The Neonatal Society Summer Meeting

June 29th – 30th 2023

University of Bristol
Welcome to Bristol
It is a pleasure to welcome you, in-person or virtually, to Bristol for The Neonatal Society Summer Meeting 2023.
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 Bristol and we are delighted to welcome our 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 hope that you enjoy the meeting,

Ela Chakkarapani
(local organiser)

Kevin Goss
(Meeting Secretary)
Thursday 29\textsuperscript{th} June 2023

9:30 Registration, coffee and exhibits

SESSION 1

9:55 Welcome

10:00 Ceri Murphy: Umbilical doppler patterns of flow in-utero affect the risk of necrotising enterocolitis in fetal growth restricted preterm infants

10:15 Claire Howarth: The effect of haemoglobin and red blood cell transfusion on gut perfusion and injury in preterm infants

10:30 Ceri Murphy: The impact of fetal growth restriction on cerebral and gut oxygenation using near infrared spectroscopy


11:00 Tea break and exhibits

11:30 Keynote Lecture: Dr Ronit Pressler, UCL
“The development and assessment of novel therapies for the treatment of neonatal seizures”

12:30 Lunch and exhibits

SESSION 2

14:00 Keynote Lecture: Prof George Davey Smith, University of Bristol
“Strengthening causal inference in antenatal and neonatal epidemiology”

15:00 Tim van Hasselt: Examining neonatal morbidity and paediatric intensive care admission following neonatal discharge - using national linked datasets

15:15 Georgina Yan: Appraisal of the usefulness of the 2022 NICHD bronchopulmonary dysplasia outcome estimator in a UK single-centre extremely preterm cohort

15:30 David Odd: The contributor and causes of death after neonatal illness

15:45 Tea break and exhibits

16:15 David Harvey Fellowship Lecture: Professor Jennifer Zeitlin, INSERM Paris
“The future of federated research for improving the health of children born preterm”

17:15 Close of day
**Friday 30th June 2023**

_9:30 Registration, coffee and exhibits_

**SESSION 3**

_9:55 Welcome_

10:00 Alexandra Bonthrone: Impaired attentional antecedents of executive functions in toddlers with congenital heart disease: an eye-tracking study

10:15 Raymond Pang: Melatonin reduces brain injury following inflammation-amplified hypoxia ischaemia in a newborn piglet model relevant to low resource settings

10:30 Bec Jackson: Impact of antenatal SARS-CoV-2 exposure on developmental outcomes within 12 months of age: a meta-analysis


_11:00 Tea break and exhibits_

11:30 Chris Gale: Establishing the safety of waterbirth for mothers and babies: The POOL observational cohort study

11:45 David Chong: Detection and quantitative analysis of patient-ventilator interactions in ventilated infants by convolutional neural networks

12:00 T’ng Chang Kwok: Network variation of postnatal dexamethasone use and BPD severity across England and Wales in infants born <28 weeks of gestation: a population-based study

12:15 Peter Fleming: Unexpected and unexplained deaths in ex-preterm infants: how effectively are we getting parents to implement safe sleep practices?

_12:30 Lunch and exhibits_

**SESSION 4**

_14:00 Young Investigator Lecture 2023: Dr Qian Yang, University of Bristol_ “Individual and joint effects of chronotype and sleep patterns on pregnancy and perinatal outcomes”

14:45 Kerry Woollfall: Timing of Stoma Closure in Neonates (ToSCiN)- a mixed methods feasibility study

15:00 Adam Smith-Collins: TRANSFER: ThReatened preterm birth, Assessment for in utero transfer; 22+0-23+6 weeks’ gestation

15:15 Don Sharkey: Novel polymer coating of nasogastric tubes to inhibit microbial biofilm formation in an in-vitro model
15:30 *Tea break and exhibits*

16:00 Prize-giving – best presentation by trainee

16:10 **The Tizard Lecture:** *Professor Caroline Crowther, University of Auckland*

“Antenatal magnesium sulphate for fetal neuroprotection: building evidence from experimental medicine, imaging, trials, and metanalysis”

17:10 Close of Meeting
Title (Upper case)

UMBILICAL DOPPLER PATTERNS OF FLOW IN UTERO AFFECT THE RISK OF NECROTISING ENTEROCOLITIS IN FETAL GROWTH RESTRICTED 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)

