation between the mother–infant dyad videorecorded at a follow-up visit at 4 months.

Results: A total of 71 infants born between 28 + 4–32 + 6 weeks + days of gestation and 56 mothers were included in the analysis; 34 mother–infant dyads allocated to SSC group and 37 mother–infant dyads allocated to control group at birth. Improved quality of mother–infant interaction was found in the SSC group when compared to standard care, both for Infant Positive Affect, Communicative and Social Skills (Cohen's D = 0.67, $P = 0.008$) and for Dyadic Emotional Tone, Reciprocity, and Regulation (Cohen's D = 0.56, $P = 0.02$). No additional accumulated effect of SSC on mother–infant interaction was found after the first 6 h.

Conclusion: Immediate parent–infant SSC after a very preterm birth is beneficial for the developing mother–infant relationship and should be supported in the clinical setting alongside other nursing and medical care provided at birth. Further, the results support the notion of an early sensitive period at birth that might provide a window of opportunity for long-term impact on infant's development.

Conflict of interest: None declared.

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PLACING PRETERM INFANTS IN POLYETHYLENE BAGS BEFORE UMBILICAL CORD CLAMPING: A RANDOMISED TRIAL

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Background: Hypothermia on admission to the neonatal intensive care unit (NICU) increases preterm infants' risk of death. We wished to determine whether placing very preterm infants in a PB before CC, compared to after CC, results in more infants with a temperature in the normal range on NICU admission.

Methods: We conducted a randomised controlled trial at a tertiary maternity hospital. Infants <32 weeks' GA for whom intensive care was planned were eligible for inclusion. Infants were randomly assigned to have a PB placed before or after CC. The primary outcome was rectal temperature within the normal range (36.5–37.5°C) on NICU admission.

Results: Between July 2020 and September 2022, 198/220 (90%) eligible infants were enrolled to this study; 99 were randomly assigned to BEFORE (43 (44%) female) and 99 (53 (54%) female) to AFTER. One infant died before the primary outcome was recorded, and was excluded from analysis. The median (IQR) GA was 29(27,31) vs. 29(27,31) weeks, and mean (SD) birthweight was 1200 (426) vs. 1138 (419) grams respectively. Baseline demographics were well matched between the groups. The proportion of infants who had normal temperature on NICU admission did not

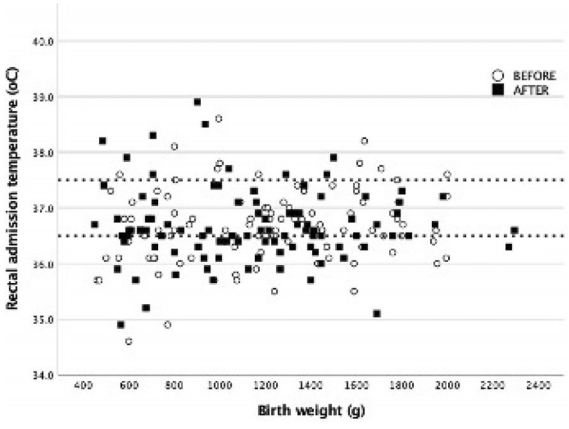


Fig. 1 Scatterplot of birthweight (g) and admission rectal temperature (°C). The area between the hatched lines represents the normal temperature range (36.5–37.5°C). Open circles = 'BEFORE'. Black squares = 'AFTER'.

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differ between the groups (BEFORE 54/99 (55%) vs. AFTER 55/98 (56%); RR 0.98, 95% CI 0.77–1.27, *P* 0.886). The proportion of infants with a temperature outside of the normal range was similar between the groups; hypothermia (BEFORE 34/99 (35%) vs. AFTER 33/98 (34%), *P* 0.880), hyperthermia (BEFORE 10/99 (10%) vs. AFTER 10/98 (10%), *P* 1.00) (Fig. 1). There were no significant differences in secondary outcomes between the groups.

Conclusions: This is the first study to examine a thermal care intervention before cord clamping. Placing a PB before CC did not increase the proportion of preterm infants with normal temperature on NICU admission. A large proportion of preterm infants had abnormal temperature at NICU admission. Further studies on thermoregulation before CC are warranted.

Conflict of interest: None declared.

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PARENTAL EXPERIENCES OF NEONATAL CARE IN SWEDEN: A NATIONWIDE STUDY ON DETERMINANTS OF EXCELLENCE

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Background: Infant- and family-centred neonatal care reduces adverse outcomes in infants and parents. In Sweden, infant- and family-centred neonatal care is standard. Most studies on parental outcomes have used qualitative techniques. This study aimed to determine proportions and determinants of excellence in neonatal care.

Methods: All neonatal units report data to the Swedish Neonatal Quality Register (SNQ). In 2020, SNQ implemented a possibility for units to let parents assess neonatal care. An SMS with a link to a questionnaire was sent to the parents within 2 weeks after discharge. This questionnaire included 15 questions in five domains, with ratings from 4 to 5. The study involved admissions from July 2020 to May 2022. The exposures were gestational age, length of stay, unit level and bed capacity. The outcome was the proportion of parents rating of neonatal care as excellent.

Results: A total 4475/13 108 (34%) parents responded. The proportions rating the care excellent varied from 65% to 90%. The domain 'Overall Impression' reached the highest proportions of excellence, whereas involvement in decision-making and information-issues reached the lowest. The largest variation in excellence between neonatal units (range 43%–80%) was found for the domain 'Participation and Involvement'. The proportion that had an excellent experience was significantly lower among parents of extremely preterm than term infants, with the largest difference

Domains and questions	Experience of excellence in neonatal care, inter-hospital range (%)	Experience of excellence in neonatal care, n/N (%)	Experience of excellence in adult somatic care n/N (%)	p-value for different experience in neonatal vs adult care
Respect and Treatment				
Q1 Did the staff treat your baby[a] with compassion and care?	80 – 95	3959/4470 (88.6)	30295/39480 (76.7)	<0.001
Q2. Were you[b] treated with respect and dignity?	65 – 89	3590/4467 (80.4)	30658/36190 (84.7)	<0.001
Q3. When the staff talked to each other about your baby[a], were you involved in the conversation?	54 – 75	2722/4117 (66.1)	13133/27406 (47.9)	<0.001
Information and Knowledge				
Q4. Did you receive enough information about your baby's[a] care/treatment?	53 – 79	2992/4466 (67.0)	24294/38588 (63.0)	<0.001
Q5. Did you receive sufficient information about where to turn after discharge from the hospital (if you needed help or had further questions)?	61 – 84	2997/4169 (71.9)	23391/36879 (63.4)	<0.001
Q6. Did the doctor/nurses (the staff) explain the treatment in a way that you[b] understood?	55 – 84	3360/4450 (75.5)	23853/36561 (65.2)	<0.001
Participation and Involvement				
Q7. Did the staff involve you in the decisions regarding your baby's[a] care or treatment?	43 – 78	2755/4270 (64.5)	23149/36350 (63.7)	0.28
Q8. Did the staff take into account your own experiences and views[b] on your baby's[a] health condition?	49 – 83	2867/3967 (72.3)	23449/34670 (67.6)	<0.001
Q9. Were you involved in the decisions regarding your baby's[a] care and treatment to the extent you wanted?	43 – 80	2995/4196 (71.4)	20855/34004 (61.3)	<0.001
Continuity, Trust/Emotional Support and Pain-Relief				
Q10. Before you[b] were discharged from hospital, was a decision made on the next step in the baby's (your) care or treatment?	61 – 85	2922/3858 (75.7)	23117/34809 (66.4)	<0.001
Q11. Did you have confidence in the staff caring for your baby?	66 – 89	3560/4466 (79.7)	NA	
Q12. If your baby experience pain during your stay in the neonatal unit, did she/he quickly receive help with pain relief?	62 – 95	2133/2596 (82.2)	NA	
Overall Impression				
Q13. Do you think that your baby's[a] current needs for care and treatment has been met?	84 – 98	4006/4460 (89.8)	28313/38550 (73.4)	<0.001
Q14. How did you experience the stay in the neonatal unit as a whole?	64 – 82	3227/4461 (72.3)	NA	
Q15. Would you[b] recommend this unit/hospital to anyone else in your situation?	73 – 93	3889/4444 (87.5)	29133/38719 (75.2)	<0.001

Table 1 Parental experience of excellence in neonatal care and patient experience of adult somatic care

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relating to a question about recommending the unit to someone else in the same situation (73% vs. 89%, adjusted odds ratio = 0.32 (95% confidence interval = 0.21–0.49)). Confidence in the staff was also lower in parents of extremely preterm than term infants (56% vs. 83%, adjusted odds ratio = 0.33 (95% confidence interval = 0.23–0.47)). Longer hospital stay affected the experience of neonatal care adversely, but level of care and bed capacity were overall unrelated to the parental experience. A higher proportion of parents of moderately preterm infants reported an excellent experience than parents of term and extremely preterm infants (Table 1).

Conclusion: A majority of parents rated neonatal care in Sweden as excellent. The less frequent ratings of excellence for some aspects of care and among parents of extremely preterm infants indicate that more could be done to optimise parental involvement and support.

Conflict of interest: None declared.

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THE INTERPLAY BETWEEN GLUCOGENIC AMINO ACIDS AND CARBOHYDRATE METABOLISMS IN REGULATING THE CLINICAL FATE OF INFECTED PRETERM NEWBORNS

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[1]University of Copenhagen

Background: Neonatal sepsis remains one of the most common morbidities in newborn preterm infants and may be related to extensive use of parenteral nutrition (PN) with high glucose levels. Using a preterm piglet model of neonatal sepsis, we have demonstrated that hyperglycaemia, induced by high glucose supply, predisposed infected animals to sepsis; whereas glucose restriction prevented sepsis but led to severe hypoglycaemia. Based on this, we hypothesized that supplementing glucogenic amino acids (GAA) in a glucose-restricted PN regime would both reduce the risk of sepsis and help maintain normoglycemia *via* enhanced hepatic gluconeogenesis.

Methods: Two experiments with similar setups were performed in caesarean-delivered preterm pigs (90% gestation). Newborn animals were inoculated with either *Staphylococcus epidermidis* (SE) or saline control (CON) and nourished with different compositions of PN until euthanasia at 15 h. Clinical signs, physiological, metabolic, and immunological responses to infection were evaluated during the study. In experiment 1, animals were allocated to PN with either restricted glucose (2 g/kg/d, rGLU) supplemented with four GAA (glutamine/valine/aspartate/asparagine, 1 g/kg/d each) or standard glucose (14.4 g/kg/d, sGLU) with saline (SAL). In experiment 2, GAA animals were compared with those only receiving restricted glucose PN (rGLU-SAL group, Fig. 1).

Results: Experiment 1: relative to standard glucose supply, restricted glucose with GAA in PN led to reduced sepsis incidence (11.1 vs. 63%) and sepsis severity outcomes (higher blood pH, lower blood bacterial density, pCO2, lactate and inflammatory response) while maintained normoglycemia. Experiment 2: Under restricted glucose provision, GAA supply provided better clinical benefits (higher blood pH, lower blood bacterial density, pCO2 and inflammatory response), together with elevated blood glucose levels. Relative to both standard and restricted glucose animals, GAA animals showed activated hepatic pathways related to gluconeogenesis, TCA cycle, oxidative phosphorylation, fatty acid metabolism, and suppressed Th1, Th2, and Th17 inflammatory pathways.

Conclusion: We demonstrated a clinically relevant nutritional regime with enriched GAA in low parenteral glucose setting to prevent sepsis and maintain glucose homeostasis in infected preterm newborns. This sepsis preventive approach should therefore be considered in future clinical trials in infection-sensitive preterm infants.

Conflict of interest: None declared.

405
GUT MICROBIOTA IN PRETERM INFANTS FED HUMAN MILK FORTIFIED WITH BOVINE COLOSTRUM

Lin Yang[1], Yan Hui[2], Per T Sangild[1], Lise Aunsholt[3], Gitte Zachariassen[4], Ping-ping Jiang[1], Dennis S Nielsen[2]

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Background: Fortification of human milk is required for proper growth of very preterm infants (VPIs). In a recent trial, fortification of human milk with bovine colostrum (BC) was shown to induce growth of VPIs similar to a conventional fortifier (*Clin. Nutr*. 42, 773–783, 2023). Effects of diet on growth depend on nutrient intake, interacting with factors such as the gut

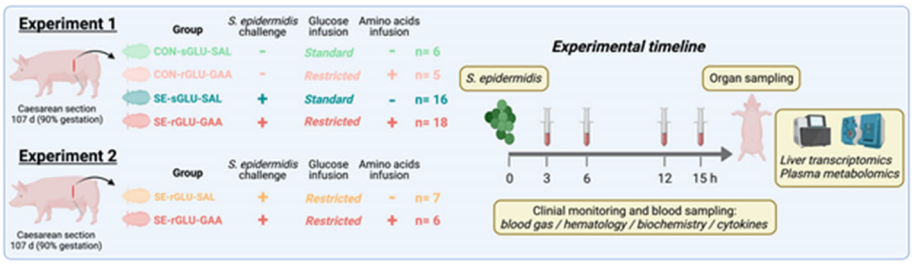


Fig. 1 Overview of the experimental design and animal procedures.

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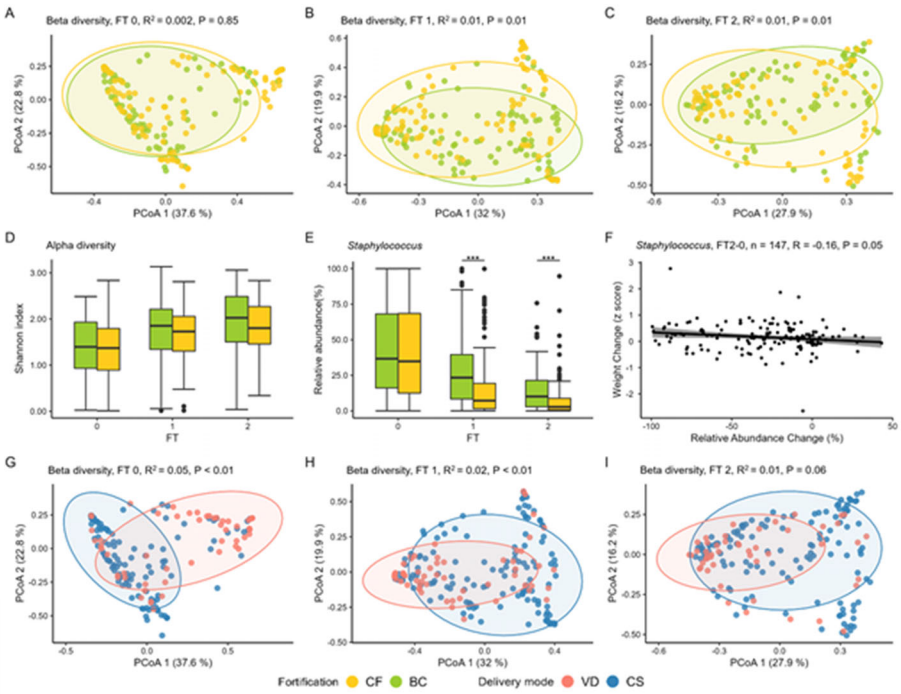


Fig. 1 Change of the gut microbiota in very preterm infants related to fortification, birth mode and growth.

microbiota (GM). We hypothesized that faecal microbiota composition in VPIs is affected by type and amount of fortifiers and is associated with growth outcomes.

Methods: Faecal samples were collected from VPIs ($n = 225$) enrolled in the trial before (time point 0, FT0), 1 (FT1) and 2 (FT2) weeks after the start of fortification with BC or a conventional fortifier (*CF*, PreNan FM85, Nestlé). The microbiota was profiled by 16S rRNA gene amplicon sequencing. Microbial species diversity (alpha diversity), microbial community structure (beta diversity) and taxa abundance were studied in relation to fortification group, birth mode and body growth.

Results: At both FT1 and FT2, infants receiving BC showed altered gut microbial community structure (beta diversity) and higher abundance of staphylococci (Wilcoxon, $P < 0.05$) but no differences in species diversity (alpha diversity) was observed between BC and *CF* groups. Across fortification groups, the change in abundance of staphylococci from FT0 to FT2 tended to negatively correlate with body weight change (change of *Z*-scores referenced to Fenton's growth chart) in the same period ($P = 0.05$, $R = -0.16$). Caesarean-delivered infants had a different gut microbial community structure from infants born vaginally only over the period FT0 to FT1 ($P < 0.05$), the gut with microbiota dominated by Firmicutes while vaginally-delivered infants by Proteobacteria (Fig. 1).

Conclusion: BC fortification induced modest, but significant effects on the developing gut microbiota in VPIs, relative to *CF*. Increased abundance of staphylococci over time tended to correlates negatively with body growth. Birth mode affects GM only shortly after birth.

Conflict of interest: The University of Copenhagen (Per T. Sangild) holds a patent on the use of colostrum for preterm infants.

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ALTERNATING FEEDING WITH COLOSTRUM AND FORMULA AFFECTS NECROTISING ENTEROCOLITIS AND GUT MICROBIOTA IN PRETERM PIGS

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Background: Exclusive feeding with bovine colostrum protects against necrotising enterocolitis (NEC) in preterm pigs, used as model for infants. If to be used in clinical practice, colostrum needs to be fed together with infant formula to avoid protein overload. It is not clear how mixed colostrum-formula feeding regimens affect NEC sensitivity and the gut microbiota. We hypothesized that mixed colostrum-formula feedings induce differential gut microbiota, potentially predisposing to NEC.

Methods: Colonic gut microbiota, profiled with 16S ribosomal RNA gene amplicon sequencing, was compared in pigs receiving exclusive colostrum (C) or formula (F) until day 5 of life (C5, F5, $n = 7$–10), followed by feeding with C or F until day 9 (*CF*, CC, FC, FF, $n = 6$–11, Exp1). Other

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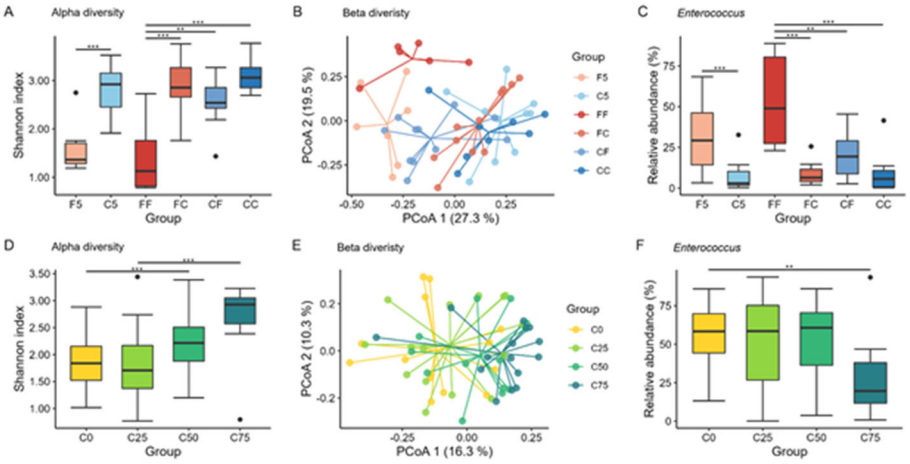


Fig. 1 Mixed feeding with colostrum and formula demonstrated different effects on the gut microbiota. Minimum 50% C feeding increased alpha-diversity (a, d), altered beta-diverstiy (b, e) and reduced enterococci (c, f).

preterm pigs received either 0, 25, 50 or 75% C (C0, C25, C50, C75), with remaining diet being F ($n = 13$–15, Exp2). Incidence of NEC was determined based on macroscopic scoring of the gut.

Results: In Exp1, pigs fed any C had higher species diversity (alpha diversity) and lower abundance of Enterococcus than pigs fed F only (CC, *CF*, FC vs. FF; C5 vs. F5, $P < 0.05$). Pigs fed any C had similar microbial community structure (beta diversity, FC or *CF* vs. CC, $P > 0.05$) that differed from pigs fed exclusive F (*CF* or FC vs. FF, $P < 0.05$). In Exp2, pigs fed >50% C had higher species diversity than pigs fed less C (C50 or C75 vs. C0 or C25, $P < 0.05$). C75 pigs had lower relative abundance of Enterococcus than C0 ones. Feeding regimen did not clearly affect NEC incidence, although groups receiving any C tended to have less NEC (67 vs. 83%, $P > 0.05$) (Fig. 1).

Conclusion: Preterm pigs fed minimum 50% C, relative to F, have a gut microbiota that differs from that in pigs fed exclusive F (e.g., higher diversity, less enterococci). Diet-induced changes in the gut microbiota that may not be able to explain the high NEC sensitivity in preterm pigs.

Conflict of interest: The University of Copenhagen (Per T. Sangild) holds a patent on the use of colostrum for preterm infants.

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PSYCHIATRIC AND BEHAVIOURAL DISORDERS IN CHILDREN BORN EXTREMELY PRETERM IN 2006 COMPARED WITH 1995: THE EPICure STUDIES

Jennifer Larsen[1], Josephine Holland[2], Puja Kochhar[2], Dieter Wolke[3], Elizabeth Draper[1], Neil Marlow[4], Samantha Johnson[1]

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Background: Changes in neonatal care over the last two decades have resulted in improved survival for children born extremely preterm (EP), but this has not yet been paralleled by improvements in neurodevelopmental outcomes. Less is known about trends over time in behavioural outcomes. The aim of this study was to investigate the prevalence of psychiatric and behavioural disorders in EP children born in 2006 compared with those born in 1995.

Methods: Comparison of two prospective longitudinal cohort studies of children born 22–25 weeks' gestation in England: EPICure (born in 1995) and EPICure2 (born in 2006). EP children in these cohorts were assessed at 11 years of age alongside a contemporaneous group of term-born children. Parents and teachers completed the Developmental and Well Being Assessment (DAWBA) from which DSM-IV research diagnoses of common mental and behavioural disorders were assigned.

Results: In EPICure 176 EP and 153 term-born children were assessed, compared with 112 EP and 143 term-born children in EPICure2. DAWBA data were obtained for 91.5% and 93.5% of EP and term-born children in EPICure, and in 67.9% and 68.5% of EP and term-born children in EPICure2 respectively. EP children in both cohorts had higher prevalence of psychiatric disorders than their term-born peers (EPICure: 26.1% vs. 9.1%; EPICure2: 38.2% vs. 3.1%). Rates of emotional disorders, attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) were higher for EP than term-born children in both cohorts.

Comparing EP children in EPICure2 with those in EPICure, there was no significant difference in the prevalence of any psychiatric disorder, emotional disorders, conduct disorders or ADHD. EP children in EPICure2 had an increased odds of ASD compared with EP children in the EPICure cohort (OR 2.8, 95% CI 1.3, 6.2); however, this difference was not significant after adjusting for confounders (Table 1).

Conclusion: Children born EP are at increased risk for mental and behavioural disorders compared with term-born peers at 11 years of age. Mental health and behavioural outcomes have

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	EPICure (22-25 weeks, England)		EPICure2 (22-25 weeks, England)		EPICure EP vs Term-born [A vs. B]				EPICure2 EP vs Term-born [C vs. D]				EPICure2 vs EPICure [C vs A]			
DAWBA Assigned Research Diagnosis	EP [A] N=161 % (n)	Term-born [B] N=143 % (n)	EP [C] N=76 % (n)	Term-born [D] N=98 % (n)	Unadj OR (95% CI)	p	Adj OR (95% CI)[a]	p	Unadj OR (95% CI)	p	Adj OR (95% CI)[a]	p	Unadj OR (95% CI)	p	Adj OR (95% CI)[a]	p
Any psychiatric disorder	26.1% (42)	9.1% (13)	38.2% (29)	3.1% (3)	3.5 (1.8, 6.9)	**<0.001**	2.7 (1.2, 5.9)	**0.013**	19.5 (5.7, 67.5)	**<0.001**	13.2 (3.6, 48.7)	**<0.001**	1.7 (1.0, 3.1)	0.060	1.2 (0.5, 2.5)	0.712
Any emotional disorder	9.3% (15)	2.1% (3)	13.2% (10)	2.0% (2)	4.8 (1.4, 16.9)	**0.015**	5.2 (1.1, 24.2)	**0.033**	7.3 (1.5, 34.3)	**0.012**	7.4 (1.5, 36.3)	**0.014**	1.5 (0.6, 3.5)	0.371	1.1 (0.4, 3.2)	0.847
Any conduct disorder	5.6% (9)	6.3% (9)	[N=75] 5.3% (4)	0.0% (0)	0.9 (0.3, 2.3)	0.795	0.5 (0.1, 1.6)	0.233	—	**0.034**[c]	—	—	1.0 (0.3, 3.2)	0.936	1.3 (0.2, 6.7)	0.780
Any ADHD	[N=147] 12.2% (18)	[N=138] 2.9% (4)	[N=56] 23.2% (13)	[N=77] 2.6% (2)	4.7 (1.5, 14.2)	**0.006**	4.4 (1.2, 16.6)	**0.030**	11.3 (2.4, 52.6)	**0.002**	9.0 (1.7, 48.5)	**0.010**	2.2 (1.0, 4.8)	0.056	1.5 (0.5, 4.2)	0.492
Any ASD	8.7% (14)	0.0% (0)	[N=75] 21.3% (16)	0.0% (0)	—	**<0.001**[c]	—	—	—	**<0.001**[c]	—	—	2.8 (1.3, 6.2)	**0.008**	1.6 (0.6, 4.6)	0.361

[a] Binary logistic regression - adjusted for sex, IMD at 11y, and severe disability (one or more of the following: Mental Processing Index >3 SD below term-born mean (<67), GMFCS/MACS ≥3, no useful hearing with aids, no useful vision or only sees gross light/movement)

[b] Binary logistic regression - adjusted for sex, gestational age, birthweight Z score, IMD at 11 years, multiple births, maternal age at birth, age at assessment (<11 and ≥11 years) and severe disability

[c] Fisher's Exact/Chi squared test as logistic regression not possible due to 0 term-born ASD diagnoses

Table 1 Prevalence of DSM-IV psychiatric and behavioural disorders in extremely preterm (22–25 weeks of gestational age) and term-born children in the EPICure and EPICure2 cohorts at age 11 years

not improved over time. Professionals involved in the follow-up of EP children should be aware of the ongoing risk of psychiatric and behavioural disorders throughout childhood following EP birth.

Conflict of interest: Neil Marlow declares financial relationships with InfanDx (ongoing), Novartis (ongoing) and Takeda (now ended) unrelated to this study. No other conflicts of interest or financial relationships to disclose.

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MYOCARDIAL STRAIN IN NEWBORN PIGLETS EXPOSED TO HYPOXIA–ISCHAEMIA RANDOMISED TO REMOTE ISCHAEMIC POSTCONDITIONING AND THERAPEUTIC HYPOTHERMIA OR HYPOTHERMIA ALONE

Sofie Schaaning[1], Lærke H Hansen[1], Ted CK Andelius[1], Hannah B Andersen[1], Mette V Pedersen[1], Regitze Pinnerup[1], Tine B Henriksen[1], Kasper J Kyng[1]

[1]Aarhus University Hospital/Department of Paediatrics

Background: Hypoxia–ischaemia (HI) at birth compromises all organs of the newborn including the cardiovascular system. Remote ischaemic postconditioning (RIPC) is a potential neuroprotective treatment following HI. The effect of RIPC may in part be attributed to effects on cardiac function. In newborn piglets subjected to global HI and randomised to either RIPC and therapeutic hypothermia (TH) or TH alone, we examined serial measures of left ventricle longitudinal (LS) and circumferential strain (CS).

Methods: Twenty-six newborn anaesthetized piglets were exposed to a standardised 45 min global HI insult, and randomised to treatment with RIPC+TH ($n = 13$) or TH alone ($n = 13$). RIPC was performed as four cycles of occluded blood flow in both hind limbs for 5 min, followed by 5 min reperfusion, repeated at 1, 12, and 24 h after the insult. Echocardiography was conducted before the insult, during the last 15 min of hypoxia, and 1, 6, 24, and 44 h after the insult. Left ventricle myocardial strain was measured, blinded to treatment group, using 2D speckle tracking. LS was measured from apical four chamber view and CS at the papillary muscle level from short axis views.

Results: Left ventricular LS and CS values of piglets exposed to RIPC+TH or TH alone were comparable between groups at all measured time intervals (Fig. 1a,b). In both groups, LS and CS decreased during hypoxia, then increased until 24 h after the insult, followed by a decline to below baseline levels at 44 h after HI.

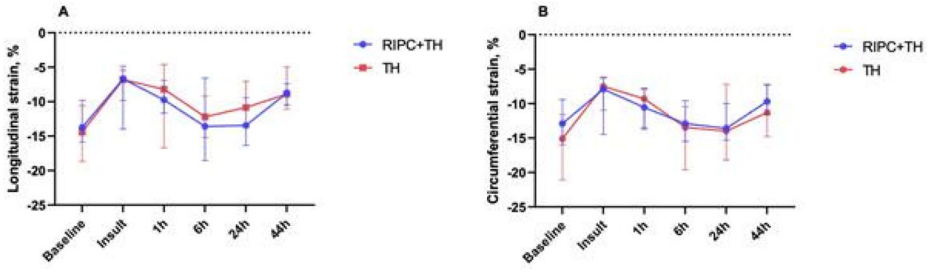


Fig. 1 Changes in (a) longitudinal strain, (b) circumferential strain before, during, and after HI. Each point represents median with interquartile range.

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Conclusions: Newborn piglets subjected to RIPC+TH versus TH alone after a standardised global HI insult had similar left ventricle LS and CS during 44 h after the insult, suggesting that RIPC did not alter myocardial strain after HI.

Conflict of interest: None declared.

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NON-INVASIVE LUNG GAS OXYGEN DETECTION IN HEALTHY TERM INFANTS: GASMAS FEASIBILITY STUDY

Jurate Panaviene[1,2,3], Konstantin Grygoryev[4], Andrea Pacheco[4,5], Pranav Lanka[4,5], Sanathana Konugolu Venkata Sekar[4,5], Roberto Chioma[1], David Healy[1,2,3], Vicki Livingstone[1,2], Stefan Andersson-Engels[4,5], Eugene Dempsey[1,2,3]

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Background: Infants admitted to neonatal unit, especially if born preterm, often have underlying respiratory problems necessitating respiratory monitoring. Gas in scattering media absorption spectroscopy (GASMAS) enables non-invasive oxygen (O_2) gas quantification by measuring O_2 light absorption within the lung.

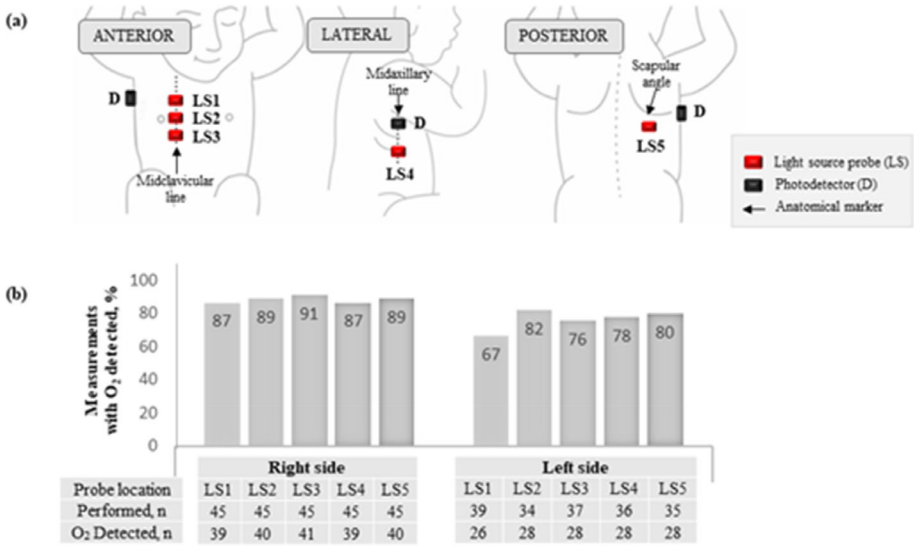
Objective: Assessment of the feasibility of GASMAS for the detection of O_2 and determination of optimal probe positioning.

Design/Methods: Healthy full-term (>37 weeks gestational age (GA)) neonates were recruited in Cork University Maternity Hospital over 7-month period. Measurements were performed using GASMAS (Neola Alpha 2, NEOLA Medical, Sweden) with near-infrared laser sources of 760 and 935 nm, specific for O_2 and H_2O absorption bands. The light source probe and photodetector were placed in five locations on each side of the infant's chest (Fig. 1a). O_2 detection was defined using multiple signal quality criteria.

Results: One-hundred healthy infants of 1–5 days age were enrolled. The mean (SD) GA was 39(1) weeks and the mean (SD) birthweight 3.6 (0.5) kg. A total of 1000 GASMAS measurements were performed. Ninety-eight of 100 infants had O_2 signal detected with at least one thoracic measurement. Interim analysis was performed after the recruitment of first 55 infants with following implementation of user interface changes for the next 45 infants. The mean percentage of measurements with detected O_2 signal across all locations had improved from 39 (2)% to 75 (2)%. No significant relationships were found between mean O_2 detection and infant ($n = 45$) birthweight ($P = 0.35$), sex ($P = 0.75$), age ($P = 0.8$), mode of delivery ($P = 0.57$), respiratory rate ($P = 0.41$). O_2 signal was less likely to be detected on the left side for the first ($P = 0.02$), second ($P = 0.04$), and third ($P = 0.01$) probe locations compared to the right (Fig. 1b).

Conclusions: This cohort study has demonstrated the feasibility of GASMAS use for non-invasive lung O_2 detection in neonates. 98% of healthy term-born infants had good quality O_2 signal detected at least once using GASMAS. The O_2 detection rate was lower for the anterior left side of the chest (second, third, and fourth intercostal space) likely due to the location of the heart, suggesting more optimal lateral and posterior locations of the probe placement.

