YOUNG INVESTIGATOR AWARD

ID 239. Longitudinal Assessment of Cardiac Function in Infants with Downs Syndrome Using Novel Echocardiography Techniques

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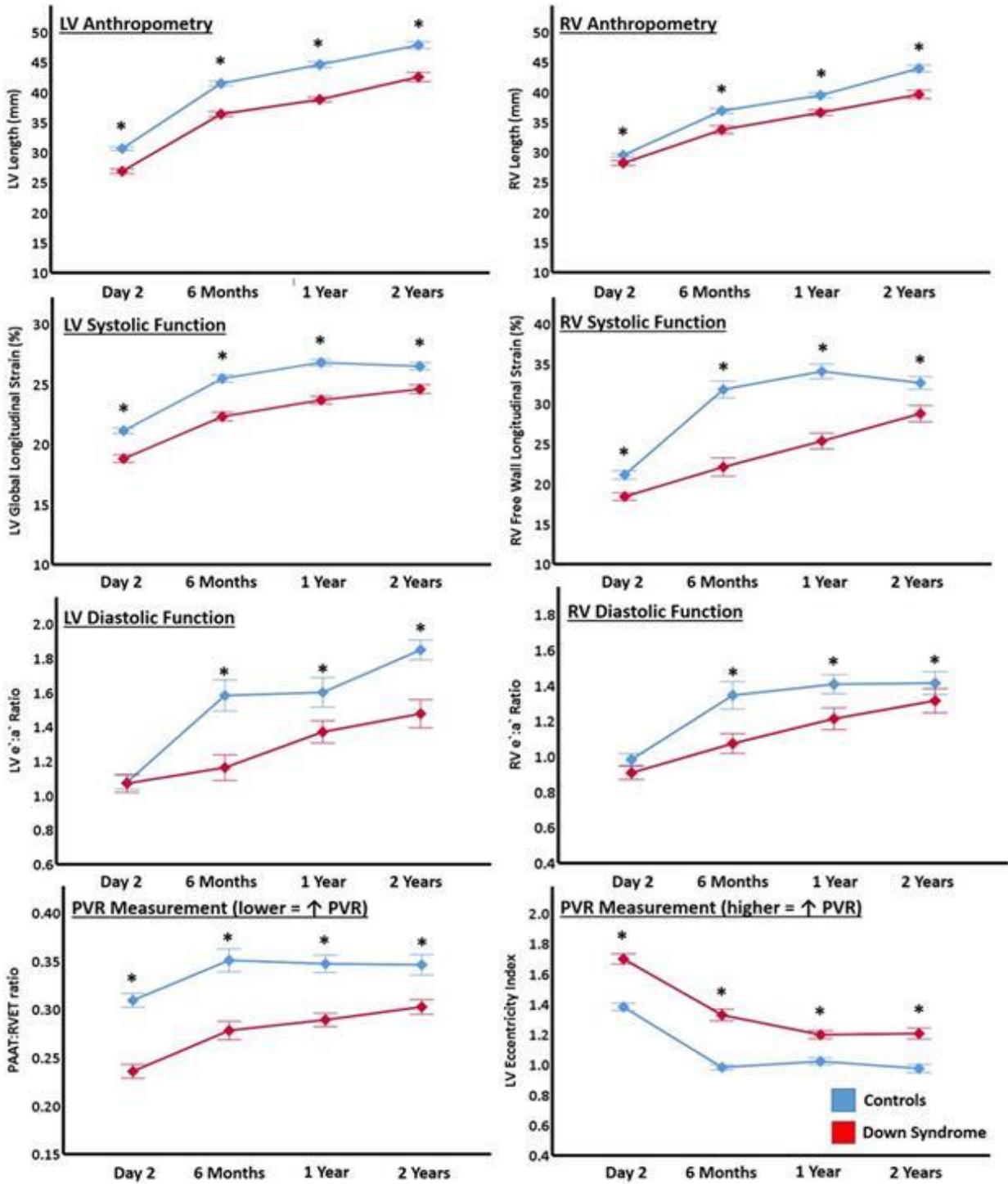
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Introduction: Infants with Down syndrome (DS) with and without congenital heart disease (CHD) can develop myocardial dysfunction and pulmonary hypertension (PH) in the neonatal period. However, data is lacking on cardiopulmonary hemodynamics beyond infancy. The objective of this study was to longitudinally characterize pulmonary hemodynamics and myocardial function in infants with DS with and without CHD over the first two years of age and compare those measurements to control infants without a diagnosis of DS.

