The Neonatal Society
Summer Meeting

June 23rd-24th 2022

University of Winchester
Welcome to Winchester

It is a pleasure to invite you to Winchester (in-person or virtually) for The Neonatal Society Summer Meeting 2022.

The aim of the society is to bring scientists and clinicians together to discuss important topics in perinatal medicine, to learn from one another and generate new ideas, to network and to meet old friends and make new ones too.

The meeting is being held at the University of Winchester and we are delighted to welcome four distinguished keynote speakers from across the world. We are also pleased to invite original abstracts, which will be presented as oral and poster presentations.

We look forward to meeting you in Winchester or virtually this summer. Registration (including accommodation) is now open at https://www.eventbrite.co.uk/e/neonatal-society-summer-meeting-2022-tickets-325853395277
Programme

Thursday 23rd June

9.30 Registration, coffee and exhibits

SESSION 1

9:55 Welcome

10:00 Ourania Kaltsogianni: A randomised crossover study of closed loop automated oxygen control in ventilated infants born at or near term

10:15 Emily van Blankenstein: Neonatal outcomes of babies born at 22-24 weeks gestation in England and Wales 2017-2020

10:30 Reena Bhatt: Recombinant surfactant protein D: a potential therapy in infants at high risk of bronchopulmonary dysplasia

10:45 Aneurin Young: Protein intake is critically important to the early growth of very preterm infants

11:00 Tea break and exhibits

11:30 Keynote Lecture: Professor Karel Allegaert, KU Leuven, Belgium
Challenges of evaluating medicines in neonates

12:30 Lunch and exhibits

SESSION 2

14:00 Karen Luyt: The contribution of newborn illness to child mortality

14:15 Janine Abramson: Trends in caffeine use in very preterm infants and association between early caffeine use, preterm brain injury, and bronchopulmonary dysplasia

14:30 Tim van Hasselt: Examining transfers of preterm infants from neonatal units to paediatric intensive care in England 2008-2018

14:45 Sena Jawad: Improving the design of neonatal clinical trials using routinely collected data

15:00 Don Sharkey: Developing novel microbial biofilm-inhibiting polymer coated neonatal devices to reduce nosocomial infections: an in-vitro study using Candida albicans

15:15 Tea break and exhibits

15:45 David Harvey Fellowship Lecture: Professor Joy Lawn, LSHTM
30 million vulnerable newborns: high impact science and care gaps to close

16:45 Close of day

**Friday 24th June**

9:30 *Registration, coffee and exhibits*

**SESSION 3**

9:55 Welcome

10:00 Charlotte Hanratty: There is no link between Birth Weight and Developmental Dysplasia of the Hip

10:15 Ahmed Ali: Histone acetylation changes in human placenta of mothers’ with preeclampsia

10:30 Sarah Sturrock: NeoMiniGut: preliminary results of a novel technique to create neonatal gut organoids

10:45 Melissa-Sue Ryan: Feasibility of using a parent-report questionnaire for two-year neurodevelopmental follow-up in infants born at 30-34 weeks’ gestational age

11:00 *Tea break and exhibits*

11:30 **Keynote Lecture: Professor Saul Faust, University of Southampton**
Treating and preventing complications of paediatric and neonatal COVID-19

12:30 *Lunch, exhibits*

**SESSION 4**

14:00 **Young Investigator Lecture 2022: Dr James Webbe, Imperial College London**

14:45 Paul Cawley: Point-of-care ultra-low field neonatal magnetic resonance T1 mapping – a novel candidate biomarker for the developing brain

15:00 Samantha Sadoo: Magnetic resonance imaging and magnetic resonance spectroscopy of neonates with encephalopathy in Uganda:
feasibility, acceptability and findings

15:15  Raymand Pang: Complementary regional neuroprotection of melatonin and azithromycin following inflammation-amplified hypoxia-ischaemia in newborn piglets

15:30  Qiaochu Wu: Cerebellar volume, microstructure, and functional outcome in early school-age children without cerebral palsy cooled for hypoxic-ischaemic encephalopathy

15:45  *Tea break and exhibits*

16:15  Prize-giving – best oral presentation and best poster by trainees

16:20  **The Tizard Lecture: Professor Arjan te Pas, University of Leiden, The Netherlands**

Advances in neonatal stabilisation and resuscitation

17:20  Close of Meeting
A RANDOMISED CROSSOVER STUDY OF CLOSED LOOP AUTOMATED OXYGEN CONTROL IN VENTILATED INFANTS BORN AT OR NEAR TERM

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

Ourania Kaltsoyanni1, Theodore Dassios1,2, Christopher Harris2, Rebecca Ann Lee1, Anne Greenough1,3

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Institution(s)

1 Women and Children’s Health, School of Life Course Sciences, Faculty of Life Sciences and Medicine, King’s College London; UK, 2 Neonatal Intensive Care Centre, King’s College Hospital NHS Foundation Trust, London, UK; 3 NIHR Biomedical Research Centre, Guy’s and St Thomas’ NHS Foundation Trust, London, UK;

Introduction (include hypothesis)

Closed loop automated oxygen control (CLAC) systems in preterm, ventilated infants have been associated with an increased percentage of time spent within the targeted oxygen saturation (SpO2) range, fewer prolonged desaturations and fewer manual adjustments to the inspired oxygen concentration (FiO2), when compared with manual oxygen control. Previous studies have not included term born infants. We have tested the hypothesis that the use of CLAC in ventilated infants born at or above thirty-four weeks gestation would reduce the incidence and duration of hypoxic episodes.

Methods (include source of funding and ethical approval if required)

A randomised crossover trial was undertaken at a tertiary neonatal unit between September 2021 and May 2022. Infants were studied on two consecutive days for six hours on each day. They were randomised to receive standard care (manual oxygen control period) or standard care with a CLAC system (automated oxygen control period) first. A planned interim analysis was carried out at half the calculated sample size to review if significant differences had already emerged. The study was approved by the Yorkshire and the Humber-Sheffield Research Ethics Committee and parents gave informed written consent for the infant to take part.

Results

Sixteen infants with a median (IQR) gestational age of 37.4 (36.6-38.8) weeks were studied at a median (IQR) postmenstrual age of 38.8 (37.4-39.8) weeks. During the automated oxygen control period, infants spent less time in hypoxia, SpO2< 92%, (median (range): 1.26 (0.02-6.34) % versus 3.24 (0.1-12.73) %, p=.033) and severe hypoxia, SpO2< 85%, (0.05 (0-3.38) % versus 0.11 (0-38.31) %, p=.043), episodes of desaturation were of shorter duration (p=.001), the median (range) time spent within target SpO2 range (92-96%) was increased (98.25 (91.82-99.95)% versus 79.62 (21.36-99.85) %, p=.001) and their median (range) FiO2 was lower (21 (21-30) % versus 22(21-42) %, p=.018). The median (range) percentage of time spent in hyperoxia was also reduced during automated oxygen control (0.09 (0-3.65) % versus 14.1 (0-74.75) %, p=.011), the episodes of hyperoxia were of shorter duration (p=.008) and fewer manual adjustments were made to the FiO2 (p=.005).