Conflict of interest: None declared.



Probe location	LS1	LS2	LS3	LS4	LS5	LS1	LS2	LS3	LS4	LS5
Performed, n	45	45	45	45	45	39	34	37	36	35
O_2 Detected, n	39	40	41	39	40	26	28	28	28	28

Fig. 1 (a) Light source (LS) and photodetector (D) positioning. Right and left side measurements were performed in anatomically corresponding locations. (b) Percentage of GASMAS measurements with O_2 detected.

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EFFECTS OF A PATENT DUCTUS ARTERIOSUS ON INTESTINAL MUCUS BARRIER IN PRETERM NEWBORNS

Nurangiz Hajiyeva[1], Nushaba Panakhova[1], Aytekin Adilova[1], Saadat Alasgarova[1], Fatima Seyidbekhova[1]
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Background: In contrast with term infants, preterm newborns have less mesenteric blood flow reserve. Their diminished reserve may increase their risk for developing intestinal ischaemia when alterations in intestinal blood flow occur. Patent ductus arteriosus (PDA) has a profound impact on mesenteric perfusion. Objective is evaluation the effects of PDA on intestinal mucosal defence ability in preterm infants.

Methods: Preterm neonates (gestational age 29–33 weeks) who were admitted to the NICU of the Paediatric Institute by name K. Faradjeva were included in this prospective observational study and were divided into two groups: the first group consisted of 20 infants with PDA and the second group consisted of 51 infants without PDA. Intestinal trefoil factor (ITF) and Mucin 2 (MUC 2) were chosen as a marker of mucosal restitution and repair. Serum ITF and MUC 2 were quantified by ELISA on 1–3 day of life (DOL). Results were compared by Mann–Whitney test.

Results: Compared with 2-nd group, the neonates with PDA had lower levels of ITF and MUC-2 (ITF – 15.0 ± 3.3 ng/ml, MUC 2 – 12.59 ± 1.79 ng/mL – in the first group and 35.8 ± 4.9 ng/mL, 14.92 ± 1.239 ng/mL, respectively – in the second group). These differences were significant only relation to ITF ($P < 0.05$).

Conclusion: The low level of ITF in preterm infants with PDA may reduce compensatory protective mechanisms of mucus layer and predispose them to intestinal pathology.

Conflict of interest: None declared.

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TRANSCUTANEOUS ELECTROMYOGRAPHY OF THE DIAPHRAGM AS A NOVEL TRIGGERING MODALITY FOR NON-INVASIVE VENTILATION

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Background: Nasal intermittent positive pressure ventilation (nIPPV) is increasingly used in clinical practice and should ideally be synchronised to the spontaneous breathing efforts of the patient. However, traditional synchronisation modalities like a flow sensor or abdominal pressure capsule are hampered by air leakage at the interface or insufficient sensitivity. Therefore, the aim of this study is to develop and test a new triggering modality based on the electrical activity of the diaphragm, measured with transcutaneous electromyography (dEMG).

Methods: A software algorithm was developed which processes raw dEMG data in real-time and detects the inspiratory efforts of the infant. First, the algorithm was tested in offline simulations and subsequently tested in real-time using an *in vitro* bench set-up. Prerecorded dEMG and flow data of mechanically ventilated infants were fed to the algorithm and the dEMG-based triggers were compared to the ventilator detected inspirations (flow-based). If the dEMG trigger lay was <200 ms pre- or post a flow trigger, it was considered a match. The main outcome measures were (1) the percentage of matched breaths (2) the detected respiratory rate (RR) based on flow and dEMG and (3) the ability to actually trigger the ventilator.

Results: Prerecorded data of 13 patients (mean GA 38.4 ± 3.0 weeks), including 16 973 flow breaths, were used in the bench. dEMG detected less (14 170 breaths, 83.5%), due to artefacts in the EMG signal or overdetection in the flow signal. 45.8% of the dEMG triggers were matched in time with inspiration, while the remaining dEMG triggers were outside the matching window. The average detected RR was similar (58.7 vs. 57.8 breaths/min) for flow and dEMG, respectively. Lastly, all dEMG-triggers were sent successfully to the ventilator which generated a corresponding pressure inflation.

Conclusion: For the first time dEMG has been used to trigger a ventilator during nIPPV. These first results show it is technically feasible to trigger a ventilator based on transcutaneous dEMG, but currently the trigger delay is too long. The next step is to optimise the triggering algorithm, before investigating the level of improvement in nIPPV synchronisation in a clinical study.

Conflict of interest: None declared considering this abstract.

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FAECAL METABOLOME IN PRETERM INFANTS FED HUMAN MILK FORTIFIED WITH BOVINE COLOSTRUM

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Background: Very preterm infants (VPIs) fed human milk require supplementation with nutrient fortifiers to achieve sufficient growth. Fortifiers composed of processed bovine milk (formula) products, lacking raw milk bioactivity, are suspected to induce inflammation and increase the risk of necrotizing enterocolitis. We hypothesized that bovine colostrum (BC), used as a fortifier to human milk, stimulates the gut microbiome of VPIs differently than a conventional fortifier (*CF*, PreNan FM85, Nestlé), thus inducing a characteristic 'healthier' faecal metabolome that correlates to growth.

Methods: Faecal samples were collected from VPIs before fortification (time point 0: FT0, 1–2 weeks of age, 100–140 mL/kg/d

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human milk) and 1 (FT1) or 2 (FT2) weeks after fortification with BC ($n = 107$) or *CF* ($n = 112$) in a randomised, controlled trial across eight Danish hospitals (Clin. Nutr. 42:773–83, 2023). The faecal metabolome was measured by proton nuclear magnetic resonance (1H NMR) spectroscopy. Metabolites were analysed according to fortification group, gestational age (GA), small for gestational age (SGA or not), delivery mode (DM), postnatal age (PA), use of antibiotics or probiotics (with false discovery rate correction).

Results: The main factors that affected faecal metabolome were fortification type and use of antibiotics. At both FT1 and FT2, faecal metabolites potentially important for growth (choline, creatine, creatinine, succinate) and essential amino acids (lysine, phenylalanine, tryptophan) were higher in BC infants relative to *CF* infants (all $P < 0.05$). Antibiotic use reduced the levels of short-chain fatty acids but favoured formation of secondary bile acids (especially at F1). At both time points, levels of acetoin and choline were higher in infants exposed to probiotics.

Conclusion: The novel BC fortifier markedly affected the faecal metabolome of VPIs. Metabolite effects may result from fortifier-related differences in dietary protein (e.g., intact vs. hydrolyzed/modified proteins) or carbohydrate (lactose vs. maltodextrin), and associated changes to the gut microbiome. The possible consequences related to clinical outcomes (e.g., growth, feeding intolerance, sepsis, NEC) are currently being investigated.

Conflict of interest: None declared.

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STOP GIVING ADULT MYDRIATIC DOSES TO PRETERM INFANTS: RESULTS FROM THE LITTLE EYE DROP STUDY

Lisa Kremer[1], **Liza Edmonds**[1], Mary Jane Sime[1], Max Berry[1], Roland Broadbent[1], Natalie Medlicott[1], Nicola Austin[1], Jane Alsweiler[1], David Reith[1]

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Background: There are multiple mydriatic regimes in use globally. In some neonatal units, preterm infants are being administered mydriatic eye drops that are equivalent to, or exceeding, what an adult would receive.

The aim of this research was to evaluate the efficacy and safety of low dose (LD, phenylephrine 1%, cyclopentolate 0.2%), compared to very low dose (VLD, phenylephrine 0.5%, cyclopentolate 0.1%), microdrop (~7 μL) for retinopathy of prematurity eye examinations.

Methods: Multicentre, prospective, randomised controlled non-inferiority clinical trial ($n = 150$). Infants were randomised to receive low dose or very low dose eye microdrops. The primary outcome was to determine if very low dose (VLD) microdrops is non-inferior to low dose (LD) microdrops for ophthalmologist determined successful retinopathy of prematurity eye examinations. Secondary analysis for ophthalmologist rated ease of screen, and exploratory analysis on Stage of ROP and iris pigment on ease of screen was performed.

Results: A total of 162 infants were enrolled in the study (LD; $n = 76$, VLD; $n = 74$; 12 withdrew). No statistically significant differences (mean ± SD) were observed between groups for gestational age (LD 27.0 ± 1.8, VLD 27.0 ± 1.9 weeks) and birthweight (LD 1031 ± 299, VLD 1062 ± 285 g). Non-inferiority of the VLD regimen for efficacy to the LD regimen was demonstrated (95% CI −0.09 to 0.03). All Māori infants had a successful eye examination (95% CI −0.02 to 0.19).

Ophthalmologist rated ease of screen as easy in most participants (RR 0.54, 95% CI 0.19 to 1.53, $P = 0.27$) despite smaller pupil dilation in the VLD group compared with the LD group (RR 0.38, 95% CI 0.21 to 0.70, $P = 0.01$). Neither iris pigmentation (adj OR 1.77, 95% CI 0.53 to 5.93, $P > 0.05$) nor presence of ROP impacted ease of ROPEE (adj OR 1.8, 95% CI 0.92 to 3.80, $P > 0.05$).

No clinically or statistically significant systemic side effects were identified in either group.

Conclusions: Phenylephrine 0.5% and cyclopentolate 0.1% VLD microdrops was non-inferior for efficacy to phenylephrine 1% and cyclopentolate 0.2% LD microdrops for ROPEE.

Stage of ROP and iris pigment does not impact ease of screen on ROPEE success rate. Using a neonatal specific mydriatic regimen will facilitate safer use of mydriatics in preterm infants.

Conflict of interest: None declared.

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VARIATION IN ANTIBIOTIC CONSUMPTION IN VERY PRETERM INFANTS: A 10-YEAR POPULATION-BASED STUDY IN NORWAY

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Background: Wide variations in antibiotic use in preterm infants have been reported across centres despite similar rates of infection. Prolonged antibiotics use in uninfected infants is associated with increased risk of necrotizing enterocolitis, bronchopulmonary dysplasia and death. Unnecessary use of broad-spectrum antibiotics is associated with increased antimicrobial

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DOT per 1000 PD	All n=5296	South-East n=2919	West n= 1217	Mid n=730	North n=430	p-value
All antibiotic treatment ^	149	159	141	161	122	0.012*
Narrow-spectrum antibiotics	108	103	109	108	70	<0.001†
Broad-spectrum antibiotics	34	42	24	31	17	<0.001~
Aminoglycosides	102	100	108	108	91	0.038*
First-generation cephalosporins	3	1	1	1	25	<0.001†
Vancomycin	27	36	18	22	8	<0.001†

DOT per 1000 PD, days of antibiotic therapy per 1000 patient days
^ when calculated "all antibiotics", one day with combination therapy is counted as one day
*Significant differences between North and Mid, North and South-East, West and South-East
† Significant differences between North and all other regions
~ Significant differences between South-East and all other regions
* Significant differences between North and South-East, North and West

resistance We aimed to describe 10-year trends in use of antibiotics and regional variations among very preterm infants in Norway.

Methods: All liveborn very preterm infants (gestational age < 32 weeks) admitted to any neonatal unit in Norway and reported to the Norwegian Neonatal Network database during 2009–2018 were included. Main outcomes are antibiotic consumption expressed as days of antibiotic therapy (DOT) per 1000 patient days (PD), regional variations in use across four health regions, rates of sepsis and sepsis-subtypes and trends of antibiotic use during the study period.

Results: We included 5296 infants; 3646 (69%) born at 28–31 weeks and 1650 (31%) born before 28 weeks gestation. The median GA and birthweight were 29 weeks and 1.2 kg, similar across the four health regions. CRIB scores, sex distribution and proportion of growth restricted infants were also similar across regions, indicating little case mix variation, but there were some differences in rates of Caesarean delivery. Overall, 80% of the included infants received antibiotic therapy. There were considerable regional differences in antibiotic consumption (Table 1); greatest variation found in the consumption of vancomycin, broad-spectrum antibiotics and first-generation cephalosporins. The most prescribed antibiotics were the combination of narrow-spectrum beta-lactams and aminoglycosides for suspected early-onset sepsis, but between 2009 and 2018 we have observed more than 50% reduction in their use from 100 to 40 DOT per 1000 PD ($P < 0.001$). In contrast, consumption of broad-spectrum antibiotics remained unchanged ($P = 0.308$) in all health regions. There were only marginal differences in rates of sepsis and no differences in sepsis-attributable mortality across regions.

Conclusion: There was a great variance both in overall antibiotic consumption and types of antibiotics used across the four health regions in Norway, with no clear correlation to sepsis subtypes or sepsis-attributable mortality. Our results highlight the need for antibiotic stewardship strategies.

Conflict of interest: None declared.

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INTRAVENTRICULAR LEVELS OF CELL-FREE HAEMOGLOBIN AND SCAVENGING PROTEINS FOLLOWING SEVERE CEREBRAL INTRAVENTRICULAR HAEMORRHAGE IN EXTREMELY PRETERM INFANTS

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Background: Cerebral intraventricular haemorrhage (IVH) is a major cause of neuro-developmental impairment in preterm infants. Cell-free haemoglobin (Hb), released into the intraventricular space due to erythrocyte lysis, is a causal initiator of pro-inflammation, oxidative stress and tissue damage. Endogenous detoxifying and scavenging proteins include haptoglobin and haemopexin. Our preclinical studies have shown that intraventricular administration of haptoglobin decreases inflammation and prevents tissue damage following IVH. Potential translation of this treatment paradigm to preterm infants requires knowledge of cell-free Hb kinetics and of intrathecal concentrations of endogenous haptoglobin and haemopexin in intraventricular CSF following IVH.

Methods: Prospective observational study at a level III NICU, Skåne University Hospital, Lund, Sweden. Sixteen extremely preterm infants with a mean (SD) gestational age at birth of 27.2 (2.7) weeks and birthweight 1042 (369) g. All infants developed either IVH grade III ($N = 11$) or periventricular haemorrhagic

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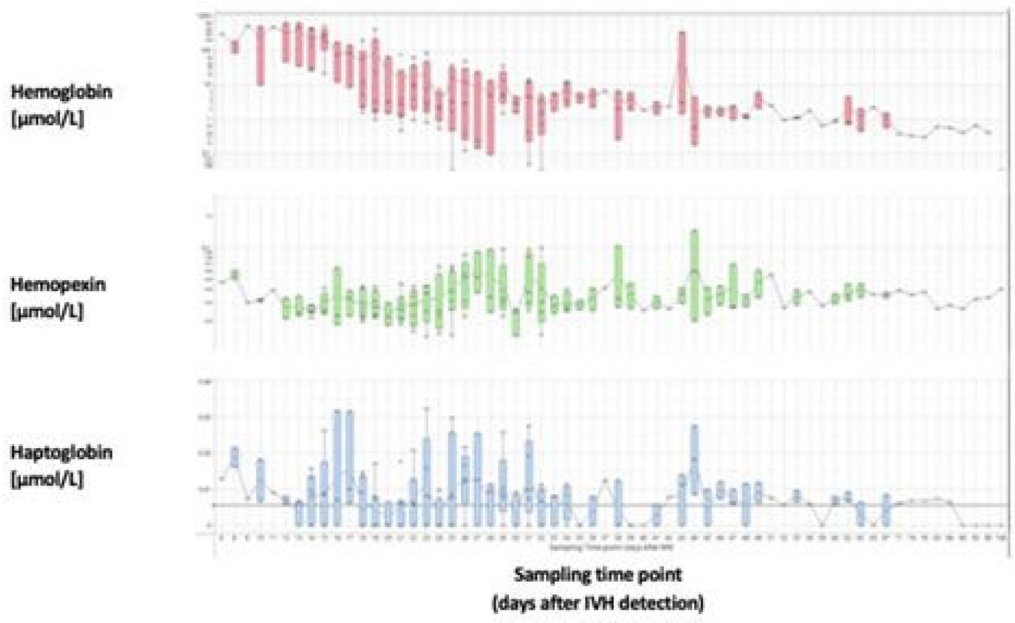


Fig. 1 Longitudinal levels of cell-free haemoglobin, haptoglobin and haemopexin in cerebrospinal fluid following severe intraventricular haemorrhage in very preterm infants. Boxplots depict medians, first/third quartile. Whiskers depict minimum and maximum.

infarction ($N = 5$) at a mean (SD) post-natal age of 3.1 (3.8) days. All infants received a neurosurgically inserted intraventricular reservoir at a mean post-natal age of 18 (11) days enabling longitudinal CSF withdrawal (approximately 10 mL/kg/day). Concentrations of cell-free Hb (spectrophotometry), haptoglobin and haemopexin (LC–MS/MS) were determined in 167 CSF samples corresponding to a mean (SD) number of 10.4 (11.6) samples per infant.

Results: Intraventricular CSF concentration of cell-free Hb decreased during a 3-week period from a median (range) of 461 (1.5–511.3) µmol/L at time-point of insertion of reservoir to 0.4 (0.1–12.0) µmol/L (Fig. 1). Concentrations of haptoglobin and haemopexin were extremely low and did not vary over time (Fig. 1).

Conclusion: Intraventricular levels of cell-free Hb decreased exponentially during the first 3 weeks following cerebral IVH. Levels of haptoglobin and haemopexin in intraventricular CSF were extremely low throughout the study period indicating a severe deficit in endogenous cell-free Hb protection resources. These novel data provide an initial basis for calculation of the amount of intrathecal haptoglobin needed to scavenge the cell-free Hb following severe IVH.

Conflict of interest: VV, SMP, KG, TG and MB are employees of CSL Behring.

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DEVELOPMENT OF A HUMAN SERUM ALBUMIN PREDICTION MODEL USING A LARGE REAL-WORLD DATASET OF TERM AND PRETERM NEONATES

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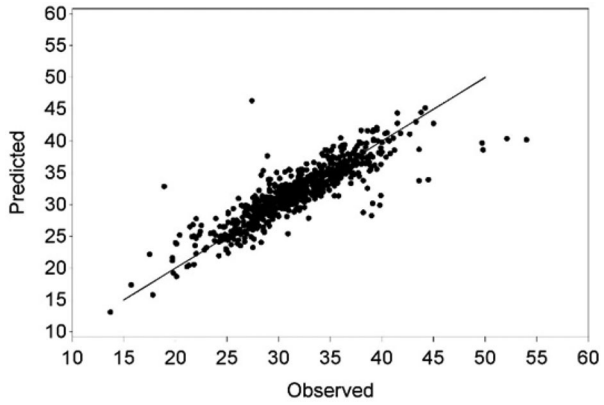
Background: Human serum albumin (HSA) is the most abundant plasma protein. Plasma levels of HSA are influenced by different factors and may alter the distribution of HSA-bound drugs. To understand drug exposure (pharmacokinetics, PK) and drug effects (pharmacodynamics, PD) in neonates, knowledge on physiology in early life is needed. This study aims to describe longitudinal trends in real-world HSA plasma levels in a large neonatal cohort, to explore the impact of maturational and non-maturational covariates on HSA plasma levels, and to develop a prediction model for HSA plasma levels in neonates.

Methods: Data from neonates admitted to the NICU of University Hospitals Leuven between June 2015 and April 2017, with post-natal age (PNA) of 28 days or less, were retrospectively collected from patient files. To define covariate effects on HSA plasma levels over time, linear mixed models were used for modelling random effects to account for the repeated measures structure of the data. Univariable analyses were performed and a multivariable prediction model was developed, using a backward model selection procedure with a 1% significance level for elimination of terms.

Results: A total of 848 neonates were included with median (IQR) gestational age (GA) of 35 (32–38) weeks and birthweight (BW) of 2400 (1640–3130) grams. Longitudinal analyses showed an increase in HSA with PNA and GA. Univariable analyses revealed a significant association of PNA, GA, BW, current weight, sepsis, ibuprofen use, respiratory support, ventilation, C-reactive protein, total and direct bilirubin, and total plasma protein with HSA plasma levels

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Method	Rho (95% CI)	R-squared
Simplified model		
All data points	0.867 (0.846; 0.884)	0.751
Weighted average over days	0.872 (0.849; 0.895)	0.762

Fig. 1 Scatterplot, with predicted and observed HSA plasma levels (g/dL), and model performance of the simplified HSA prediction model. (Rho = Pearson correlation).

(P-value <0.05). Taking interaction with time into account, a complex HSA prediction model was developed with high model performance ($R^2 = 77.5\%$). Next, a clinically applicable, more simplified HSA prediction model was developed containing 10 statistically significant covariates (model performance $R^2 = 76.2\%$).

Conclusion: The developed HSA prediction models, based on a large cohort of term and preterm neonates, integrate multiple (non-)maturational covariates providing an accurate prediction of HSA plasma levels in neonates. Together with drug albumin-binding data, these can be used in neonatal PK/PD analyses to improve modelling and unbound drug exposure prediction and, consequently, drug dosage in neonates.

Conflict of interest: None declared.

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BIOREACTANCE-DERIVED THORACIC FLUID CONTENT (TFC) AND RESPIRATORY DISTRESS IN PRETERM INFANTS

Lizelle Van Wyk[1], Johan Smith[1], John Lawrenson[1], Carl J Lombard[2], Willem-Pieter de Boode[3]

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Background: The most common respiratory pathology in preterm neonates is respiratory distress of the newborn (RDS) for which the mainstay of treatment is nasal continuous positive airway pressure (nCPAP) and surfactant replacement therapy (SRT). Thoracic fluid content (TFC) is a non-invasive thoracic electrical biosensing technology (TEBT) parameter. TFC has been shown to correlate RDS and TTN (transient tachypnoea of the newborn) in term and late-preterm infants. Bioreactance, a type of TEBT, has not been used to determine the effect of different respiratory support modes on TFC in preterm infants.

Methods: This was a retrospective descriptive study of TFC data collected during a prospective method comparison study utilising bioreactance and transthoracic echocardiography measuring cardiac output in preterm neonates. TFC, TFCd (dynamic TFC) and TFCd0(change from baseline) were measured at predefined times pre- and post-intervention (CPAP and CPAP+SRT groups) and compared to infants requiring no respiratory support (NONE group). Parents provided informed consent and the study was approved by the Stellenbosch University HREC.

Results: 63 infants were included. The mean gestational age was 31.3 (±2.7) weeks and mean birthweight 1563 (±3)g, of which 63% were ≤32 weeks and 46% were <1500 g. 31% of infants had RDS and 22% TTN. 22% of infants required no respiratory support, 57% CPAP only and 21% required CPAP with SRT. TFC and TFCd0 differed at all time points between NONE and CPAP/ CPAP+SRT groups but not between CPAP and CPAP+SRT groups. TFC and TFCd0 were significantly associated with gestational age as well as pre- and post measurements in the CPAP and CPAP+SRT groups.

Conclusion: This is the first study of TFC in preterm neonates utilising bioreactance technology to show an effect of various respiratory support methods on TFC. TFC changed with CPAP and SRT administration even after accounting for gestational age and birthweight. TFC and TFCd0 may be able to be used to determine the severity of RDS and predict SRT requirement. More research is required to confirm these findings.

Conflict of interest: L Van Wyk declares technology support by Amayezu Medical, South Africa. WP de Boode declares research support by Cheetah Medical.

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TRENDS OF INFANT MORTALITY DUE TO NEONATAL ENCEPHALOPATHY AND BIRTH ASPHYXIA (NE) IN INDIA, 1990–2019

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Background: Reducing infant and neonatal mortality is a crucial objective of the United Nations sustainable development goals (SDGs), particularly for low and middle-income countries. This study aims to analyse the trends in infant mortality rate (IMR), NE-related infant mortality rate (NE-IMR), and neonatal mortality rate (NMR) in India over the past three decades.

Methods: We utilised the Global Health Data Exchange tool to obtain data on annual NE-related death counts from 1990 to 2019, categorised by age (early: 0–6 days, late: 7–27 days, post-neonatal: >28–365 days) and location (https://ghdx.healthdata.org/). We extracted UN Population Prospects data for India's annual birth cohorts from 1990 to 2019. To summarise and model the data, we calculated and compared the overall NE-IMR trends using the Joinpoint regression programme from the National Cancer Institute. Statistical significance was set at <0.05. We assessed NE-related mortality using the human capital approach, value of statistical life (VSL), and value of statistical life year (VSLY) methods.

Results: Among more than 811 million births, 4.4 million (UI: 3.6, 5.3) deaths were attributed to NE. The relative contribution of NE to total infant mortality decreased from 22.1% in 1990 to

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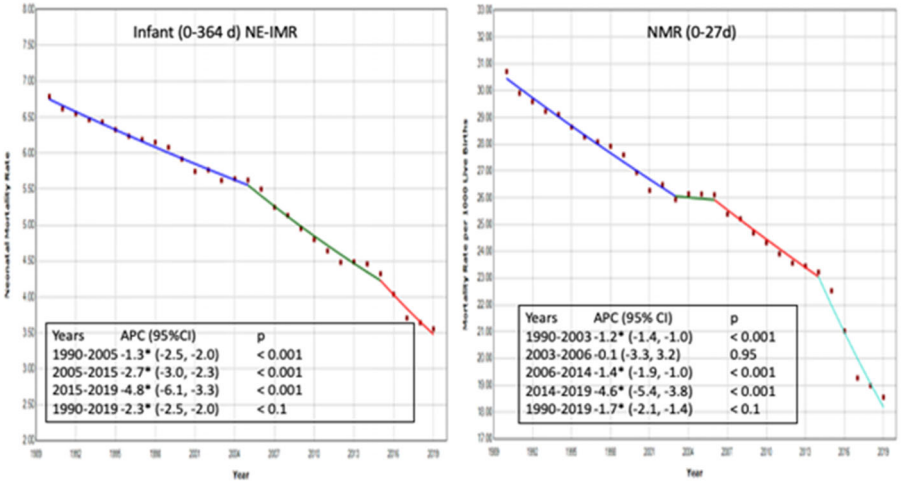


Fig. 1 Trends in NE-IMR (left) and NMR (right). We noted three joinpoints for NE-IMR and four joinpoints for NMR.

19.2% in 2019. Over the study period, NE-IMR and NMR decreased from 6.8 to 3.6 and 29.2 to 18.2 per 1000 live births, respectively. We observed a 39.6% (UI: 33.2, 43.7) reduction in IMR from 1990 to 2019, while NE-IMR decreased by 47.6% (UI: 43.4, 51.3). The annual percentage change (APC) for NE-IMR and NMR was −2.3% (95% CI: −2.5, 2) and −1.7% (95% CI: −2.1, −1.4), respectively (Fig. 1). In 2019, there was substantial interstate variation in NE-IMR (see Fig. 1a). The economic losses associated with NE-related infant mortality ranged from 25 to 51 billion USD.

Conclusions: In India, there has been remarkable progress in reducing NE-related mortality compared to the overall reduction in neonatal mortality over the past 30 years. As NMR serves as a crucial indicator for social development and economic progress, targeted investments are necessary to sustain this progress by expanding coverage and addressing data gaps. These efforts are crucial for achieving the SDG target of single-digit NMR by 2030.

Conflict of interest: None declared.

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ENHANCING decision-making IN NEONATAL INTENSIVE CARE UNITS: A CLINICAL DECISION SYSTEM FOR EARLY PREDICTION OF NEONATAL MORTALITY AND LENGTH OF STAY

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Background: The use of early predictive models for neonatal mortality and Length of Stay (LOS) in Neonatal Intensive Care Units (NICUs) greatly enhances decision-making capabilities. We developed an intelligent system that employs the 'Case-Based Reasoning' (CBR) methodology to effectively predict neonatal mortality and LOS.

Methods: The web-based CBR system, based on K-Nearest Neighbourhood (KNN) algorithm, was developed to predict neonatal mortality and LOS. A dataset of 1682 neonates, consisting 17 variables for mortality and 13 variables for LOS prediction, was used in the development process. The system's performance was evaluated using 336 retrospectively collected data. Furthermore, the system was successfully implemented and externally validated in a NICU.

Results: In the internal validation, the system showed a high accuracy of 97.02% and an F-score of 0.984 for mortality prediction in the balanced case base. The RMSE for LOS was 4.78 days. The external validation on the balanced case base, showed a significant accuracy of 98.91% and F-score of 0.993 for mortality prediction. The RMSE for LOS was 3.27 days. This system is available at http://neonatalcdss.ir/

Conclusion: The positive results observed in terms of performance showed that this system can be effectively employed to enhance neonatal care.

Keywords: Artificial intelligence, case-based reasoning, clinical decision support system, length of stay, neonatal intensive care units (NICUs), neonatal mortality.

Conflict of interest: None declared.

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BEHAVIOUR AND QUALITY OF LIFE IN 5-YEAR-OLD CHILDREN BORN VERY PRETERM AFTER EARLY HIGH-DOSE RECOMBINANT HUMAN ERYTHROPOIETIN: A RANDOMISED CLINICAL TRIAL

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Background: The Swiss Epo Neuroprotection Trial was launched to examine the potential neuroprotective effect of recombinant human erythropoietin (rhEpo) on the neurodevelopment of very preterm newborns. According to the results of the primary and secondary outcome analyses, rhEPO had no effect on the study participants' cognitive abilities, neuro-motor outcomes, or somatic growth at ages 2 and 5 years, respectively. We report here the findings of secondary analyses of pre-specified parent-reported behavioural outcomes of the study children and their health-related quality of life (HRQoL) at age 5 years.

Methods: This randomised, double-blind, placebo-controlled, multicentre trial was conducted in five level-III perinatal centres in Switzerland. Between 2005 and 2012, infants born between 26 weeks 0 days' and 31 weeks 6 days' gestation were recruited. Infants were assigned to receive either rhEpo (3000 IU/kg) or placebo (saline, 0.9%) intravenously three times during the first 42 h after birth. Two standardised questionnaires, the Strengths and Difficulties Questionnaire and the Kidscreen-27, were used to evaluate the pre-specified parent-reported measures of behavioural outcomes and health-related quality of life (HRQoL), respectively, of their children at the age of 5 years. The last outcome assessment was completed in 2018.

Results: Among the 448 randomised infants, 228 infants were allocated to the rhEpo group and 220 to the placebo group. Questionnaires data were available for 317 (71%) children at a mean (SD) age of 5.8 (0.4) years (gestational age 29.3 (1.6) weeks at birth; birthweight 1220 (340) grams; 128 (40%) females). The mean (SD) total difficulties score in the rhEPO group ($M = 8.41$, $SD = 5.60$) was similar to that of the placebo group ($M = 7.76$, $SD = 4.81$, $P = 0.37$). No evidence for a difference in any other outcome measurements was observed between groups.

Conclusion: The findings of the current secondary outcome analyses provide no evidence in support of a relationship between prophylactic early high-dose rhEpo administration and behavioural outcomes or HRQoL in 5-year-old children born very preterm.

Trial Registration: NCT00413946.

Conflict of interest: None declared.

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STRESS EXPOSURE DURING NICU ADMISSION: THE CHALLENGES FACED BY PRETERM INFANTS

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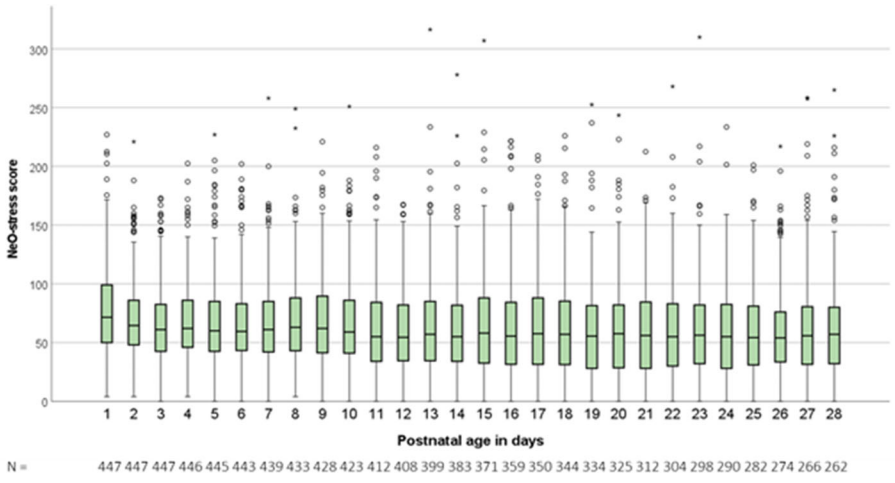


Fig. 1 Stress exposure during the first 28 days of life in preterm infants with a gestational age less than 29 weeks.

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Background: NICU admission is known as a potentially very stressful period in the preterm infants' life with an important impact on the short and long-term development of the child. This study aims to describe stress exposure for preterm infants born with a gestational age below 29 weeks during the first 28 days of NICU admission.

Methods: This is a national multicentre observational cohort study with a 1-year inclusion period in all nine Dutch NICUs. All premature infants born in the Netherlands with a gestational age below 29 weeks were eligible for inclusion. Data collection included patient characteristics and the previously developed NeO-stress score, consisting of 38 items including their severity index. The stress score were calculated per day for all infants and a cumulative score during the first 28 days was determined for the infants that were admitted this complete period.

Results: A total of 447 patients, 74% of all eligible patients, were included in this study. These 262 boys (59%) and 185 girls (41%) had a median gestational age of 27 weeks and 2 days (IQR 26 + 1 to 28 + 2 weeks) and a birthweight between 450 and 1635 g. NeO-stress scores per day ranged from 0 to 317 with a median score of 59.5 (IQR 37.5–84.5). Median stress exposure per day was highest on the day of admission (71.5, IQR 50–99) and showed an overall decrease during the first 28 days ($r = -0.12$, $P < 0.001$), see Fig. 1. The cumulative stress score during the first 28 days ($N = 262$), was negatively correlated with gestational age ($r = -0.50$, $P < 0.001$).