Methods: This was a prospective observational cohort study carried out in three tertiary neonatal intensive care units in Dublin, Ireland. Infants with DS with and without CHD and controls underwent serial echocardiograms at birth, 6 months, 1 year and 2 years of age to assess biventricular systolic and diastolic function using deformation analysis and tissue Doppler velocities. Pulmonary vascular resistance (PVR) was assessed using LV eccentricity index and pulmonary artery acceleration time (PAAT).

Results: Seventy infants with DS (48 with CHD and 22 without CHD) were compared to 60 controls. Infants with DS had a lower gestation (37.7 ± 2.1 vs. 39.6 ± 1.2 weeks, p<0.01) and birth weight (3.02 ± 0.68 vs. 3.56 ± 0.42 Kg, p<0.01), and a higher maternal age (37 ± 4 vs. 34 ± 4 years, p<0.01). Infants with DS exhibited smaller LV and RV lengths and lower LV and RV systolic function over the two year period (Figure). LV diastolic function was lower in infants with DS beyond Day 2. RV diastolic function was lower in infants with DS at 6 months and 1 year (Figure). PVR was higher in the DS group throughout the study period (Figure). A diagnosis of DS was an independent significant predictor of all the described measurements at 2 years, independent of CHD status and gestation at birth (all p<0.05).

Conclusion: Infants with DS exhibit impaired maturational changes in myocardial growth, systolic and diastolic function, independent of CHD and gestation at birth. PVR remains elevated universally in children with DS over the two years of age, suggesting that long term follow up is required to further characterise the clinical impact of those findings.

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Maturational changes in myocardial size, systolic and diastolic performance and pulmonary vascular resistance over the two year period

None declared

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ID 188. HYPERGLYCEMIA AND GROWTH RATE IN VERY LOW BIRTH WEIGHT INFANTS - FROM BIRTH UNTIL POSTMENSTRUAL AGE 36 WEEKS

<u>Miss Johanna Karlsson[1]</u>, RD PhD Johannes van Den Berg[1], MD PhD Yonas Berhane[1], RD PhD Elisabeth Stoltz Sjöström[2], MD PhD Estelle Naumberg[1], MD PhD Magnus Domellöf[1], MD PhD Itay Zamir[1]
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Background
Hyperglycemia is common in very low birth weight infants (VLBW, <1500g) during the admission period at the neonatal intensive care unit. This might reflect underlying increased resistance for insulin, an important regulatory hormone that affects infant growth. Growth failure in early infancy is associated with neurodevelopmental abnormalities. The objective of this study was to investigate the associations between hyperglycemia and growth rate from birth until postmenstrual age (PMA) 36 weeks in VLBW infants.

Methods
The Very low birth weight infants – glucose and hormonal profiles over time (LIGHT) study is a prospective observational study that included 50 VLBW infants born during 2016-2019 and treated at Umeå University Hospital. Detailed data regarding glucose concentrations and growth parameters (weight, length and head circumference) were registered prospectively and Z-scores were calculated. A growth restriction phase was defined from birth until the day nadir weight z-score was reached and the entire period was defined from birth to PMA 36 weeks.

Results
Considering growth outcomes during growth restriction phase, for each day with hyperglycemia > 10 mmol/L during this period there was a decrease of 0.14 (95% CI 0.06-0.22, P=0.001) and 0.05 (95% CI 0.01-0.10, P=0.024) in length and head circumference Z-scores, respectively. Considering growth during the entire study period, for each day with hyperglycemia > 10 mmol/L during growth restriction phase there was a decrease of 0.10 (95% CI 0.03-0.18, P=0.005) and 0.20 (95 % CI 0.10-0.29, P<0.001) in weight and length Z-scores, respectively. A decrease of head circumference Z-scores by 0.05 (95% CI 0.01-0.10, P=0.027) during the entire study period was observed for each day with hyperglycemia > 8 mmol/L during growth restriction phase.