Conclusions

Closed-loop automated oxygen control in ventilated infants born at or near term appears to be beneficial, as it was associated with a reduction in the incidence and duration of hypoxic episodes, increased percentage of time spent in the target oxygen range, reduced time spent in hyperoxia and fewer manual adjustments to the inspired oxygen concentration. Whether it improves long term outcomes merits testing in an appropriately designed randomised controlled trial.

References (include acknowledgement here if appropriate)


Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee X ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: X ☐

Senior author supporting presentation on day of meeting: Professor Anne Greenough
NEONATAL OUTCOMES OF BABIES BORN AT 22-24 WEEKS GESTATION IN ENGLAND AND WALES 2017-2020

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

Emily van Blankenstein¹, Lucy K Smith², Grenville Fox³, Mario Martinez-Jimenez⁴, Sarah E Seaton⁵, Stavros Petrou⁶, Cheryl Battersby¹

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Institution(s)

1. School of Public Health, Faculty of Medicine, Imperial College London, UK
2. Department of Health Sciences, University of Leicester
3. Children's Services, Guy's and St. Thomas’ NHS Foundation Trust
4. Centre for Health Economics & Policy Innovation, Department of Economics & Public Policy, Imperial College London Business School
5. Nuffield Department of Primary Care Health Sciences, University of Oxford

Introduction (include hypothesis)

In 2019, the British Association of Perinatal Medicine (BAPM) updated their guidance from a recommendation of no active (survival-focused) care for infants born <23+0 weeks (1), to recommending a risk-based approach from 22+0 weeks (2). Therefore, more infants born at 22+0 to 23+6 weeks will meet the risk-threshold for survival-focused care, with implications for resources and service planning. We examine recent trends in outcomes of infants born at 22+0 to 24+6 weeks’ gestation using the National Neonatal Research Database (NNRD).

Methods (include source of funding and ethical approval if required)

Babies born at 22+0 to 24+6 weeks’ gestation between 01/01/2017–31/12/2020 and admitted to neonatal units in England or Wales were included. We explored their characteristics, length of stay and outcomes, including: survival to discharge, severe necrotising enterocolitis (NEC), severe brain injury (BI). Composite outcomes of survival without bronchopulmonary dysplasia (BPD), severe NEC, retinopathy of prematurity (ROP), and severe BI, and survival without severe NEC, ROP and severe BI were examined. We explored changes over two epochs (2017 – 2018 and 2019 – 2020) and by gestation group. This study is part of the NIHR-funded neoWONDER programme of research (3) (Research Ethic Committee approval 21/EM/0130, IRAS 293603).

Results

Preliminary results are shown in table 1. The number of admissions for babies born at 22 weeks rose from 27 to 82, whilst admissions at 23 weeks remained similar between the two epochs, and fell for those born at 24 weeks. Babies born at 22 weeks in the earlier epoch had a higher median birthweight than those born in the later epoch (535g vs 495g). Across all gestations, median length of admission was ≤10 days for those who died, and ≥118 days for those who survived. In both epochs, few babies born at 22 weeks survived to discharge (11 and 18), and fewer than 10 in both epochs survived without major morbidities as defined by the composite outcomes.

Conclusions

There was a close to three-fold increase in the number of babies born at 22 weeks and admitted to neonatal units in the more recent epoch. Survival decreased from 41% to 22%; we speculate this reduction may be due to a lower threshold for active care offered at birth. However, we are unable to infer change in practice without data for number of babies alive at onset of labour, and whether survival-focused care was provided at birth; this is currently being explored with Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK).

References (include acknowledgement here if appropriate)


Acknowledgements: Julia Lanoue, Neonatal Data Analysis Unit data analyst, and the UK Neonatal Collaborative
### Table 1: Characteristics and outcomes

<table>
<thead>
<tr>
<th></th>
<th>22 weeks</th>
<th>23 weeks</th>
<th>24 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admitted to neonatal unit, n</td>
<td>27</td>
<td>83</td>
<td>494</td>
</tr>
<tr>
<td></td>
<td>490</td>
<td>803</td>
<td>700</td>
</tr>
<tr>
<td>Survived to neonatal discharge, n (%)</td>
<td>11 (41)</td>
<td>18 (22)</td>
<td>228 (46)</td>
</tr>
<tr>
<td></td>
<td>247* (51)</td>
<td>534 (67)</td>
<td>496** (71)</td>
</tr>
<tr>
<td>Length of stay in days, median (IQR)</td>
<td>146 (124 – 158)</td>
<td>151 (141 – 169)</td>
<td>132 (116 – 154)</td>
</tr>
<tr>
<td>Survived</td>
<td>135 (121 – 155)</td>
<td>118 (103 – 141)</td>
<td>121 (107 – 139)</td>
</tr>
<tr>
<td>Died</td>
<td>2 (1 – 6)</td>
<td>4 (2 – 9)</td>
<td>6 (2 – 17)</td>
</tr>
<tr>
<td>Birthweight, median (IQR)</td>
<td>535 (489 – 580)</td>
<td>495 (470 – 550)</td>
<td>575 (535 – 621)</td>
</tr>
<tr>
<td></td>
<td>580 (525 – 620)</td>
<td>675 (620 – 730)</td>
<td>665 (615 – 725)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>16 (59)</td>
<td>47 (57)</td>
<td>265 (54)</td>
</tr>
<tr>
<td>Delivered by c-section, n (%)</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>36 (7)</td>
</tr>
<tr>
<td>Multiple pregnancy, n (%)</td>
<td>12 (44)</td>
<td>16 (19)</td>
<td>111 (22)</td>
</tr>
<tr>
<td>Antenatal steroids n (%)</td>
<td>None</td>
<td>23* (28)</td>
<td>76** (15)</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
<td>26* (32)</td>
<td>137** (28)</td>
</tr>
<tr>
<td>Admitted to level 3 unit at birth, n (%)</td>
<td>23 (85)</td>
<td>73 (88)</td>
<td>389 (79)</td>
</tr>
<tr>
<td>Severe NEC, n (%)</td>
<td>&lt;10</td>
<td>13 (16)</td>
<td>67 (14)</td>
</tr>
<tr>
<td>Severe BI, n (%)</td>
<td>&lt;10</td>
<td>28 (34)</td>
<td>162 (33)</td>
</tr>
<tr>
<td>Survived without severe NEC, BPD, ROP, severe BI, n (%)</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>&lt;10*</td>
</tr>
<tr>
<td>Survived without severe NEC, ROP, severe BI, n (%)</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>97 (20)</td>
</tr>
</tbody>
</table>

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All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☑

Senior author supporting presentation on day of meeting: Dr Cheryl Battersby
**Title (Upper case)**

RECOMBINANT SURFACTANT PROTEIN D: A POTENTIAL THERAPY IN INFANTS AT HIGH RISK OF BRONCHOPULMONARY DYSPLASIA.

**Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)**

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**Institution(s)**

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**Introduction (include hypothesis)**

Bronchopulmonary dysplasia (BPD) affects up to 40% of infants born <30 weeks gestational age1 and is associated with long term respiratory morbidity. Inflammation plays a key role in the development of BPD. Surfactant Protein D (SP-D) has several immunomodulatory functions in the lung2. We employed a preterm lamb model of ventilator associated lung injury to test the hypothesis that a recombinant fragment SP-D (rfhSP-D) reduces levels of pro-inflammatory cytokines and may therefore have therapeutic potential in preterm infants.