Conclusion: Our preliminary results show that there is an overall very high, but variable, daily stress exposure in preterm infants during NICU admission with an overall decrease over time during the first 28 days. Gestational age is negatively associated with the cumulative exposure to stress. A better understanding of other factors associated with the level of stress is important in order to determine ways to decrease this stress and its negative consequences. These factors will be analysed and available to present at the congress.

Conflict of interest: None declared.

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MANAGEMENT OF NEONATAL PAIN IN THE NICU WITH SKIN-TO-SKIN CONTACT

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Introduction: Advances in neonatology have significantly reduced morbidity and mortality, but neonatal pain, discomfort, and stress remain significant problems in neonatal intensive care units (NICUs), especially for preterm infants. Although significant progress has been made in the treatment and prophylaxis of neonatal pain in many NICUs, the early and long-term outcomes of pain and stress in these vulnerable infants compel the continued search for healing pain- and stress-reducing interventions. Therefore, the aim of our research was to study how skin-to-skin contact influences neonatal pain intensity in preterm infants in the NICU.

Material and Methods: The study included 140 preterm infants with gestational age less than 34 weeks, who were treated in the NICU of the regional perinatal centre. For the laboratory evaluation of pain and the effectiveness of skin-to-skin contact (SSC) in pain relief the level of pain markers (dopamine, serotonin, endorphin) were determined before (baseline level) and after rooming-in and skin-to-skin contact of an infant with mother. The level of dopamine, β-endorphin, serotonin in urine samples was determined by enzyme-linked immunosorbent assay.

Results: The study included 19 extremely preterm (13.6%), 52 very preterm (51.4%), and 49 moderate preterm infants (35%). There were 74 (52.9%) males and 66 (47.1%) females. The mean gestational age (GA) of the study population was (31.1 ± 2.4) weeks, the mean birthweight – (1591.46 ± 439.51) grams. There was a significant decrease in the dopamine level in preterm infants after SSC in comparison with baseline values (132.20 (104.80; 183.70) pg/mL vs. 85.99 (69.35; 112.20) pg/mL), $P < 0.001$, before and after intervention). The β-endorphin and serotonin levels simultaneously significantly increased after SSC compared to baseline values (29.87 (20.61; 46.94)) pg/mL vs. 40.09 (26.81; 70.63) pg/mL, $P = 0.009$ before and after SSC, and (22.30 (15.13; 31.65) ng/mL vs. 25.49 (20.45; 40.08) ng/mL, $P = 0.011$, respectively).

Conclusions: Kangaroo mother care with skin-to-skin contact is effective intervention for neonatal pain management. The level of dopamine as a pain hormone reduced after regular SSC and pain-relieving markers β-endorphin and serotonin reliably increased in preterm infants in response to the SSC.

Conflict of interest: None declared.

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TRANSLATING AN 'APP' PREDICTING SURVIVAL AND DISABILITY IN INFANTS BORN EXTREMELY PRETERM INTO CLINICAL PRACTICE

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Background: We have shown in two previous surveys that clinicians grossly overestimate mortality and disability rates in infants born extremely preterm. Consequently, we developed NIC-PREDICT: a Smartphone application ('app') and web-based tool (NIC-PREDICT: https://nic-predict.com.au/) that predicts infant mortality, and survival with and without major disability at 8 years in infants born 23–27 weeks' gestation. The aim of this study was to determine if clinicians could predict outcome in these infants more accurately using NIC-PREDICT.

Methods: The NIC-PREDICT app was released for clinical use in the state of Victoria on 17/7/2021. We sent an electronic survey to midwives, nurses, obstetricians, and neonatologists working in tertiary and non-tertiary hospitals in Victoria in 2022. Clinicians were asked to use the NIC-PREDICT app to estimate the three mutually exclusive outcomes of (1) infant mortality, (2) survival with major disability, and (3) survival without major disability for six different scenarios where a liveborn infant was

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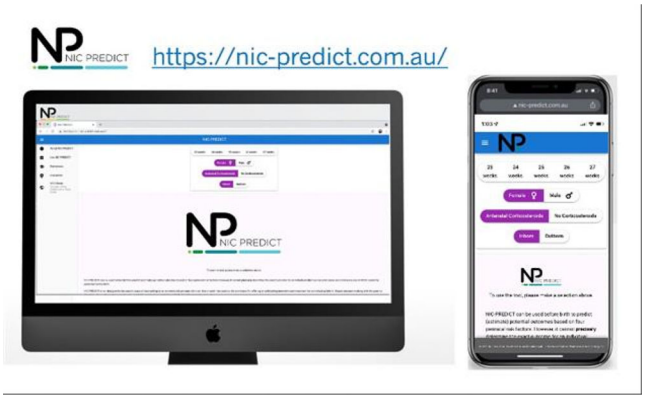


Fig. 1 NIC-PREDICT web-based platform and Smartphone application (app).

offered active care after birth. The proportions who completed the survey (responded to all six scenarios) and the proportions of those who were able to use the app correctly and provided 100% accurate results for all scenarios were determined. Estimates of the three outcomes were compared with true rates.

Results: A total of 85 clinicians responded, but only 70 (82%) completed the survey. Of the 70 who completed the survey, overall accuracy was 76% (321/420) for the 6 scenarios. Mortality overall was overestimated by only 0.7% (95% CI −0.7, 2.1), which was a substantial improvement on the previous surveys in 2010 (6.7%, 95% CI 3.7, 9.7) and 2020 (14.4%, 95% CI 12.3, 16.6). Survival with no disability overall was underestimated by only −0.7% (95% CI −3.0, 1.7). However, survival with disability was overestimated by 4.9% (95% CI 1.7, 8.0) $P = 0.003$ (Fig. 1).

Conclusion: Most perinatal clinicians who responded can correctly use the NIC-PREDICT app to predict expected outcomes in infants born extremely preterm who are offered active care. However, further training is needed to ensure all perinatal clinicians who are likely to use NIC-PREDICT are able to use it correctly. Undue pessimism about major disability remains an ongoing concern.

Conflict of interest: None declared.

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REFERENCE VALUES OF THROMBOLASTOMETRY PARAMETERS IN HEALTHY TERM NEONATES

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Background: Rotational Thromboelastometry (ROTEM) as a point of care test is an attractive tool for rapid global evaluation of haemostasis. In adults and guide for transfusion therapy. According to the concept of developmental haemostasis, the levels of most of the coagulation factors are lower in the newborn and they are related to gestational and post-natal age. Conventional tests of coagulation such as prothrombin time (PT)-partial thromboplastin time(PTT) are of limited utility in predicting haemorrhage and guiding transfusion therapy in critically ill neonates. Currently, no reference ranges exist for all ROTEM assays in neonates, limiting its use in this vulnerable population. The establishment of reference ranges for standard extrinsically activated (EXTEM), intrinsically activated (INTEM) and fibrinogen polymerisation (FIBTEM) ROTEM assays, in whole blood samples in a relatively large sample of healthy term neonates and to determine the impact of gender, delivery mode, haematocrit on ROTEM parameters.

Methods: This single centre observational study included 226 full term neonates with appropriate birthweight for gestational age, born in the General Hospital of Nikaia, 'AghiosPanteleimon', Piraeus, over a 3 year period (2017–2020). EXTEM, INTEM and FIBTEM assays were performed on the 2nd–3rd day of life simultaneously with any occasion for blood testing for various medical conditions.

Results: Reference ranges (2.5th and 97.5th percentiles) were obtained for clotting time (CT), clot formation time (CFT), α-angle, clot firmness at 10 min (A10), maximum clot firmness (MCF), and lysis index at 60 min (LI60, %). Reference ranges for EXTEM were CT 38–78 s, CFT 49–148 s, A10 40–65 mm, and MCF 47–69 mm, LI60 83%–98%. For INTEM, CT 134–270 s, CFT 50–142 s, A10 41–63 mm, and MCF 48–67 mm, LI60 85%–97%, and finally, for FIBTEM: CT 36–85 s, A10 9–25 mm and MCF 10–26 mm, LI60 92%–100%. Haematocrit values were positively correlated with CT, CFT and negatively with A10, MCF values.

Conclusion: This study provides, for the first time, reference ranges for ROTEM EXTEM/INTEM/FIBTEM values simultaneously in healthy term neonates. The combined evaluation of ROTEM tests increases its diagnostic accuracy, contributing to the expansion of ROTEM use in the neonatal population.

Conflict of interest: None declared.

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PLASMA AMINO ACID LEVELS ASSOCIATE WITH GROWTH IN PRETERM INFANTS FED FORTIFIED HUMAN MILK

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Background: Preterm infants fed human milk require nutrient fortification to reach acceptable in-hospital growth rates. It is unclear how different fortification products affect amino acids (AAs) in plasma and how individual AAs relate to in-hospital growth and growth-promoting hormones. Using infants

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randomised to two different fortification products, we hypothesized that plasma AAs associate with in-hospital growth during the first weeks after the start of fortification and that this may be mediated by insulin-like growth factor 1 (IGF-1).

Methods: Very preterm infants ($n = 225$, mean gestational age, 29 weeks) were randomised to fortification with a conventional fortifier (*CF*, PreNan, Nestlé, hydrolyzed whey protein) or bovine colostrum (BC, Biofiber-Damino, intact whey, casein, immunoglobulins), starting at post-natal day 8–9 until 35 weeks postmenstrual age aiming for similar growth (*Clin. Nutr*. 42, 773–783, 2023). Total protein provision was similar, but AA levels differed between fortification products. Growth was measured as ΔZ weight scores from birth until end of intervention. Preprandial plasma levels of 20 AAs and IGF-1 were measured after one (T1) and 2 weeks of fortification (T2). Analyses were adjusted for gestational age at birth, small for gestational age, fortifier type and post-natal age.

Results: BC increased nine AAs (+11–42% for alanine, arginine, glycine, histidine, phenylalanine, proline, serine, tyrosine and valine), total AAs (+9–11%) and combined branched-chain AAs (BCAA) (+15–17%) at both T1 and T2 relative to *CF*. IGF-1 was unaffected by fortification type but associated positively with arginine, asparagine, lysine, methionine, threonine and valine as well as total and essential AAs at both time points. Regardless of fortification type, alanine, arginine, asparagine, cysteine, glutamine, lysine, methionine, threonine and tyrosine along with total and essential AAs at T1 and T2 associated positively with growth, whereas IGF-1 only associated with growth at T1.

Conclusion: One and 2 weeks after the start of fortification, fortification-derived protein seems linked to in-hospital growth through numerous individual growth-associated plasma AAs. Although BC provided similar growth, it increased the growth-associated AAs alanine, arginine and tyrosine. IGF-1 may partly mediate arginine, asparagine, lysine, methionine and threonine growth effects. More studies are needed to define the optimal AA composition of fortifiers.

Conflict of interest: PT Sangild holds a patent in BC, but has declined any share of potential revenue arising from commercial exploitation of the patent. Other authors declare no conflicts of interest.

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THERAPY WITH A FRAGMENT OF RECOMBINANT SURFACTANT PROTEIN D DEMONSTRATES NO TOXICITY IN VENTILATED AND NON-VENTILATED TRANSLATIONAL MODELS

Reena Bhatt[1], Tania Castillo-Hernandez[1], Ariel Finkielsztein[1], Martin Kemp[2], Boris Kemp[3], Neil Marlow[1], Jens Madsen[1], Howard Clark[1]

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Introduction: Bronchopulmonary dysplasia (BPD) affects up to 40% of infants born <30 weeks gestational age, with inflammation playing a key role in its development. Surfactant Protein D (SP-D) has several immunomodulatory functions in the lung. We employed two translational models; a preterm lamb model of ventilator-associated lung injury and a non-ventilated mini-pig model to test the hypothesis that a recombinant fragment SP-D (rfhSP-D) is non-toxic when administered as intratracheal (IT) therapy while reducing inflammation and may have therapeutic potential in preterm infants.

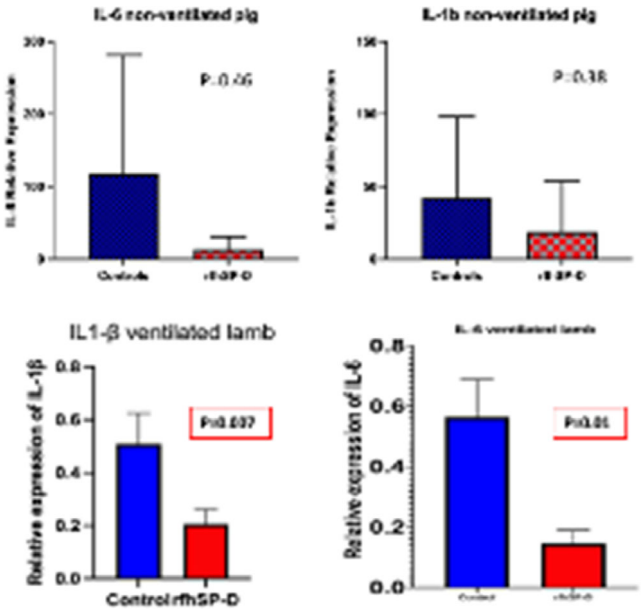


Fig. 1 Expression of IL-1β and IL-6 in ventilated and non-ventilated models. Expression of pro-inflammatory cytokines was lower in the treated animals in both models. Mean + SD, compared using Mann–Whitney test, $P < 0.05$ = statistical significance.

Methods: The studies were funded by MRC and conducted with animal ethics approval. Sixteen mechanically ventilated preterm lambs and 18 non-ventilated mini pigs were randomised to either IT rfhSP-D or control (IT 0.9% saline). Lambs were treated with 24 mg of rfhSP-D administered at 20, 140 and 260 min. Mini-pigs were treated with three doses of 4 mg/kg rfhSP-D at 0, 12 and 24 h. SP-D levels and cell infiltrates were measured in terminal bronchoalveolar lavage, and PCR was used to analyse the expression of IL-1β, IL-6, IL-8 and TNF-α in homogenised lung tissue.

Results: IT administration of rfhSP-D in non-ventilated mini pigs was shown to be effective and was cleared from the BAL within 72 h of administration. There was no increase in expression of pro-inflammatory cytokines, expression was lower in the treated animals but not statistically significant ($P > 0.05$). There was no significant difference in the cell infiltrates between the treated and untreated groups. In ventilated preterm lambs expression of all pro-inflammatory cytokines was lower in the treated animals and expression of IL-1β and IL-6 was significantly lower in the IT rfhSP-D group ($P = 0.007$ and $P = 0.01$, respectively) (Fig. 1).

Conclusion: IT administration is effective in delivering rfhSP-D and there is good clearance from the lungs. IT rfhSP-D in these translational models showed no toxic effect on pro-inflammatory cytokines and in the ventilated model was shown to significantly reduce potent pro-inflammatory cytokines such as IL-1β and IL-6, which are known to have a role in the

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development of BPD. These results support that rfhSP-D is likely to have a therapeutic benefit in preterm infants at risk of BPD.

Conflict of interest: None declared.

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THE EFFECT OF ANTENATAL MAGNESIUM SULPHATE EXPOSURE ON PATENT DUCTUS ARTERIOSUS IN PREMATURE INFANTS

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Background: Magnesium sulphate ($MgSO_4$) has been shown to be effective for neuroprotection of the fetus. Extracellular magnesium causes ductus arteriosus closure to be delayed. There is conflicting evidence from studies regarding the relationship between antenatal $MgSO_4$ administration and patent ductus arteriosus (PDA). This study aims to evaluate the association between antenatal $MgSO_4$ exposure and PDA.

Methods: Preterm infants born between 240/7 and 316/7 weeks were included. Infants who died during the first 72 h of life and had significant congenital abnormalities were excluded. Echocardiographic and clinical evaluations were used to define PDA and haemodynamically significant PDA (hsPDA). The treatments were planned in accordance with the unit's standard protocols.

Results: The study included 300 preterm infants, 32.6% ($n = 98$) of whom were exposed to antenatal $MgSO_4$. The gestational age (GA) and the birthweight (BW) of infants were lower ($P = 0.012$ and $P < 0.001$, respectively) and the exposure to antenatal steroids was higher in the $MgSO_4$ group ($P = 0.039$). While hsPDA rates were pretending to be higher in the infants who exposed antenatal $MgSO_4$ (OR: 2.034, 95% CI: 1.161–3.564, $P = 0.012$), with adjustment for antenatal steroid administration, GA, and BW; hsPDA incidences were found to be similar (OR: 1.6, 95% CI: 0.849–3.118, $P = 0.146$). The rates of PDA ligation and open PDA at discharge were similar between groups. A cumulative MgSO4 dose of greater than 20 g was associated with an increased risk of hsPDA (crude OR: 2.476, 95% CI: 0.893–6.864, $P = 0.076$; adjusted OR: 3.829, 95% CI: 1.068–13.728, $P = 0.039$). However, the cumulative dose had no impact on the ligation rates or open PDA at discharge. The rates of prematurity-related morbidities and mortality were similar (Table 1).

Conclusion: This study showed that antenatal $MgSO_4$ exposure increased the incidence of hsPDA but had no effect on the rates of PDA ligation or open PDA at discharge. Based on the results, antenatal $MgSO_4$ administration with an established neuroprotective effect should not be regarded with concern.

Conflict of interest: None declared.

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CONGENITAL DIAPHRAGMATIC HERNIA (CDH): ARTIFICIAL INTELLIGENCE FOR AUTOMATIC LUNG AND LIVER SEGMENTATION IN MAGNETIC RESONANCE IMAGES, AND LIVER HERNIATION CLASSIFICATION

Luana Conte[1,2], Ilaria Amodeo[3], Giorgio De Nunzio[1,2], Genny Raffaeli[3,4], Irene Borzani[5], Nicola Persico[4,6,7], Giuseppe Como[3],

	Exposed to $MgSO_4$ (n=98) n (%)	Not exposed to $MgSO_4$ (n=202) n (%)	Crude OR (95%CI)	p	Adjusted OR* (95%CI)	p
Any PDA (at first ECHO)	49 (50)	96 (47.5)	1.104 (0.681-1.789)	0.687	0.778 (0.443-1.369)	0.384
Moderate to large PDA (at first ECHO)	39 (39.8)	69 (34.2)	1.274 (0.774-2.097)	0.340	0.863 (0.480-1.550)	0.621
Medical treatment (hsPDA)	30 (30.6)	36 (17.8)	2.034 (1.161-3.564)	**0.012**	1.600 (0.849-3.018)	0.146
PDA ligation[a]	6/49 (12.2)	14/96 (14.6)	0.714 (0.250-2.040)	0.699	0.370 (0.115-1.197)	0.097
PDA on discharge[b]	13 (15.1)	17 (9.7)	1.666 (0.769-3.610)	0.193	1.206 (0.517-2.812)	0.664
Subgroup analysis for GA < 28 weeks						
Any PDA (at first ECHO)	31 (81.6)	42 (75)	1.476 (0.533-1.476)	0.452	1.229 (0.418-3.613)	0.708
Moderate to large PDA (at first ECHO)	28 (73.7)	35 (62.5)	1.680 (0.682-4.141)	0.258	1.368 (0.524-3.572)	0.522
Medical treatment (hsPDA)	23 (60.5)	20 (35.7)	2.760 (1.180-6.455)	**0.018**	2.763 (1.148-6.653)	**0.023**
PDA ligation[a]	6/28 (21.4)	12/35 (34.3)	0.523 (0.167-1.636)	0.262	0.457 (0.139-1.502)	0.197
PDA on discharge[b]	7/26 (26.9)	11/37 (29.7)	0.871 (0.285-2.661)	0.808	0.642 (0.197-2.097)	0.463

*Adjustments for Antenatal steroids exposure, gestational age and birth weight, in the subgroup analysis for antenatal steroid exposure and birth weight
[a]Only the patients who have moderate-large PDA(at first ECHO) were included.
[b]Patients who died before discharge or required PDA ligation were excluded.
Only one patient whose gestational age <28 w, required transcatether PDA closure procedure after discharge in antenatal $MgSO_4$ group. No patient whose gestational age <28 w, required transcatether PDA closure procedure after discharge in the other group.
ECHO: echocardiography

Table 1 Comparison of PDA between groups

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Background: Congenital Diaphragmatic Hernia (CDH) is a rare malformation characterised by a diaphragmatic defect that allows intrathoracic herniation of abdominal viscera, affecting lung development and leading to lung hypoplasia and post-natal pulmonary hypertension. Fetal MRI is a reliable technique for prenatal CDH evaluation, since it allows the assessment of several factors impacting neonatal survival, mainly lung size and liver position. However, manual segmentation of MRI sections is time-consuming and prone to errors. Recently, Artificial Intelligence-based technologies have been utilised in the neonatal field to support medical data analysis. The purpose of this study was to automate lung and liver segmentation in MRI so as to enable reliable automatic prediction of prognostic factors in newborns affected by this severe disease.

Methods: We proposed the use of nnU-Net, a free and user-friendly deep-learning automatic segmentation system, for the automated contouring of lungs and liver in 39 MR images of CDH-affected fetuses. Segmentation quality was assessed by the Jaccard coefficient, a measure of similarity defined as the size of the intersection of the manual and the automatic regions of interest (ROIs), divided by the size of their union: values close to 1 indicate fully overlapped regions. We also built a Machine Learning (ML) classifier system to predict liver herniation based on Pyradiomics shape features computed from the manual and automatic segmentations of lungs and liver.

Results: nnU-Net yielded good automatic segmentations, with most Jaccard coefficients around 0.60–0.70 for the lungs and 0.75–0.80 for the liver. Pyradiomics features were partly reproducible in the manually and automatically segmented ROIs, which is a sign of reliability of the automatic segmentations. The ML procedure for liver herniation prediction, based on nnU-Net segmentations, gave high ROC AUC values (0.91) similarly to those based on manual segmentations (see Fig. 1).

Conclusions: To the best of our knowledge, this work is the first attempt at the automatic segmentation of lungs and livers in MRI of fetuses affected by CDH. The study suggests that the automatic segmentation approach is feasible, with promising results, and can be useful in ML applications such as predicting liver herniation.

Conflict of interest: None declared.

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PREVALENCE OF EPILEPSY AND PATHOLOGICAL EEG IN A NORWEGIAN SAMPLE OF CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDER (FASD): IMPACT ON COGNITION AND ADAPTIVE FUNCTIONING

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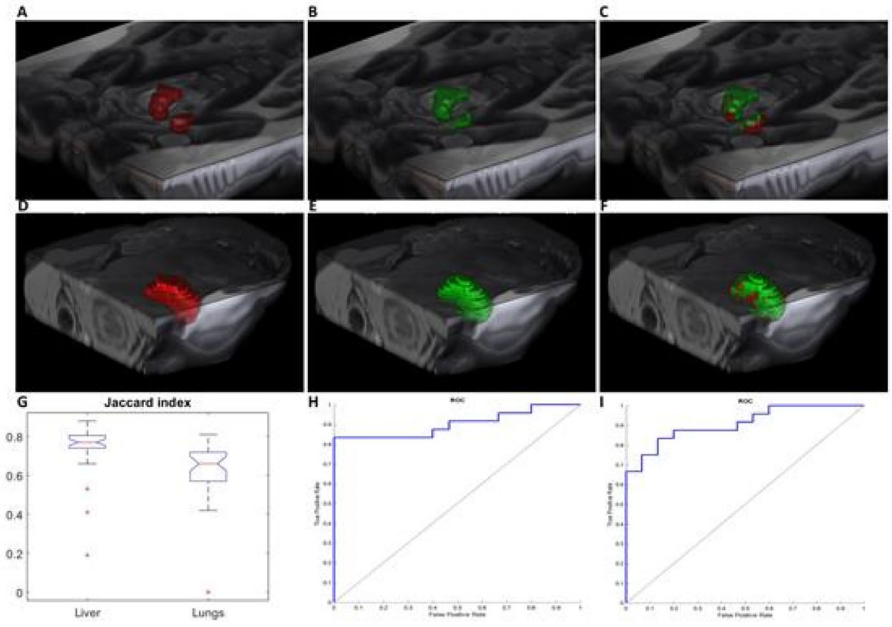


Fig. 1 Lung (1st row) and liver (2nd row) segmentation results: manual (a, d), automatic (b, e), overlaps (c, f), Jaccard coefficients (g). ROC curves for liver herniation prediction (H: manual, I: automatic ROIs).

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Background: Fetal Alcohol Spectrum Disorder (FASD) is an umbrella term describing a combination of developmental, cognitive and behavioural disabilities after prenatal alcohol exposure. Data on prevalence are limited, but it is estimated that the current prevalence of FASD in populations of younger school children as high as 2%–5% in the US and other Western countries. Increased prevalence of epilepsies and pathological EEG have been reported. This study aimed to examine the prevalence of epilepsy, EEG pathologies and its implication on cognitive and adaptive functioning.

Methods: Cross-sectional study on 148 children with FASD, assessed multidisciplinary and with EEG recording. Group comparisons and regression analyses were used to test the associations between epilepsy and EEG on FASD subgroups and neurocognitive performance in children with presence or absence of ADHD as comorbidity.

Results: The incidence of epilepsy was 6% compared to 0.7%–0.9% in children in general. Pathological EEG was seen in 21% of children with FASD. ADHD was confirmed in 64% of the children, evenly distributed between children in different FASD subgroups. Children with epilepsy and/or pathological EEG findings did not have lower cognitive and adaptive scores compared to the total FASD group. However, significantly lower scores of the IQ indices processing speed and working memory were found in children with frontal EEG-pathologies (but without epilepsy) compared to FASD children without such findings, irrespective of ADHD status, sex or preterm birth, indicating executive function deficits.

Conclusion: We found a 6.7–8.6 fold increased prevalence of epilepsy in the FASD group. A pathological EEG was found in a many children throughout all FASD subgroups, even in absence of an epileptic disorder. Irrespective of epilepsy, ADHD and FASD subgroup, children with frontal EEG pathologies showed significantly reduced processing speed and working memory, which may justify medical treatment.

Conflict of interest: None declared.

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THE IMPACT OF EXTREME TEMPERATURES ON BIRTH OUTCOMES: A NATIONWIDE POPULATION-BASED STUDY

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Background: The aim of this study was to investigate the causal impact of *in utero* exposure to extreme temperatures on key birth outcomes, i.e., birthweight, low birthweight (LBW), small-for-gestational-age (SGA), and preterm birth (PTB) in the Netherlands. Moreover, we examined the role of socioeconomic status (SES) as moderator for the effect of interest.

Methods: We included singleton births that occurred in the Netherlands between 2003 and 2017 ($N = 2\,476\,772$). Daily weather measurements were linked to the Dutch perinatal registry using maternal residential postcode. The exposure corresponded to the number of days during the gestation period in which the daily mean temperature fell into each of mutually exclusive temperature bins, where the 8–12°C bin was used as reference. Logistic regression models were used to assess the effect of temperature exposure on birth outcomes. To identify a causal effect our approach exploited the unpredictability of daily temperature fluctuations while accounting for seasonal and underlying trends. Interaction terms between the exposure and SES indicators (household income, education, and neighbourhood SES) were used to investigate the effect heterogeneity across levels of SES.

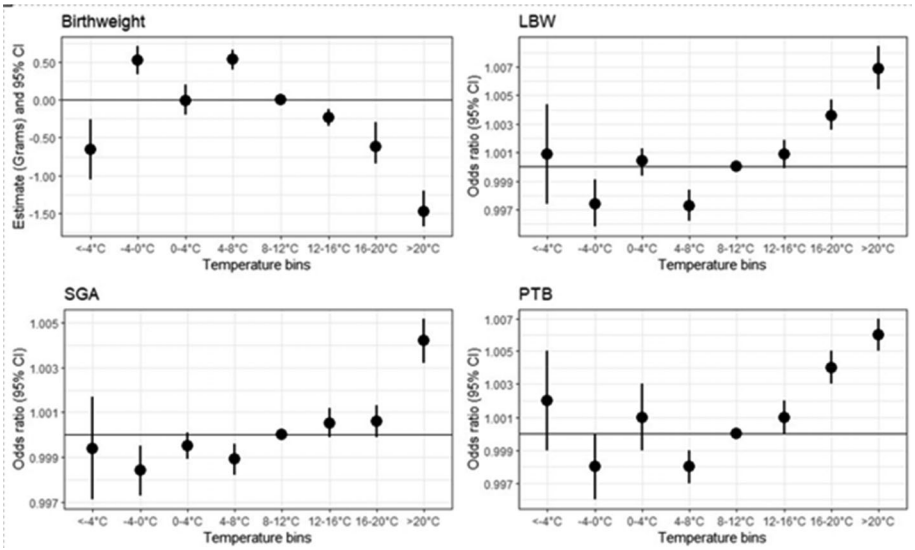


Table 1 The effect of *in utero* exposure to one additional day falling in certain temperature bin on birth outcomes (relative to a day with a mean temperature of 8–12°C)

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Results: *In utero* exposure to an additional hot day (mean temperature > 20°C), relative to a day within the 8–12°C range, was related to increased odds of LBW (OR (95% CI) = 1.007 (1.005, 1.009)), SGA (OR (95% CI) = 1.004 (1.003, 1.005)), and PTB (OR (95% CI) = 1.006 (1.005, 1.007)), and a reduction in birthweight of 1.47 g (95% CI = 1.20, 1.60). Additionally, exposure to an additional cold day (<−4°C) was related to a reduction of birthweight by 0.66 g (95% CI = 0.27, 1.05). We observed that SES moderated the effect of *in utero* temperature exposure on birth outcomes and that the observed effect was the most detrimental for births in low SES households (Table 1).

Conclusion: We found that exposure to extreme temperature during pregnancy has an adverse impact on birth outcomes in the Netherlands. The projected increases in extreme temperatures in the face of the climate crisis may further exacerbate health disparities in early-life.

Conflict of interest: None declared.

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ASSOCIATION BETWEEN MATERNAL MIGRATION BACKGROUND AND MORTALITY AMONG EXTREMELY PRETERM INFANTS

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Background: Disparities exist in perinatal outcomes and evidence is increasing that differential care provision across population subgroups may in part be responsible. In the Netherlands, when delivery is imminent at 24–25 weeks of gestation, a decision whether or not to offer active neonatal care is made in agreement with parents following counselling. We investigated the relationship between maternal migration background and admissions to and mortality within NICUs at the edge of viability.

Methods: National population-based study using individually-linked data of births in the Netherlands with household-level income tax records and municipality and mortality registers. The primary study population consisted of livebirths (2010–2017) between 24 + 0 weeks and 25 + 6 weeks of gestation. We explored the link between maternal migration background (i.e., first-or-second-generation migrant mother) and admissions to NICUs and mortality within the first week, month, and year of life. We estimated logistic regressions adjusted for year of birth, maternal age, parity, household income, sex, gestational age, multiple birth, and small-for-gestational age. We included unit-specific fixed effects.

Results: Among the 1405 livebirths, 546 (39%) had mothers with maternal migration background. One thousand two hundred and forty-three infants (89%) were admitted to a NICU. Three hundred and sixty-one (26%) of those died within the first week of life, 544 (39%) in the first month, and 652 (46%) in the first year of life. Infants born to first- or second-generation migrant mothers tended to be more likely to be admitted to a NICU (OR 1.37, 95% CI 0.93–2.04). In the fully adjusted model, infants born to migrant mothers had lower odds of mortality within the first week (OR 0.77, 95% CI 0.54–1.09), first month (OR 0.71, 95% CI 0.53–0.95), and first year of life (OR 0.69, 95% CI 0.52–0.91). Findings were robust in sensitivity analyses. These disparities were not observed for babies born at 26–27 weeks of gestation (Table 1).

Conclusion: Infants born to migrant mothers at the edge of viability had lower odds of mortality within the first year of life. This is unlikely to be explained by differences in care across NICUs. Further research is needed to understand the underlying mechanisms driving these disparities, including

	Model 1	Model 2	Model 3
NICU admissions (N=1,405)	1.22 [0.86,1.73]	1.47 [1.00,2.14]	1.37 [0.93,2.04]
First-week mortality (N=1,243)	0.69 [0.51,0.94]	0.66 [0.47,0.92]	0.77 [0.54,1.09]
First-month mortality (N=1,243)	0.76 [0.60,0.98]	0.66 [0.50,0.88]	0.71 [0.53,0.95]
First-year mortality (N=1,243)	0.76 [0.60,0.96]	0.63 [0.48,0.82]	0.69 [0.52,0.91]

Odds ratio of first-or-second generation migration background. Reference category = no migration background. 95% confidence intervals in brackets.
Model 1: unadjusted model including time trends.
Model 2: adjusted for potential confounders - sex, gestational age, multiple births, SGA, congenital anomalies, parity, maternal age at birth, and household income quintile.
Model 3: adjusted for potential confounders and including consortia fixed effects.

Table 1 Association between migration background and NICU admissions and mortality

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differential parental preferences for active care of extremely preterm infants.

Conflict of interest: None declared.