Conclusion
Hyperglycemia during the first weeks of life is associated with reduced weight, length and head circumference growth rate during the admission period in VLBW infants. Such changes might influence growth and neurodevelopment later in life. Further studies are needed to elucidate possible mechanisms and treatment modalities for this common and modifiable clinical condition.
None declared

ID 54. A RANDOMISED TRIAL OF PROPHYLACTIC OROPHARYNGEAL SURFACTANT FOR PRETERM INFANTS

Doctor Madeleine Murphy[1], Prof Jan Miletin[2], Dr Hans Jørgen Guthe[3], Dr Claus Klingenberg[4], Dr Vincent Rigo[5], Prof Richard Plavka[6], Dr Kajsa Bohlin[7], Dr Almerinda Pereira[8], Dr Tomas Juren[9], Prof Colm O'Donnell[1]
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Background: Preterm infants are at high risk of developing respiratory distress syndrome (RDS). Endotracheal surfactant is effective in preventing and treating RDS; however, intubation is invasive and associated with adverse effects. Half of infants born <29 weeks' gestation initially managed with continuous positive airway pressure (CPAP) are ultimately intubated for surfactant. Administration of surfactant into the pharynx has been reported in preterm animals and humans and may be effective. We wished to determine whether giving oropharyngeal surfactant at birth reduces the rate of endotracheal intubation for respiratory failure in preterm infants within 120 hours.

Methods/design: Infants born before 29 weeks' gestation who were free of major anomalies were enrolled to this unblinded study at 9 centres in 6 European countries. They were randomly assigned to receive oropharyngeal surfactant at birth in addition to CPAP or CPAP alone. The primary outcome was intubation within 120 hours of birth, either for bradycardia and/or apnoea despite respiratory support in the delivery room, or for pre-specified respiratory failure criteria in the neonatal intensive care unit. Secondary outcomes included incidence of mechanical ventilation, chronic lung disease, and death before hospital discharge.

Results: A total of 251 infants were included in the study; 126 infants were assigned to oropharyngeal surfactant and 125 infants to control. The groups were well matched at study entry; their mean (SD) gestational age was 26 (2) vs 26 (2) weeks, and their mean (SD) birth weight was 874 (261) vs 851 (253) g respectively. There was no difference between groups in the rate of intubation at 120 hours [79/126 (63) vs 81/125 (65) %, p=0.793] (table). There were no differences between the groups in the rate or duration of mechanical ventilation; the rates of bronchopulmonary dysplasia, chronic lung disease, or postnatal steroid use; or in the rate of death before hospital discharge.

Conclusion: Administration of surfactant into the oropharynx immediately after birth in addition to CPAP compared to CPAP alone did not reduce the rate of intubation amongst infants born before 29 weeks' gestation in the first 5 days of life.

Table. Outcome measures

	OP Surfactant N=126	Control N=125	P value
Primary intention-to-treat analysis			
Intubated within 120 hours of life	79 (63)	81 (65)	0.793
GA < 26 weeks	40/48 (83)	35/44 (80)	0.789

GA 26 − 28⁺⁶ weeks	39/78 (50)	46/80 (57)	0.429
Other outcome measures			
Pneumothorax, n (%)	21 (17)	9 (7)	0.031
Pulmonary hemorrhage, n (%)	6 (5)	5 (4)	0.999
Mechanical ventilation, n (%)	77 (62)	81 (66)	0.511
Days of mechanical ventilation, median (IQR)	1 (0, 8)	2 (0, 7)	0.445
Postnatal corticosteroids, n (%)	27 (22)	29 (24)	0.762
Days of respiratory support, median (IQR)	53 (27, 73)	50 (26, 72)	0.798
BPD, n (%)	72 (70)	73 (69)	0.882
CLD, n (%)	26 (26)	29 (29)	0.637
Medical treatment for PDA, n (%)	26 (21)	37 (30)	0.110
Surgical treatment for PDA, n (%)	2 (8)	2 (5)	0.99
Necrotising enterocolitis, n (%)	10 (8)	13 (10)	0.259
IVH grade 3 or 4, n (%)	8 (6)	8 (7)	0.999
Cystic PVL, n (%)	4 (3)	4 (3)	0.999
ROP treated with laser or intravitreal injections, n (%)	13 (10)	10 (8)	0.339
Death before hospital discharge, n (%)	23 (19)	22 (19)	0.999
Survival without BPD at hospital discharge, n (%)	31 (25)	32 (26)	0.884
Survival without CLD at hospital discharge, n (%)	71 (58)	72 (60)	0.794
Duration of hospitalisation, median (IQR), days	73 (53, 92)	75 (53, 88)	0.798
Home oxygen therapy, n (%)	3 (3)	10 (9)	0.048

BPD, bronchopulmonary dysplasia; CLD, chronic lung disease; PDA, patent ductus arteriosus; IVH, intra-ventricular haemorrhage; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity

Table. Outcome measures
Chiesi Farmaceutici, manufacturers of poractant alfa (Curosurf), supplied the study drug free of charge; they had no role in study design; and no role in data collection, analysis or interpretation.