**Methods (include source of funding and ethical approval if required)**

The study was funded by MRC and ethical approval from the University of Western Australia animal ethical committee. 30 preterm lambs delivered by caesarean section at gestational age 124 days. 24 lambs were mechanically ventilated and received endotracheal surfactant at 10minutes. Lambs were split into 3 treatment arms intratracheal (IT) rfhSP-D, intravenous (IV) rfhSP-D and control (IT 0.9% saline). Treatment with 24mg of rfhSP-D or 0.9% saline was administered at 20,140 and 260 minutes. Lambs were euthanised at 300minutes. Lung tissue was homogenised, and quantitative PCR was used to analyse levels of IL-1β, IL-6, IL-8 and TNF-α.

**Results**

Intratracheal administration of 24mg (approx. 8mg/kg) rfhSP-D improved compliance of the lungs when compared to the IV rfhSP-D and control group (p=0.03 in the IT group). The rfhSP-D (both IT and IV) treated groups generally had lower peak inspiratory pressure requirements compared to the control group.

The control (saline) group had the highest expression of all the cytokines measured. Expression of IL-1β and IL-6 were significantly lower in the IT rfhSP-D group (p=0.007 and p=0.01 respectively) compared to the control group. IL-8 and TNF-α expression was lower in the IT rfhSP-D group compared to the control group but not statistically significant (p=0.08 and p=0.7 respectively). IV administration of rfhSP-D did not have a significant impact on the expression of the pro-inflammatory cytokines measured.

**Conclusions**

IT rfhSP-D in preterm lambs reduces the expression of pro-inflammatory cytokines such as IL-6 and IL-1β and does not inhibit the action of standard surfactant therapy. These results support the use of this rfhSP-D as a therapy in preterm infants at risk of BPD.

**References (include acknowledgement here if appropriate)**


**Check box if presenting author is a trainee:** basic science trainee [ ] clinical trainee [ ]

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: X

Senior author supporting presentation on day of meeting: Professor Clark
Title (Upper case)

PROTEIN INTAKE IS CRITICALLY IMPORTANT TO THE EARLY GROWTH OF VERY PRETERM INFANTS

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

Aneurin Young1,2,3, Guo Cheng3, Sarah Ennis3, R Mark Beattie1,2, Mark J Johnson1,2.

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Institution(s)

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2. NIHR Southampton Biomedical Research Centre (BRC)
3. University of Southampton

Introduction (include hypothesis)

Infants born very preterm (before 32 weeks postmenstrual age) frequently fail to keep pace with the weight gain and head circumference (HC) growth of the equivalent fetus in utero. The early growth of these infants is affected by myriad interacting factors which are poorly understood, but likely include features of the pregnancy, perinatal complications and nutritional care. This study aimed to describe the factors which are most influential for growth of very preterm infants during the first 42 days of life.

Methods (include source of funding and ethical approval if required)

Prospectively recorded demographic, clinical, nutritional and growth data from one level 3 neonatal unit were collated. Multiple linear regression was used to explore influences on change in weight standard deviation score (SDS) and HC SDS. Backward stepwise selection with AIC was used to identify the most predictive factors. Candidate factors used for model selection included: gestation, sex, birthweight SDS, umbilical artery doppler status, perinatal steroids and magnesium sulphate, total energy intake and intake of protein, carbohydrate and fat. Work was funded by NIHR Southampton BRC. National REC ID: 14/SC/1275.

Results

Weight information was available for 309 infants and HC data for 276 infants. Median gestation at birth was 27+4 weeks (range 23+3 to 31+5) and mean birthweight was 970g (SD ±250g). Mean weight SDS change from birth to day 42 of life was -0.6 (SD ±0.6) and mean HC SDS change was -0.9 (SD ±1), demonstrating growth velocity falling short of expectations for the equivalent fetus. Eight factors were identified as important determinants of weight gain, including a significant influence of protein intake (an increase in 1g/kg/day of protein intake associated with a reduced weight SDS deficit of 0.5 after correction, p<0.001). Seven factors were identified to influence change in HC SDS, including a significant effect of protein intake (1g/kg/day increase in protein intake associated with reduced HC SDS deficit of 0.44, p<0.001). Accounting for energy intake in models did not significantly change the magnitude or statistical significance of the influence of protein intake on growth parameters, suggesting a protein effect independent of energy intake.

Conclusions

Protein intake is critically important to the early weight gain and head circumference growth of very preterm infants. Further work is required to identify the optimal range of protein intake for these infants, along with ideal ratios between macronutrients, to support healthy growth and development.

References (include acknowledgement here if appropriate)


All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Mark J Johnson
THE CONTRIBUTION OF NEWBORN ILLNESS TO CHILD MORTALITY

Authors (Presenting author underlined)


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Institution(s)

National Child Mortality Database, Child Mortality Analysis Unit, Bristol Medical School, University of Bristol

Introduction (include hypothesis)

The aim of this work was to investigate how many deaths in the first 10-years of childhood are associated with neonatal illness, the specific neonatal conditions involved, and causation of death.

Methods (include source of funding and ethical approval if required)

Deaths between April 2019-March 2021 (24-months), reported to the National Child Mortality Database were identified. Child death review data were linked with neonatal care records (BadgerNet). Neonatal care was defined as receiving care in a neonatal unit after birth, in addition to those who died in the first day of life outside of a neonatal unit (‘Likely neonatal illness’). Characteristics of the population were identified, then using a Poisson model, the relative mortality risk in three age categories (<1 year, 1-4 years and 5-9 years) estimated, stratified by neonatal illness, and by specific neonatal conditions. Populations at risk were estimated from ONS data.

Results

4829 children died before their 10th birthday. Half (n=2406) occurred within the first 4-weeks of life. Overall, 71.6% of deaths had evidence of neonatal illness; 82.7% of deaths <1 year, 38.4% between 1-4 years, and 27.3% between 5-9 years. In the oldest age group (5-9 years) 13.9% of deaths were of children born preterm and 3.2% were of children who had Hypoxic-Ischaemic Encephalopathy after birth (Fig 1). Children with neonatal illness were 14 times (RR13.82 (95% CI 13.00-14.71)) more likely to die before their 10th birthday than those without neonatal illness. Increased risk was seen in all age groups, (<1 year; RR 25.78 (95%CI:23.69-23.06), between 1-4 years; RR 3.69(95% CI:3.12-4.37), between 5-9 years RR 2.08(95%CI:1.72-2.52).

Conclusions

We describe the first national, population level evaluation of the impact of neonatal illness on child mortality. For children who died, after 22 weeks of gestational age, the majority of deaths under 10 years occurred in the first year of life. However, a third of deaths in the next 4 years, and a quarter of deaths in children between 5-9 years of age were also linkable to neonatal illness.

References (include acknowledgement here if appropriate)

The National Child Mortality Database Programme is commissioned by the Healthcare Quality Improvement Partnership as part of the National Clinical Audit and Patient Outcomes Programme.