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A GLOBAL SURVEY ON NEONATAL SEDATION AND ANALGESIA: IMPACT OF THE SOCIO-DEMOGRAPHIC INDEX (SDI)

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	Low & Low-Middle		Middle		Middle-High		High		p-value
Written guideline for analgesia and sedation in NICU:									
- Yes	35 (44.9)		95 (45.5)		226 (66.5)		230 (66.5)		
- No	43 (55.1)		114 (54.5)		114 (33.5)		116 (33.5)		< 0.001*
Adherence to analgesia and sedation guidelines:									
- Very low (< 20%)	11 (22.4)		28 (22.6)		21 (8.5)		11 (4.5)		
- Low (20-50%)	10 (20.4)		33 (26.6)		58 (23.6)		46 (18.7)		
- High (50-80%)	20 (40.8)		46 (37.1)		110 (44.7)		110 (44.7)		
- Very high (> 80%)	8 (16.3)		17 (13.7)		57 (23.2)		79 (32.1)		< 0.001*
Use of scales to measure pain in sick neonates:									
- Very low (< 20%)	45 (59.2)		80 (39.2)		83 (24.6)		49 (14.3)		
- Low (20-50%)	15 (19.7)		57 (27.9)		69 (20.4)		47 (13.7)		
- High (50-80%)	9 (11.8)		37 (18.1)		84 (24.9)		78 (22.7)		
- Very high (> 80%)	7 (9.2)		30 (14.7)		102 (30.2)		169 (49.3)		< 0.001*
Who is responsible for applying pain scales in your NICU:									
- Nurses	19 (26.8)		64 (32.8)		152 (46.3)		271 (80.9)		
- Doctors	24 (33.8)		44 (22.6)		37 (11.3)		4 (1.2)		
- Both	28 (39.4)		87 (44.6)		139 (42.4)		60 (17.9)		< 0.001*
Medical staff paying attention to scales when measured by nurses:									
- Very low (< 20%)	30 (44.1)		52 (28)		49 (15.9)		38 (11.4)		
- Low (20-50%)	12 (17.6)		66 (35.5)		87 (28.2)		82 (24.6)		
- High (50-80%)	17 (25)		45 (24.2)		103 (33.4)		121 (36.2)		
- Very high (> 80%)	9 (13.2)		23 (12.4)		69 (22.4)		93 (37.8)		< 0.001*
Pain scales used in NICU:	Yes	No	Yes	No	Yes	No	Yes	No	
- PIPP/PIPP-R	31 (39.7)	47 (60.3)	57 (27.3)	152 (72.7)	136 (39.6)	205 (60.1)	78 (22.4)	270 (77.6)	< 0.001*
- NPASS	14 (17.9)	64 (82.1)	48 (23)	161 (77.0)	103 (30.2)	238 (69.8)	124 (35.6)	224 (64.4)	0.001*
- NIPS	16 (20.5)	62 (79.5)	77 (36.8)	136 (65.1)	103 (30.2)	238 (69.8)	61 (17.5)	287 (82.5)	< 0.001*
- CRIES	30 (38.5)	48 (61.5)	73 (34.9)	187 (89.5)	94 (27.6)	247 (72.4)	16 (4.6)	332 (95.4)	< 0.001*
- CONFORT	11 (14.1)	67 (85.9)	22 (10.5)		63 (18.5)	278 (81.5)	78 (22.4)	270 (77.6)	0.004*
Use of analgosedation in neonatal procedures:	Yes	No	Yes	No	Yes	No	Yes	No	
- Mechanical ventilation	49 (62.8)	29 (37.2)	129 (61.7)	80 (38.3)	245 (71.8)	96 (28.2)	196 (56.3)	152 (43.7)	< 0.001*
- Brief respiratory techniques (BRT)	49 (62.8)	29 (37.2)	114 (54.5)	95 (45.5)	256 (75.1)	85 (24.9)	307 (88.2)	41 (11.8)	< 0.001*
- Vascular access techniques (VAT)	31 (39.7)	47 (60.3)	117 (56.0)	92 (44.0)	224 (65.7)	117 (34.3)	167 (48.0)	181 (52.0)	< 0.001*
- Surgical techniques (ST)	65 (83.3)	13 (16.3)	196 (93.8)	13 (6.2)	316 (92.7)	25 (7.3)	325 (93.4)	23 (6.6)	0.017*
- Hypothermia	13 (16.7)	65 (83.3)	72 (34.4)	137 (65.6)	230 (67.4)	111 (32.6)	240 (69)	108 (31)	< 0.001*
- Other techniques (OT)	40 (51.3)	38 (48.7)	105 (50.2)	104 (49.8)	213 (62.5)	128 (37.5)	179 (51.4)	169 (48.6)	0.008*
Premedication used for neonatal intubation:									
- Very low (< 20%)	34 (45.9)		102 (50.2)		93 (28.0)		49 (14.4)		
- Low (20-50%)	16 (21.6)		36 (17.7)		70 (21.1)		28 (8.2)		
- High (50-80%)	16 (21.6)		25 (12.3)		61 (18.4)		59 (17.4)		
- Very high (> 80%)	8 (10)		40 (19.7)		108 (32.5)		204 (60.0)		< 0.001*
Combination of medication used for neonatal intubation:	Yes	No	Yes	No	Yes	No	Yes	No	
- Opioid analgesia (OA)	54 (69.2)	24 (30.8)	151 (72.2)	58 (27.8)	294 (86.2)	47 (13.8)	268 (77)	80 (23.0)	< 0.001*
- Non opioid analgesia (NOA)	13 (16.7)	65 (83.3)	22 (10.5)	187 (89.5)	13 (3.8)	328 (96.2)	73 (21)	275 (79.0)	< 0.001*
- Hypnotic (HY)	38 (48.7)	40 (51.3)	96 (45.9)	113 (54.1)	160 (46.9)	181 (53.1)	73 (21.0)	275 (79.0)	< 0.001*
- Anesthetic (AN)	14 (17.9)	64 (82.19	16 (7.7)	193 (92.3)	49 (14.4)	292 (85.6)	106 (30.5)	242 (69.5)	< 0.001*
- Muscle relaxants (MR)	15 (19.2)	63 (80.8)	26 (12.4)	183 (87.6)	69 (20.2)	272 (79.8)	161 (46.3)	187 (53.7)	< 0.001*
- Atropine	23 (29.5)	55 (70.5)	36 (17.2)	173 (82.8)	102 (29.9)	239 (70.1)	204 (58.6)	144 (41.4)	< 0.001*
Sedoanalgesia for preterm used during mechanical ventilation:									
- Very low (< 20%)	39 (52.7)		92 (44.7)		99 (29.4)		119 (34.9)		
- Low (20-50%)	13 (17.6)		54 (26.2)		92 (27.3)		99 (29.0)		
- High (50-80%)	12 (16.2)		34 (16.5)		66 (19.6)		69 (20.2)		
- Very high (> 80%)	10 (13.5)		26 (12.6)		80 (23.7)		54 (15.8)		< 0.001*
Combination of medication for neonatal intubation:	Yes	No	Yes	No	Yes	No	Yes	No	
- Opioid analgesia (OA)	62 (70.5)	16 (20.5)	182 (87.1)	27 (12.9)	318 (93.3)	23 (6.7)	320 (92.0)	28 (8.0)	0.001*
- Non opioid analgesia (NOA)	26 (33.3)	52 (66.7)	56 (26.8)	153 (73.2)	64 (18.8)	277 (81.2)	83 (23.9)	265 (76.1)	0.021*
- Hypnotic (HY)	32 (41.0)	46 (59.0)	127 (60.8)	82 (39.2)	163 (47.8)	178 (52.2)	149 (42.8)	199 (57.2)	< 0.001*
- Anesthetic (AN)	5 (6.4)	73 (93.6)	9 (4.3)	200 (95.7)	15 (4.4)	326 (95.6)	44 (4.5)	333 (95.7)	0.869
- Muscle relaxants (MR)	12 (5.4)	66 (84.6)	7 (3.3)	202 (96.7)	19 (5.6)	322 (94.4)	25 (7.2)	323 (92.8)	0.002*
Way of administration of analgosedation for preterm babies:	Yes	No	Yes	No	Yes	No	Yes	No	
- Continuous infusion	34 (43.6)	44 (56.4)	91 (43.5)	118 (56.5)	135 (39.6)	209 (60.1)	139 (39.9)	209 (60.1)	0.750
- Bolus	34 (43.6)	44 (56.4)	66 (31.6)	143 (68.4)	70 (20.5)	271 (79.5)	108 (31.0)	240 (69.0)	< 0.001*
- Continuous infusion & bolus as rescue	23 (29.5)	55 (70.5)	84 (40.2)	125 (59.8)	189 (55.4)	152 (44.6)	217 (62.4)	131 (37.6)	< 0.001*
- Bolus followed by continuous infusion	13 (16.7)	65 (83.3)	62 (29.7)	147 (70.3)	75 (22)	266 (78)	128 (36.8)	220 (63.2)	< 0.001*
Way of administration of relaxants for preterm babies:	Yes	No	Yes	No	Yes	No	Yes	No	
- Continuous infusion	9 (11.5)	69 (88.5)	38 (18.2)	171 (81.8)	44 (12.9)	297 (87.1)	71 (20.4)	277 (79.6)	0.032*
- Bolus	19 (24.4)	59 (75.6)	50 (23.9)	159 (76.1)	110 (32.3)	231 (67.7)	151 (43.4)	197 (56.6)	<0.001*
- Continuous infusion & bolus as rescue	7 (9.0)	71 (91.0)	16 (7.7)	193 (92.3)	35 (10.3)	306 (89.7)	44 (12.6)	304 (87.4)	0.292
- Bolus followed by continuous infusion	5 (6.4)	73 (93.6)	15 (7.2)	194 (92.8)	18 (5.3)	323 (94.7)	56 (16.1)	292 (83.9)	<0.001*
- Never use muscle relaxants	40 (51.3)	38 (48.7)	102 (48.8)	107 (51.2)	158 (46.3)	183 (53.7)	92 (26.4)	256 (73.6)	<0.001*
Use of sedoanalgesia for term during mechanical ventilation:									
- Very low (< 20%)	32 (43.2)		74 (35.9)		54 (16.0)		64 (18.9)		
- Low (20-50%)	13 (17.6)		56 (27.2)		66 (19.6)		78 (23.0)		
- High (50-80%)	13 (17.6)		38 (18.4)		86 (25.5)		84 (24.8)		
- Very high (> 80%)	16 (21.6)		38 (18.4)		131 (38.9)		113 (33.3)		< 0.001*
Combination of medication for terms during mechanical ventilation:	Yes	No	Yes	No	Yes	No	Yes	No	
- Opioid analgesia (OA)	62 (79.5)	16 (20.5)	184 (88.0)	25 (12.0)	325 (5.3)	16 (4.7)	330 (94.8)	18 (5.2)	< 0.001*
- Non opioid analgesia (NOA)	18 (23.1)	60 (76.9)	52 (24.9)	157 (75.1)	66 (19.4)	275 (80.6)	85 (24.4)	263 (75.6)	0.342
- Hypnotic (HY)	47 (60.3)	31 (39.7)	148 (70.8)	61 (29.2)	237 (69.5)	104 (30.5)	230 (66.1)	118 (33.9)	0.281
- Anesthetic (AN)	4 (5.1)	74 (94.9)	18 (7.7)	193 (92.3)	29 (8.5)	312 (91.5)	32 (9.2)	316 (90.8)	0.675
- Muscle relaxants (MR)	18 (23.1)	60 (76.9)	7 (3.3)	202 (96.7)	40 (11.7)	301 (88.3)	60 (17.2)	288 (82.8)	< 0.001*
Way of administration of analgosedation for tem babies:	Yes	No	Yes	No	Yes	No	Yes	No	
- Continuous infusion	30 (38.5)	48 (61.5)	86 (41.4)	123 (58.9)	125 (36.7)	216 (63.3)	137 (39.4)	211 (60.6)	0.754
- Bolus	33 (42.3)	45 (57.7)	54 (25.8)	155 (74.2)	67 (19.6)	274 (80.4)	110 (31.6)	238 (68.4)	< 0.001*
- Continuous infusion & bolus as rescue	23 (29.5)	55 (70.5)	90 (43.1)	119 (56.9)	190 (55.7)	151 (44.3)	209 (60.1)	139 (39.9)	< 0.001*
- Bolus followed by continuous infusion	18 (23.1)	60 (76.9)	57 (27.3)	152 (72.7)	86 (25.2)	255 (74.8)	142 (40.8)	206 (59.2)	< 0.001*
Way of administration of muscle relaxants for term babies:	Yes	No	Yes	No	Yes	No	Yes	No	
- Continuous infusion	7 (9.0)	71 (91.0)	47 (22.5)	162 (77.5)	49 (14.4)	292 (85.6)	85 (24.4)	263 (75.6)	< 0.001*
- Bolus	27 (34.6)	51 (65.4)	68 (32.5)	141 (67.5)	125 (36.7)	216 (63.3)	162 (46.6)	186 (53.4)	0.004*
- Continuous infusion & bolus as rescue	7 (9.0)	71 (91.0)	14 (6.7)	195 (93.3)	39 (11.4)	302 (88.6)	59 (17.0)	289 (83.0)	0.003*
- Bolus followed by continuous infusion	11 (14.1)	67 (85.9)	23 (11.0)	186 (89.0)	38 (11.1)	303 (88.9)	70 (20.1)	278 (79.9)	0.003*
- Never use muscle relaxants	32 (41.0)	46 (59.0)	73 (34.9)	136 (65.1)	116 (34.0)	225 (66.0)	64 (18.4)	284 (81.6)	< 0.001*
Combination of medication for asphyxiated neonates undergoing hypothermia:	Yes	No	Yes	No	Yes	No	Yes	No	
- Opioid analgesia (OA)	55 (70.5)	23 (29.5)	154 (73.7)	55 (26.3)	294 (86.2)	47 (13.8)	303 (87.1)	45 (12.9)	< 0.001*
- Non opioid analgesia (NOA)	11 (14.1)	67 (85.9)	20 (9.6)	189 (90.4)	28 (8.2)	313 (91.8)	33 (9.5)	315 (90.5)	0.459
- Hypnotic (HY)	25 (32.1)	53 (67.9)	66 (31.6)	143 (68.4)	110 (32.2)	231 (67.6)	121 (34.8)	227 (65.2)	0.849
- Anesthetic (AN)	1 (1.3)	77 (98.7)	3 (1.4)	206 (98.6)	5 (1.5)	336 (98.5)	5 (1.4)	343 (98.6)	^NS
Use of local analgesia to perform lumbar puncture:									
- Very low (< 20%)	53 (72.6)		138 (69.3)		149 (45.3)		171 (50.3)		
- Low (20-50%)	9 (12.3)		22 (11.1)		36 (10.9)		23 (6.8)		
- High (50-80%)	4 (5.3)		17 (8,5)		37 (11.2)		34 (10.0)		
- Very high (> 80%)	7 (9.6)		22 (11.1)		107 (32.5)		112 (32.9)		< 0.001*
Medication used for local analgesia in lumbar puncture:									
- EMLA	26 (39.4)		59 (33.7)		239 (78.4)		210 (73.2)		
- Tetracaine gel	40 (60.6)		107 (61.1)		61 (20.0)		74 (25.8)		
- Lidocaine	0 (0.0)		9 (5.1)		5 (1.6)		3 (1.0)		< 0.001*

PIPP: Premature Infant Pain Profile; PIPP- R: Premature Infant Pain Profile-Revised; N-PASS: Neonatal Pain Agitation and Sedation Scale; NIPS: Neonatal Infant Pain Scale; CRIES: Crying, Requires Oxygen Saturation, Increased Vital Signs, Expression, Sleeplessness; NFCS: Neonatal Facial Coding System; NFCS-R: Neonatal Facial Coding System-Revised; DAN: Douleur Aigué Nouveau-né scale; BIPP: Behavioral Infant Pain Profile; COMFORTneo: Comfort neo scale. BPN: Bernese Pain Scale Neonates; EDIN: Échelle Douleur Inconfort Nouveau-Né, neonatal pain, and discomfort scale; BRT: Brief respiratory techniques (intubation; surfactant administration by minimally invasive techniques); VAT: Vascular access techniques (peripheral cannular insertion, central long lines insertion, heel prick, skin-breaking procedures [phlebotomy, intramuscular and subcutaneous injection]); ST: Surgical Techniques (abdominal tube insertion, suprapubic puncture or catheter insertion, pelvis catheter insertion or nephrostomy, cerebral ventricular puncture, pericardial puncture, bone marrow puncture, post-surgical pain management); AO: Opioid analgesia (morphine, fentanyl, remifentanyl); HY: Hypnotics (midazolam, dexmedetomidine); AN: Anesthetics (ketamine, propofol); MR: Muscle relaxants (cisatracurium, pancuronium, rocuronium, vecuronium, succinyl-choline); NOA: Non-opioid analgesics (paracetamol). ^NS: No significant.

Table 1 This table represents the responses to our questionnaire in the form of frequencies and percentages (in brackets), distributed in columns according to the socio-demographic index

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Background: Use of sedation and analgesia drugs in neonates varies in routine clinical practice between NICUs. Differences are focused on the indication for use, dosages, ways of administration, availability of clinical guidelines for pain management, and adherence to them. Commonly these drugs are used 'off label' since most of them have not been approved for the neonatal period, and even long-term adverse effects have been described. The aim of this survey was to describe the use and management of sedation and analgesia in newborns admitted to NICUs globally, and find differences based on a socio-demographic index (SDI).

Methods: A questionnaire with 28 questions was developed following the modified-Delphi technique. Survey circulated through professional societies and neonatal work groups. To establish the impact of the country's socio-demographic level on analgesia and sedation practices, we used the SDI. SDI is constructed based on the geometric mean of three indicators: income *per capita*, average years of schooling among people aged 15 years or older, and the total fertility rate. SDI values are scaled from 0 (highest fertility, lowest income, and lowest education) to 1 (highest income, highest education, and lowest fertility).

Results: From May to November 2022, 1305 responses from all continents were obtained. After depuration of the database, 976 were analysed. 60.2% of those surveyed reported having an analgosedation guideline in their unit. Adherence to them was high or very high (67.4%). NICUs with the capacity to treat neonates less than 28 weeks had guidelines more significantly ($P < 0.05$), although this fact had no impact on adherence to them ($P = 0.310$). Procedures in which sedation and analgesia were more frequently used were insertion of a chest tube (81.3%), post-surgical management (76.1%), endotracheal intubation (73.4%), and mechanical ventilation (63.4%). SDI had a significant impact on most neonatal pain management variables (Table 1).

Conclusions: There is variability in the use of sedative and analgesic drugs in the NICU globally, so efforts must be made to promote practice with less variability and based on clinical evidence. Global socio-demographic differences have significant impact on how pain is managed in neonates.

Conflict of interest: None declared.

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NEWBORN'S NEURAL REPRESENTATION OF INSTRUMENTAL AND VOCAL MUSIC AS REVEALED BY fMRI: A DYNAMIC EFFECTIVE BRAIN CONNECTIVITY STUDY

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Background: Music is ubiquitous, both in its instrumental or vocal forms. The ontogeny of instrument and voice neural representation has yet to be defined.

Aim: To assess the origins of the ability to discriminate instrumental or vocal melodies, 45 newborns were scanned using functional magnetic resonance imaging while listening to a melody played by a musical instrument, a flute or sang by a female voice.

Methods: To investigate the dynamic task-based effective connectivity, we employed a psychophysiological interaction of co-activation patterns (PPI-CAPs) analysis, using the auditory cortices as seed region, to investigate moment-to-moment changes in task-driven modulation of cortical activity during an fMRI task.

Results: Our findings revealed unique, condition-specific, dynamically occurring patterns of co-activation (PPI-CAPs). During vocal condition, auditory cortex co-activated with sensorimotor and salience network, while during instrumental condition, it co-activated with visual and superior frontal cortex. In line with adult studies, the vocal condition was recognised as relevant stimulus (salience activation) in CAP1, it induced somatomotor network activations, evoking motor responses. In CAP2 a cognitively oriented network with temporal pole activation rTPG, while the instrumental condition activated (CAP3/4) visual imaginary and mind wandering networks. Common neural signatures for vocal and instrumental melodies were found in the precuneus and posterior cingulate gyrus, indicating a perceived musicality of the sound stimuli.

Conclusions: This study adds knowledge on the dynamic brain connectivity underlying the newborns capability of early and specialised auditory processing, highlighting the relevance of dynamic approaches to study brain function in newborn populations.

Conflict of interest: None declared.

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EFFECT OF SUPPLEMENTAL DONOR HUMAN MILK COMPARED TO PRETERM FORMULA ON NEURODEVELOPMENT OF VERY LOW BIRTHWEIGHT INFANTS: 5.5-YEAR FOLLOW-UP OF A RANDOMISED CLINICAL TRIAL

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Background: Use of supplemental pasteurised donor human milk (PDHM), when maternal milk is unavailable, reduces the risk of necrotizing enterocolitis versus preterm formula (PTF) among very low birthweight (VLBW, <1500 g) infants. In the Donor Milk for Improved Neurodevelopmental Outcomes trial, we reported more VLBW infants supplemented with PDHM compared to PTF had a 18 month cognitive score indicative of neuroimpairment (*JAMA* 2016; 316(18):1897–1905). This study reports the impact of supplement-type on neurodevelopment at school entry.

Methods: VLBW infants were fed either PDHM or PTF for 90 days or to discharge, whenever maternal milk was unavailable. The primary outcome was the Full Scale IQ (FSIQ) on the Wechsler Pre-school and Primary Scale of Intelligence (WPPSI-IV) at 5.5 years. Secondary outcomes included WPPSI-IV subscales. In exploratory analyses, executive function was assessed using the NEPSY-II and BRIEF.

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Results: Of 316 infants (363 enrolled, 37 died, 10 withdrawn), 158 children participated in this follow-up study ($n = 80$ PDHM, $n = 78$ PTF). Mean birthweight and gestation in the follow-up study was 1013 (SD, 264) g and 27.8 (2.5) weeks, and 53% were male. Twenty-six (33%) children in the PDHM group and 21 (27%) in the PTF group received only mother's milk. Median (IQR) %total feeds as maternal milk was 69% (30%, 95%) in the PDHM group and 70% (11%, 96%) in the PTF group. As randomised, mean WPPSI-IV FSIQ scores were 91.2 and 98.3 in the PDHM and PTF groups, respectively (fully adjusted effect: −7.2 (95% CI: −13.0, −1.5); $P = 0.01$). No statistically significant differences were found in executive function. In three-way analysis where children fed exclusively mother's milk were considered separately, differences in mean WIPPSI-IV FSIQ scores between PDHM (90.8, 95% CI: 85.6, 96.1) and PTF (97.1, 95% CI: 91.5, 102.8) groups were no longer statistically significant; neither were other measures of neurodevelopment.

Conclusion: Use of supplemental PDHM compared with PTF during hospitalisation did not improve neurodevelopment. Notably, NICU care, including PDHM processing optimization has evolved significantly since the original trial. Strategies to promote mother's milk feeding, and improve processing of PDHM to retain important nutrients and bioactive components continue to be urgently required.

Grants: Funding provided by the Canadian Institutes of Health Research. SU is the medical director of the Rogers Hixon Ontario Human Milk Bank and DO serves on its advisory committee.

637 (EXPECTING)
SAFETY AND EFFICACY OF HIGH DOSES NEBULIZED SALBUTAMOL COMPARED WITH PLACEBO ON TRANSIENT TACHYPNOEA OF THE NEWBORNS (TTN): A TRIPLE BLIND PHASE II/III PARALLEL RANDOMISED CONTROLLED TRIAL

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Objective: To evaluate the safety and efficacy of nebulized salbutamol in 2.5 and 1.25 doses on transient tachypnoea of the newborn (TTN) compared to the placebo.

Design: Triple blind phase II/III parallel randomised controlled trial. Registered as: IRCT20190328043133N1.

Setting: Two university-affiliated hospitals with neonatal intensive care units (nICU).

Participants: Newborns with a confirmed diagnosis of TTN, with gestational age >35 weeks and gestational weight >2 kg. Cases of asphyxia, meconium aspiration and persistent pulmonary hypertension (PPHN) were excluded.

Methods: Ninety eligible patients were randomly allocated in three intervention groups (2.5 mg salbutamol, 1.25 salbutamol and placebo), and a single dose nebulized product was prescribed 6 h after the birth. Safety outcomes included post-intervention tachycardia, hyperglycaemia, hypokalaemia and changes in blood pressure measured. To evaluate the efficacy, the duration of post-intervention tachypnoea, TTN clinical score and clinical and para-clinical respiratory indices were assessed. Parents, outcome assessors and data analyser were blind to the intervention.

Results: There was no adverse reaction, including tachycardia, hypokalaemia and jitteriness. Both groups of salbutamol recipients showed significant improvement regarding respiratory rate, TTN clinical score and oxygenation indices compared to the placebo (P-values <0.001). Non-statistically significant higher hospital stay was observed in the placebo group. Single 2.5 mg salbutamol nebulization showed a little better outcomes than the dose of 1.25, although we could not find statistical superiority.

Conclusion: The newly-applied single high-dose of 2.5 mg nebulized salbutamol is safe in treating TTN and leads to notable faster improvement of respiratory status without any considerable adverse reaction.

Keywords: Respiratory outcomes, safety outcomes, salbutamol, tachypnoea, transient tachypnoea of the newborn.

Conflict of interest: None declared.

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MATURATIONAL TRENDS OF NEONATAL SLEEP OBTAINED BY FULLY AUTOMATED SLEEP ANALYSIS

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Background: The physiological importance of coherent sleep for our health and wellbeing cannot be overemphasised. Understanding the contextual framework of neonatal sleep in the organisation of brain networks carries clinical potential. These neonatal sleep patterns have been described based on visual scoring. This study aims to describe normative results of neonatal sleep using a fully automated sleep staging.

Method: In 79 preterm infants (GA 23 6/7–33 6/7 weeks), multichannel-EEG was performed between 36 and 45 4/7 weeks PMA. All infants have a normal BSID-III score at 24 months. Polysomnography was performed overnight (mean duration of 16 h (±2 h)). This sleep staging algorithm consists of five sequential steps: artefact detection, data cleaning, sleep state classification, reliability analysis and hypnogram construction. The sleep staging step classifies each 30-segment as one of four sleep states: LVI, ASI, QS-HVS or QS-TA. The reliability step checks whether predictions are reliable by identifying artefacts and uncertain predictions. Ultimately, during hypnogram construction, each 30-s segment is labelled as LVI, ASI, QS-HVS, QS-TA, Artefact, Uncertain or Transitional Sleep (TS).

Results: In all age groups (36–37, 38–39, 40+ PMA weeks), approximately two thirds of the recording are labelled as sleep, the remaining as unreliable due to artefacts or uncertainty. Using Kaplan–Meier Survival curves for sleep bouts per age group and the Cox regression model, a significant affect of PMA on sleep bout duration is found for AS, QS-HVS and QS-TA. The QS-HVS state becomes more dominant, whereas time spent in QS-TA decreases. Sleep cycles last a little less than 1 h, and the sleep time is around 55 min. No differences in duration are found between PMA-age groups. Approximately 60% of a sleep epoch consists of AS and approximately 37% of QS., and 3% is attributed to TS. We observed an increasing percentage of artefacts with PMA, interpreted as a surrogate for movement or awake (Fig. 1).

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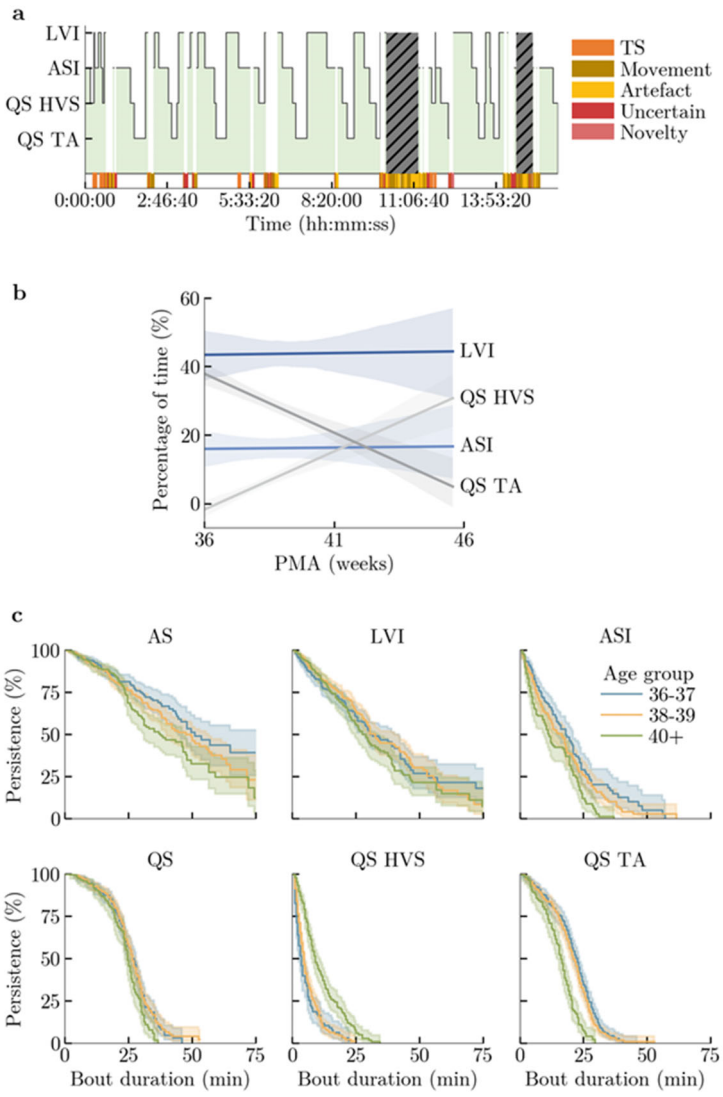


Fig. 1 (a) Hypnogram. (b) Regression lines (95% CI) for the sleep state distributions as function of PMA. (c) Kaplan–Meier curves for the sleep bout durations for each sleep state per age group.

Conclusion: This 'quantitative sleep' modelling approach is congruent with visual scoring in literature. This model can contribute to a pipeline for automated reporting of sleep parameters by mapping datasets from different neonatal cohorts, which offers improved diagnostic characterisation of neonatal sleep–wake architecture.

Conflict of interest: None declared.

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TRENDS IN MORTALITY AND NEUROLOGICAL INJURIES IN VERY PRETERM OUTBORN AND INBORN SURVIVORS CARED FOR IN AUSTRALIAN AND NEW ZEALAND NEONATAL INTENSIVE CARE UNITS: 1995 TO 2019

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Background: Very preterm infants (VPT), born outside (outborn) tertiary centres with on-site neonatal intensive care units (NICUs), are known to have higher rates of mortality and neurodevelopmental impairment than those inborn. This group

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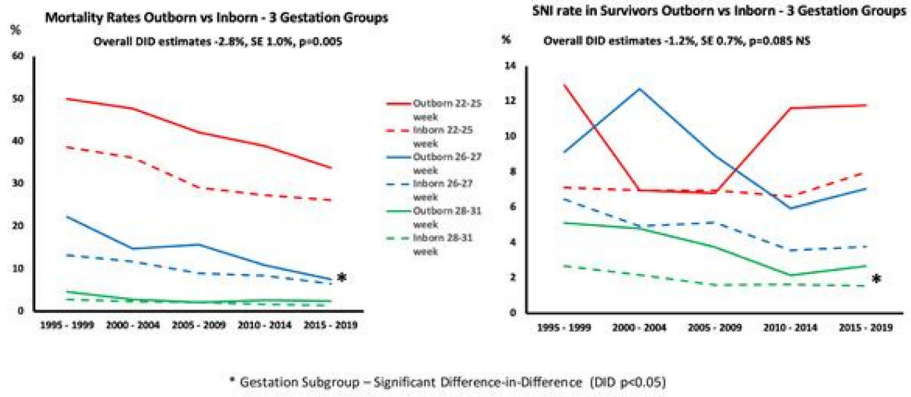


Fig. 1 Variations in mortality and survivor SNI rates for VPT outborn and inborn infants cared for in Australian and New Zealand NICUs 1995–2019.

sought to examine whether contemporary clinical practice and established coordinated regional retrieval services, has improved the outcomes for high-risk outborn infants over the preceding 25 years (1995–2019).

Methods: A retrospective cohort study of the ANZNN NICU population database, for infants born at 22–31 weeks gestational age (GA) and admitted to ANZ tertiary NICUs. Outborn and inborn infants were compared for trends in mortality at discharge and survival with serious neurological injury (SNI; presence of intraventricular haemorrhage grade 3/4 or periventricular leukomalacia) for infants born at 22–25 weeks, 26–27 weeks and 28–31 weeks GA, across five epochs (1995–1999, 2000–2004, 2005–2009, 2010–2014 and 2015–2019).

Results: 9370 (12%) of 78 517 VPT infants, were outborn. The outborn mortality was higher than for inborns (10% vs. 7%, $P < 0.001$); the VPT mortality rate gap narrowed over time from Epoch 1 to Epoch 5 (Epoch-1: 14.1% outborn v 9.8% inborn, $P < 0.001$; Epoch-5: 7.4% v 5.9% respectively, $P < 0.01$). While inborn mortality improved, the Difference-in-difference (DID) analysis showed overall outborn mortality improvement surpass that of inborns (estimate 2.8%, SE 1.0%, $P = 0.005$). Reduction of mortality and SNI rate among survivors of the three gestational age groups varied for both outborn and inborn infants (Fig. 1). Improvements, including fewer SNI outborn survivors, were seen in the higher gestation subgroups. Least favourable outcomes were seen in 22–25 weeks GA outborn infants, having highest mortality rate compared to their inborn counterparts, as well as an increase in SNI survivors.

Conclusion: Survival to discharge increased and SNI among survivors decreased among VPT NICU infants in Australia and New Zealand from 1995 to 2019. Despite improving performance over and above the inborn gains, outborn VPT infants continue to have higher mortality and SNI among survivors than the inborns. Notwithstanding the evolution of regionalised neonatal retrieval services, it remains critical to support optimal maternal transport of pregnancies especially those born at <26 weeks GA to prevent death and neurodevelopmental disability in survivors.

Conflict of interest: None declared.

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CHANGING BURDEN OF SYSTEMIC POST-NATAL CORTICOSTEROIDS USE IN INFANTS BORN BELOW 28 WEEKS OF GESTATION IN ENGLAND AND WALES FROM 2011 TO 2020

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Background: Post-natal corticosteroids (PNCs) are used in premature infants to facilitate extubation and reduce bronchopulmonary dysplasia (BPD). Due to neurotoxicity concerns, their use decreased in the 2000s. Increased exposure (the burden) to PNCs is associated with worse neurodevelopment outcomes. This study aimed to explore changes in the burden of PNCs use across a national population.