ID 286. PREDICTING ACUTE ADVERSE EVENTS IN NEONATES USING AUTOMATED VITAL SIGN PATTERN ANALYSIS

Mrs Katja Adolphson[1,2], Mr Antoine Honoré[1,2,3], Dr David Forsberg[1,2], Mr Alexander Mildalen Stalhammar[1,2], Dr Kerstin Jost[1,2], Dr Eric Herlenius[1,2]

1Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden, 2Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden, 3Department of Information Science and Engineering, KTH, Stockholm, Sweden

Background: Infants in a neonatal intensive care unit (NICU) are at risk of a variety of adverse events, such as systemic infections, necrotizing enterocolitis and major bleeding. These usually present with initial subtle changes of physiological parameters but may lead to life-threatening situations. Earlier recognition of such events would be of importance in daily clinical practice. Recent development of Clinical Decisions Support Systems indicate that the use of machine learning to detect changes in vital sign patterns enable early diagnosis of neonatal pathologies. Most studies have focused on sepsis and specific subgroups of the NICU population, such as very low birth weight infants. Earlier detection of adverse events in the whole NICU population could reduce morbidity and mortality.

Methods: We performed an observational study on a representative NICU cohort admitted to Karolinska University Hospital, using high frequency vital signs including heart rate, respiratory rate and oxygen saturation. We assessed the ability of a Gaussian Mixture Model based machine learning algorithm to detect sepsis, necrotizing enterocolitis, central nervous system infection, pneumonia, intraventricular hemorrhage and lung bleeding up to 24 hours before clinical suspicion. We compared the ability of the algorithm to detect all adverse events to detection in subgroups of infections and sepsis.

Results: Our study included 342 infants with 41 patients experiencing 52 adverse events. Our algorithm could detect events 24 hours before diagnosis with an area under the receiver operating characteristics curve of 0.69 for the prediction of all adverse events, 0.80 for infections and 0.75 for sepsis.

Conclusion: Several adverse events in NICU patients can be predicted 24 hours before clinical discovery with a machine learning algorithm based on continuous vital sign characteristics. The algorithm is more useful to detect systemic infections, probably since they constitute a more uniform group compared to all adverse events in this study. We use several parameters from standard monitoring in a representative NICU cohort to detect a broader spectrum of complications compared to earlier investigations, and thus explore new applications of vital sign pattern analysis. This potentially provides new tools for the clinician in the diagnosis of neonatal disease, enabling earlier therapeutic interventions and saved lives.

None declared

ID 466. DEVELOPMENT AND PSYCHOMETRIC EVALUATION OF THE CO-PARTNER TOOL FOR COLLABORATION AND PARENT PARTICIPATION IN NEONATAL CARE

Doctor Nicole Van Veenendaal[1,2], **MSc Jennifer Auxier[3]**, Doctor Sophie van der Schoor[2], Professor Linda Franck[4], MSc Mireille Stelwagen[2], Doctor Femke de Groof[5], Professor Hans van Goudoever[1], MSc, PhD Iris Eekhout[6], Professor Henrica de Vet[7], MSc Anna Axelin[3], Doctor Anne van Kempen[2]

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BACKGROUND Active parent participation in neonatal care and collaboration between parents and professionals during infant hospitalization in the neonatal intensive care unit (NICU) is beneficial for infants and their parents. A tool is needed to support parents and to study the effects and implementation of parent-partnered models of neonatal care.

METHODS We developed and psychometrically evaluated a tool measuring active parent participation and collaboration in neonatal care within six domains: Daily Care, Medical Care, Acquiring Information, Parent Advocacy, Time Spent with Infant and Closeness and Comforting the Infant. Items were generated in focus group discussions and in-depth interviews with professionals and parents. The tool was completed at NICU-discharge by 306 parents (174 mothers and 132 fathers) of preterm infants. Subsequently, we studied structural validity with confirmatory factor analysis (CFA), construct validity, using the Average Variance Extracted and Heterotrait-Monotrait ratio of correlations, and hypothesis testing with correlations and univariate linear regression. For internal consistency we calculated composite reliability (CR). We performed multiple imputations by chained equations for missing data.