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒
**Title (Upper case)**

TRENDS IN CAFFEINE USE IN VERY PRETERM INFANTS AND ASSOCIATION BETWEEN EARLY CAFFEINE USE, PRETERM BRAIN INJURY, AND BRONCHOPULMONARY DYSPLASIA

**Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)**

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**Institution(s)**

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2Children’s Hospital, University Hospitals of Derby and Burton NHS Foundation Trust

**Introduction (include hypothesis)**

Caffeine reduces the risk of bronchopulmonary dysplasia (BPD) and improves neurodevelopmental outcomes in very preterm infants (VPTs). Caffeine may have neuroprotective effects and observational studies suggest starting caffeine early could improve neurodevelopmental outcomes. We hypothesised that caffeine use has increased, and that more infants are started on caffeine early. Secondly, we hypothesised that early caffeine use is associated with a reduced risk of preterm brain injury and BPD in VPT infants.

**Methods (include source of funding and ethical approval if required)**

Retrospective cohort study using routinely recorded data (National Neonatal Research Database) of VPT infants (<32 weeks’ gestational age (GA) admitted for >3 days to neonatal units in England and Wales from 2012-2020. Data on caffeine use were extracted from daily prescribing records. Early caffeine use was defined as first use on calendar day 1 or 2 after birth. Prevalence of caffeine use was calculated overall, and by GA group and year of admission. Adjusted odds ratios (aOR) for preterm brain injury (using National Neonatal Audit Programme definition of intraventricular haemorrhage, posthaemorrhagic ventricular dilatation or periventricular leukomalacia) and BPD at 36 weeks’ postmenstrual age were calculated. Ethical approval was granted by the Sheffield REC.

**Results**

Of 60,464 infants, 46,310 (77%) received caffeine. Use increased from 65% of all infants in 2012 to 85% in 2020, (86% to 93% in infants <28 weeks’ GA and 56% to 80% in infants 28-31 weeks’ GA). Amongst infants prescribed caffeine, the median (IQR) number of days of use also increased from 5 (3-13) days in 2012 to 9 (4-19) days in 2020. Caffeine was started early in 56% of those who received caffeine, increasing from 41% in 2012 to 68% in 2020 (36% to 72% in infants <28 weeks’ GA and 44% to 66% in infants 28-31 weeks’ GA). Amongst infants who received any caffeine, the aOR for brain injury was lower in those who received caffeine early compared to those who received it later (early caffeine, 4.781/25.856 (18.5%) vs. late caffeine, 3.894/20.454 (19.0%), aOR=0.95, 95% CI 0.90-1.00, p=0.043). The aOR for BPD was also lower (early caffeine, 9.566/25.856 (37.0%) vs. late caffeine, 7.880/20.454 (38.5%), aOR=0.89, 95% CI 0.85-0.93, p<0.001).

**Conclusions**

With increased and earlier use of caffeine, we found a small reduction in preterm brain injury and BPD associated with early caffeine even after adjustment for confounders including need for mechanical ventilation on day 1. The optimal time of starting caffeine is unknown. A recent RCT was stopped early due to a trend towards higher mortality in the early caffeine group. RCTs are needed to ensure that early caffeine use is safe and effective.

**References (include acknowledgement here if appropriate)**


Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☐

Senior author supporting presentation on day of meeting: Shalini Ojha
EXAMINING TRANSFERS OF PRETERM INFANTS FROM NEONATAL UNITS TO PAEDIATRIC INTENSIVE CARE IN ENGLAND 2008-2018

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

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Institution(s)

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²Neonatal Medicine, School of Public Health, Faculty of Medicine, Imperial College London

Introduction (include hypothesis)

Transfers of preterm born infants from neonatal care to paediatric intensive care (PIC) are necessary for varied reasons including emergency surgery, closure of patent ductus arteriosus (PDA), or ongoing long-term respiratory support for bronchopulmonary dysplasia (BPD). Due to increasing survival of extreme preterm infants with chronic morbidity, we sought to investigate the demand on PIC services for management of complications of prematurity.

Methods (include source of funding and ethical approval if required)

PICANet is the national PIC audit and research database. All PIC admissions aged <2 years in England 2008-2018 were analysed. PICANet reports PIC admissions from neonatal units. Summary statistics produced: frequencies/percentages or median/IQR. NHS Readcodes for primary admission diagnosis analysed. Corrected gestational age (CGA) at admission was calculated. No formal statistical tests reported. PICANet has Research Ethics Committee approval (05/MRE04/17). This project was funded by the NIHR (DF: Ref NIHR301761).

Results

Over the 10 year period there were 99,071 PICU admissions aged <2 years (67,623 individual patients). 14,527 (14.7%) were direct transfers from neonatal care. 43.1% of these neonatal transfers were born preterm; 15.7% born <28 weeks; 9.3% had missing data for gestation. Examining the 2288 transfers born <28 weeks, for those occurring when the baby was <40 weeks CGA (n=1729) the most frequent admission diagnoses were: PDA (n=454, 26.3%); necrotising enterocolitis (n=391 22.6%); hydrocephalus (n=83, 4.8%). For infants born <28 weeks transferred at >40 weeks CGA (n=559) the most common diagnoses were: BPD (n=58, 10.4%); respiratory insufficiency (n=32, 5.7%); respiratory syncytial virus bronchiolitis (n=21, 3.8%). Neonatal transfers born at term (n=6864) were most commonly admitted for cardiac disease. For infants born <28 weeks transferred at <40 weeks median PIC length of stay (LOS) was 2.7 days, 2.7% stayed >28 days; for transfers >40 weeks median LOS was 5.2 days, 10.0% stayed >28 days.

Conclusions

Transfers from neonatal to paediatric intensive care of preterm infants form a considerable proportion of PICU admissions. Infants born extremely preterm (<28 weeks) have a high proportion of gastrointestinal and cardiovascular PIC admissions before term CGA, and then respiratory admissions when they are post-term.

References (include acknowledgement here if appropriate)

N/A

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☒

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Dr Chris Gale
Title (Upper case)

IMPROVING THE DESIGN OF NEONATAL CLINICAL TRIALS USING ROUTINELY COLLECTED DATA

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

Jawad S¹, Prevost AT², Modi N¹, Gale C¹

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Institution(s)

¹Neonatal Medicine, School of Public Health, Imperial College London, Chelsea and Westminster Hospital Campus
²Nightingale-Saunders Clinical Trials and Epidemiology Unit, King's College London

Introduction (include hypothesis)

Clustering, when individuals in a group tend to have similar outcomes, occurs naturally in neonatal data due to the presence of multiple births and neonatal units of care. Accounting for clustering in the design of studies is highly encouraged in the literature (1) to preserve statistical power. However, the lack of published cluster estimates, a measure of the similarity of outcomes of individuals in the same cluster, is a barrier to conducting well designed neonatal trials (2). This study aims to use routinely recorded data to estimate these clusters to add to the published literature and to present their impact on the design of future neonatal trials.

Methods (include source of funding and ethical approval if required)

Data from all neonatal unit admissions in England, Scotland and Wales in the National Neonatal Research Database from January 2016 to January 2020 were included in the analyses. Intracluster correlation coefficients (ICCs) and 95% confidence intervals were calculated for all infants for both multiple births and neonatal units for core neonatal outcomes and other outcomes commonly used in trials. Design effects, a sample size inflator for cluster trials, were then estimated and the effect of clustering on sample size were calculated using typical neonatal trial scenarios. Estimates are presented for all infants as well as by gestational age group based on typical trial populations.