Methods: Routinely recorded data were extracted for infants born <28 weeks gestation in England and Wales across two 5-year periods (Epoch 1 = 2011–2015 and Epoch 2 = 2016–2020). Systemic PNCs use was defined as ≥three consecutive days of dexamethasone or methylprednisolone and ≥ seven consecutive days of hydrocortisone use. Cumulative PNCs exposure was the total number of days infants received PNCs divided by the neonatal stay duration. PNCs practices across the two epochs were compared using multivariable regression adjusting for case-mix differences and clustering within units. Cumulative exposure was modelled using generalised linear model with logit function and binomial distribution. Missing data was imputed five times using multivariable imputation by chained equation.

Results: Of the 23 166 infants included, 4400 (19%) infants received PNCs, with 3531 (15%), 1187 (5%) and 28 (0.1%) receiving dexamethasone, hydrocortisone and methylprednisolone respectively. Infants in Epoch 2 were more likely to receive PNCs (aOR 1.50, 95% CI 1.30–1.73) with longer cumulative exposure by 4.5% (95% CI 2.2–6.9) than in Epoch 1. PNCs were commenced 6.3 days earlier in Epoch 2, primarily driven by earlier hydrocortisone use. Dexamethasone use increased by 35% in Epoch 2 and commenced 3.5 days earlier than in Epoch 1. Mortality decreased across the two epochs with increasing BPD and

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Infant characteristics	Epoch 1 (2011 – 2015) (N = 12,045)	Epoch 2 (2016 – 2020) (N = 11,121)	Treatment effect[1] Odds ratio / Marginal effects of the mean (95% CI)	p value
Birth characteristics				
Gestational age at birth	26+1 (24+6 – 27+0)	26+0 (24+5 – 27+1)		
Birthweight	810 (680 – 960)	805 (660 – 960)		
Male sex, n (%)	6,554 (54)	6,026 (54)		
Antenatal corticosteroids use, n (%)	10,550 (88)	10,062 (90)		
Systemic postnatal corticosteroids				
Dexamethasone / hydrocortisone / methylprednisolone use, n (%)	1,936 (16)	2,464 (22)	1.50 (1.30 – 1.73)	<0.001
Age started (day)	27 (18 – 41)	23 (15 – 35)	-6.3 (-9.1 – -3.5)	<0.001
Cumulative exposure (%)	13 (8 – 24)	15 (9 – 30)	4.5 (2.2 – 6.9)	<0.001
Duration of use (day)	14 (9 – 26)	15 (10 – 27)	2.3 (0.3 – 4.3)	0.02
Length of neonatal stay (day)	122 (101 – 146)	117 (97 – 141)	-7.4 (-11.9 – -3.0)	0.001
Dexamethasone				
Dexamethasone use, n (%)	1,613 (13)	1,918 (17)	1.35 (1.22 – 1.50)	<0.001
Age started (day)	28 (19 – 43)	26 (19 – 38)	-3.5 (-5.7 – -1.4)	0.001
Cumulative exposure (%)	11 (7 – 19)	12 (8 – 21)	1.3 (-0.6 – 3.1)	0.2
Duration of use (day)	12 (8 – 22)	13 (9 – 24)	0.3 (-1.6 – 2.3)	0.7
Length of neonatal stay (day)	122 (103 – 147)	121 (102 – 145)	-3.8 (-7.4 – -0.3)	0.04
Hydrocortisone				
Hydrocortisone use, n (%)	410 (3)	777 (7)	2.03 (1.40 – 2.94)	<0.001
Age started (day)	24 (13 – 42)	13 (2 – 35)	-9.4 (-16.4 – -2.4)	0.009
Cumulative exposure (%)	19 (9 – 34)	19 (11 – 47)	6.7 (1.8 – 11.6)	0.007
Duration of use (day)	17 (11 – 31)	14 (10 – 32)	3.4 (-2.0 – 8.8)	0.2
Length of neonatal stay (day)	122.5 (95 – 154)	111 (73 – 142)	-12.4 (-22.1 – -2.7)	0.01
Methylprednisolone				
Methylprednisolone use, n (%)	10 (0.08)	18 (0.2)	1.73 (1.06 – 2.83)	0.03
Age started (day)	151.5 (131 – 166)	119 (94 – 156)	13 (-62 – 88)	0.7
Cumulative exposure (%)	3 (2 – 8)	4 (3 – 5)	-0.9 (-3.6 – 1.7)	0.5
Duration of use (day)	5 (3 – 9)	6.5 (4 – 9)	-2.0 (-10.9 – 7.0)	0.6
Length of neonatal stay (day)	179.5 (167 – 217)	153.5 (135 – 167)	-3.3 (-106.8 – 100.2)	0.9
Outcome				
Death, n (%)	2.727 (23)	2,293 (21)	0.87 (0.81 – 0.94)	<0.001
Bronchopulmonary dysplasia[2], n (%)	6,282 (68)	6,193 (70)	1.16 (1.04 – 1.30)	0.009
Severe Grade 2/3 bronchopulmonary dysplasia[2], n (%)	3,352 (36)	3,541 (40)	1.20 (1.11 – 1.30)	<0.001

Table 1 Comparison of birth characteristics, postnatal corticosteroids usage and outcomes between Epoch 1 (2011 – 2015) and Epoch 2 (2016 – 2020) after adjustment for case-mix and clustering of infants within units. Data presented as median (interquartile range) unless stated otherwise. OR = odds ratio. MEM = marginal effects of the mean.
[1]Epoch 1 (2011 – 2015) was used as a reference for the treatment effect measures of odds ratio for categorical variables and marginal effects of the mean for continuous variables.
[2]Respiratory outcomes were obtained for infants who survived to neonatal discharge. Severe bronchopulmonary dysplasia was defined using the Grade 2 or 3 BPD definition by Jensen et al 2019, which is respiratory pressure support requirement at 36 weeks postmenstrual age.

Table 1 Comparison of birth characteristics, post-natal corticosteroids usage and outcomes between Epoch 1 (2011–2015) and Epoch 2 (2016–2020) after adjustment for case-mix and clustering of infants within units

more severe Grade 2/3 BPD in survivors (Table 1). By 2020, 492/1866 (26%) infants received PNCs with a median (IQR) cumulative exposure of 16.5% (9.7–37.0) and more survivors had BPD (72%) or severe Grade 2/3 BPD (41%).

Conclusion: Extremely preterm infants are exposed to PNCs at an increasingly earlier age and for a longer duration. These trends are associated with increasing survival but worsening respiratory morbidity especially more severe BPD. As survival improves, we need new, targeted approaches to reduce the severity of respiratory disease which has life-long implications in these infants.

Conflict of interest: All authors declare no competing interests. TCK received the Action Medical Research training fellowship, supported by the Albert Gubay Foundation, as part of this study.

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DELAYING THE CLAMPING OF THE CORD USING AN OVINE PRETERM MODEL: WHAT'S THE OPTIMAL DURATION?

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Background: Current guidelines recommend delaying umbilical cord clamping for 30–60 s after birth in vigorous preterm neonates. There is insufficient evidence for optimal cord management in preterm infants needing resuscitation.

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Objectives: To compare effect of early cord clamping ventilation (ECCV) and various time frames of delayed cord clamping ventilation (DCCV) on: (a) primary outcome – (i) combined HR ≥100 bpm & peripheral SpO_2 ≥ 80% by 5 min, (ii) time to achieve primary outcome; (b) secondary outcomes – gas exchange/ haemodynamics.

Methods: Following instrumentation, a total of 21 preterm lambs (126–128d, ~28wk human neonates) were asphyxiated by umbilical cord occlusion to achieve HR < 90 bpm. The lambs randomised: (1) ECCV (Controls): cord clamped immediately and ventilated. (2) DCCV (Study): cord intact while ventilation initiated (2a) DCCV1 – cord clamp@1 min; (2b)DCCV2 – @2 min; (2c) DCCV3 – @3 min; (2d) DCCV5 – @5 min. Initial supplemental oxygen of 60% was used in all groups and titrated based on recommended preductal SpO_2. Data on gas exchange and haemodynamics collected for first 10 min (Fig. 1). All lambs in DCCV5 achieved the primary composite outcome HR of ≥100 bpm and peripheral SpO_2 of ≥80% by 5 min. The time

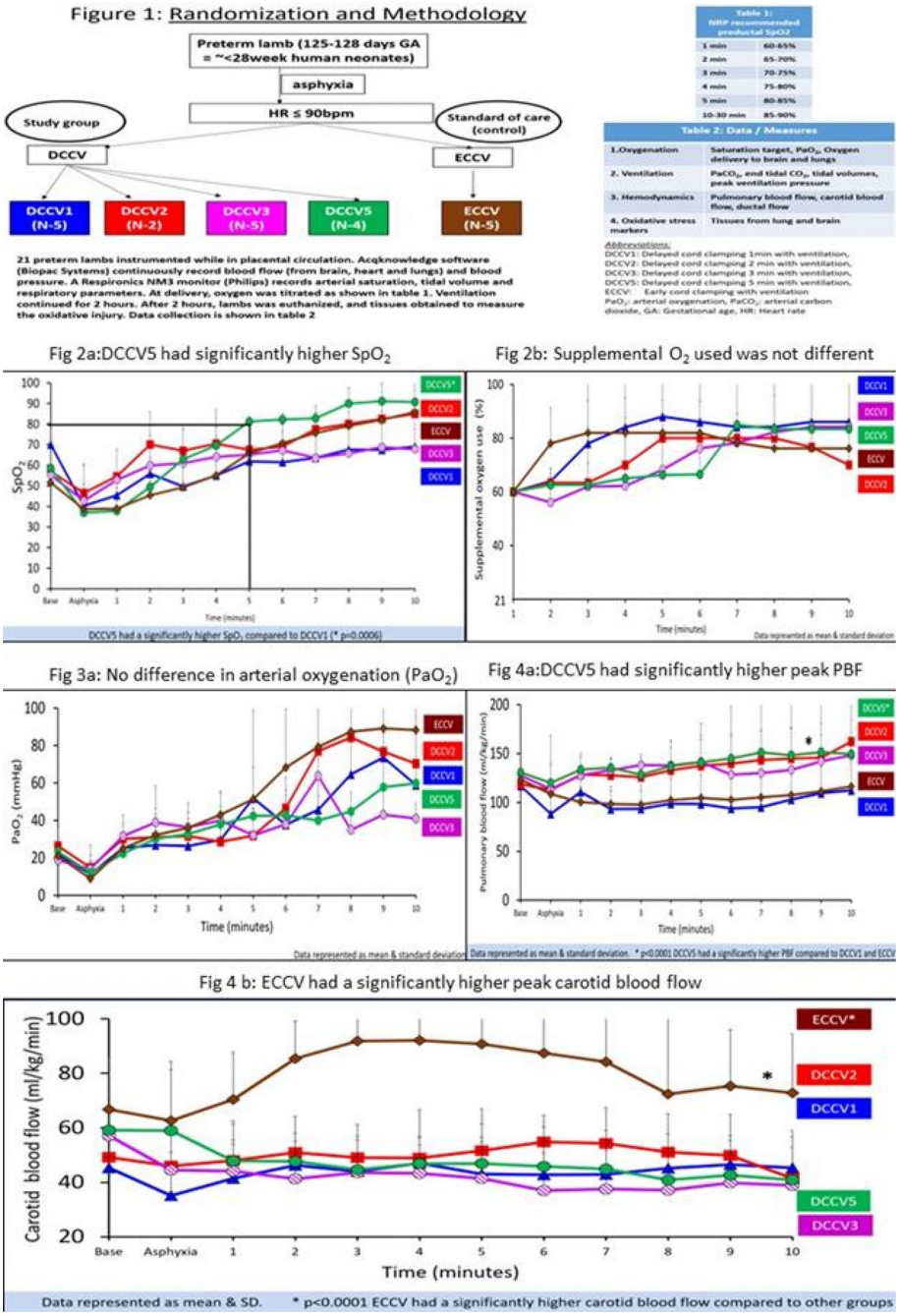


Fig. 1 Randomisation and methodology. **Fig. 2** (a) Peripheral arterial saturation. (b) Supplemental oxygen used between groups. **Fig. 3** Arterial oxygenation between groups. **Fig. 4** (a) Peak pulmonary blood flow between groups. (b) Peak carotid blood flow between groups.

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taken to achieve the primary outcome in DCCV5 (5 ± 0 min) was significantly lower (p-0.003) compared to DCCV1 & ECCV. There was no statistical difference between the groups' supplemental O_2 exposure and arterial oxygenation (Figs 2a,b,3). Arterial pH was not different between groups. Arterial carbon dioxide was significantly higher (p-0.0001) in ECCV & DCCV1 compared to DCCV5. Pulmonary blood flow was significantly higher (p-0.0001) in DCCV5 compared to ECCV & DCCV1(Fig. 4a). Carotid blood flow was highest in the ECCV group and was statistically different ($P < 0.0001$) compared to other groups(Fig. 4b). In an asphyxiated preterm ovine model, resuscitation with an intact cord for 5 min increased the incidence of primary outcome, decreased the time to achieve primary outcome and improved gas exchange by increasing pulmonary blood flow. Our results suggest that resuscitating an asphyxiated preterm infant with an intact cord could help with transition better than ECCV.

Conflict of interest: None declared.

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POST-NATAL DEPRESSION, BONDING AND ATTACHMENT IN PARENTS WHO DID OR DID NOT CUDDLE THEIR INFANTS COOLED FOR HIE

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Background: Children cooled for neonatal hypoxic-ischaemic encephalopathy (HIE) experience cognitive impairments associated with altered brain connectivity. Enhancing parent–infant bonding and addressing parental mood can improve cognitive development. We investigated whether parents cuddling their babies during cooling therapy influenced mother-infant bonding and post-natal depression, and examined post-natal depression and father infant attachment in fathers.

Methods: Two multicentre cohort studies were conducted involving families of infants receiving therapeutic hypothermia for HIE. The CoolCuddle study (October 2019 to November 2020) evaluated cuddling during cooling and intensive care and included 27 families. The CoolBonding study (February to November 2021) recruited families of 48 infants undergoing cooling and intensive care for HIE in England and Wales. Mothers completed the Mother-Infant Bonding Scale (MIBS) and Edinburgh Post-natal Depression Scale (EPDS) at 5–7 days and 8 weeks postpartum. Fathers completed the Paternal Post-natal Attachment Scale (PPAS) at 8 weeks. In the CoolBonding study, fathers also completed EPDS at 5–7 weeks and 8 weeks. Using multiple linear regression, association between the exposure, cuddle during cooling, and MIBS (lower score implies improved bonding), EPDS and breast feeding rates were assessed controlling for date of birth, site, severity of HIE and antidepressants use during pregnancy. Fathers' EPDS scores were compared between discharge and 8 weeks using independent samples t test.

Results: Thirty-five families had cuddle exposure (CoolCuddle: 27; CoolBonding: 8). There were no significant differences in baseline characteristics including gestation, sex, birthweight, Apgar score at 10 min, cord pH and severity of HIE between exposed and non-exposed group. Exposure to cuddle was independently associated with reduced MIBS and EPDS score at 5–7 days postpartum. At 8 weeks, MIBs and maternal EPDS were significantly associated with each other (Table 1). Fathers' EPDS scores significantly decreased by 8 weeks postpartum (5.7 (3.31) vs. 27.2 (2.97), $P < 0.0001$). There was no association between cuddle and PPAS or breast feeding.

Conclusion: Cuddling during cooling therapy for HIE improves mother-infant bonding and post-natal mood. Fathers of infants cooled for HIE exhibit post-natal depression symptoms at discharge, which significantly improves by 8 weeks. Our findings illustrate importance of psychological support for parents of infants undergoing cooling.

Conflict of interest: None declared.

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THE INCIDENCE OF NECROTIZING ENTEROCOLITIS DURING THE COVID-19 PANDEMIC IN SWEDEN: A POPULATION-BASED COHORT STUDY

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Introduction: COVID-19 pandemic has changed routines in neonatal intensive care units (NICUs), mostly by stricter infection

Models	Outcome	Predictors	Regression coefficient	95% CI	P value
1	MIBS at 5-7 days	Cuddle	-2.9	-4.88, -1.05	0.003
2	EPDS at 5-7 days	Cuddle HIE severity	-4.9 2.83	-7.74, -2.07 0.08, 5.59	0.001 0.04
3	MIBS at 8 weeks	MIBS at 5-7 days EPDS at 8 weeks	0.22 0.31	0.01, 0.43 0.18, 0.43	0.04 0.001
4	EPDS at 8 weeks	MIBS at 8 weeks	1.26	0.83, 1.71	0.001

Table 1 Association between Cuddling and MIBS, maternal EPDS at 5–7 days and 8 weeks postpartum. Covariates: date of birth, site, HIE severity, antidepressants during pregnancy. MIBS and EPDS (models 3 and 4)

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	Infants born during Covid-19 pandemic (n=4272)	Infants born before Covid-19 pandemic (n=8967)	P value
C-section, n(%)	2530(59.22)	5053(56.35)	**0.002**
Acute section among sections,n(%)	2376(93.91)	4686 (92.74)	0.056
Ablation, n(%)	377(8.94)	801(9.46)	0.344
*Preeclampsia/eclampsia, n(%)	650(15.42)	1239(14.64)	0.243
*PPROM(<v37) n(%)	715(16.96)	1410(16.66)	0.680
*Chorioamnionitis, n(%)	111(2.63)	213(2.52)	0.700
Gestational diabetes, n(%)	158(3.75)	271(3.20)	0.108
Number of feti 1,singletone 2,twins 3,triples 4,quadruples	 3188(74.63) 1013(23.71) 71(1.66) 0(0.00)	 6634(73.98) 2159(24.08) 170(1.90) 4(0.04)	0.457
*Antenatal steroids, n(%)	2455(69.35)	4951(69.35)	0.847
IUGR, n(%)	474(11.25)	999(11.80)	0.357
Female, n(%)	2001(46.84)	4114(45.88)	0.300
Gestational age, median (IQR)	32.86(30.29-34.14)	32.86(30.14-34.14)	0.925
Infants born <28 weeks,	571(13.37)	1244(13.87)	0.428
Birthweight, median(IQR)	1860(1370-2263)	1865(1335-2260)	0.547
APGAR, median (IQR)	9(8-10)	9(7-10)	0.375
RDS, n(%)	1236(28.93)	2503(27.91)	0.223
IVH Grade 1,n(%) IVH Grade 2, n(%) IVH Grade 3, n(%) IVH Grade 4, n(%)	148(3.77) 61(1.55) 40(1.02) 60(1.53)	263(3.17) 165(1.99) 78(0.94) 99(1.19)	0.085
hsPDA medically treated, n(%)	228(5.34)	516(5.75)	0.330
hsPDA, surgically treated, n(%)	31(0.73)	100(1.12)	**0.034**
Parenteral nutrition, n(%)	1643(38.46)	3368(37.56)	0.318
Days of parenteral nutrition, median(IQR)	7(4-12)	7(4-13)	0.123
Early onset sepsis (positive culture),n(%)	22(0.52)	61(0.68)	0.256
Early onset infection(positive culture)	40(0.94)	86(0.96)	0.889
Late onset sepsis(positive culture), n(%)	137(3.21)	371(4.15)	**0.008**
Late onset infection(positive culture), n(%)	252(5.91)	640(7.17)	**0.007**
NEC, n(%)	61(1.43)	174(1.94)	**0.037**
Surgical NEC verified, n(%)	29(0.68)	66(0.74)	0.715
SIP, n(%)	14(0.33)	39(0.43)	0.361
Probiotics, n(%)	499(11.68)	232(2.59)	**0.000**
Oxygen need at 36 weeks, n(%)	282(6.60)	681(7.59)	**0.040**
Death, n(%)	165(3.86)	336(3.75)	0.745

(*= not complete data, missing data <5%)(PPROM = Premature rupture of membranes, IUGR= Intrauterine growth restriction, RDS= respiratory distress syndrome, IVH= intraventricular hemorrhage, hsPDA= hemodynamically significant patent ductus arteriosus, NE= necrotizing enterocolitis, SIP= spontaneous intestinal perforation)

Table 1 Cohort of preterm newterms (born <35 weeks of gestation) in Sweden 2017–2021

control measures and restricting visitor presence. The effect of the pandemic restrictions in the NICUs has not yet been studied. Necrotizing enterocolitis (NEC) is a disease characterised by intestinal inflammation and bacterial invasion. The objective of this study was to investigate whether the incidence of NEC has changed during the COVID-19 pandemic in Sweden and if it was associated with a change in the frequency of extremely preterm births.

Methods: Data were retrieved from the Swedish Neonatal Quality Register (SNQ) for infants registered from 1 January 2017 to 31 December 2021 born below a gestational age of 35 weeks. The registry completeness is 98%–99%. The diagnosis of NEC was the primary outcome. Generalised linear model were used to calculate the risk ratio for NEC.

Results: A total of 13 239 premature infants born were included in the study. Two hundred and thirty-five (1.8%) infants developed NEC, 91 of which (38% of all NEC cases) required surgical treatment. Eight thousand nine hundred and sixty-seven infants were born before COVID-19 pandemic restrictions and 4272 during. Median gestational age at birth was 32.8 weeks in both periods. Table 1 shows patients characteristics. The incidence of NEC was significantly lower during COVID-19 pandemic compared to the prior period (1.43% vs. 1.94% *P* value 0.037), but not the incidence of surgical NEC (0.89%

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vs. 1.14%, *P* value 0.192). The crude Risk ratio (RR) of developing NEC was (0.74, 95% CI (0.55–0.98), *P* value 0.038), but when adjusted for region, gestational age at birth, probiotics, intra-uterine growth restriction and Chorioamnionitis the RR was 0.80 95% CI (0.60–1.06), *P* value 0.112. The incidence of late onset sepsis with positive culture was also significantly lower during COVID-19 pandemic (3.21% vs. 4.15, *P* value 0.008).

Conclusion: Under the COVID-19 pandemic the incidence of NEC was significantly diminished compared to the previous period despite the same frequency of extremely preterm births. This could partially be explained by the simultaneous introduction of probiotics and the normal variation of NEC over time. The incidence of late onset sepsis was also decreased during the COVID-19 pandemic.

Conflict of interest: None declared.

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SURVIVAL ACCORDING TO SEX AT BIRTH AMONG EXTREMELY PRETERM FETUSES: A PAN-EUROPEAN STUDY FROM THE 'RECAP PRETERM' PLATFORM OF COHORT AND REGISTER DATA

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Background: Many studies show that females born extremely preterm have lower mortality than males. However, results are not completely concordant across studies, and survival differences may have changed over time. Erroneous beliefs about biological differences in survival could be self-perpetuating. We examined the consistency of male–female survival differences among extremely preterm (EP: 22–26 weeks gestational age (GA)) births in relation to survival to hospital discharge across multiple countries and epochs.

Methods: Population-based data from Nordic (Denmark, Finland, Norway and Sweden) Registries spanning 1967–2016 and cohorts (ACTION (Italy, 2003–2005), EPIBEL (Belgium, 1999–2000), EPICE (19 regions in 11 European countries, 2011–2012), EPICure-2 (England, 2006), EPIPAGE-2 (France, 2011), EST0203 (Estonia 2002–2003), EXPRESS (Sweden, 2004–2007), and PIPARI (Finland, 2001–2006)) were analysed using the RECAP Preterm platform (https://platform.recap-preterm.eu) which controls transmission of potentially identifiable data. We used modified Poisson regression models to estimate relative risks (RR) of survival for live births, including adjustment for GA (for cohorts) and GA, year, maternal age and multiple status (for Registries), with sub-analyses of Registry data by epoch (before 1990, 1990–1999, 2000–2016) and by epoch and GA; results were pooled using R package 'metafor'.

Results: 23904 live births were analysed (Registries: 17432; cohorts: 6472); 11 093 (46.4%) were female. Overall, male survival (6354 of 12 811, 49.60%) was lower than for females (6145 of 11 093, 55.40%; unadjusted pooled risk ratio (RR) 0.95, 95% confidence interval (CI) 0.92–0.98, $P < 0.001$; pooled RR adjusted for GA 0.95, 95% CI 0.93–0.98, $P = 0.002$). Fully-adjusted pooled RRs (aRR) for the Register data were 0.94 (95% CI 0.83–1.07, $P = 0.347$) during the first, 0.99 (95% CI 0.98–1.00, $P = 0.035$) during the second and 0.95 (95% CI 0.90–1.00, $P = 0.046$) during the third epoch. No statistically significant differences were seen according to GA other than at 26 weeks' GA in 2000–2016 (pooled aRR 0.98, 95% CI 0.97–0.99) (Table 1).

Time period	23 weeks	24 weeks	25 weeks	26 weeks
Pre-1990	0.94 (0.82 – 1.07)[a]	1.00 (0.87 – 1.15)[a]	0.91 (0.73 – 1.15)[a]	0.99 (0.97 – 1.02)
1990-1999	1.15 (0.88 – 1.51)[a]	0.86 (0.67 – 1.11)[a]	0.99 (0.96 – 1.01)	1.00 (0.99 – 1.01)
2000-2016	0.94 (0.84 – 1.05)[a]	0.98 (0.96 – 1.00)	0.99 (0.98 – 1.00)	0.98 (0.97 – 0.99)

[a] Data from Denmark not available as insufficient numbers of live births.

Table 1 Risk ratios (95% confidence intervals) according to gestational age for male relative to female survival to 6 months from Nordic Registries (Denmark 1978–2016, Finland 1987–2016, Norway 1967–2016 and Sweden 1974–2016)

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Conclusions: More live births were male, but survival to hospital discharge was better for live born females. Although point estimates generally pointed to a female survival advantage, there was evidence of differences according to country and time period. Perceived biological differences may be mediated by social context.

Grants: This is a demonstration project of the RECAP Preterm project which received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733280.

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EFFECT OF KANGAROO CARE IN THE NICU ON PRE-ADOLESCENT OUTCOMES IN GUJARAT, INDIA: 10-YEAR NICU FOLLOW-UP

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Background: Kangaroo care is a lifesaving intervention for neonates in resource-limited settings. Real-world evidence of its efficacy on longitudinal outcomes of growth, cognitive development, morbidity and mortality among an Indian cohort is not well studied.

Methods: This prospective cohort study followed a cohort of children who were hospitalised in a NICU in rural India between 2011 and 2014 with follow-up home visits conducted between 2021 and 2022. Standardised and validated methods were used to measure height, weight, reading ability and mathematics skills in addition to survey-based data collection for demographics, family characteristics and major morbidity history. Data were combined with hospital EMR data from their NICU hospitalisation. This combined dataset was used to calculate propensity scores for receiving kangaroo care and a fragility index to adjust for possible confounding by indication in the NICU setting. Multivariable regression models were used to estimate treatment effects at the time of follow-up.

Results: In total, 442 of the 708 children or their families were recontacted in the follow-up period. Among the living children, those who received kangaroo care were older and more likely to be male ($P < 0.001$). Receiving kangaroo care was associated with decreased odds of mortality, anthropometric failure or cognitive delay (Table 1). Adjustments for baseline fragility or their propensity to receive kangaroo care did not considerably change these associations.

Table 1. Distribution of preadolescent physical growth, cognitive, comorbidity, and Mortality outcomes stratified by Kangaroo Care status in the NICU.

Outcome	Received KC-179	Did Not Receive KC-126	p-value
CIAF			
no	70 (43.21)	38 (31.93)	0.055
yes	92 (56.79)	81 (68.07)	
Can Add			
no	44 (25.0)	43 (34.13)	0.084
yes	132 (75.0)	83 (65.87)	
Read Words			
no	45 (25.57)	44 (34.92)	0.079
yes	131 (74.43)	82 (65.08)	
Cognitive Delay			
no	117 (66.48)	69 (54.76)	**0.039**
yes	59 (33.52)	57 (45.24)	
Comorbidity Composite			
no	143 (79.89)	102 (80.95)	0.818
yes	36 (20.11)	24 (19.05)	
Overall Composite among living			
no	59 (32.96)	23 (18.25)	**0.004**
yes	120 (67.04)	103 (81.75)	
Outcome	**Received KC-204**	**Did Not Receive KC-238**	**p-value**
Died			
no	180 (88.24)	132 (55.46)	**0.000**
yes	24 (11.76)	106 (44.54)	
Overall composite			
no	60 (29.41)	29 (12.78)	**0.000**
yes	144 (70.59)	209 (87.82)	

Table 1 Distribution of preadolescent physical growth, cognitive, comorbidity, and Mortality outcomes stratified by Kangaroo Care Status in the NICU.

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Conclusion: This represents the first longitudinal study of kangaroo care among children in India and found that not only was kangaroo care associated with reduced mortality among high-risk neonates, but those who survived to early childhood also had a lower likelihood of having physical or cognitive deficits.

Conflict of interest: None declared.

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METABOLIC SHIFT OF *BIFIDOBACTERIUM LONGUM* SUBSP. *INFANTIS* IN RESPONSE TO ACID STRESS IS ASSOCIATED WITH FAILURE TO PREVENT SEPSIS IN PRETERM INFANTS

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Background: Early alterations of the gut microbiome are considered as drivers of sepsis risk in preterm infants. *Bifidobacterium longum* (*B. longum*) containing probiotics are frequently supplemented to preterm infants with the aim to restore early microbiome distortions and to prevent adverse outcome. However, the effect of the probiotics on sepsis prevention is inconclusive, and we herein hypothesized that their metabolic features are key modulators of sepsis risk.

Methods: We conducted a prospective longitudinal study in preterm infants during the period of highest vulnerability for late-onset sepsis (LOS; faecal sampling: days 7, 14, and 21 of life). 108 infants received routine supplementation with *B. longum* subspecies infantis plus Lactobacillus acidophilus and were compared to 126 infants who did not receive probiotics. Following metagenomic sequencing and determination of metabolic profiles *via* nuclear magnetic resonance (NMR) spectroscopy, we assessed microbial community function using metabolic network modelling.

Results: Administration of probiotics led to an early colonisation of the probiotic bacteria in the preterm infant gut in line with an increase of faecal concentrations of most metabolites. In our cohort, 70/234 preterm infants developed LOS and had distinct microbiome features preceding sepsis: (i) increased abundance of *Staphylococcus epidermidis* and reduced prevalence of *Veillonella* sp., especially in co-occurrence with *B. longum*, and (ii) increased rates of branched-chain and aromatic amino acids along with decreased rates of acetate and lactate in infants supplemented with probiotics. Our data suggest that *B. longum* switches metabolism as a response to acid stress (low pH) which may be a crucial determinant for the failure to prevent sepsis. These specific features are associated with impaired ecological succession and reduced establishment of secondary fermenting microorganisms.

Conclusions: Further studies are needed to identify the targets for metabolic shifts prior to LOS development in order to optimise probiotic interventions and to facilitate multi-site collaborative efforts to define the patient groups that benefit most.

Conflict of interest: None declared.

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TWO-YEAR OUTCOMES IN A RANDOMISED CONTROLLED TRIAL OF LESS INVASIVE SURFACTANT ADMINISTRATION (LISA) IN PRETERM INFANTS SUPPORTED WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

Peter Dargaville[1,2], Omar Kamlin[3], Francesca Orsini[4], Xiaofang Wang[4], Tony De Paoli[1], Howard Clark[5], Roger Soll[6], Samantha Johnson[7], Jeanie Cheong[3,4], John Carlin[4,8], Peter Davis[3], for the OPTIMIST-A study investigators

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Background: Definitive studies of the longer-term effects of LISA are lacking. We aimed to evaluate, in preterm infants 25–28 weeks' gestation, the effect of LISA on neurodevelopment and respiratory health during the first 2 years of life.

Methods: In this blinded randomised controlled trial (OPTIMIST-A, ACTRN12611000916943), infants supported with CPAP and requiring FiO_2 ≥0.30 before 6 h received LISA (200 mg/kg poractant alfa delivered *via* thin catheter) or sham treatment (control), with continuation of CPAP thereafter unless predefined intubation criteria were met. Beyond the previously reported in-hospital outcomes (JAMA 2021; 326:2478), data were gathered on respiratory health and further hospitalisations in the first 2 years and presence of neurodevelopmental disability (NDD: moderate–severe cognitive or language impairment, cerebral palsy, vision or hearing impairment) at 2 years corrected age (CA). Modes of outcome ascertainment were i) parent-completed online questionnaire including the Parent Report of Children's Abilities – Revised (83%); ii) face-to-face assessment including Bayley III psychometric testing (10%); or iii) abbreviated questionnaire (7%). Primary outcome was the composite of death or NDD. Treatment effects were estimated as relative risk (RR) with 95% confidence interval (CI), adjusted for gestation strata and site clustering.

Results: 485 infants were randomised at 33 sites. Data were available at 2 years CA in 453 infants (LISA: N = 224 (29 deaths <2 years; 195/212 survivors with follow-up data); control: N = 229 (24 deaths; 205/220 survivors with follow-up data)). The treatment groups showed good prognostic balance (Table). Incidence of death or NDD was similar in the two groups, as were the rates of the primary outcome components (death, NDD) (Table 1). There was, however, an important difference favouring the LISA group in need for hospitalisation in the first 2 years for any illness (RR 0.78; 95% CI: 0.66–0.92) and for respiratory illness (RR 0.66; 95% CI: 0.54–0.81), as well as a reduction in wheezing and breathing difficulty, use of bronchodilator therapy and diagnosis of asthma (Table 1).**CONCLUSION:** Application of LISA in the first 6 h may considerably reduce the burden of respiratory illness in the first two years of life, with no effect on neurodevelopmental outcome at 2 years *CA*.

Conflict of interest: Prof. Dargaville received support from Chiesi Farmaceutici (provision of surfactant at reduced cost).