RESULTS A 31 item tool for parent participation and collaboration in neonatal care was developed. CFA revealed high factor loadings of items within each domain. Internal consistency was 0.558 to 0.938. Convergent validity and discriminant validity were strong. Higher scores correlated with less parent depressive symptoms (r=-0.141, 95%CI -0.240; -0.029, p=0.0141), less impaired parent-infant bonding (r=-0.196, 95%CI -0.302; -0.056, p<0.0001), higher parent self-efficacy (r=0.228, 95%CI 0.117; 0.332, p<0.0001), and higher parent satisfaction (r=0.197, 95%CI 0.090; 0.308, p=0.001). Parents in a family integrated care model had higher scores than in standard care (beta 6.020, 95%CI 4.144; 7.895, p<0.0001) and mothers scored higher than fathers (beta 2.103,95%CI 0.084; 4.121, p=0.041).

CONCLUSION The CO-PARTNER tool explicitly measures parents' participation and collaboration with professionals in neonatal care incorporating their unique roles in care provision, leadership, and connection to their infant. The tool consists of 31 items within six domains with good face, content, construct and structural validity.

None

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ID 362. Resuscitation after cardiac arrest in a newborn piglet model of LPS induced sepsis; randomization to epinephrine versus placebo and the effects on ROSC and markers of CNS outcome

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Background
Most cardiac arrests (CA) in newborns are presumed of hypoxic origin, yet a number of preexisting conditions, e.g. sepsis, have been associated with high risk of requiring resuscitation. Epinephrine is part of the resuscitation guidelines; however, epinephrine may not be the optimal treatment in sepsis associated CA (SA-CA), as epinephrine and sepsis are both potential risk factors of adverse neurologic outcome. We aimed to investigate the effect of epinephrine vs. placebo on 1) return of spontaneous circulation (ROSC), 2) time-to-ROSC, and 3) markers of CNS outcome, in a piglet model of neonatal SA-CA.

Methods
Sepsis was induced in 30 newborn piglets by continuous infusion of lipopolysaccharide (LPS) from Escherichia coli. After four hours of LPS infusion, hypoxia was induced by clamping the endotracheal tube until CA (mean arterial blood pressure <20 mmHg and heart rate <60 bpm). CPR was initiated five minutes after CA. The animals were randomized to either CPR + intravenous epinephrine or CPR + placebo (saline). The primary outcome was ROSC and secondary outcomes were time-to-ROSC and markers of CNS outcome measured by magnetic resonance imaging and -spectroscopy (MRI/MRS) 14 hours after ROSC.

Results
We found no difference in ROSC (RR = 0.93 (95 % CI: 0.70 to 1.18)) or time-to-ROSC between animals resuscitated with epinephrine compared to placebo. The Lac/NAA ratio in frontal cortex was significantly lower in animals that received epinephrine (median Lac/NAA ratio; epinephrine: 0.17 vs. placebo: 0.39; p = 0.02); though, all remaining MRS measures showed no difference between the two groups (Figure 1). We found no difference between groups in MRI measures of cerebral edema, cerebral oxygenation, or cerebral perfusion.