Results

A total of 417,675 infants from 184 neonatal units were included in the analysis. The ICCs for multiple births ranged from 0 to 0.5957 while those for neonatal units ranged from 0.0008 to 0.0642. Design effects for multiple births ranged from 1.0 to 1.08 for all outcomes in the trial scenarios. This implies that to adjust adequately for multiple birth clustering, the sample size for an individual trial needs to be multiplied by a factor of 1.0 to 1.08 (depending on the outcome and trial population). This effect was expectedly much higher for neonatal unit clustering, with sample sizes needing to be inflated 1.10 to 3.50 times. The combined presence of both multiple births and neonatal unit clustering translates to increasing individual sample size calculations from anywhere between 1.10 to 3.78 times. Design effects varied widely between outcomes and gestational age groups.

Conclusions

The use of routinely recorded data has enabled the calculation of precise cluster estimates for a variety of key neonatal trial outcomes. Moreover, this study has clearly presented the implications of these cluster estimates on the sample size of trials. These results should enable a more reliable design for future neonatal trial to increase statistical power and trial efficiency.

References (include acknowledgement here if appropriate)


Check box if presenting author is a trainee: basic science trainee □ clinical trainee □

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: □

Senior author supporting presentation on day of meeting: Chris Gale
DEVeLOPING NOVEL MICROBIAL BIOFILM-IHNIBITING POLYMER COATED NEONATAL DEVICES TO REDUCE NOSOCOMIAL INFECTIONS: AN IN-VITRO STUDY USING CANDIDA ALBICANS

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

Don Sharkey, Claire Saxby, Chester Blackburn, Sophie Goodwin, Kiril Kalenderski, Dave Hampton, Derek Irvine, Paul Williams, Morgan Alexander

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Institution(s)
Centre for Perinatal Research, School of Pharmacy, Faculty of Engineering and School of Life Sciences, University of Nottingham, UK and Camstent Ltd, Cambridge, UK.

Introduction (include hypothesis)
Late-onset infections (LOIs) in preterm infants cause severe illness (20-38%), death (13-19%), are associated with neurodevelopmental impairment (NDI), and increase NHS costs by ~£19,000/infection. Preterm infants can acquire nosocomial LOI from medical devices including endotracheal tubes (ETTs) and nasogastric tubes (NGTs). We have developed a rapid, high throughput polymer discovery platform1,2 to screen for materials that inhibit microbial biofilm formation and can be used to coat common neonatal medical devices. We aimed to identify candidate polymers and coat ETTs and NGTs to compare their biofilm-inhibiting properties.

Methods (include source of funding and ethical approval if required)
Using our polymer discovery platform, we selected candidate polymers to coat neonatal ETT and NGT sections. NGT sections were exposed to infant milk formula for 30mins. Triplicate control and coated sections underwent 24-h incubation with C. albicans, a common neonatal biofilm-forming yeast. Confocal fluorescence microscopy (three sample areas/section) and image analysis were used to quantify biofilm biomass. Kruskal Wallis with Dunn’s multiple comparisons analysis compared controls to polymers with significance set at P<0.05. Funded by the Medical Research Council CiC, EPSRC, and NIHR CYP MedTech Cooperative POC fund.

Results
IBNA-DEGMA and IBNA-TEGMA were identified as potential anti-biofilm polymers. Devices coated in a 90:10 ratio (IBNA:DEGMA or TEGMA) significantly resisted biofilm formation (Table) and exemplified in the two figures below uncoated (marked bioluminescence of C. albicans biofilm formation) and 10% TEGMA coated (minimal growth) ETT sections.

<table>
<thead>
<tr>
<th>Device</th>
<th>Control</th>
<th>Homopolymer</th>
<th>10% DEGMA</th>
<th>10% TEGMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETT</td>
<td>100.3±38.9</td>
<td>5.9±5.1*</td>
<td>1.6±1.2***</td>
<td>2.0±1.7***</td>
</tr>
<tr>
<td>NGT</td>
<td>12.5±7.9</td>
<td>1.2±1.1***</td>
<td>2.4±2.4**</td>
<td>2.3±2.9**</td>
</tr>
</tbody>
</table>

Table: Confocal biomass (µg/cm²) analysis of control and polymer coated devices (n=9/device). *P<0.05, **P<0.01, ***P<0.001. Homopolymer=IBNA coating only

Conclusions
A rapid, high throughput polymer discovery platform allows identification of polymers capable of inhibiting microbial biofilm formation on commonly colonised neonatal medical devices. Development and clinical evaluation of these polymers could reduce the burden of neonatal nosocomial LOI and improve outcomes.

References (include acknowledgement here if appropriate)

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Don Sharkey
There is no link between Birth Weight and Developmental Dysplasia of the Hip

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University of Southampton
Princess Anne Hospital

Developmental Dysplasia of the Hip (DDH) has been linked to high birth weight and packaging disorders, though evidence is limited. This has implications on screening strategies. This study aimed to establish whether birth weight was truly associated with the incidence of DDH.

This cohort study analysed the birth weights of all babies born at our institution over a 24 month period, between 01/01/2017 and 01/01/2019. Babies with DDH and those without DDH were compared. Babies were excluded if born before 38 weeks, had incomplete data, or were a non-singleton pregnancy. Sub-analysis was performed for DDH severity (dysplastic versus subluxed / dislocated hips) and gender. Statistical analysis was performed using SPSS.

There were 10113 babies born at our institution during the selected timeframe, of which 884 were excluded for prematurity, 336 for being non-singleton and 19 for incomplete data. This left 8874 for analysis, of which 95 babies had confirmed DDH. Both the Non-DDH and DDH data sets had normal distribution (Shapiro-Wilkes, p=0.308 and 0.629 respectively), with mean birth weights of 3477.7g with DDH and 3492.8g without DDH. No difference in birth weight was found (Independent T test, p=0.789). Females had a lower birth weight than males (3293.1g versus 3416.6g (P<0.001)) yet have a higher incidence of DDH (ratio 6:1 in this dataset). No significant difference was found between birth weights of females with and without DDH (p=0.068), nor between males with and without DDH (p=0.513). There were no significant differences in birth weights even when only displaced hips were analysed (p=0.543).

This study discredits the belief that DDH may be related to higher birth weight, thus casting doubt on the link to DDH being a packaging problem in utero. This therefore allows future research to prioritise investigation of alternative aetiologies.

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously:

Senior author supporting presentation on day of meeting:
# HISTONE ACETYLATION CHANGES IN HUMAN PLACENTA OF MOTHERS' WITH PREECLAMPSIA

**Authors** (Presenting author underlined. If no author is a Society member, please provide the name of the member introducing the author to the Society)

Ahmed S. Ali $^{1,2,3}$, Manthan Patel $^2$, Pradeepa Madapura $^2$, Ajay K. Sinha $^{1,2}$

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**Institution(s)**

1-Neonatal Unit, Royal London Hospital, London, UK. 2- Centre for Genomics and Child Health, Queen Mary University of London, London, UK. 3-Assiut University Children Hospital, Assiut, Egypt

**Introduction (include hypothesis)**

Preeclampsia (PET) has acute and chronic effects on mothers and infants. Epigenetics marks regulates placental development and may have a role in development of PET, a disease of placental origin (1). Histone modification affects gene expression. DNA repeat elements are implicated in normal placental development as cis-regulatory elements (CREs) for gene expression. Altered histone modification at these repeats could affect expression of gene under its regulation in preeclampsia. We profiled genome wide histone acetylation (H3K27ac and H4K16ac) levels in normal and preeclampsia placental tissue samples along with the transcriptomics.