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Table: Baseline variables and outcomes

BASELINE VARIABLES	LISA	Control		
Gestation, weeks	27.3 (26.3–28.1)	27.3 (26.4–28.0)		
Birth weight (g)	932 (780–1065)	905 (777–1070)		
Male sex	116/224 (52%)	109/229 (48%)		
Multiple birth	84/224 (38%)	71/229 (31%)		
Antenatal steroids (any)	204/224 (91%)	210/229 (92%)		
Caesarean delivery	184/224 (82%)	180/229 (79%)		
Apgar score at 5 min	8 (7–9)	8 (7–9)		
Age at randomisation (h)	2.7 (1.6–4.0)	2.6 (1.7–3.6)		
Immunised <2 yrs against: RSV Influenza	119/175 (68%) 91/173 (53%)	128/185 (69%) 104/184 (57%)		
Family history of asthma (in parents or siblings)	50/177 (28%)	53/188 (28%)		
OUTCOMES	**LISA**	**Control**	**Adjusted relative risk (95% CI)**	**P value**
Death or NDD*	78/215 (36.3%)	79/219 (36.1%)	1.00 (0.81 to 1.24)	0.99
Death prior to 2 years CA	29/224 (12.9%)	24/229 (10.5%)	1.23 (0.69 to 2.19)	0.48
NDD in survivors to 2 years CA	49/186 (26.3%)	55/195 (28.2%)	0.94 (0.71 to 1.25)	0.69
Cognitive or language impairment	42/183 (23.0%)	47/195 (24.1%)	0.96 (0.73 to 1.27)	0.77
Cerebral palsy (equivalent to GMFCS level ≥2)	9/195 (4.6%)	15/204 (7.4%)	0.63 (0.36 to 1.11)	0.11
Visual impairment	0/193 (0.0%)	5/204 (2.5%)	Not estimable	-
Hearing impairment	4/194 (2.1%)	4/205 (2.0%)	1.06 (0.31 to 3.61)	0.93
One or more hospitalisation† with any illness in first 2 years	77/194 (39.7%)	104/204 (51.0%)	0.78 (0.66 to 0.92)	0.003
One or more hospitalisation† with respiratory illness in first 2 years	49/195 (25.1%)	78/204 (38.2%)	0.66 (0.54 to 0.81)	<0.001
Parent-reported wheezing/breathing difficulty	73/180 (40.6%)	104/194 (53.6%)	0.76 (0.63 to 0.90)	0.002
Any bronchodilator therapy	57/180 (31.7%)	83/194 (42.8%)	0.74 (0.57 to 0.96)	0.026
Parent report of physician diagnosis of asthma	8/180 (4.4%)	23/194 (11.9%)	0.37 (0.19 to 0.73)	0.004

Table 1 n/N (%) or median (interquartile range). *Primary outcome not determinable for 9 infants (LISA), 10 infants (control). †Excluding birth hospitalisation. GMFCS, gross motor function classification system; RSV, respiratory syncytial virus

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PREDICTORS OF CEREBELLAR HAEMORRHAGE VOLUME AND LOCATION IN PRETERM INFANTS

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Background: Cerebellar haemorrhage (CbH) contributes to motor and cognitive disabilities in preterm infants. Location and size of CbH has been shown to be important for neurodevelopment outcomes. A complicated neonatal course including haemodynamic disturbances may be related to an increased risk for CbH, vermis involvement and larger CbH volumes.

Objective: To define risk factors related to cardiovascular insufficiency in preterm infants for CbH location and volume.

Methods: Early-life and term-equivalent age (TEA) brain MRIs were performed in a prospective cohort of very preterm infants born <32 weeks postmenstrual age (PMA). Presence of CbH (T1, T2 and SWI) was assessed by a paediatric neuroradiologist. A cut-off of 4 mm was used to distinguish punctate versus large haemorrhages. Vermis haemorrhage was noted. CbH volume was measured by manual segmentation using Display software by two trained raters. Hypotension requiring treatment, presence of a PDA requiring treatment, and the SNAPii Score (used to quantify illness severity in first 12 h of life) together with other comorbidities were recorded., Outcome variables for uni- and multivariate regression analyses were presence of CbH, presence of vermis haemorrhage, CbH severity (punctate vs. large), and CbH volume.

Results: A total of 309 very preterm infants (27.6 ± 2.3 week PMA at birth) were included. 60 infants (18.3%) had CbH, classified as punctate in 43 infants (71.3%) and vermis involvement in 14 (23.3%). Median CbH volume was 19 mm3 (range 1-411 mm3). 42 infants with CbH had both early-life and TEA

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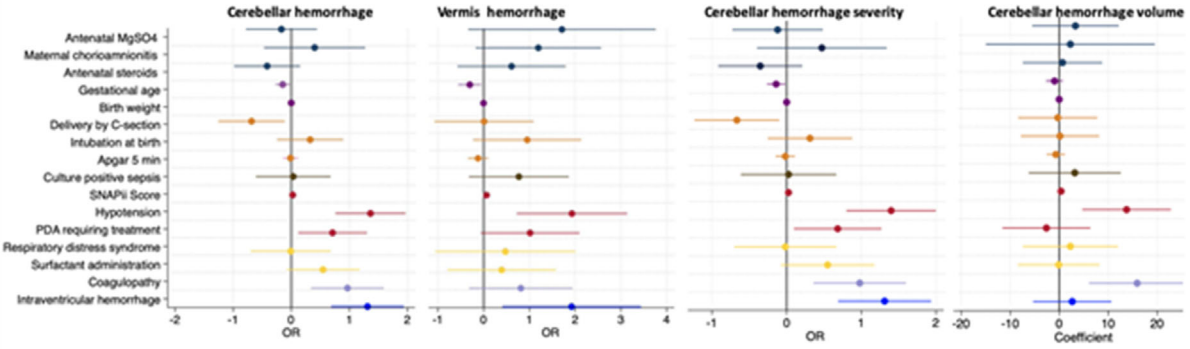


Fig. 1 Univariable regression.

MRI; CbH was not detected on the early-life scan in 4 infants. Univariable regression analyses are presented in Fig. 1. On multivariable regression, hypotension (OR 2.80, 95% CI 1.34–5.84, $P = 0.006$) and IVH (OR 2.36, 95% CI 1.17–4.72, $P = 0.01$) were significantly associated with CbH. Although hypotension was not a significant risk factor for vermis involvement (OR 3.49, 95% CI 0.90–13.48, $P = 0.07$), it was the only independent predictor of larger CbH volumes (4.35 mm3, 95% CI 1.04–7.67, $P = 0.01$).

Conclusion: This study highlights the important role that haemodynamic disturbances play in CbH, with hypotension being an independent risk factor for large CbH. Further investigations are needed regarding risk factors for vermis haemorrhage.

Conflict of interest: None declared.

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ARTERIAL BLOOD PRESSURE AND CEREBRAL OXYGENATION DURING THE IMMEDIATE NEONATAL TRANSITION AFTER BIRTH - A PROSPECTIVE OBSERVATIONAL STUDY

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Background and Aims: The aim of this study was to investigate the influence of arterial blood pressure on cerebral tissue oxygenation index (cTOI) and cerebral fractional tissue oxygen extraction (cFTOE) in preterm and term neonates during the immediate neonatal transition after birth.

Methods: For this purpose, we conducted a prospective observational study. Neonates received oscillometric blood pressure measurements at minutes 5, 10, and 15 after birth , and continuous cTOI monitoring with near-infrared spectroscopy and continuous monitoring of arterial oxygen saturation (SpO2) with pulse oximetry during the first 15 minutes after birth. cFTOE was calculated out of cTOI and SpO2. Preterm neonates receiving respiratory support and term neonates without medical support (control group) were analyzed. cTOI and cFTOE at minutes 5, 10, and 15 were correlated to systolic (SABP), diastolic (DABP), and mean arterial blood pressure (MABP) in both groups.

Results: In the 24 included preterm neonates (gestational age 34.4 weeks (33.7 - 35.1)) requiring respiratory support, cTOI correlated positively with DABP at minute 5 and with MABP and SABP at minute 15. cFTOE correlated negatively with all blood pressure values at minutes 5, 10 and 15. In the 51 included stable term neonates (gestational age 38.7 weeks (38.4 - 39.0)), blood pressure values did not correlate with crSO2 nor cFTOE at any time point (Table1).

Conclusion: In compromised preterm neonates requiring respiratory support, crSO2 and cFTOE were associated with

Table 1)

		5 minutes after birth				10 minutes after birth				15 minutes after birth			
		Term neonates		Preterm neonates		Term neonates		Preterm neonates		Term neonates		Preterm neonates	
		cTOI	cFTOE	cTOI	cFTOE	cTOI	cFTOE	cTOI	cFTOE	cTOI	cFTOE	cTOI	cFTOE
SABP	p	0.79	0.11	0.12	0.01*	0.91	0.27	0.48	0.04*	0.19	0.97	0.04*	0.00***
	r	-0.04	-0.23	0.37	-0.62	0.02	-0.16	0.16	-0.41	0.19	-0.01	0.41	-0.62
MABP	p	0.51	0.35	0.26	0.04*	0.28	0.98	0.22	0.04*	0.74	0.34	0.05*	0.00***
	r	-0.10	-0.14	0.28	-0.48	-0.15	-0.01	0.27	-0.43	0.05	0.13	0.37	-0.63
DABP	p	0.74	0.36	0.02*	0.03*	0.18	0.90	0.12	0.00**	0.50	0.16	0.00**	0.00**
	r	-0.05	-0.14	0.53	-0.50	-0.19	0.02	0.34	-0.59	-0.10	0.20	0.50	-0.55

cTOI cerebral tissue oxygenation index, cFTOE cerebral fractional tissue oxygen extraction, SABP systolic arterial blood pressure, DABP diastolic arterial blood pressure, MABP mean arterial blood pressure.

*p<0,05, **P<0,01; ***P<0,001

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arterial blood pressure at different time points during the first 15 minutes after birth, while no such associations were observed in stable term neonates.

Conflict of interest: The authors have no conflicts of interest to declare.

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LUNG AND BRAIN PROTECTION IN VLBW INFANTS AFTER ANTENATAL STEROID COURSE: DOES TIMING MATTER?

Flavia Pozzi[1], **Paolo Massirio**[2], Francesco Vinci[2], Irene Bonato[2], Maria Grazia Calevo[3], Dario Paladini[4], Federico Prefumo[5], Mariasavina Severino[6], Domenico Tortora[6], Andrea Rossi[6,7], Diego Minghetti[2], Mariya Malova[2], Luca Ramengi[2,8]

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Background: Antenatal corticosteroids (ACS) are widely used in pregnancies at risk of preterm birth to target lung maturation, but their role in brain development is debated. Some studies suggest that protective effect on lung vanishes if more than 7 days has passed between administration and birth. The aim of our study was to evaluate effects of complete course of ACS (ccACS) on lung and brain with attention to timing and with the help of MRI, known to be more sensitive to intraventricular haemorrhage (IVH) than previously used cranial ultrasound (Parodi *et al*., 2015).

Methods: All VLBW infants admitted to our NICU from January 2019 to December 2021 were included. Clinical data including timing of ACS and respiratory outcome were registered. Term-equivalent age MRI scans were reviewed to identify IVH, white matter lesions (WML), and cerebellar haemorrhage (CBH). Linear measurements of brain size were carried out and total maturation score was calculated. Lung and brain parameters were compared between infants with and without ccACS, and between subgroups of infants with time between steroid administration and birth being less versus more than 7, 14 and 21 days.

Results: Out of 189 infants included, 139 (73,5%) received ccACS. Infants with ccACS presented higher 5 min Apgar score ($p = 0.001$), lower use of surfactant ($p = 0.005$) and a trend for lower rate of intubation (60.4% vs. 76%, $p = 0.06$). We have not observed significant reduction of beneficial effect on lungs in infants delivered more than 7, 14 or 21 days after ACS. On MRI infants with ccACS had less WML ($p = 0.02$) and less severe IVH ($p = 0.04$). In the extremely preterm (<28 weeks) subgroup at higher risk of IVH we have observed a significant reduction of IVH in infants receiving ccACS less than 7 days before birth. No significant differences were observed between groups in brain size and maturation.

Conclusion: According to our data, timing of ACS does not matter for the lung protection. Nevertheless, reduction of IVH in extremely preterm infants seems to be more pronounced when less than 7 days has passed from ACS administration to birth. Our study suggests a reduction of WML following ccACS.

Conflict of interest: None declared.

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THE EFFECTS OF MATERNAL MAGNESIUM SULPHATE THERAPY ON EARLY NEONATAL OUTCOMES

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Background: Magnesium sulphate (MgSO4) is frequently used for maternal and fetal neuroprotection in the presence of premature labour in pregnant women with preeclampsia/eclampsia. However, there are concerns about the adverse effects of this practice on neonatal morbidities. Therefore, we aimed to evaluate the effects of maternal MgSO4 therapy on early neonatal outcomes.

Methods: In this retrospective study, babies born at/or before 34 weeks of gestation whose mothers received intravenous (IV) MgSO4 therapy (bolus dose of 6 g over 30 min, followed by a continuous infusion of 2–3 g/h) for at least 12 h before delivery were included in the study, from November 2022 to May 2023. Control group consisted of babies born in the same study period at the similar gestational weeks. The groups were compared in terms of short-term neonatal clinical outcomes.

Results: A total of 64 newborns were evaluated for the study (32 babies in each group). The mean gestational age and birthweight of all subjects were 29.2 ± 2.7 week and 1213 - $\pm$ 361 g. Male to female ratio was 1.6:1.0, without any difference between the groups. The newborns exposed to maternal MgSO4 had a higher incidence of hypotonia and lower 1- and 5-min Apgar scores compared to control babies ($p < 0.001$). However, there was no association between these adverse outcomes and maternal serum magnesium concentrations both at delivery and during the treatment, or cumulative dose of MgSO4. Study groups did not differ in terms of the neonatal morbidities such as patent ductus arteriosus, bronchopulmonary dysplasia, and necrotizing enterocolitis.

Conclusion: Antenatal MgSO4 therapy may lead to hypotonia and lower Apgar scores in premature babies regardless of maternal serum magnesium levels. Further studies are needed to clarify the effects of maternal MgSO4 therapy on early neonatal outcomes.

Conflict of interest: None declared.

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THE PREDICTIVE ROLE OF EARLY QUALITATIVE AND QUANTITATIVE (A)EEG ON LONG-TERM NEURODEVELOPMENTAL OUTCOMES IN EXTREMELY PRETERM INFANTS

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Background: Extremely preterm (EP) infants (<28 weeks of gestation) are at great risk for long-term neurodevelopmental impairments. Early continuous amplitude-integrated electroencephalography (aEEG) with raw EEG traces holds a high potential for predicting later outcomes in the preterm population. This study aimed to determine whether and which qualitative and quantitative (a)EEG features obtained within the first post-natal days predict EP infants' neurodevelopmental outcomes at pre-school and early school age.

Methods: This study used a retrospective cohort of 369 EP infants who underwent routine (a)EEG monitoring during their first post-natal three days. From pre-processed (a)EEG signals, we extracted an extensive feature set, including three types of qualitative parameters (background pattern, sleep–wake cycles, and seizure activity) and four groups of quantitative metrics (amplitude, spectral content, connectivity, and discontinuity). The extracted (a)EEG features were fed into machine learning (ML)-based regression and classification models to assess their predictive value for cognitive, motor, and behavioural problem outcomes at two and five years of age. Potential confounders were corrected in the prediction analysis.

Results: The ML-based regression analyses showed statistically significant but relatively weak predictive performance (R = 0.12–0.23) for most (11/13) outcomes. However, the binary classifiers showed acceptable performance in identifying EP infants with delayed full-scale and verbal intellectual quotient scores at five years from those with optimal scores, achieving 68% and 72% (both permutation P-value <0.001) balanced accuracy, respectively.

Conclusion: These results highlight the potential benefits of early post-natal (a)EEG monitoring, along with using ML approaches, to automatically recognise EP infants with impaired outcomes, shedding light on developing an explainable prognostic tool that aids in decision-making and therapy planning in this population.

Conflict of interest: None declared.

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THE ROLE OF CEREBRAL, RENAL, AND ABDOMINAL NIRS TO DETECT SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN VERY PRETERM INFANTS: A PILOT STUDY

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Background: Haemodynamically significant patent ductus arteriosus (hsPDA) is characterised with systemic hypoperfusion and pulmonary overcirculation. Systemic hypoperfusion with subsequent decrease of tissue oxygenation can be detected using near-infrared spectroscopy (NIRS) applied at cerebral, renal, and abdominal area. The aim of this study is to evaluate the use of regional saturation (cerebral/CrSO2, renal/RrSO2, and abdominal/SrSO2) to detect hsPDA in very preterm infants.

Methods: Forty-one very preterm infants (birthweight < 1500 g and gestational age < 32 weeks) were monitored continuously with cerebral, renal, and abdominal NIRS immediately after birth until ductus arteriosus was closed. All infants were prospectively evaluated using echocardiography to detect hsPDA within 24-h after birth daily during NIRS application. Echocardiography criteria to diagnose hsPDA were the following: 1). ductal diameter ≥ 1.5 mm, 2). La:Ao ratio ≥ 1.5, 3). LPA diastolic velocity > 0.2 m/s and 4). Absent or retrograde diastolic flow

Variable	No-hsPDA (n=30)	hsPDA (n=11)	p
Gestational Age(weeks), median (IQR)	29.5 (26;30)	29 (28;30)	0.76
Birth Weight (gram), median (IQR)	1010 (772;1291)	1100 (750;1170)	0.54
Male (%)	14 (73.7)	5 (26.3)	0.95
Apgar 1 – min, median (IQR)	4 (3;6)	5(4;6)	0.26
Apgar 5-min, median (IQR)	6 (5;7)	7 (5;7)	0.63
Age of Diagnosis PDA (hours), median (IQR)		48 (24;72)	
Full Cover antenatal steroid (%)	8 (80)	2 (20)	0.77
Caesarean section (%)	23 (71.9)	9 (28.1)	0.54
IUGR (%)	9 (69.2)	4 (30.8)	0.49
UTI (%)	11 (78.6)	3 (21.4)	0.43
Surfactant (%)	26 (76.5)	8 (23.5)	0.27
Mechanical Ventilation (%)	23 (79.3)	6 (20.7)	0.16

Table 1 Baseline characteristics

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at superior mesenteric artery (SMA), anterior cerebral artery (ACA), or renal artery. Mean value of regional NIRS during its application were compared between hsPDA and no-hsPDA group.

Results: Of 41 infants, there were 11 infants with hsPDA and 30 with no hsPDA. A lower mean (±SD) of CrSO2 was detected in hsPDA group (65 ± 8.1) than in no hsPDA group (75 ± 6.3) ($P < 0.001$). The median (IQR) of RrSO2 was lower in hsPDA group (60.4 (54; 76) than in no hsPDA group 83.5 (77; 82) ($P < 0.001$)). Abdominal regional saturation were also lower in hsPDA group with median of 30 (22; 38) vs. 37.5 (30; 54) in no hsPDA group ($P = 0.032$) (Table 1).

Conclusion: Lower cerebral, renal, and abdominal regional saturations were associated with the presence of hsPDA in preterm infants.

Conflict of interest: None declared.

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ISOLATED CHRONIC FETAL HYPOXEMIA RESULTS IN VASCULAR REMODELLING IN FETAL LAMBS MAINTAINED ON EXTEND

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Background: Severe fetal hypoxia has been associated with failed transition of the fetal circulation at birth causing persistent pulmonary hypertension of the newborn. However, animal models have not been able to achieve fetal hypoxia without concurrent reductions in nutritional delivery or increased maternal stress. Consequently, the implications isolated fetal hypoxia on lung development remains unclear.

Method: In this study, we used an EXTra-uterine Environment for Neonatal Development (EXTEND) to artificially reduce oxygen delivery (DO2) to the fetus (DO2 = 15 mL/min.kg). Preterm fetal lambs (105–110 days GA) were isolated by caesarean section and supported on EXTEND for 7 days reaching canalicular stage of lung development (n = 10) in hypoxic (n = 5) or normoxic (n = 5) condition; or 17 days reaching saccular stage of lung development (n = 8) in hypoxic (n = 4) or normoxic (n = 4) condition. Study of vascular remodelling included vascular and capillary density, neo-muscularization of vessels and medial wall thickness of distal arteries and was assessed through immunohistochemistry and immunofluorescence.

Results: In our study, aberrant vascular remodelling was observed with a significant reduction in the total number of vessels by 37% and capillary density by 7% after 17 days in hypoxic conditions. Arteriolar medial wall thickness was similar for both 7-day normoxic and hypoxic group but increased by 13% after 17 days in hypoxic conditions (P = 0.0002). Small distal arteries (20–50 μm in diameter) comprised the most significantly increased medial wall thickness (P = 0.03). In addition, vessels showed a 10% increase in partially muscularized vessels after 7 days in hypoxic conditions (P = 0.03) with similarly increased trend in partially muscularized vessels after 17 days in hypoxic condition.

Conclusion: These preliminary data show that isolated fetal hypoxia drives vascular remodelling consistent with vasculopathy observed in persistent pulmonary hypertension of the newborn.

Conflict of interest: Alan W. Flake holds multiple patents related to EXTEND technology and is a Paid Medical Consultant for Vitara Biomedical Inc. Marcus Davey is listed as inventor on EXTEND device patents.

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A RANDOMISED TRIAL OF ROUTINE OR SELECTIVE APPLICATION OF A FACE MASK FOR BREATHING SUPPORT OF PRETERM INFANTS AT BIRTH

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Background: Most preterm infants breathe spontaneously at delivery. Despite this, the majority have a face mask applied immediately, usually before their heart rate has been determined. Application of a face mask may inhibit spontaneous breathing.

Objectives: To determine whether selectively applying a face mask to give positive pressure ventilation (PPV) to preterm infants for apnoea or bradycardia only, rather than routinely giving face mask continuous positive airway pressure (CPAP) resulted in fewer infants receiving PPV in the first 5 min of life.

Methods: Infants born before 32 weeks' gestation were randomly assigned before birth to 'Routine' or 'Selective' groups, stratified by gestational age (GA) (<28 and 28 + 0–31 + 6 weeks). 'Routine' infants had a face mask applied to give CPAP as soon as possible after birth. 'Selective' infants were placed supine to breathe spontaneously and were not to receive mask CPAP before 5 min of life. Infants in both groups were given mask PPV for apnoea or bradycardia (heart rate < 100 bpm). All other aspects of DR care were the same. The primary outcome was face mask PPV in the first 5 min of life. Secondary outcomes in the DR included use of face mask CPAP, face mask PPV, endotracheal intubation, and chest compressions; and heart rate and oxygen saturations at 5 min. Secondary outcomes in the NICU included endotracheal ventilation and surfactant administration.

Results: We enrolled 200 infants; 102 were randomly assigned to 'Routine' (mean (SD) GA 28 (2) weeks and birthweight (BW) 1152 (423) g) and 98 to 'Selective' (mean (SD) GA 28 (3) weeks and BW 1118 (440) g). There was no difference in the proportion of babies who received PPV in the first 5 min of life (53/102 (52%) vs. 62/98 (63%), P = 0.106) between the groups. More infants in the Routine group received mask CPAP in the DR, in accordance with the protocol. There were no differences between the groups in other secondary outcomes.

Conclusions: Selective application of a face mask for PPV did not result in fewer preterm infants receiving PPV in the DR.

Conflict of interest: None declared.

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	Routine n =102	Selective n = 98	p value
Primary outcome: Mask PPV first 5 min *	53 (51)	62 (63)	.106
$23^{+0} - 27^{+6}$	28/43 (65)	33/42 (79)	.168
$28^{+0} - 31^{+6}$	25/59 (42)	29/56 (52)	.312
DR outcomes			
Face mask CPAP *	98 (96)	68 (69)	< .001
Face mask PPV *	53 (52)	63 (64)	.077
Endotracheal intubation *	15 (15)	17 (17)	.611
Chest compressions *	3 (3)	4 (4)	.661
HR at 5 minutes (beats/min) #	144 (28)	142 (27)	.667
Oxygen saturation at 5 minutes #	85 (17)	78 (24)	.120
NICU outcomes			
Endotracheal intubation during admission *	60 (59)	59 (60)	.842

* = (%)
# = median (IQR)
Abbreviations: PPV, positive pressure ventilation; DR, delivery room; CPAP, continuous positive airway pressure; HR, heart rate; IQR, interquartile range

Table 1 Outcomes

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PARENTAL TOUCH TRIAL (PETAL): A MULTICENTRE RANDOMISED CONTROLLED TRIAL INVESTIGATING PARENTAL TOUCH AS AN INTERVENTION TO RELIEVE NEONATAL PAIN AND REDUCE PARENTAL ANXIETY

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Background: Tactile stimulation, such as kangaroo care, massage and brushing, are reported to reduce pain in infants. The aim of this clinical trial was to establish whether parental touch, optimised for C tactile (CT) fibre activation and delivered prior to an acutely painful clinical procedure, can reduce neonatal pain.

Methods: In this multicentre randomised controlled trial, neonates born ≥35 weeks gestational age, without neurological abnormalities, and requiring a heel lance during the first 7 post-natal days were eligible. Neonates were randomised to receive gentle stroking

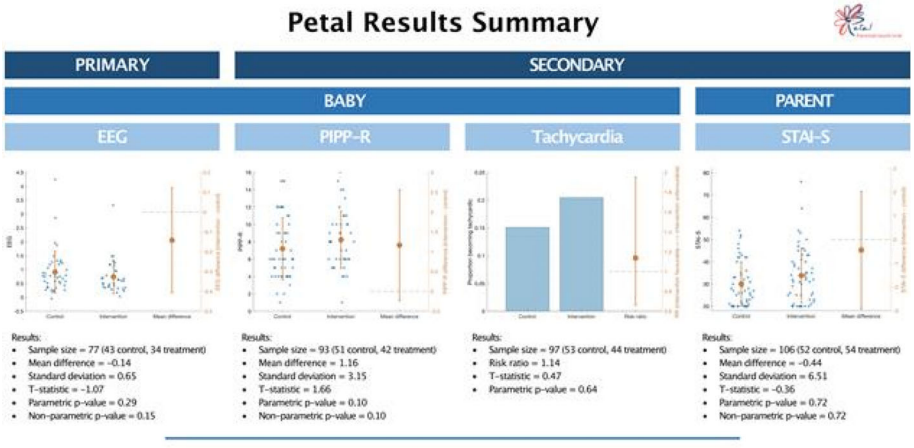


Fig. 1 The intervention and control columns display raw data and mean ± SD (overlying bars). The third column shows adjusted intervention minus control mean difference/risk ratio, 95% CI, and null value (dashed line).

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for 10 s either shortly before (intervention group) or after (control group) a clinically-required heel lance. The parent delivered the intervention to the neonate's lower leg, ipsilateral to the side of the heel lance, at a speed of 3 cm/s optimised for CT fibre activation. The primary outcome was the magnitude of noxious-evoked brain activity, recorded by EEG, following the heel lance. Secondary outcomes were the Premature Infant Pain Profile – Revised (PIPP-R) score, development of tachycardia post heel lance, and parental anxiety measured with the State–Trait Anxiety Inventory State (STAI-S). The trial and statistical analysis plan were registered (ClinicalTrials.gov: NCT04901611; ISRCTN: 14135962).

Results: We enrolled 112 participants between 1 September 2021 and 7 February 2023. The magnitude of noxious-evoked brain activity following the heel lance was not significantly different between the control and intervention groups (difference in means −0.14, $P = 0.15$; Fig. 1). In addition, no significant differences between control and intervention arms were observed in the secondary outcomes (difference in PIPP-R means 1.16, $P = 0.10$; tachycardia risk ratio 1.14, $P = 0.64$; difference in STAI-S means −0.44, $P = 0.72$; Fig. 1).

Conclusion: Parents stroking their infant's leg at 3 cm/s for 10 s prior to a heel lance did not significantly change infants' noxious-evoked brain activity, PIPP-R score, development of tachycardic episodes, nor parental STAI-S scores. The lack of an effect of the intervention on the primary outcome is not consistent with previous observational research demonstrating the analgesic effects of gentle CT-fibre-stimulating experimental brushing. These conflicting findings could highlight important differences between experimental brush stimulation and parental stroking under research conditions.

Grants: LB is funded by a BLISS (a neonatal charity promoting parental involvement) research grant. RS, EA, FM and CH are named applicants on this grant, but not funded by it.

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IMPACT OF AMPLITUDE-INTEGRATED ELECTROENCEPHALOGRAPHY FINDINGS DURING CARDIAC SURGERY ON NEURODEVELOPMENTAL OUTCOME

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Background and Aims: Perioperative brain injury is common in young infants undergoing cardiac surgery (CS). We aimed to determine the relationship between intra-surgical electrical seizures and the background pattern of amplitude-integrated electroencephalography (aEEG) with brain damage biomarkers and 2-year neurodevelopmental outcome in infants undergoing CS.

Methods: A total of 120 infants undergoing CS underwent aEEG monitoring during surgery. Seizure activity and aEEG background pattern were recorded and analysed. Brain damage biomarkers (protein s100b and neuronal specific enolase (NSE)) were analysed immediately after surgery and 72 h post. Survivors underwent neurodevelopmental outcome assessment using the Bayley Scales at 2 years.

Results: Sixty-one per cent of the patients were operated with less than one month. Cardiopulmonary bypass was used in 58.47%. Intraoperative electrical seizures occurred in 22.87%. Seizures were more frequent in surgeries with higher Aristoteles score ($P = 0.001$). Those patients with seizures presented higher levels of s100b immediately after surgery ($P = 0.0019$). Mean time of seizure burden was 30 min (9.6–71.4). Seizure burden was correlated with time of aortic clamps (rho = 0.60; $P < 0.05$) and temperature (rho = −0.32; $P = 0.02$). Those surgeries that require Aortic clamp presented worse aEEG patterns. There is no correlation between seizures or aEEG pattern and Bayley scores at 2 years.

Conclusions: Patients with seizures presented higher levels of S100B. Aortic Clamp and hypothermia are the main risks for intra-operative seizures and abnormal background patterns. Intraoperative seizures were common in this cohort of infants but did not impact on 2-year neurodevelopmental outcome. Post-surgical monitorization will be important to determine the impact of the recovery of the aEEG patterns on the long-term outcome.

Conflict of interest: None declared.

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SUPPLEMENTATION WITH DOCOSAHEXAENOIC ACID (DHA) AND ARACHIDONIC ACID (AA) TO EXTREMELY PRETERM APPEARS TO ALLEVIATE THROMBOCYTOPENIA AS A RISK FACTOR FOR SEVERE RETINOPATHY OF PREMATURITY (ROP)

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Background: Low levels of docosahexaenoic acid (DHA) and arachidonic acid (AA) and low platelet counts are associated with retinopathy of prematurity (ROP), but the nature of their association is unknown.

Method: Longitudinal serum DHA, AA, and protein levels were analysed, and platelet count was recorded during the first post-natal month in Swedish infants born <28 weeks gestational age (GA), 2016 to 2019, randomised to receive post-natal enteral supplementation of AA/DHA or standard nutrition (controls). Thrombocytopenia was defined as a platelet count <100 $\times 10^9$/L. Association between levels of DHA, AA, platelet counts, and platelet-related proteins were assessed during the infants' first post-natal month and associated with the development of severe ROP (ROP Stage 3 and treated). Analyses were adjusted for GA, birthweight (BW) standard deviation and randomised AA/DHA supplementation. The interaction between AA/DHA supplementation and thrombocytopenia was investigated.

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Results: The 178 infants had a mean BW of 806 ± 200 g and a mean GA of 25.6 ± 1.4 weeks. Thrombocytopenia first post-natal month was present in 28% of the controls and 20% of the AA/DHA supplemented group (adj. $P = 0.32$). Thrombocytopenia first post-natal month was found to be a risk factor for severe ROP overall (adj. OR 2.48, 95% CI 1.03 5.99, $P = 0.043$); however, there was a numerical difference in the risk factor effect in the control group (adj. OR 4.27, 95% CI 1.23 14.83, $P = 0.022$) compared to the AA/DHA group (adj. OR 1.37, 95% CI 0.34 5.46, $P = 0.66$), p for interaction 0.28. DHA and/or AA levels were positively associated with levels of platelet-related proteins such as platelet-derived growth factor subunits A and B (PDGFA and PDGFB) and negatively with tissue plasminogen activator (TPA); in contrast, the association with severe ROP was the opposite.

Conclusions: Post-natal enteral supplementation with AA/DHA to extremely preterm infants numerically reduced early thrombocytopenia as a risk factor for severe ROP. Levels of AA and DHA were associated with levels of platelet-related proteins, and we hypothesize that the effect of AA/DHA supplementation on severe ROP may be modulated through platelet activation and function.

Conflict of interest: None declared.

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LONGITUDINAL ASSESSMENT OF BRAIN DEVELOPMENT AND LONG TERM OUTCOMES IN EXTREMELY PRETERM INFANTS UP TO 9 YEARS OF AGE

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Background: Premature infants exhibit distinct pattern of brain development compared to full-term, but this has been evaluated longitudinally in only a small number of studies. This longitudinal study aims to analyse serial magnetic resonance imaging (MRI) scans of extremely preterm infants (<28 weeks of gestation) to assess brain development and injuries and investigate their relationship with long-term outcome.

Methods: One hundred-thirty-four extremely preterm infants born at the Wilhelmina Children's Hospital in Utrecht, The Netherlands (2008–2012) were included. Serial MRI images were collected at around 30 and 40 weeks of postmenstrual age and at 9 years. Neonatal MRI images were analysed using the dHCP Structural-Pipeline, 9 years images were segmented using Freesurfer. Most relevant maternal and perinatal data were collected and the presence of brain injury at term was assessed using the Kidokoro MRI score. Follow up at 9 years was performed using Movement Assessment Battery for Children (Movement-ABC) and Wechsler Intelligence Scale for Children version-V (WISC-V) tests. Adjusted correlation analysis was conducted between the volumes and their ratios to the total brain volume, and the outcome scores, with correction for gender and age at scan.