Conclusion
Resuscitation with epinephrine compared to placebo did not affect ROSC or time-to-ROSC after neonatal SA-CA. Based on Lac/NAA ratio, the brain damage in frontal cortex was less severe in animals resuscitated with epinephrine. Remaining MRI/MRS biomarkers of brain damage showed no difference between groups. This study provides evidence that epinephrine is a safe treatment to apply during resuscitation with regards to CNS outcome. Yet, epinephrine was nonessential to achieve ROSC, and other therapies might prove more beneficial in neonatal SA-CA.
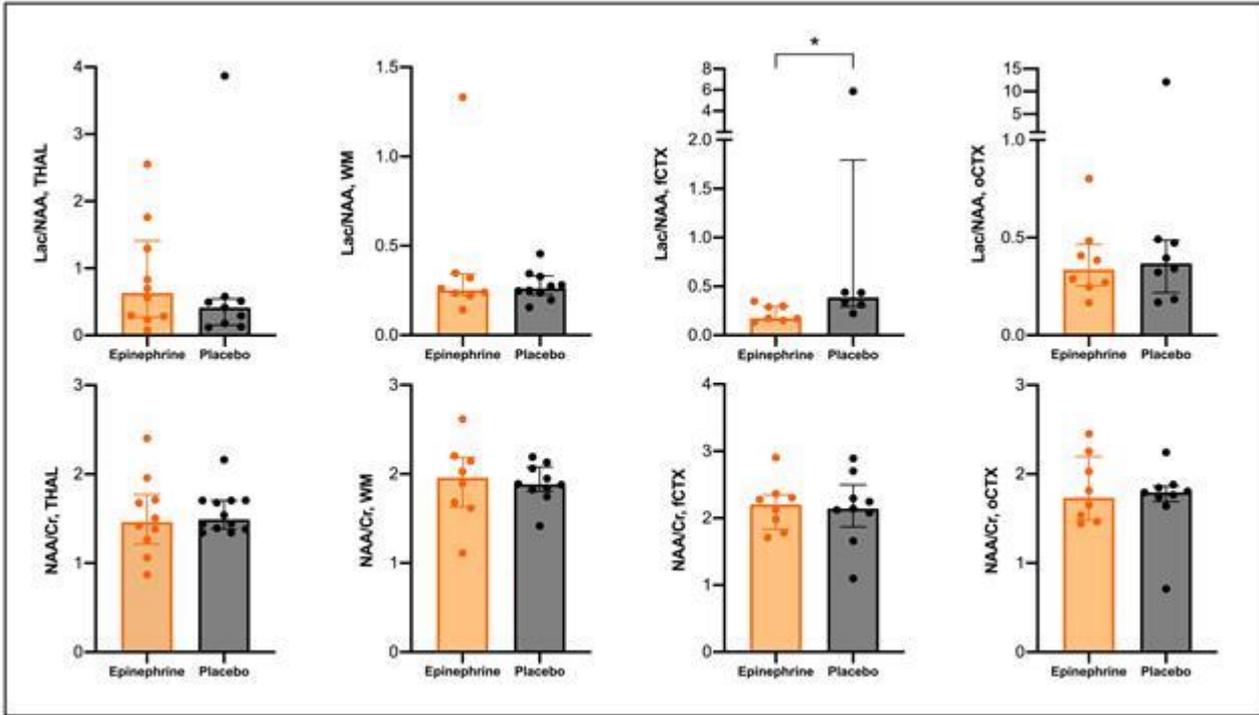
Figure 1. Magnetic resonance spectroscopy. NAA; N-acetyl-aspartate, Cr; creatine, THAL; thalamus, WM; white matter, fCTX; frontal cortex, oCTX; occipital cortex. Scatter plots with superimposed medians (IQR). *p<0.05 epinephrine vs placebo.

None declared

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ID 401. MUSIC IMPACTS BRAIN CORTICAL MICROSTRUCTURAL MATURATION IN VERY PRETERM INFANTS

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[1]Division of Development and Growth, Department of Woman, Child and Adolescent, University Hospitals of Geneva, Geneva, Switzerland, [2]Division of Neonatal and Intensive Care, Department of Woman, Child and Adolescent, University Hospitals of Geneva, Geneva, Switzerland, [3]Department of Radiology and Medical Informatics; Center of BioMedical Imaging (CIBM), University of Geneva, Geneva, Switzerland