**Methods (include source of funding and ethical approval if required)**

Six control, five mild preeclampsia (PET) and four severe PET were recruited from Royal London Hospital between the period of May 2021 to March 2022. PET was diagnosed based on ISSHP criteria. Fresh postnatal placental samples were taken and frozen directly in -80°C. Histone acetylation was assessed by Cut&TAG technique (cleavage under targets and tagmentation). The data was analysed for differential and co-occupancy of these histone acetylations at various genomic elements including repeats. Further, we performed RNA-seq and carried out integrative analysis to study differential gene expression regulation by these histone marks. The study has ethical committee approval (HRA 21/55/0010) and was funded from British Counsel in Egypt.

**Results**

Differential histone acetylation is observed in preeclampsia at differentially expressed genes as down-regulated genes show loss of histone acetylation and up-regulated genes different levels of H3K27ac and H4K16ac. Comparison of H3K27ac and H4K16ac at repeat elements identified novel subclasses that could function as CREs. There was an enrichment of H4K16ac and H3K27ac at the subclasses of Long Terminal Repeats (LTRs) such as LTR5, HERVs, LTR9, LTR16, LTR33, MER39, MER41 and THE1. While many of these subfamilies showed enrichment for enhancer mark H3K4me1, few were enriched for promoter mark H3K4me3. This indicates a role of histone acetylation in regulating potential CREs function of these elements in preeclampsia. Altered levels of H4K16ac and H3K27ac was observed in severe PET for the genes known to be implicated in preeclampsia such as CRT, FLT1, DLX5, FOS, LEP, HK2, and GATA3. Functional annotation of differentially acetylated regions showed GO terms linked with placental development, DNA damage, osmotic stress, and immune regulation.

**Conclusions**

This study assessing histone acetylation in human placental tissue showed novel epigenetic marks are altered in preeclampsia, particularly in the severe form. These histone acetylations regulate the CRE function of repeat elements that regulate the target gene expression. Novel repeat subfamilies which could act as potential enhancers are affected in preeclampsia and thus resulting in dysregulated gene expression.

**References (include acknowledgement here if appropriate)**


Check box if presenting author is a trainee:  basic science trainee ☐  clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: XX

Senior author supporting presentation on day of meeting: Dr Ajay K. Sinha
Title (Upper case)
NeoMiniGut: preliminary results of a novel technique to create neonatal gut organoids

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)
Dr Suzy Lim, Dr Sarah Sturrock, Dr Joseph Salem, Professor Kirsty Le Doare

Corresponding author e-mail address: sarah.sturrock@nhs.net

Institution(s)
Centre for Neonatal and Paediatric Infection, St George’s, University of London

Introduction (include hypothesis)
Gut colonisation is an important source of invasive pathogens causing neonatal sepsis. Understanding how bacteria adhere to and invade neonatal gut tissue, and the immune system response, is crucial to preventive strategies. Intestinal organoids – 3D multicellular structures containing the cell types found in intestinal tissue – can be invaluable to understanding disease pathogenesis(1), but to date intestinal organoid creation has been limited to adult tissue. We have successfully grown organoids from preterm neonatal gut samples.

Methods (include source of funding and ethical approval if required)
Neonates aged under 4 months undergoing abdominal surgery involving the small or large bowel either as an emergency or elective procedure were eligible for inclusion. A 0.5-1cm section of resected healthy margin was taken as the research tissue sample. The tissue sample was thoroughly washed before being minced and the intestinal crypts isolated and cultured in basement membrane matrix to form organoids. Resulting organoids were split and propagated before being stored in liquid nitrogen for future research.

Results
To date, 5 participants have been recruited to the NeoMiniGut study. 100% of approached families have consented to participation in the study. Participants have ranged from 25 to 39 weeks gestational age, and have undergone laparotomies for stoma reversal, intestinal perforation, and necrotising enterocolitis. Organoids have been created from ileal, jejunal and stoma tip samples. Organoid culture has been successful in 80%, with a total of >1000 organoids created and stored for future research to date. The unsuccessful organoid culture used a tissue sample from a participant with widespread severe necrotising enterocolitis.

Conclusions
This study’s preliminary results have shown a high success rate for culture of gut organoids from neonatal patients, including those who are premature and those who have active gut infection and disease. Family responses to the study have been positive. Neonatal organoid culture represents a promising field to increase understanding of the pathogenesis and possible preventive targets in neonatal gut infection.

References (include acknowledgement here if appropriate)

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: X

Senior author supporting presentation on day of meeting: Kirsty Le Doare
Title (Upper case)

FEASIBILITY OF USING A PARENT-REPORT QUESTIONNAIRE FOR TWO-YEAR NEURODEVELOPMENTAL FOLLOW-UP IN INFANTS BORN AT 30-34 WEEKS’ GESTATIONAL AGE (GA)

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

Melissa-Sue Ryan, John McIntyre, Samantha Johnson, Shalini Ojha

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Institution(s)

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2. Neonatal Intensive Care Unit, Children’s Hospital, University Hospitals of Derby and Burton NHS Trust, Derby
3. Department of Health Sciences, University of Leicester

Introduction (include hypothesis)

Preterm infants have significant risk of adverse neurodevelopmental outcomes1,2 with high health, social, and educational costs.2 While pathways exist for follow-up of extremely premature infants, more mature infants are not routinely assessed. We investigated the feasibility of using parent rating scales3,4 to assess language, cognitive, and motor skills at 24-month corrected GA for ex-30-34 weeks’ GA infants.

Methods (include source of funding and ethical approval if required)

54 infants were identified from Royal Derby Hospital’s electronic patient records (EPR). Two were excluded (complex congenital conditions). Parents of 52 infants (25 female; 24-months CGA between 01/12/2021-30/04/2022) were offered paper or online questionnaires (Parent Report of Children’s Ability-3 with motor components of the Ages and Stages-3). Basic demographic and clinical information were collected from EPRs. The study is part of the neonatal unit’s quality improvement for achieving 24mo-follow-up of all infants admitted for neonatal care.

Results

We received 29/52 (56%) responses (10 were not contactable; 1 declined; 12 questionnaires not returned).

24/29 (83%) preferred online questionnaires with a greater overall response rate (online, 24/32 (75%) vs. paper 5/9 (56%)).

There was no difference in clinical, maternal, or socio-economic characteristics of responders vs. non-responders (Table 1).

Questionnaires were scored using published cut-offs for developmental delay. 7/24 had moderate/severe delay (at least 2SD below expected: 3, global delay, 4 with isolated motor deficits).

Conclusions

Collection of 24mo-outcomes is feasible using questionnaires, although response rate was low. Prospective engagement of families may improve rates. Some more mature premature infants have moderate/severe neurodevelopmental delay. Follow-up is essential to ensure correct support can be given for these infants.