Results: Segmentation analysis was performed only on good-quality scans ($N = 77$ at 30 wks, $N = 129$ at 40 wks and $N = 105$ at 8–12 y) obtaining volumes of 87 brain regions. No significant correlations were observed volumes at 30 wks post-menstrual age and long term outcomes. Brain volumes at term-equivalent age were significantly and positively correlated with 9 years intelligence quotient, with the strongest correlation observed for cortical grey matter and the brainstem. Moreover, Kidokoro total white matter injury score at term negatively correlated with long-term motor and cognitive scores at 9 years. Cortical grey matter and basal ganglia volumes measured at 9 years MRI were also significantly correlated with 9 years total intelligence quotient.

Conclusions: Our findings underscore the long-term impact of preterm birth on neurodevelopment and highlight the crucial role of term equivalent age MRI for prognosis and long term outcome prediction. Early diagnosis and identification of high-risk infants are crucial and can potentially provide an important window for intervention.

Conflict of interest: None declared.

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DEFINING OPTIMAL BODY COMPOSITION OUTCOMES AT TERM EQUIVALENT AGE IN INFANTS BORN VERY PRETERM

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Background: The growth calculator (www.growthcalculator.org) is an innovative tool that accounts for variability in weight gain observed during the first weeks after birth and defines the optimal growth 'trajectory' for very preterm infants. However, body composition outcomes of infants who grow within this newly defined optimal target have not been characterised. We hypothesized that infants with growth trajectories within target from birth to 36 weeks of postmenstrual age (PMA) defined by the growth calculator tool would have the highest fat-free mass (FFM) accretion at 36 weeks PMA.

Methods: We analysed anonymous growth and body composition data from preterm infants born in the United States, Canada, Germany, and Austria. Infants included had body composition measurements using air-displacement plethysmography around term equivalent age or hospital discharge. To test our hypothesis, we entered birth and 36-week anthropometric data in the 'growth calculator' application and determined individualised trajectories for each study participant.

Results: A total of 1026 infants were included. The median gestational age (GA) and birthweight were 28 weeks (IQR, 26–30) and 1020 g (SD, 352), respectively. There were significant differences in body fat percentage (%BF) and FFM accretion at 36 weeks PMA across 5 gestational age groups. In very preterm

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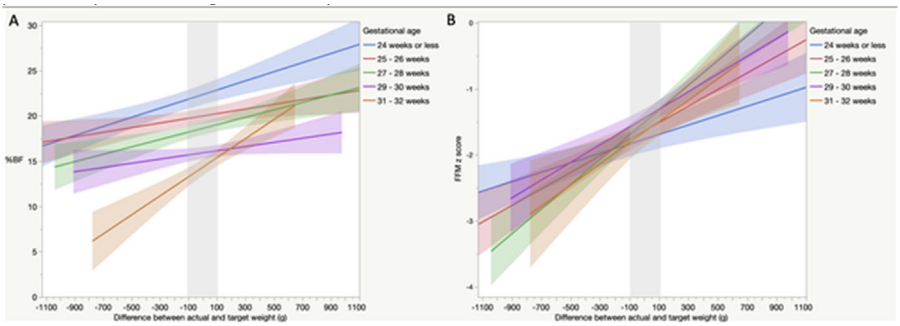


Fig. 1 Body fat percentage (a) and fat-free mass accretion (b) at term equivalent age across five gestational age groups.

infants with growth trajectories within target, %BF at 36 weeks PMA had a strong correlation with GA (Fig. 1a). FFM z scores at 36 weeks PMA ranged from −2 to −1.5 across GA groups (Fig. 1b).

Conclusion: This analysis provides strong scientific justification to redefine optimal body composition outcomes in infants born very preterm. Future studies should identify nutritional strategies that increase the probability of achieving these newly defined outcomes.

Grants: This study was partially supported by an unrestricted grant from the Neonatal Network.

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THE EFFECT OF HIGHER protein-energy INTAKES AND STIMULATION OF PHYSICAL ACTIVITY ON GROWTH OF PRETERM INFANTS: A NESTED DESIGN RANDOMISED CLINICAL TRIAL

Chiara Biagetti[1], Alessio Correani[1], Ilaria Giretti[1], Maria Paola Bellagamba[1], Rita D'Ascenzo[1], Beatrice Bartolomei[1], Ilaria Burattini[1], Enrica Ferretti[1], Annamaria Peretti[1], Domenico Galotto[1], Paola Cogo[2], Virgilio P Carnielli[1]

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Background: Increasing protein and energy intake above the anabolic capacity of a given individual may result in increased lipogenesis and excessive fat deposition. We hypothesized that combining a physical stimulation programme to increased nutritional intakes would have improved growth and body composition of preterm infants born before 32 weeks (W) of gestation.

Methods: We performed a pilot randomised controlled trial with a 2-by-2 factorial design involving infants born between 24 + 0 W and 31 + 6 W, who were randomly assigned to Standard Nutrition (N0: protein intake 3.6 g/kg/d and energy intake 135 kcal/kg/d) or Enhanced Nutrition (N+: protein intake 4.6 g/kg/d and energy intake 145 kcal/kg/d) and to Physical Stimulation (S+: flexion/extension of the 4 limbs and other motion exercises of the shoulder girdle and of the hips 4 times/day at least 5 days a week) or No Physical Stimulation (S0) from birth to 36 W postmenstrual age (PMA). Growth and body composition (assessed by skinfold and ultrasound muscle and adipose tissue thickness measurements of limbs) were evaluated until 36 W PMA.

Results: One hundred and twenty-seven infants met inclusion criteria and were included in the per protocol final analysis (N + S + =32; N + S0 = 33; N0S + =30; N0S0 = 32). No differences were found in demographics and in the main complications of prematurity between the groups. N+ patients showed improved weight gain from birth to 36 W PMA (weight gain Birth-36 W: 13.8 ± 2.1 vs. 12.4 ± 2.3 g·kg-1·d-1, N+ vs. N0 respectively, p = 0.001; delta weight SDS birth-36 W PMA: −0.7 ± 0.5 vs. −1.0 ± 0.5, N+ vs. N0 respectively, p = 0.001). Physical stimulation was not associated with any clinically and statistically significant effect on growth. Neither the nutritional intervention, nor the physical stimulation programme affected body composition until 36 W PMA. No significant interaction was found between nutrition and physical stimulation on growth and body composition during the study period.

Conclusion: In very preterm infants (24 + 0–31 + 6 weeks), enhanced nutrition was associated with a higher weight gain from birth to 36 W PMA but no other statistically and clinically significant differences were found. We could not demonstrate any growth advantage in receiving the physical stimulation programme, nor there was any interaction between nutrition and physical stimulation.

Conflict of interest: None declared.

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THE RISK OF RETINOPATHY OF PREMATURITY IN EXTREMELY LOW GESTATIONAL AGE NEONATES INCREASES WITH EACH EPISODE OF CULTURE-PROVEN SEPSIS

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Background: Retinopathy of prematurity (ROP) is a major morbidity mainly in very premature preterm infants causing visual impairment including blindness. Timely diagnosis, treatment and prevention are critical. There is growing evidence of a contributing role of infection and inflammation in the pathogenesis of

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ROP. We herein hypothesized that extremely low gestational age newborns (ELGANs) having survived one or more episodes of sepsis are more likely to develop any ROP and/or progression to higher-stage disease.

Methods: We analysed the impact of culture-proven sepsis on ROP risk in ELGANs enrolled in the German Neonatal Network multicentre study. Stepwise multivariable logistic regression analyses controlled for confounding.

Results: n = 12 563 infants were included (median gestational age 26 6/7 weeks, birthweight 840 g). 6177/12563 infants (49.2%) were diagnosed with any ROP, comprising 2700 infants (21.5%) with stage 1 disease, 2163 (17.2%) with stage 2 ROP, 1282 (10.2%) with Stage 3 and 32 (0.3%) with stage 4 disease. 829/12563 infants (6.6%) required treatment for higher-stage ROP. Stepwise multivariable logistic regression identified neonatal sepsis as an independent risk factor. The number of sepsis episodes was directly related to the risk increase – with a 1.4-fold increase at one (95% CI 1.2–1.6, $p < 0.001$), and a 1.8-fold and 4.7-fold increase at two (95% CI 1.3–2.3, $p < 0.001$) and three episodes (95% CI 2.3–9.7, $p < 0.001$). Moreover, neonatal sepsis was associated with progression to higher-stage disease – with a 1.4-fold risk at one (95% CI 1.2–1.7, $p < 0.001$), a 1.9-fold risk at two (95% CI 1.4–2.5, $p < 0.001$), and a 2.3-fold risk at three sepsis episodes (95% CI 1.4–3.8, $p = 0.001$).

Conclusion: The risk of ROP and higher-stage ROP in ELGANs increases with each episode of neonatal sepsis. Future studies ought to investigate underlying mechanisms and may help to direct future ROP screening.

Conflict of interest: CH: grants (BMBF, Chiesi, DFG). EH: grants/travel/honoraria (Chiesi, Pfizer, Merck Sharp&Dohme, Sanofi, AstraZeneca). AS: consultancy/honoraria (Apellis, Allergan, Bayer, Novartis, Roche). WG: grants (BMBF); honoraria (Chiesi, Abbott). No other disclosures.

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THE PROTECTIVE ROLE OF ACTIVE SLEEP IN MATURATION OF THE POSTERIOR LIMB OF THE INTERNAL CAPSULE

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Background: Preterm brain development is influenced by a plethora of factors. Days of invasive ventilation (DOV) and maturation of the posterior limb of the internal capsule (PLIC – part of the sensorimotor tracts) are among the most predictive for future outcome in preterm infants. Although sleep is also thought to be essential for brain development, it is rarely considered as a moderator of brain development. Animal research has found an association between active sleep (AS) and development of the white matter expressed by sensorimotor pathways (e.g. the corticospinal tract; CST). The aim of the current research was to explore the role of AS in preterm CST – and more specifically PLIC – maturation.

Methods: In a retrospective cohort of 50 preterm infants (born 24.6–29.4 weeks gestational age, 52% female) sleep states were continuously measured during 5–7 consecutive days between 29 + 0 and 31 + 6 weeks postmenstrual age. Every minute sleep stages were predicted using an in-house developed sleep staging algorithm. Furthermore, a DTI scan was made at term equivalent age as part of standard care. Infants without overt brain injury or congenital malformations and with a good quality DTI scan were included. After quality assessment, tract based spatial statistics (TBSS) analysis was performed, followed by region of interest analysis of the bilateral PLIC. Finally, the CST was analysed using tractography. For all analyses, DOV, gestational age at birth and postmenstrual age at scan were included as covariates.

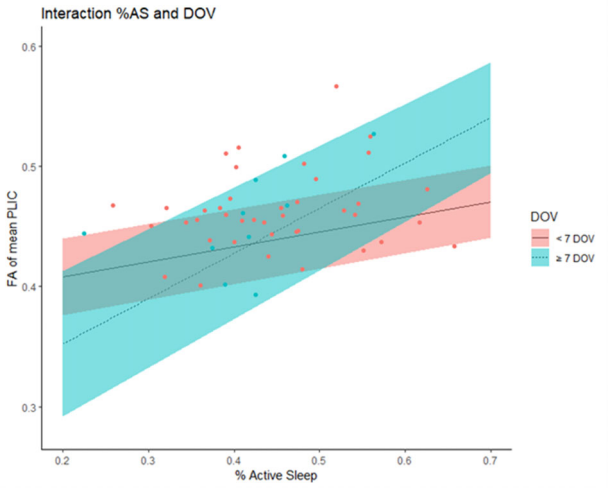


Fig. 1 Interaction between DOV and %AS for FA values of the bilateral PLIC.

Results: TBSS analyses suggested a positive trend, associating AS with fractional anisotropy (FA) of the medial lemniscus and left inferior CST ($P < 0.10$). However, DOV was negatively associated with FA throughout the brain ($P < 0.05$). Furthermore, analyses showed a significant interaction effect between AS and DOV for FA of the PLIC ($P = 0.01$; Fig. 1) and for radial diffusivity of the PLIC ($P = 0.03$).

Conclusion: In very preterm infants, invasive ventilation has a negative effect on white matter tract maturation throughout the brain. However, active sleep may play a protective role for the most vulnerable infants by supporting the maturation of the PLIC, which is crucial for long-term neurodevelopmental outcomes.

Conflict of interest: None declared.

892
THE IMPACT OF CHORIOAMNIONITIS ON LUNG FUNCTION DEVELOPMENT OVER THE FIRST 18 MONTHS IN EXTREMELY PRETERM INFANTS

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Background: Histological chorioamnionitis (HCA) is one of the major causes of preterm birth. HCA is associated with decreased incidence of early respiratory distress syndrome and, probably, with a later increase of bronchopulmonary dysplasia. Less is known about the impact of HCA on the developing lung in terms of lung function measurements, particularly in the most immature infants. Since poor lung function is tracking through life, an impact of HCA may affect long-term the respiratory morbidity after preterm birth. We aimed to investigate if extremely preterm born infants exposed to chorioamnionitis have impaired lung function during the first 18 months.

Methods: Placenta samples were collected from extremely preterm born infants (< 28 weeks gestational age) at Karolinska University Hospital. Chorioamnionitis was diagnosed histologically. The infants were followed up and lung function testing performed as part of clinical routine, at age 3- and 18-months postmenstrual age, by Tidal Volume Rapid Thoracoabdominal Compression (TVRTC) and Raised Volume-Rapid Thoracic Compression Technique (RVRTC).

Results: Twenty-nine infants (14 boys/15 girls) born extremely preterm with a median gestational age of 25 weeks (range 23-27 weeks) were included. HCA was detected in 18 (62%) of the placentas. At postmenstrual age 3 months there was a trend towards higher expiratory flows in the HCA group (HCA vs non-HCA; FEV0.5 p=0.06, FVC p=0.06 for, FEF25-75 p=0.046, VmaxFRC p=0.55). At 18 months of age, lung function results were similar, between groups (HCA vs non-HCA; FEV0.5 p=0.9, FVC p=0.86, FEF25-75 p=0.83,VmaxFRC p=0.93). No gender-related differences were observed for HCA vs non-HCA exposed infants.

Conclusion: Exposure to chorioamnionitis did not adversely affect lung function in the first 18 months of life in this cohort of extremely preterm infants. The observed tendency towards enhanced lung function in early testing needs to be further investigated and difficult to interpret due to the small sample size. Pulmonary outcome after extreme preterm birth is multifactorial and the impact of chorioamnionitis may differ in conjunction with other factors or in subgroups of infants.

Conflict of interest: None declared.

898
NEONATES <3 MONTHS WITH LATE-ONSET SEPSIS DISPLAY SPECIFIC SIGNATURES OF THE IMMUNE-MICROBIOME INTERACTION

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Background: Infants <3 months with fever are at high risk of invasive bacterial infection (IBI), resulting in frequent exposure to empiric antibiotic therapy. A possible sepsis-predisposing profile of the immune-microbiome interaction has not yet been explored in this specific cohort as well as the long-term consequences of early sepsis and antimicrobial exposure on the microbiome.

Methods: Previously healthy infants <3 months with fever/suspected infection were included, clinically characterised and divided into subgroups of bacterial and viral infections and 'symptoms of unknown cause' due to detailed diagnostics that were performed (sepsis workup, multiplex PCR, enterovirus diagnostics). Immunophenotyping (B- and T cell subsets, regulatory T cells) and sequencing of the gastrointestinal microbiome were used to investigate sepsis-predisposing profiles in comparison to healthy children without infection. Follow-up included clinical examinations and microbiome profiling at one year of age.

Results: N = 51 infants with fever and sepsis work-up were enrolled. Invasive bacterial infection was diagnosed in 25 (49%) patients. Infants with suspected LOS displayed a decreased abundance of regulatory CD4+ FoxP3+ T cells as compared to healthy controls, which was most pronounced in the subgroup of infants with IBI. Further, we observed distinct microbiome characteristics, that were associated with sepsis, such as a reduced microbial diversity (Shannon diversity index: $P = 0.007$) and a reduced abundance of bifidobacteria, especially *Bifidobacterium longum* (canonical correspondence analysis: $P = 0.03$). Significant relations between microbiome signatures and immune cells, such as the association between the abundance of *B. longum* and regulatory T cell-frequencies, were observed in healthy babies but not in infants with sepsis ($P = 0.001$). In children with early sepsis and consecutive antibiotic therapy, we demonstrate long-term changes in the gastrointestinal microbiome at one year of age, such a reduced abundance of Bifidobacterium breve as compared to healthy controls.

Conclusion: Our exploratory data indicate specific immune-microbiome profiles that are associated with neonatal late-onset sepsis as well as consequences of early sepsis with antibiotic therapy for the gastrointestinal microbiome at one year of age.

Conflict of interest: None declared.

907
EARLY HUMAN MILK FORTIFICATION IN PRETERM INFANTS BORN AT 28 WEEKS OF GESTATION OR LESS: A MASKED RANDOMISED TRIAL

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Background: The use of unfortified human milk for enteral nutrition during the first two weeks after birth often results in protein and energy deficits among preterm infants. To address this issue, the administration of fortified human milk soon after birth has been explored as a potential solution, with the aim of improving growth and increasing fat-free mass (FFM) accretion in these infants.

Methods: We conducted a masked, randomised trial involving extremely preterm infants born at 28 weeks or less. The infants, who were fed either maternal or donor milk, were randomly assigned to two groups: one receiving a diet fortified with a human-based product (intervention group) and the other receiving a standard, unfortified diet (control group). This practice continued until the feeding day when a standard bovine-based fortifier was ordered (around post-natal day 14). The caregivers were blinded to the group assignments. The primary outcome was fat-free mass (FFM)-for-age z score at 36 weeks of postmenstrual age (PMA).

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Results: Between 2020 and 2022, a total of 150 infants were enrolled and randomised. The mean birthweight was 795 ± 250 g, and the median gestational age was 26 weeks. Eleven infants died during the observation period. The primary outcome was assessed in 105 infants. The FFM-for-age z scores did not show significant differences between the intervention and control groups (−1.7 vs. −1.6, respectively). However, the intervention group exhibited higher length gain velocities in cm/week from birth to 36 weeks PMA ($p = 0.04$), and the decline in head circumference-for-age z scores from birth to 36 weeks PMA was less pronounced in this group (−0.9 vs. −1.3; $p = 0.01$).

Conclusions: In extremely preterm infants, fortifying human milk diets soon after birth does not lead to increased FFM accretion at 36 weeks PMA. However, it may contribute to higher length gain velocities and reduced declines in head circumference-for-age z scores.

Conflict of interest: The authors have no conflicts of interest relevant to this article to disclose. Dr. Salas patented an instrumented feeding bottle and received consulting fees for participation in advisory board meetings.

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EARLY AND EXCLUSIVE ENTERAL NUTRITION IN VERY PRETERM INFANTS: A RANDOMISED TRIAL

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[1]University of Alabama at Birmingham

Background: Feeding preterm infants slowly is a common practice, but early and exclusive enteral nutrition could improve growth outcomes and reduce hospitalisation costs.

Methods: This parallel group randomised controlled trial included 102 infants born very preterm (28 to 32 weeks of gestation). Infants randomised to the intervention group received 60–80 ml/kg/day of either maternal or donor milk within the first 36 h after birth. The control group received 20–30 ml/kg/day (standard trophic feeding volumes). The primary outcome was the number of full enteral feeding days (>150 ml/kg/day) within the first 2 post-natal weeks. All study participants underwent a complete growth and body composition assessment at end of the first 2 post-natal weeks. Stool samples were also collected around 2 weeks after birth.

Results: The mean birthweight was 1477 ± 334 g. Half of the infants were male, and 44% were black. Early and exclusive enteral nutrition within the first 36 h after birth increased the number of full enteral feeding days (9 vs. 8 days; $P < 0.01$) and fat-free mass-for-age z-scores (−1.5 vs. −2.0; $P = 0.02$). No differences in microbiome diversity were found, but the intervention group had greater length-for-age z-scores (−0.9 vs. −1.5) and lower hospitalisation costs (mean difference: −$28754).

Conclusions: In infants born very preterm, early and exclusive enteral nutrition increases the number of full enteral feeding days. This feeding practice may also improve fat-free mass accretion, increase length, and reduce hospitalisation costs.

Conflict of interest: The authors have no conflicts of interest relevant to this article to disclose. Dr. Salas patented an instrumented feeding bottle and received consulting fees for participation in advisory board meetings.

913
EARLY BRAIN ACTIVITY AND DEVELOPMENT OF THE CENTRAL SULCUS

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Introduction: A delay in the sulcation of the central sulcus in extremely preterm born infants may potentially contribute to impaired motor outcome later in life. Therefore, the identification of early biomarkers that can assist in predicting neurodevelopmental outcomes would be highly advantageous. The current study investigates the relationship between early brain activity and central sulcus maturation between 30 and 40 weeks of gestation in infants born extremely preterm (GA < 28 weeks), without major brain injury.

Methods: In the current study, 26 infants (GA Mean = 26.8, SD = 1.0, Birthweight mean = 948, SD = 179) were included and monitored with continuous two-channel aEEG during the first 72 h after birth and scanned twice using MRI around 30 weeks post-menstrual age (PMA) and term-equivalent age. Theta power was calculated from raw EEGs. Central sulcus (CS) length, and CS surface growth were calculated as the difference (delta) of the CS length and surface between the 30- and 40-weeks MRI scans. Relative CS length and surface growth were calculated by adjusting the absolute values for global gyrification index. Linear correlations were performed between theta power and absolute CS length and surface growth. Correlations were adjusted for GA and age at scan.

Results: Significant correlations were observed between spectral theta power on day two and right hemisphere central sulcus length growth ($r = -0.478$, $P = 0.021$), bilateral length growth ($r = -496$, $P = 0.024$) and left ($r = -0.444$, $P = 0.034$), right ($r = -0.528$, $P = 0.01$) and bilateral ($r = -0.517$, $P = 0.012$) surface growth.

Conclusion: These results suggest that early spectral theta power may be a possible predictor of central sulcus maturation. Whether these results may provide a new biomarker for early prediction of motor impairment is worth to be investigated in future studies. The ability to predict brain development and subsequent outcomes using non-invasive neuromonitoring, early after birth, could be beneficial in providing timely treatment and interventions due to the increased plasticity of the young preterm's brain.

Conflict of interest: None declared.

918
CHEST COMPRESSION RATES OF 60/MIN VERSUS 90/MIN DURING NEONATAL CARDIOPULMONARY RESUSCITATION: A RANDOMISED CONTROLLED ANIMAL TRIAL

Marlies Bruckner[1,2], Megan O'Reilly[2,3], Tze-Fun Lee[2,3], Po-Yin Cheung[2,3], Georg Schmölzer[2,3]

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Background: A 3:1 compression-to-ventilation ratio with 90 chest compressions (CC) and 30 inflations to achieve approximately 120 events per minute is the current consensus of science and treatment recommendations (CoSTR) for neonatal resuscitation. However, the optimal CC rate to optimise coronary and cerebral perfusion during cardiopulmonary resuscitation (CPR) remains unknown. The aim was to compare CC rates of 60/min with 90/min and their effect on the time to return of spontaneous circulation (ROSC), survival, haemodynamic, and respiratory parameters. We hypothesized that asphyxiated newborn piglets that received CC at 60/min versus 90/min during cardiopulmonary resuscitation would have a shorter time to ROSC.

Methods: Newborn piglets (n = 7/group) were anaesthetised, tracheotomized and intubated, instrumented and exposed to 45 min normocapnic hypoxia followed by asphyxia and cardiac arrest. Piglets were randomly allocated to a CC rate of 60/min or 90/min. CC were performed using an automated CC machine using CC superimposed with sustained inflation. Haemodynamic parameters, respiratory parameters, and applied compression force were continuously measured.

Results: The mean (IQR) time to ROSC was 97 (65-149)sec and 136 (88-395)sec for CC rates of 60/min and 90/min, respectively (p = 0.31). The number of piglets that achieved ROSC was 5 (71%) and 5 (71%) with 60/min and 90/min CC rates, respectively (p = 1.00). Haemodynamic parameters (i.e., diastolic and mean blood pressure, carotid blood flow, stroke volume, end-diastolic volume, left ventricular contractile function) and respiratory parameters (i.e., minute ventilation, peak inflation and peak expiration flow) did not differ with a CC rate of 60/min compared to 90/min.

Conclusion: Time to ROSC, survival, haemodynamic, and respiratory parameters were not significantly different between CC rates of 60/min versus 90/min. Different CC rates during neonatal resuscitation warrant further investigation.

Conflict of interest: None declared.

923
MODIFIED DELPHI CONSENSUS IDENTIFYING UK NEONATAL TRANSPORT RESEARCH PRIORITIES. A COMPARISON OF HEALTH-CARE PROFESSIONALS AND PARENT PERSPECTIVES IN PRIORITY SETTING

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Background/Aim: Over the last decade we have observed significant advances in care provision within neonatal transport in the UK. Due to lack of high impact neonatal transport specific research studies, updates in clinical practice have been informed by neonatal/scientific based research, leaving many unanswered questions raised by neonatal transport service providers and users.

Our study aims to identify the top ten UK neonatal transport research priorities most important to healthcare professionals and parents and observes differing perspectives between these cohorts. This abstract presents Phase 2 survey results.

Method: Using key principles outlined by the James Lind Alliance priority setting guidance, a three phased modified Delphi consensus was formulated and conducted over a 2-year period.

Phase 2 Research priorities meeting consensus (n=22)	Parent scores (n=55)		Healthcare professional scores (n=99)	
	Score ≥ 4 (%)	Mean±SD	Score ≥4 (%)	Mean±SD
1. Preventing harm with equipment failure in neonatal transport	100	4.80 ± 0.40	89.9	4.53 ± 0.80
2. Investigating the risk of neonatal transport	90.9	4.49 ± 0.72	91.9	4.33 ± 0.70
3. Sedation and pain relief during transport	94.6	4.55 ± 0.60	86.9	4.33 ± 0.77
4. Impact of transfer on babies with birth-related brain injury	83.7	4.31 ± 0.79	90.9	4.44 ± 0.69
5. Optimal temperature management during transfer	85.5	4.18 ± 0.77	86.9	4.27 ± 0.78
6. Dealing with bereavement and death in transport	87.3	4.44 ± 0.76	83.8	4.21 ± 0.93
7. Invasive ventilation techniques during transport	92.7	4.49 ± 0.64	80.8	4.11 ± 0.82
8. Long term neurological outcomes for transported babies	74.5	4.22 ± 0.88	86.9	4.22 ± 0.72
9. Impact of vibration exposure during transfer	76.4	4.05 ± 0.97	85.9	4.22 ± 0.76
10. Exploration of timely in utero transfer	80.0	4.27 ± 0.91	82.8	4.28 ± 0.90
11. Assessments methods for babies' stress and discomfort during transfer	92.7	4.49 ± 0.69	74.7	3.96 ± 0.95
12. Ambulance design exclusive to neonatal transport	80	4.20 ± 0.99	81.8	4.14 ± 0.81
13. Development of better restraining systems (safety harness) for the baby	74.6	4.15 ± 0.85	83.8	4.21 ± 0.79
14. Effects of acceleration and deceleration forces to babies during neonatal transfer	70.9	4.04 ± 0.99	85.8	4.24 ± 0.74
15. Respiratory outcomes for transported preterm babies	90.9	4.44 ± 0.76	74.7	4.01 ± 0.89
16. Carbon dioxide monitoring in transport	76.4	4.18 ± 0.91	81.8	4.07 ± 0.75
17. Family support away from home for those with transferred babies	89.1	4.40 ± 0.83	73.7	3.92 ± 0.95
18. Impact of noise exposure during transfer	65.5	3.95 ± 0.93	85.9	4.26 ±0.80
19. Use of non-invasive ventilation such as CPAP and high flow during transport	83.6	4.29 ± 0.79	73.7	3.94 ± 0.86
20. Outcomes for babies transferred for surgical management	78.2	4.27 ± 0.85	76.8	3.92 ± 0.88
21. Mental health issues associated with families of transported babies	76.3	4.05 ± 0.95	75.8	3.90 ± 0.92
22. Benchmarking system for important measures/outcomes in neonatal transport	65.5	3.91 ± 0.87	80.8	3.98 ± 0.86

Table 1 Phase 2 survey, Comparison of parent and healthcare professionals scores (Percentage score ≥ 4 and Mean ± SD) of the 22 research priorities that met consensus after analysis of n = 154 survey responses

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The Phase 1 and 2 surveys were sequentially disseminated to healthcare professionals and parents. Each respondent was asked to rank each priority against a 5-point Likert scale. Consensus was defined where >75% of respondents had given score ≥ 4, those meeting consensus were discussed in the final Delphi priority setting virtual workshop.

Results: Total of 269 survey responses were analysed from healthcare professionals (n = 161) and parents (n = 115) over two sequential surveys. Phase 1 survey (n = 115 responses): 23/43 research priorities met consensus; 6 new priorities were added after screening of free text responses. Phase 2 survey (n = 154 responses), 22/29 research priorities met consensus, differences between parent and healthcare professional scoring shown in (Table 1). Research priorities encompassing areas of transport risk, thermoregulation and pain and sedation during transport scored highly by both cohorts. Marked differences were observed around priorities exploring transport environment exposures, these were scored highly by healthcare professionals compared to parents. Priorities focusing on infant outcomes showed parents held respiratory outcomes to be of greater importance compared to healthcare professionals whose focus was towards long-term neurological outcomes.

Conclusion: Differing perspectives observed during priority setting are often reflective of an individual's experience. Engagement of parent perspectives, alongside healthcare professionals has played an invaluable role within this priority setting project; generating holistic neonatal transport research priorities most relevant to today's service providers and their users' needs This evidently will yield greater impact, through targeted funding and research resources.

Conflict of interest: None declared.

929
CAN OPEN LUNG STRATEGY IN THE DELIVERY ROOM REDUCE CPAP FAILURE IN VERY PRETERM INFANTS? RANDOMISED CONTROLLED TRIAL USING TWO DIFFERENT PRESSURE RANGES (OpenCPAP-DR)

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Background: Recommended standard CPAP pressures for delivery room management of very preterm infants may not meet the needs of individual babies. In this study, we aimed to compare the influence of individualised CPAP therapy applied with lung

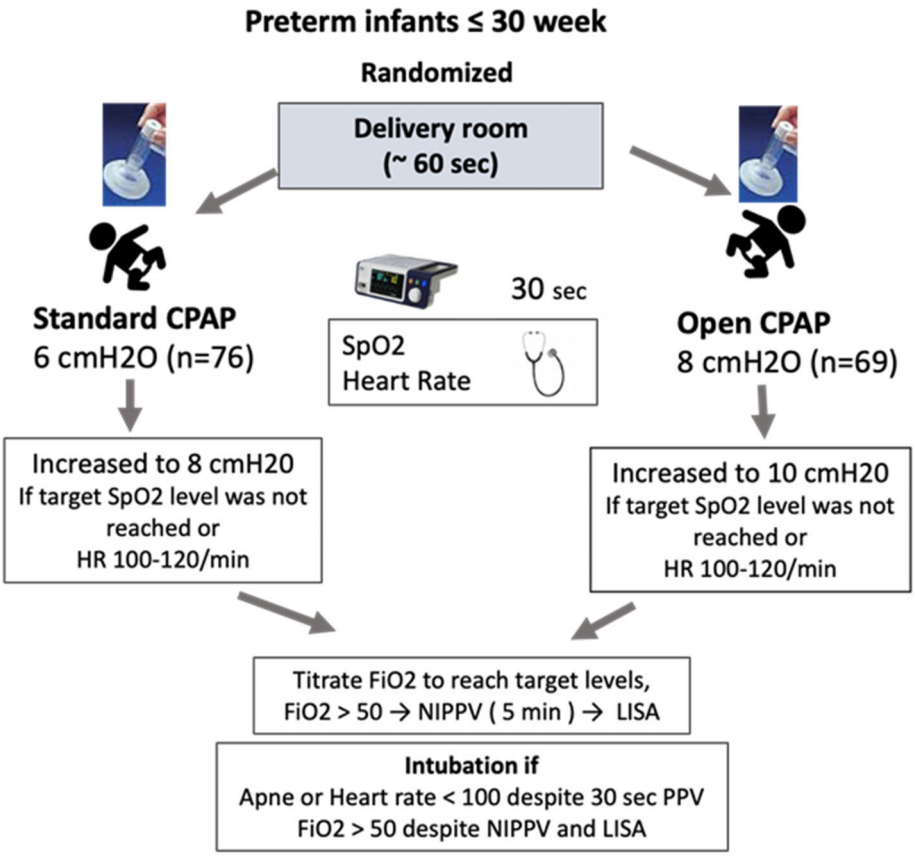


Fig. 1 Study protocol.

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recruitment using different PEEP ranges on physiological parameters, and CPAP failure.

Methods: Eligible infants ≤30 weeks of gestation were randomised into standardCPAP or openCPAP groups according to initial CPAP levels of 6 or 8 cmH2O under 30% FiO_2 following the initial steps of resuscitation. The heart rate(HR) and preductal saturation(SpO2) were evaluated every 30 s. Starting pressures were increased to the upper limit of 8 cmH2O for the standardCPAP group and 10 cmH2O for the openCPAP group if the heart rate and oxygen saturation targets were not achieved. FiO_2 level was titrated if the target saturation was not reached with the upper pressure limits, and LISA threshold was $FiO_2 > 50\%$. CPAP failure was defined as NIPPV, LISA or invasive MV requirement in the first 72 h. Primary outcomes were FiO_2 and SpO2 level at 5th /10th minutes, LISA requirement and CPAP failure within the first 72 h (Clinical Trial NCT05031650).