BACKGROUND
Preterm birth disrupts important micro and macrostructural neurodevelopmental processes taking place from mid-fetal stage to birth, a critical period of activity dependent plasticity. Music interventions have been used in neonatal intensive care units (NICU), aiming to modulate early brain networks development during this critical period. Such interventions have been shown to impact early brain functional networks' known to be negatively affected by prematurity, but literature is still scarce regarding its impact on brain structure.
METHODS
In order to evaluate if a music intervention might induce brain macro- or microstructural changes, multi-shell diffusion imaging data was acquired longitudinally in 54 very preterm infants (VPT), randomized into a music or control group and undergoing an MRI before the intervention (during the 33th week gestational age) and at its end, at term-equivalent-age (TEA). Data were analysed using a longitudinal whole-brain fixel-based analysis (FBA) complemented by NODDI microstructural analysis.
RESULTS
Between the 33th week and TEA, a longitudinal increase of fiber density (FD), fiber cross-section (FC) and fiber density cross-section (FDC) in all major cerebral white matter (WM) fibers in VPT. In cortical grey matter (GM) regions, while FC and orientation dispersion index (ODI) increase longitudinally, the FD and FDC decrease. When comparing VPT music and control groups, the early music intervention resulted in a longitudinal significantly superior increase of FC and ODI in certain cortical regions, namely in the right middle temporal gyrus, the right precuneus/posterior cingulate gyrus and the left insulo-orbito-temporopolar complex.
CONCLUSION
Important macro and microstructural changes, measured by multi-shell diffusion imaging, are taking place in human WM and GM between the 33th week and TEA, corresponding to tissue-specific developmental maturation processes. Early music intervention, as an activity stimulating process, can increase the complexity of important cortical regions implied in auditory, cognitive and specially socio-emotional processing.
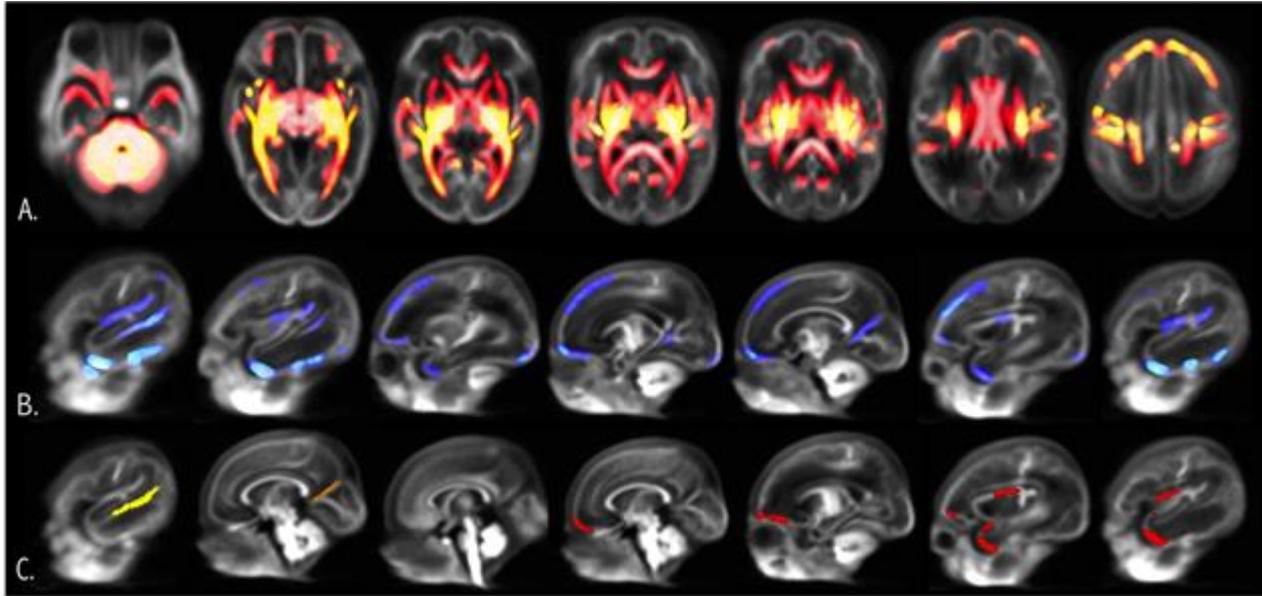
WM fibers with increased FD/FC/FDC (A) and cortical GM regions with increased FC (B) in VPT from 33th week GA to TEA; GM regions with increased FC in music group.
WM fibers with increased FD/FC/FDC (A) and cortical GM regions with increased FC (B) in VPT from 33th week GA to TEA; GM regions with increased FC in music group.

None declared

ID 541. ASSOCIATION OF ANTENATAL CORTICOSTEROIDS ON SURVIVAL AND RESPIRATORY OUTCOMES OF VERY PREMATURE INFANTS – A POPULATION-BASED COHORT STUDY IN ENGLAND AND WALES FROM 2010 TO 2017

Doctor T'ng Chang Kwok[1], Doctor Don Sharkey[1]
[1]*University Of Nottingham, Nottingham, United Kingdom*

Background
Antenatal corticosteroids (ANCs) prevent neonatal mortality and respiratory morbidity. However, much of the evidence was derived from women delivering at 28–34 weeks gestational age (GA). Intensive care is increasingly being considered for babies born from 22+0 weeks GA based on individualised risks that encompass ANCs use. We aimed to explore the impact of a partial and complete ANCs course on outcomes of extremely preterm infants.

Methods
Routinely collected data from infants <32 weeks GA admitted to 185 neonatal units in England and Wales from 2010 to 2017 were extracted. ANCs were defined as none, partial or complete course. Outcomes were death before discharge, respiratory support requirement at one week old, 36 weeks of corrected GA (bronchopulmonary dysplasia (BPD)) and discharge. Logistic regression exploring the effect of ANCs on these outcomes stratified by GA was adjusted for a-priori risk factors (birthweight, gender, multiple pregnancy, prolonged rupture of membranes, chorioamnionitis, congenital anomaly, birth in a tertiary centre and birth year) and clustering within units using robust variance estimator. The number needed to be exposed (NNE) for benefit/harm was derived from adjusted odds ratios and unexposed exposure rates.