References (include acknowledgement here if appropriate)


Check box if presenting author is a trainee: basic science trainee  clinical trainee X

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: X

Senior author supporting presentation on day of meeting: Shalini Ojha, Consultant Neonatoalogist
Table 1. Responses to 24mo corrected gestational age neurodevelopmental questionnaire for infants born at 30-34 weeks’ gestational age

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Responders N = 29</th>
<th>Non-responders N = 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age in weeks, median (IQR)</td>
<td>33 (32 to 34)</td>
<td>33 (32 to 33)</td>
</tr>
<tr>
<td>Birth weight in grams, median (IQR)</td>
<td>2260 (1685 to 2500)</td>
<td>1949 (1560 to 2096)</td>
</tr>
<tr>
<td>Females, n (%)</td>
<td>11 (38)</td>
<td>14 (61)</td>
</tr>
<tr>
<td>Length of hospital stay in days, median (IQR)</td>
<td>17 (8 to 29)</td>
<td>18 (12 to 30)</td>
</tr>
<tr>
<td>Co-morbidities, n(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>11 (38)</td>
<td>9 (39)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1 (3)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Necrotising enterocolitis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Any intraventricular haemorrhage</td>
<td>0</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Maternal characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years, median (IQR)</td>
<td>30 (25 to 35)</td>
<td>29 (26 to 34)</td>
</tr>
<tr>
<td>Index of multiple deprivation score, median (IQR)</td>
<td>15893 (7875 to 29253)</td>
<td>13329 (5602 to 26609)</td>
</tr>
</tbody>
</table>

Neurodevelopmental scores of responders (n=29)

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>IQR</th>
<th>Min</th>
<th>Max</th>
</tr>
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<tbody>
<tr>
<td>Parent Report of Children’s Ability- Revised</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-verbal cognition standard score *</td>
<td>98</td>
<td>89-107</td>
<td>53</td>
<td>124</td>
</tr>
<tr>
<td>Total language standard score*</td>
<td>92</td>
<td>80-101</td>
<td>53</td>
<td>119</td>
</tr>
</tbody>
</table>

* where standard scores have mean of 100 and SD of 15

Ages and Stages Questionnaire-3 (motor scale only)

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fine motor scale</td>
<td>50</td>
<td>40-60</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>Gross motor scale</td>
<td>50</td>
<td>45-60</td>
<td>25</td>
<td>60</td>
</tr>
</tbody>
</table>
Title (Upper case)

Point-of-Care Ultra-low Field Neonatal Magnetic Resonance T1 Mapping – a Novel Candidate Biomarker for the Developing Brain

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

F. Padorno1,2 & P. Cawley1,3, L. Dillon1, E. Hughes1, J. Almalbis1, J. Robinson1, A. Maggioni1, M. De La Fuente Botella1, D. Cromb1, A. Price1, L. Arlinghaus4, J. Pitts1, S. Deoni1, S. Williams3,6, S. Malik1, J. O’Muircheartaigh1,3, S. J. Counsell1, M. Rutherford1,3, T. Arichi1,3, A. D. Edwards1,3, J. V. Hajnal1

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Introduction (include hypothesis)

Ultra-low field (ULF) point-of-care MRI allows image acquisition without interrupting medical provision, with neonatal clinical care being an important potential application. Knowledge of the tissue longitudinal relaxation time, known as T1, is key for subsequent structural image contrast optimisation, and could represent a potential biomarker for brain development. We describe an optimised strategy for neonatal T1 mapping at ULF and present T1 data over a range of gestational ages. We hypothesised that T1 would change as a function of postmenstral age, as seen at higher field strengths.

Methods (include source of funding and ethical approval if required)

MRI data were acquired from infants using a 64mT Hyperfine Swoop portable MRI system at St Thomas’ Hospital, London. Scans occurred in natural sleep or following Chloral Hydrate sedation where prior clinical 3T MRI was undertaken. All required intensive care therapies and monitoring were continued during scanning. In each infant, multiple inversion-recovery turbo spin echo sequences were acquired with differing inversion and repetition times. An analysis pipeline incorporating motion correction generated proton density and T1 maps. Regions of interest were placed in the cerebral deep grey matter, frontal white matter and cerebellum. Weighted linear regression was used to describe T1 as a function of postmenstral age. Study Ethics: IRAS 263765 & 77927 (Funding: Medical Research Council, Belinda and Melinda Gates Foundation).

Results

A total of thirty-three exams were acquired from twenty-eight infants with mean age at first scan: 13 days, range: [1, 94], mean postmenstral age at scan: 39.2 ± 0.9 weeks, range: [31.4, 49.0]). A linear reduction of T1 with postmenstral age was observed in all measured brain tissue, most markedly within the frontal white matter - Figure 1. An example axial T1 Map, for infant with postmenstral age 34.0 weeks, is shown in figure 2.

Conclusions

Neonatal T1 values at ULF are shorter than those previously described at standard clinical MRI field strengths. T1 reduces with postmenstral age and is thus a candidate biomarker for perinatal brain maturation.

References (include acknowledgement here if appropriate)

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: -
### MAGNETIC RESONANCE IMAGING AND MAGNETIC RESONANCE SPECTROSCOPY OF NEONATES WITH ENCEPHALOPATHY IN UGANDA: FEASIBILITY, ACCEPTABILITY AND FINDINGS

**Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)**

Sadoo S\(^1\), Nanyunja C\(^2\), Mambule I\(^1,2\), Mugalu J\(^3\), Torrealdea F\(^4,5\), Bainbridge A\(^4,5\), Nabawanuka A\(^6\), Swambale J\(^6\), Perogorletti-Baruteau K\(^4,6\), Srinivasan L\(^4,6\), Gilbert G\(^7\), Mathieson SR\(^7\), Lubowa S\(^8\), Ssebombo H\(^8\), Wintermark P\(^10\), Boylan GB\(^8\), Nakimuli A\(^1,9\), Robertzon NJ\(^1,4\), Nyirenda M\(^1,2\), Cowan FM\(^1,3\), Kowooya M\(^1,2\), Tann CJ\(^1,2\)

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### Introduction (include hypothesis)

The majority of infants with neonatal encephalopathy (NE) are born in low- and middle-income countries where the aetiology, nature and timing of brain insult has not been well defined. Brain magnetic resonance imaging and spectroscopy (MRI/S) can support detection and description of perinatally acquired brain lesions. We aimed to assess the feasibility, acceptability and findings from neonatal brain MR imaging in Uganda.

### Methods (include source of funding and ethical approval if required)

Neonates (≥36 weeks) were recruited to a prospective feasibility cohort study at Kawempe National Referral Hospital, Uganda. Sarnat staging classified severity. Survivors underwent MRI/S (1.5 T) after collaborative protocol development and training. Images were evaluated for quality, and scored (Rutherford\(^1\)). MRS data was fitted using TARQUIN to obtain brain lactate (Lac):N-acetyl aspartate (NAA) peak-area ratios in deep gray matter\(^2\) and sensitivity confirmed using the SPECTRE MRS phantom. Feasibility and acceptability were assessed by the number of recruited participants consenting to, and successfully undergoing MRI/S, of diagnostic quality. Ethics: LSHTM, Uganda Viral Research Institute. Funding: Bill & Melinda Gates Foundation

### Results

Of 51 participants, 13 died early; of 38 survivors 27 underwent MRI and 24 MRS (median 11 days (IQR 11-16.4)); all were of diagnostic quality. Reasons for not imaging 11 survivors were Covid-19 lockdown (6), loss to follow-up (3) and withdrawal (2). Of the 27 imaged, 17 (63%) had moderate-severe NE. Non-imaged infants had more severe NE, higher electrographic seizure burden and higher mortality. Severe abnormalities on MRI were seen equally in the basal ganglia/thalami (BGT); score 2/3 in 4 neonates (14.8%), and white matter (WM); score 3 in 4 neonates (14.8%). Seven (25.9%) scans were considered predictive of adverse 2-year outcome and all had moderate-severe NE. Lac:NAA ratio was 0.09-0.26 (median 0.15) amongst those with predicted adverse outcome vs. 0.08-0.24 (median 0.12) amongst others. Milder MRI abnormalities were common; in moderate-severe NE, WM 76.5%, BGT 35%; in mild NE, WM 60%, BGT 10%.