Results: Among the 145 successfully randomised infants, 76 were in the standardCPAP group and the remainder in the openCPAP group. Mean gestational age and birthweights were 28.23 ± 1.64 weeks and 1144 ± 306 g respectively. The need of PEEP adjustment to the upper limit was higher in the standardCPAP group(51.3% vs. 30.4%, $p = 0.012$). There were no significant difference between the groups in terms of FiO_2 levels at 5th/10th minutes, LISA need in the delivery room or in the NICU. CPAP failure rate was higher in the standardCPAP group (72.4% vs. 55.1%, $p = 0.038$). Incidence of morbidities including pneumothorax, and/or mortality were similar (Fig. 1).

Conclusion: This is the first clinical trial specifically assessed the effect of lung recruitment strategy using different PEEP levels in the delivery room management of very preterm infants. An individualised PEEP strategy starting with a PEEP level of 8 cmH2O seems to promote better lung aeration, and increased CPAP success. Further studies evaluating individualised PEEP strategy in delivery room accompanied with objective lung volume monitoring are needed.

Conflict of interest: None declared.

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PERINATAL STROKE LESION VOLUME AND TOPOLOGY ARE RELATED TO COGNITIVE IMPAIRMENT AT EARLY SCHOOL-AGE

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Background: Perinatal arterial ischaemic stroke (PAIS) leads to major developmental disabilities, such as motor and cognitive sequelae, as well as epilepsy, language disorders and behavioural problems. Early MRI offers the ability to accurately predict motor disabilities in later life. However, it is still very challenging to predict the effect of PAIS on other developmental domains. This study aims to create voxel-based lesion-symptom maps to identify specific PAIS features associated with adverse cognitive development at early childhood.

Methods: A total of 94 term-born neonates with PAIS, born between 2000 and 2016, from the Hospital for Sick Children in Toronto (SickKids), Canada (n = 45) and the University Medical Center in Utrecht (UMCU), the Netherlands (n = 49) were included who had a neonatal MRI available (performed at a mean age of 4.1 ± 3.0 days after birth). Stroke lesion volumes were semi-automatically segmented and used for univariate voxel-based lesion symptom mapping (VLSM). Cognitive development was assessed at a mean age of 5.2 (0.8) years by the Wechsler Pre-school and Primary Scale of Intelligence (WPPSI), that yielded full scale intelligence quotient (FSIQ), verbal and performance intelligence quotient (VIQ and PIQ) and performance speed index (PSI).

Results: Cognitive impairment, defined as a FSIQ below −1 SD, was associated with lesions in the left temporo-parietal lobe including the postcentral gyrus and the superior and middle temporal gyrus. In the UMCU, but not in the SickKids, cohort, impaired performance speed (PSI below −1 SD) was associated with lesions in the right parietal lobe, specifically the inferior parietal lobe. Stroke lesion volume was negatively correlated with all cognitive subscores and cut-offs were calculated for stroke volume to predict cognitive impairment, ranging between 4.9% and 6.0% of total intracranial volume.

Conclusion: In this multicentre study, we were able to accurately delineate, in a semi-automatic method, stroke lesions on early MRI in a large cohort of 94 patients with PAIS and found that stroke lesion volume and topology on neonatal MRI are associated with cognitive development at early school-age.

Conflict of interest: None declared.

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'SCAN THE LINE' QIP: POINT OF CARE ULTRASOUND SCAN (POCUS) FOR LONG LINE (CVL) TIP CONFIRMATION IN NICU

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Background: Central venous line / long line placement in neonates is a common procedure. Malpositioned lines can lead to significant morbidity and mortality. Therefore, X-rays are routinely performed to confirm correct placement of the line. Currently, X-ray is the gold standard, however, point of care ultrasound scans (POCUS) are becoming more widely used as a way of assessing line tip position. In addition, POCUS allows the clinician

	Pre implementation of POCUS (Oct 2021 – Apr 2022) *N – 56*	Post implementation of POCUS (May 2022 – Apr 2023) *N - 29*
Number of X-rays done to confirm LL tip position	80 1.43/LL insertion	33 1.14/LL insertion
Number of LL adjustments required *(lines removed not included as POCUS would not have changed outcome)	40% (22) *(1 line removed)	12.5% (3) *(5 lines removed)

Table 1 Compares number of X-rays and LL adjustments required with and without POCUS

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to manipulate the line to the correct position in real-time. We identified that post Long Line (LL) insertion, infants were having multiple X-rays and line adjustments which had a number of negative implications.

Aim: Quality Improvement Project (QIP) on POCUS/Real-Time Ultrasound to confirm LL tip position.

The project specifically aims to reduce the exposure to radiation associated with LL insertion and reduce the risk of line infection or line loss by reducing the number of line adjustments required.

Methods: Setting – Tertiary Neonatal Intensive Care Unit (NICU). Step 1 – Literature review on POCUS for LL tip position. Step 2 – Retrospective data analysis on number of X-rays and line adjustments (October 2021–April 2022). Step 3 – Implementation of POCUS to confirm line tip position (May 2022). Step 4 – Prospective data collection regarding the number of X-rays and line adjustments (May 2022–April 2023).

Results: In total, 116 long lines were analysed. 56 prior to the introduction of POCUS and 60 post introduction (29 of these lines used POCUS).

Gestation ranged from $22+6$ to $37+4$ weeks and birthweight from 450 g to 2830 g.

Post introduction of POCUS there was a reduction in the number of X-rays from 1.43/LL to 1.14/LL, and the percentage of lines requiring adjustment reduced from 40.0% to 12.5% (Table 1).**Discussion/Conclusion:** Introduction of POCUS to confirm LL tip position in NICU significantly reduced the number of X-rays done and line adjustments. POCUS was associated with better positioned lines, decreased irradiation and cost. The main limitation is, prospectively not all LL insertions used POCUS due to lack of POCUS-trained staff. The next step is to develop a training package to train all medical staff on POCUS to identify LL/CVL tip position.

Conflict of interest: None declared.

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DECODING SLEEP PATTERNS IN PRETERM INFANTS: LEVERAGING CONVOLUTIONAL NEURAL NETWORKS AND multi-modal FEATURE EXTRACTION FROM near-Infrared SPECTROSCOPY

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Background: Sleep is important for brain development in (pre) term infants. Accurate and non-invasive monitoring of sleep stages active sleep (AS) and quiet sleep (QS) is essential for assessing the quality of sleep, guiding clinical interventions, and thereby optimising sleep in the neonatal intensive care unit (NICU). Cerebral Near-Infrared Spectroscopy (NIRS) is more and more common in the NICU, and signals are affected by physiological processes that can be potentially used for sleep quantification. We aimed to assess AS and QS by means of a single (NIRS) sensor.

Methods: A single NIRS sensor was placed on the forehead and NIRS was recorded at 100 Hz in 10 preterm infants admitted to our NICU. We extracted eight features from the raw NIRS signals, including heart rate (HR) and respiratory rate (RR). These features were then fed to a deep convolutional neural network (CNN) model to classify AS versus QS. We assessed the performance of the proposed CNN model in two cross-validation approaches (i.e., data pooling and leave-one-subject-out (LOSO)). The accuracy, balanced accuracy, F1-score, and Kappa were assessed. We also compare the performance of the classifier with six benchmark classifiers including K-Nearest Neighbours, Naive Bayes, Support Vector Machines, Random Forest, AdaBoost, and XGBoost.

Results: The results showed an outperformance of the proposed CNN model over the benchmark classifiers in terms of accuracy (average at 88%), balanced accuracy (94%), F1-score (91%), and Kappa (95%) in the data pooling cross-validation. Likewise, the model outperformed the benchmark classifiers in the LOSO cross-validation approach.

Conclusion: The study demonstrated that using a single Near-Infrared Spectroscopy (NIRS) sensor and a deep convolutional neural network (CNN) model can effectively classify active and quiet sleep stages in preterm infants in the neonatal intensive care unit. This research suggests that the combination of NIRS and CNN holds great potential for optimising neonatal sleep monitoring and thereby guiding interventions to improve the quality of sleep in infants admitted to the NICU.

Conflict of interest: None declared.

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HOW TO DEFINE POST-NATAL GROWTH FAILURE? THE ANALYSIS OF PGF INCIDENCE WITH THE USE OF FOUR DIFFERENT DEFINITIONS

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Background: Maintaining optimal growth is one of the great challenges in the population of premature newborns, especially those with very low birthweight (<1500 g). Some studies suggest that growth impairment may impact future neurodevelopment and long-term metabolic and cardiovascular effects. Due to multiple different definitions used in the literature, the incidence of post-natal growth failure (PGF) and its consequences are very difficult to evaluate. The aim of this retrospective study is to determine the incidence of PGF depending on different definitions.

Methodology: We included 146 newborns with VLBW hospitalised in our department between 2018 and 2021. Patients with congenital disorders were excluded. We gathered data on the perinatal period, maternal and neonatal morbidities. Infants' measurements, such as body weight, head circumference (HC), and length, were collected during hospitalisation. We assessed the growth pattern with Fenton charts as a reference. *Z*-scores

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were calculated using Fenton Peditools. The group was subdivided based on birthweight into SGA (<10 centiles) and non-SGA newborns (>10 centiles). In the analysis, we applied four longitudinal definitions of PGF: (1) decrease of weight z-score > 1 from birth to discharge; (2) decrease of weight z-score > 2 from birth to discharge; (3) decrease of weight z-score > 1 from nadir to discharge; (4) simultaneous decrease of weight, HC, and length z-score > 1 from birth to discharge.

Results: Depending on the applied definition, the incidence of post-natal growth failure varied greatly from 10.96% (def. 2) up to 56.85% (def. 1). We found that when using definitions 2, 3, or 4, it was significantly more likely to diagnose post-natal growth failure in SGA newborns in comparison to non-SGA group.

Conclusions: Unifying the definition of PGF is crucial to evaluating its risk factors and incidence. Proper growth evaluation plays an important role in the management of preterm VLBW newborns in the NICU. Appropriate identification of patients with growth impairment may impact their nutritional support in the future and assessment of probable long-term consequences.

Conflict of interest: None declared.

990
CONTEMPORARY PATTERNS OF BRAIN INJURY IN INFANTS WITH NEONATAL ENCEPHALOPATHY IN THE THERAPEUTIC HYPOTHERMIA ERA

Aisling Garvey[1,2], Eniko Szakmar[2,3], Hoda El-Shibiny[2], Helene Meunier[4], Brian Walsh[1,2,5], Sara Cherkerzian[2], Mohamed El-Dib[2], Terrie Inder[2,6]

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Background: Brain injury in Neonatal Encephalopathy (NE) has historically been classified into injury to the deep grey matter, white matter/watershed area or global injury. However, injury in other areas have been described. This study aimed to describe contemporary patterns of brain injury in infants with NE in the era of therapeutic hypothermia (TH) and to examine potential risk factors associated with different patterns of injury.

Methods: Retrospective analysis of all infants with NE admitted for TH to the Brigham and Women's Hospital, a tertiary NICU (January 2016–December 2021). MRIs were performed after rewarming and scored independently by 3 reviewers blinded to outcome and grade of encephalopathy using the Weeke scoring system. Mann–Whitney U Tests were performed to compare risk factors in infants with and without different patterns of injury.

Results: Two-hundred and eighty-nine infants with all grades of NE were included with a median gestational age of 39.3 weeks (IQR 37.5–40.1) and median birthweight of 3.13 kg (IQR 2.72–3.54). Of these, 196 (68%) had abnormal MRI findings. Locations of injury are outlined in Table 1.

Injury to the grey matter was associated with the requirement for extensive resuscitation (chest compressions $P < 0.001$, epinephrine $P < 0.001$), lower 10-min Apgar scores ($P = 0.003$), worse post-natal gas measurements (pH $P = 0.043$, base deficit $P = 0.033$, lactate $P = 0.031$) and the requirement for inotropes in the NICU ($P = 0.013$).

	n (%)
MRI Findings	
Normal MRI (score of 0)	93 (32)
Abnormal MRI (score of ≥1)	196 (68)
Location of Injury	n (% of those with injury)
Deep Grey Matter	47 (24)
Thalamus	22 (11)
Basal Ganglia	23 (12)
PLIC	22 (11)
Brainstem	6 (3)
Perirolandic Cortex	11 (6)
Hippocampus	7 (4)
White Matter	89 (45)
Cortex	32 (16)
White Matter (not PWML)	47 (24)
PWML	32 (16)
Hemorrhage	26 (13)
Optic Radiation	16 (8)
Corpus Callosum	22 (11)
Cerebellar	34 (17)
Signal abnormalities	12 (6)
Hemorrhage	32 (16)

PLIC, posterior limb of the internal capsule; PWML, punctate white matter lesions

Table 1 Description and location of brain injury noted on MRI scans

Injury to the white matter was associated with a lower birthweight ($P = 0.005$), risk of chorioamnionitis ($P = 0.033$), lower umbilical pH values ($P < 0.001$), lower 5- and 10-min Apgar scores ($P = 0.021$ and 0.015 respectively) and the requirement for intubation ($P = 0.004$).

Infants with grey or white matter injury had a higher clinical ($P = 0.003$; $P = 0.001$) and EEG grade ($P = 0.002$; $P = 0.048$) of NE and were more likely to require intubation ($P = 0.022$; $P = 0.004$). These infants had a higher incidence of seizures ($P < 0.001$) and death ($P = 0.003$), and had longer hospital stays ($P < 0.001$). Cerebellar injury was associated with vaginal delivery ($P = 0.043$) and incidence of PPV ($P = 0.043$).

Conclusion: Areas of brain injury noted in infants with NE extend beyond the hallmark patterns of basal ganglia/thalamus and watershed areas and are associated with different risk factors which may aid in the short-term prediction of outcome.

Conflict of interest: None declared.

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HIGHER LEVELS OF ANTISECRETORY FACTOR IN MOTHERS OWN MILK IS ASSOCIATED WITH REDUCED INCIDENCE OF SEPSIS IN PRETERM INFANTS

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Background: Antisecretory Factor (AF) is a protein present in breastmilk that regulates inflammatory processes. AF can be increased by commercially available dietary supplements, classified as food for special medical purposes. A small RCT has shown increased AF levels in breast milk and a preventive effect on mastitis. Inflammation and inflammatory reactions contribute to preterm birth and trigger complications leading to major morbidities in in preterm infants with significant impact on long-term health, parental stress, and societal costs.

We aimed to investigate the level of AF in mothers' own milk (MOM) in relation to sepsis and other neonatal morbidities in preterm infants.

Methods: Samples of breastmilk and infant plasma were collected at 1, 4, and 12 weeks after birth from 38 mothers and their 49 infants born before 30 weeks gestation. AF-compleasome in MOM was determined by a sandwich enzyme-linked immunosorbent assay (ELISA) and inflammatory markers in infant plasma by a panel of 92 inflammatory proteins. Neonatal treatments and outcomes as sepsis, necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), patent ductus arteriosus (PDA), intraventricular haemorrhage (IVH), and retinopathy of prematurity (ROP) were recorded.

Results: The level of AF in MOM week 1 was lower for infants with later sepsis compared to no sepsis ($P = 0.005$). Corrected for nutritional intake of MOM, higher levels of AF decreased the risk for sepsis, OR 0.24. AF in MOM week 1 was negatively correlated to inflammatory proteins in infant plasma week 4, markedly IL-8, which was also associated with infant sepsis. A higher AF-compleasome in MOM week 1 was inversely associated with the number of inflammatory morbidities in the infant (any combination of sepsis, NEC, BPD, PDA, IVH and/or ROP) (Spearman's rho -0.361, $P = 0.01$, Kruskal Wallis test $P = 0.048$).

Conclusion: Naturally high amounts of antisecretory factor in mothers' own milk during the first week after birth, is associated with lower risk for sepsis and less inflammation in the preterm infant. AF in MOM may be an important component in the anti-inflammatory and protective effects of breastmilk for preterm-born infants, and maternal dietary supplementation to increase AF a possible target for future interventions.

Conflict of interest: None declared.

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ESTIMATION OF EEG-MATURATIONAL AGE IN PRETERM INFANTS USING DEEP LEARNING MODELS

Johannes Mader[1], Manfred Hartman[2], Laura Gschwandtner[2], Katrin Klebermass-Scherhof[1], Tobias Werther[1], Angelika Berger[1], Tillmann Kluge[2], Vito Giordano[1]

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Background: The brain of preterm infants is developing very rapidly in an environment different form mother's womb. Hence monitoring the neurological development of such patients is important. Since manual EEG analysis is very tedious, research has recently been focusing on automatic recognition algorithms using machine learning.

The aim of this study was to train and compare four featureless machine learning models for estimating the EEG maturational age (EMA) of preterm infants using EEG data collected from amplitude-integrated electroencephalography (aEEG) monitors.

Methods: This was a retrospective data analysis considering 590 EEG recordings from 197 preterm infants with a mean (std) gestational age at birth of 25.8 (2.1) weeks and 30.2 (3.8) weeks post maturational age (PMA) at the day of recording. We excluded patients with major neurological conditions and recordings performed under sedation. The analysis was performed on the raw three-channel EEG (C3-P3, C4-P4, C3-C4) signal recorded with aEEG monitors.

The patient dataset was split into 149 patients for training and 48 patients for testing. Three different convolutional neural network (CNN) models and one hybrid (CNN and long-term memory) model were trained to estimate the PMA based on four channel EEG data using a 6-fold validation. All models were evaluated on the independent test data set to determine the best performing model architecture.

Results: The largest CNN model had the best performance classifying, on average, 74% of all recordings correctly within 1 week of PMA and 95% of all recordings within 2 weeks, see Fig. 1, outperforming previously published models. The mean standard deviation of that model was 5.9 days within a patient or 6.6 days for all recordings.

Furthermore, we looked at the impact of wide and short convolutional filters in the input layer of the CNN models and found that wide filters have a greater impact on the performance.

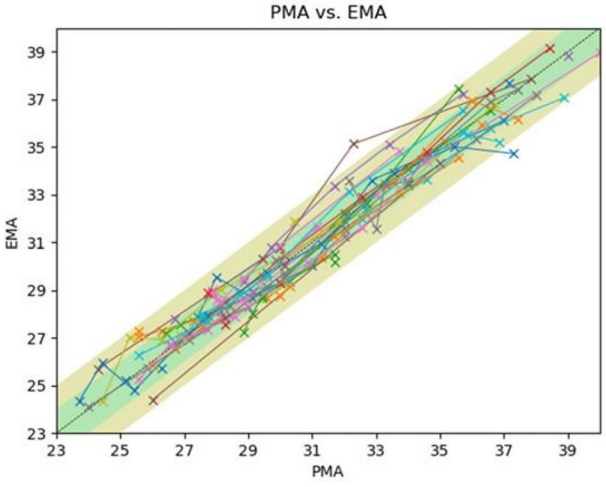


Fig. 1 PMA and estimated EMA of all recording of the test dataset. Recordings from the same patient are coloured the same and are connected by a line.

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Conclusion: Automated EMA estimation can accurately track the neurological developmental of preterm infants. Using aEEG monitors instead of conventional EEG monitors could improve the applicability of such algorithms in clinical settings, especially when access to EEG experts or multichannel EEG monitors is limited.

Conflict of interest: I am employed *via* a project funded by the FWF.

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IDENTIFY CORRELATION BETWEEN SENTINEL EVENTS AND BRAIN LESIONS IN HYPOXIC–ISCHAEMIC ENCEPHALOPATHY (HIE)

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Introduction: Perinatal asphyxia(PA) is a unpredictable event that can result in post asphyxial encephalopathy. In most cases it is not possible to identify an underlying sentinel event(SE). Outside the presence of SE, the only way to predict asphyxia is abnormalities in the cardiotocographic tracing. Acute damage during PA is associated with typical lesions of the basal ganglia(BG), the thalami(T) and the posterior limbs of the internal capsule(PLIC). However, SE and related brain lesions are rarely investigated together.

Methods: It was a retroprospective study included term newborns with HIE treated with hypothermia(HT). Details regarding the antenatal and perinatal medical history were obtained. Brain lesions were detected such as abnormal signal or diffusion restriction at the first MRI performed 3 to 5 days after HT. They were classificated in typical lesions (T, BG, diffuse BGT + WM, PLIC and perilondic cortex) and atypical (other cortex regions and white matter including minor lesions such as punctate white matter lesions PWML, optic radiation abnormalities). We divided the newborns in: presence(PSE) or absence(ASE) of SE.

Results: 78 newborns treated with HT were included. In PSE patients 22/78 (28.2%), more severe umbilical artery pH values ($P = 0{,}002$) and a pathological CGT 14/22 (63.6% vs. 35.7% of ASE group, $P = 0.03$) emerged. MRI brain lesion was present in 26/78 (33.3%) of 11/26 (42.3%) PSE patients. In PSE group MRI lesions (11/22) were significantly more frequent than ASE group 15/56 (50% vs. 26.8%, $P = 0.05$ respectively); typical lesions in 8/11 (72.7%) vs. 7/15 (46.7%), respectively. In particular, typical thalamic, perirolandic lesions and PLIC alterations ($P = 0.02$; $P = 0.05$; $P = 0.04$; $P = 0.04$, respectively) were present in PSE group. aEEG alterations (48.3%) had a positive correlation for typical MRI lesions at all levels (<0.001) but not for the atypical ones ($P = 0.2$).

Conclusion: The nature of the insult causing typical lesions is consistent with an acute/profound ischaemic insult, highly plausible in case of a SE. Conversely the presence of atypical abnormalities like white matter alterations suggest a more chronic kind of insult to the brain, reinforced by the lack of significant aEEG alterations. Further studies are needed to identify the potential iatrogenic role of HT in case of white matter damage.

Conflict of interest: None declared.

1025
IMPLEMENTATION OF NUTRITIONAL CARE BUNDLE WITHIN A NEONATAL UNIT IN A STEPWISE, GRADUATED APPROACH USING QI METHODOLOGY

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Introduction: Preterm nutritional care makes up several components of the Perinatal Excellence to Reduce Injury in Premature Birth (PERIPrem) bundle of care, improving mortality and brain injury in preterm babies. British Association of Perinatal Medicine (BAPM) recommends that all preterm babies should ideally receive buccal colostrum/expressed breast milk(EBM) within 6 h of birth, alongside receiving parenteral nutrition(PN) within 8 h of birth and to have their first dose of probiotics with their first non-nutritive feed as soon as possible after birth.

Methods: XPRES is a team-based QI project comprising key stakeholders from both neonatal and maternity teams – including medical, nursing, advance nurse practitioners and infant feeding leads. We have involved parents at several stages of our QI PDSA cycles to guide successful implementation. Using QI methodology, the XPRES team has now gone through 7 PDSA cycles. Initially focusing on improving time of preterm babies receiving 1st buccal colostrum/EBM, the XPRES group has now got 5 nutritional arms to our QI group: buccal colostrum, donor human milk (DHM), enteral feeds, probiotics, parenteral nutrition(PN). With each advancing PDSA cycle, we gradually added different interventions including educational tools, guidelines, training packages, as well as parental surveys to help improve outcomes across the five arms. At each cycle, both quantitative and qualitative data was collected from parental surveys, BadgerNet data, prospective and retrospective ward based data collection.

Results: Table 1 highlights what was achieved during each PDSA cycle. It is evident there is vast improvement in most areas of the various arms of the nutritional care bundle.**Discussion:** Our QI group highlights the experience of a tertiary neonatal care centre to achieving a successful nutritional care bundle optimising preterm nutrition. The XPRES QI group took a stepwise approach, engaging key stakeholders at each stage, allowing the unit to personalise interventions, and set targeted goals thereby maximising success at each cycle – this is in an effort to work towards achieving an ideal nutritional care bundle. The next stage would be to measure overall success of the five arms of the nutritional care bundle including NNAP measures like NEC rates.

Conflict of interest: None declared.

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PDSA cycle	Outcome measured	Interventions	Results
PDSA 1	Improving time of receiving 1st buccal colostrum	Staff education, Patient & staff questionnaires	• Overall improvement in time of 1st buccal colostrum to baby by 7.6 hours across all gestation by end of 3rd PDSA cycle. • 16.8 hour overall reduction in <28 weeker group.
PDSA 2	Improving time of receiving 1st buccal colostrum	XPRES packs	
PDSA 3	Improving time of receiving 1st buccal colostrum	XPRES trolley & Maternity boxes	
PDSA 4	Improving time of receiving 1st buccal colostrum	Education and raising awareness Involvement of maternity teams and parents as stakeholders Presentation in MatNeoSip, maternity QIPS, Maternity safety champions meeting	• Time of administration of first buccal colostrum halved from 18 hours to 9.9 hours across all age groups.
	Nutritional guidelines	Hypoglycaemia, Enteral feeding,	
	Introduced Probiotics	Probiotics guidelines and implementation	• Probiotics introduced. 75% of babies received it.
PDSA 5	Introduced DHM	Education, Parental surveys, Road shows	• 35% of babies <32 weeks received 1st buccal colostrum within 6 hours. • 35% of babies whose parents consented to DHM received it. • 63% on EBM at discharge.
		PN & Enteral feeding guideline	
	Holistic nutritional care	EBM, TPN, DHM, probiotics, enteral feed at discharge	
PDSA 6	Review of current practice	Evidence based recommendations at maternity and neonatal roadshows to raise awareness and optimise preterm nutrition	• 80% of babies <32weeks received 1st buccal colostrum within 6hours of birth. • 78% received DHM following consent. • 57% on regular EBM by day2, and 80% by day 14. • 85% on EBM/breastfeeding at discharge.
PDSA 7	Improving PN delivery	PN toolkit and staff training	Current PDSA cycle in progress.
	Enteral feeding	Guidelines aligned to ESPHAGN recommendations	
	Nutritional care	Continue educational roadshows to maintain standards and awareness	

Table 1 Highlights the stages of the PDSA cycles, as well as the interventions and outcomes achieved at each stage

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PERSISTENT ALTERATION OF microRNAs IN NEONATAL HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE) IN THE FIRST 6 H AFTER BIRTH

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Background: HIE remains a serious cause of neurological morbidity in neonates. Initial therapeutic intervention is time sensitive and early diagnosis of HIE remains subjective. We have previously identified miRNAs which are consistently altered in umbilical cord blood and wished to establish if these miRNAs would be detectable and altered on post-natal blood sampling in the first 6 h after birth.

Methods: Infants with HIE and healthy controls born in Cork University Maternity Hospital (CUMH) from 2018 to 2020 from the Multimodal Assessment of Newborns at Risk of Neonatal Hypoxic Ischaemic Encephalopathy (MONiToR) study. Inclusion criteria for sample selection were term infants born with HIE (and matched controls) in CUMH from 2018 to 2020, who were ≥36 gestational weeks of age. HIE grade (mild, moderate, or severe) was determined based on modified Sarnat score within 6 h. Whole blood was collected within the first 6 h (T0) after delivery *via* Neoteryx dried blood spot microsampling. A custom qPCR panel of 19 candidate miRNAs and three housekeeping miRNAs for normalisation was analysed in all infants. Benjamini-Hochberg (BH) correction was applied to correct for multiple testing.

Results: In total 41 infants were included in the study (controls, $n = 13$, and HIE, $n = 28$ (12 mild, 14 moderate, 2 severe)); and whole blood samples were analysed using in the custom qPCR panel. Comparing infants with mild and moderate HIE at T0 vs. control infants at T0, 8 miRNAs were significantly altered after BH adjustment including miR-374a and miR-181b which we have previously validated in cord blood. Subsequently, comparing infants eligible for therapeutic hypothermia (TH) at T0 (moderate and severe HIE) vs. infants not eligible for TH at T0 (controls and mild), 2 miRNAs were altered; miR-205 was upregulated (Fold Change = 7, BH adj. *P*-Value <0.001) and miR-181b was downregulated (Fold Change = −1.5, BH adj. *P*-Value <0.001).

Conclusion: Altered miRNA expression persists in the first 6 h of life and can be detected using a minimally invasive microsampling method. These miRNAs should be further explored to identify their potential as bedside biomarkers for rapid detection of hypoxic brain injury.

Conflict of interest: None declared.

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IMPACT OF BEING BORN SMALL FOR GESTATIONAL AGE ON RENAL DRUG CLEARANCE

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Background: The pharmacokinetics of drugs in neonates vary largely, as a result of variation in for instance gestational age (GA), birthweight, and post-natal age (PNA). Current research has not paid specific attention to neonates born small for gestational age (SGA) as compared to appropriate for gestational age (AGA) counterparts. We aim to determine the influence of being born SGA on the clearance (CL) and volume of distribution (Vd) of gentamicin and amikacin in neonates.

Methods: We used already available datasets of patients treated with gentamicin or amikacin (Table 1). For both drugs, we used the previously published two compartment model in NONMEM 7.4 and a covariate analysis was performed in which the influence of SGA (i.e., a birthweight less than the 10th percentile of the birthweight for their GA) and *Z*-score of birthweight for GA were tested, in addition to birthweight or GA and PNA, on CL and bodyweight on Vd.

Results: After including SGA in the covariate model, in addition to birthweight and PNA, CL proved to be 19% higher in SGA neonates compared to AGA neonates for both gentamicin and amikacin ($P < 0.001$, respectively). When SGA was added as covariate in the GA and PNA model, gentamicin and amikacin CL was significantly decreased with 30% and 32% ($P < 0.001$), respectively, for SGA compared to AGA neonates. Overall, the birthweight and PNA + SGA model described the data significantly better than the GA and PNA + SGA model for both gentamicin and amikacin CL ($P < 0.001$). In addition to bodyweight, SGA was not a covariate for Vd.

	Gentamicin [4,5]	Amikacin [6–9]
Number of patients (n)	733	944
Gestational age (weeks)	35 (23-42.1)	32 (24-42)
Postmenstrual age (weeks)	35.29 (23.1-43.3)	33 (24-55)
Postnatal age (days)	3 (1-30)	3 (1-30)
Birthweight (g)	2390 (440-5240)	1780 (420-5420)
Bodyweight (g)	2385 (440-5420)	1920 (420-5420)
Co-administration of ibuprofen (n(%))	76 (10.4%)	52 (5.5%)
Small for gestational age (n(%))	84 (11.5%)	121 (12.8%)
Birthweight Z-score	0.11 (-4.1 - 4.8)	-0.17 (-3.4 - 4.0)

Values are expressed as median [range]

Table 1 Patient demographics of the gentamicin and amikacin dataset

Conclusion: Being small for gestational age has an important impact on the clearance of gentamicin and amikacin. If dosing is based on birthweight, CL for SGA neonates is 19% underestimated, potentially because the maturation for SGA neonates is further developed than predicted by their birthweight. If dosing is based on GA, CL for SGA neonates is 30% overestimated, probably because the maturation for SGA neonates is behind as predicted by their GA. These results imply that SGA should be included into dosing guidelines for renally cleared drugs in neonates.

Conflict of interest: None declared.

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DIAGNOSTIC UTILITY OF FULL BLOOD COUNT SCREENING IN NEONATES BORN TO MOTHERS WITH MODERATE–SEVERE THROMBOCYTOPENIA

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Background: Maternal thrombocytopenia during pregnancy is relatively common. However, the relationship between maternal and neonatal thrombocytopenia is poorly understood. We aimed to determine whether a correlation exists between platelet counts of neonates born to thrombocytopenic mothers (<100 × 10^9/L) and maternal counts, given the non-evidence based practice of screening these neonates with an early full blood count (FBC).

Methods: We identified records from 557 thrombocytopenic mothers and the 337 associated newborn charts from 2018 to

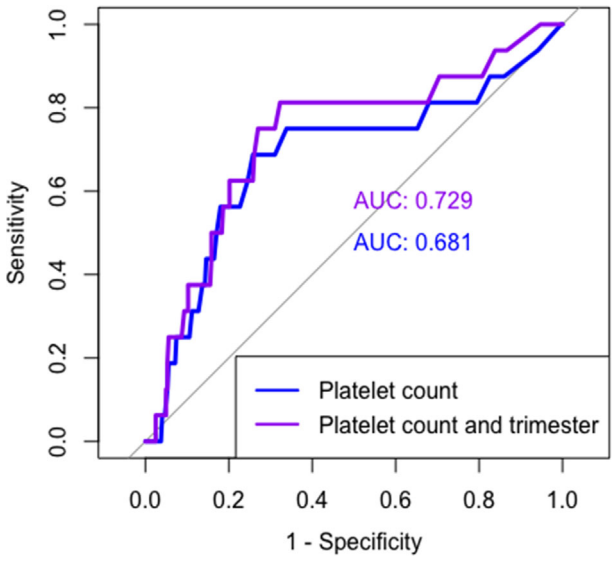


Fig. 1 ROC curve with AUC for maternal platelet count alone (as continuous variable) versus <80 × 10^9/L (as dichotomous variable) in identifying neonatal thrombocytopenia.

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2022. Mothers with a maternal platelet count <100 × 10^9/L prior to delivery during present gestation were included. Any thrombocytopenia that occurred outside of pregnancy or in the postpartum period was excluded. Receiver operator characteristic (ROC) curves were generated using the 'pROC' statistical package on R and Area under the Curve (AUC) examined. Coordinates of the 'best' fit model were examined using the 'pROC' statistical package.

Results: A total of 550 FBCs were taken in neonates of mothers with thrombocytopenia. Sixteen neonates with clinically significant thrombocytopenia (Platelet count <100 × 10^9/L) were identified. 'Number(s) needed to treat' (NNT) was 78 FBCs for infants requiring treatment and 183 FBCs to identify a clinically significant haemorrhage. Maternal platelet count alone was not a significant predictor of neonatal thrombocytopenia (Fig. 1). The addition of trimester of onset of thrombocytopenia did not significantly improve predictive power. The coordinates of the best platelet count threshold for this dataset were then derived from the ROC curve and determined that a threshold of 78 × 10^9/L maternal platelets offered the best sensitivity (74%) and specificity (68%) in this cohort.

Conclusion: Screening FBCs based on maternal platelet counts <100 × 10^9/L has a poor diagnostic yield and accuracy.

Conflict of interest: None declared.

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