Results
59,296 infants were included with 3,568 (5.7%) missing data. Women receiving complete ANCs increased from 62% in 2010 to 70% in 2017, particularly in infants <24 weeks GA where they doubled.

For a complete ANC course, the NNE to prevent one death increases exponentially from 4 (95% CI 3–5) to 88 (95% CI 56–318) in infants ≤23 and 31 weeks GA respectively. Similar findings were found in infants receiving partial ANCs course (Figure). Infants <25 weeks GA who received a complete ANCs course were more likely to receive invasive ventilation in the first week of life and require a longer duration of invasive ventilation (p<0.001). The reverse was seen for GA >25 weeks. No association was found between a complete ANCs course with BPD and respiratory support at discharge.

Conclusion
ANCs, including a partial course, appear to be more efficacious at reducing neonatal mortality with increasing prematurity. Early, but not late, respiratory morbidity also appears better especially in infants >25 weeks GA.
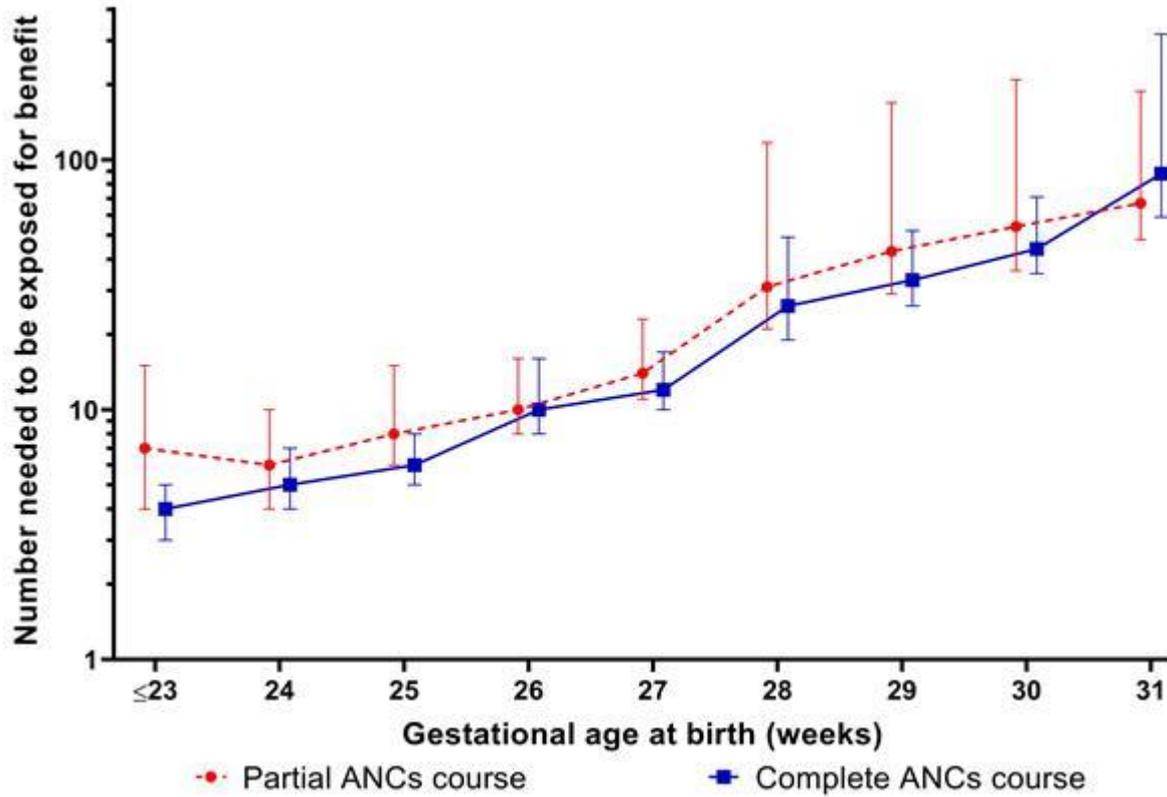
Figure. Number needed to be exposed (95% confidence interval) to complete and partial antenatal cortico-steroids (ANCs) to prevent one death by gestation. Log scale Y-axis and datapoints interleaved for clarity.

None declared