### Conclusions

MRI/S is a feasible and acceptable research tool in this Ugandan setting. Patterns of brain injury differed from those in UK trial cohorts with less BGT injury seen and lower Lac:NAA. This must partly relate to the high pre-scan mortality amongst NE infants in this low resource setting without NICU, but may also represent differences in the aetiology, nature and timing of injury, with important implications for developing effective NE interventions.

### References (include acknowledgement here if appropriate)


Check box if presenting author is a trainee: basic science trainee □ clinical trainee ✓

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ✓

Senior author supporting presentation on day of meeting: Cally Tann
COMPLEMENTARY REGIONAL NEUROPROTECTION OF MELATONIN AND AZITHROMYCIN FOLLOWING INFLAMMATION-AMPLIFIED HYPOXIA-ISCHAEMIA IN NEWBORN PIGLETS

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

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Introduction (include hypothesis)

Infection and inflammation are independent risk factors for neonatal encephalopathy (NE) in Sub-Saharan Africa (Tann 2018). There are safety and efficacy concerns of therapeutic hypothermia (HT) in some LMIC (Thayyil 2021). Alternative therapies are therefore needed. In newborn piglets subjected to inflammation-amplified hypoxia-ischaemia (IA-HI), while matter (WM) injury predominates and HT is ineffective (Martinello 2021). Aim: To assess safety and efficacy of azithromycin (AZI) and melatonin (MEL) monotherapies in piglets after IA-HI.

Methods (include source of funding and ethical approval if required)

The study was funded by Wellbeing of Women and Bill & Melinda Gates Foundation. Piglets underwent IA-HI injury by *E. coli* lipopolysaccharide pre-sensitisation (2µg/kg bolus + 1mcg/kg/h infusion for 12h) and acute HI injury at 4h into the infusion by carotid artery occlusion and reduction in FiO₂. At 1h after HI, piglets were randomised to intravenous vehicle (n=10), AZI 20mg/kg over 1h (n=8) or MEL 30mg/kg over 2h (n=8), repeated at 24h and 48h. Continuous electroencephalogram (aEEG) and 1H MRS Lactate/N-acetyl aspartate (Lac/NAA) peak ratio were acquired at 60h. Piglets were euthanised at 65h and brain assessed by immunohistochemistry.

Results

We observed no differences in insult severity between treatment groups and no adverse haemodynamic effects of AZI and MEL (QTc prolongation and systemic hypotension).

At interim analysis of the primary outcome measures, AZI reduced mean Basal Ganglia & Thalamus (BGT) Lac/NAA by -0.17 (95% CI, -0.56 to 0.22) Log₁₀ units. Bayesian analysis using non-informative priors indicated a 82.8% probability of treatment superiority (Prsuper). MEL reduced mean WM Lac/NAA by -0.35 (95% CI, -0.86 to 0.15) Log₁₀ units with a Prsuper of 90.8%. AZI improved background aEEG activity at 55-60h (Prsuper 95.5%); no significant improvement in aEEG activity was observed in the MEL group. AZI suppressed microglial activation (Iba-1) in 4 of 8 regions assessed (deep grey matter: caudate & thalamus and WM: periventricular WM and internal capsule). MEL suppressed microglial activation in the sensorimotor and cingulate cortex.

Conclusions

AZI preserved cerebral energy metabolism in BGT and reduced neuro-inflammation in deep grey matter and WM. MEL reduced Lac/NAA in WM and suppressed neuro-inflammation in the cortex. The combination of AZI and MEL was safe and led to protection in different brain regions. Early phase clinical trials in LMIC are needed.

References (include acknowledgement here if appropriate)


Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☑

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☑

Senior author supporting presentation on day of meeting: N J Robertson
CEREBELLAR VOLUME, MICROSTRUCTURE, AND FUNCTIONAL OUTCOME IN EARLY SCHOOL-AGE CHILDREN WITHOUT CEREBRAL PALSY COOLED FOR HYPOXIC-ISCHAEMIC ENCEPHALOPATHY

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)

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Introduction (include hypothesis)

Children cooled for hypoxic-ischaemic encephalopathy (HIE) who do not develop cerebral palsy (CP) have altered supratentorial brain structure at school age,2 despite most having a normal or only mild changes on neonatal MRI.3 We hypothesise that in this population, who had normal looking cerebellums on neonatal MRI, cerebellar development will similarly be altered at school age compared to matched controls and any changes found will be associated with motor and cognitive scores.

Methods (include source of funding and ethical approval if required)

T1-weighted (23 cases, 26 controls) and diffusion-weighted (19 cases, 24 controls) MR images were obtained in 6-8-year-olds, cooled for HIE without CP. Volumes (raw and normalised by total brain volume (TBV)), mean diffusivity (MD) and fractional anisotropy (FA) were measured from 9 cerebellar regions using the SUIT atlas.4 These regions were (combining left and right): anterior lobe, superior posterior lobe (hemispheres and vermis), inferior posterior lobe (hemispheres and vermis), flocculonodular lobe, dentate nucleus, interposed nucleus and fastigial nucleus. Outcomes were assessed using full-scale IQ (WISC-IV) and total motor score (MABC-2).

Results

Cerebellar volumes were smaller in cases (FDR-corrected p<0.05) in the anterior lobe (15.8 vs 17.1 cm³), superior posterior lobe of the hemispheres (76.4 vs 81.1 cm³) and vermis (2.47 vs 2.64 cm³), inferior posterior lobe of the vermis (2.50 vs 2.65 cm³), dentate nucleus (2.74 vs 3.04 cm³), interposed nucleus (0.402 vs 0.442 cm³), and fastigial nucleus (0.0746 vs 0.0838 cm³). FA was lower in cases in the inferior posterior lobe of the hemispheres (0.194 vs 0.209). No differences were found in volumes normalised to TBV or in MD. ANCOVA revealed that cases had a stronger association between interposed nucleus volume and full-scale IQ than controls, with age, sex and TBV included as covariates (p=0.02). For all other cerebellar regions, the association between functional outcome and regional volume, FA or MD did not differ between cases and controls (p>0.05).

Conclusions

In cooled children compared to controls, normalised cerebellar volumes did not differ and only the inferior posterior lobe hemispheres had altered FA. In children cooled for HIE without severe abnormalities on neonatal scans and normal appearing cerebellum there is minimal impact on cerebellar development by early school-age.

References (include acknowledgement here if appropriate)


Check box if presenting author is a trainee: □ basic science trainee ☒ clinical trainee □

All authors have approved the abstract, actual, or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

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