Murphy, C\textsuperscript{1,2}; Willis, M\textsuperscript{1}; Asamoah, F\textsuperscript{3}; Howarth, C\textsuperscript{1,2}; Fleming, P\textsuperscript{1,2}; Banerjee, J\textsuperscript{4,5}; Aladangady, N\textsuperscript{1,2}

Corresponding author e-mail address: Ceri.murphy1@nhs.net

Institution(s)

1: Homerton University Hospital NHS Trust 2: Queen Mary University of London 3: NHS England 4: Imperial College Healthcare NHS Trust 5: Imperial College London

Introduction (include hypothesis)

Compromised placental flow leads to fetal growth restriction (FGR) and these infants have poor outcomes and increased mortality. There is a lack of evidence regarding how individual flow patterns (FGR without abnormal dopplers, redistribution of flow, absent end diastolic flow (AEDF) and reversed EDF (REDF)) affect risk, making clinical decisions challenging (e.g., in identifying infants who require, and in implementing higher risk feeding regimens).

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

The systematic review was conducted according to PRISMA guidelines and registered with the PROSPERO database\textsuperscript{1}. Two independent researchers searched for articles published in English between 2005-2022. Inclusion criteria: Studies comparing risk of NEC in FGR v AGA or FGR v FGR preterm infants <37 weeks gestational age (GA). Exclusion criteria: studies investigating multiple births only.

6 groups studied: (1) FGR, no abnormal doppler; (2) AEDF; (3) REDF; (4) A/REDF; (5) any abnormal doppler (including redistribution, AEDF, REDF), (6) appropriately grown (AGA).

Results

Group 1 v Group 6: (19 studies; 81,450 infants) [NEC 62% greater in Group1 (LogOR 0.62 CI 0.41-0.83 p<0.0001], (Figure 1A). Group 5 v Group 6: (6 studies; 1,600 infants) [NEC 77% greater in Group5 (LogOR 0.77 CI 0.4-1.14 p<0.0001)].

Group 1 v Group 5: (4 studies; 1,480 infants) [NEC 63% greater in Group5 (LogOR -1.37 CI -2.31, 0.44 p<0.004)], (Figure 1B). Group 1 v Group 4: (2 studies; 1,426 infants) [NEC 61% greater in Group4 (LogOR -1.39 CI -2.11-0.66 p<0.0001). Group2 v Group3: (2 studies; 149 infants) [NEC 21% greater in Group3 (LogOR 0.21 CI 0.530.95 p=0.578)], (Figure 1C).

Conclusions

The meta-analysis demonstrated that preterm with FGR are at a higher risk of developing NEC with or without documented abnormal placental blood flow patterns. This could be due to studies not reporting abnormal Dopplers in a standardised or appropriate manner. Perinatal mechanistic studies with standardised methodology are required to identify the relationship between these abnormal blood flow patterns with development of NEC. The findings may help guide targeted NEC preventative strategies for this high-risk group.

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: Narendra Aladangady
Figure 1: Forest plot depicting odds of NEC in A:FGR with no abnormal doppler versus AGA infants, B:no abnormal doppler versus infants with any abnormal doppler, C: REDF versus AEDF
THE EFFECT OF HAEMOGLOBIN AND RED BLOOD CELL TRANSFUSION ON GUT PERFUSION AND INJURY IN 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)

Claire Howarth1, Christian Mifsud2,3, Jayanta Banerjee4, Simon Eaton2, Terence Leung5, Paul Fleming1, Joan Morris4, Narendra Aladnagady1

Corresponding author e-mail address: Claire.howarth@nhs.net

Introduction (include hypothesis)

Necrotising enterocolitis (NEC) carries significant morbidity and mortality in preterm infants11. The association between anaemia and/or red blood cell transfusions (RBCT) and NEC is controversial and incompletely understood. The aim of this study was to evaluate a range of known biomarkers of gut injury and identify potential tissue injury associated with RBCT and anaemia. We hypothesised that anaemia (through gut hypoperfusion and hypoxia) and/or RBCT (through a reperfusion injury) would cause gut injury evidenced by raised tissue biomarkers or changes in Near Infrared Spectroscopy (NIRS).

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

We conducted a prospective observational study in preterm infants born at <30 weeks gestation (REC reference: 16/LO/1353). Each infant was monitored for gut perfusion and injury weekly from birth until 36 weeks post conceptional age or discharge with 60 minutes NIRS measurements of splanchnic tissue oxygenation index (sTOI) and splanchnic fractional oxygenation extraction (sFTOE), stool calprotectin, urine intestinal (I-FABP) and liver (L-FABP) fatty acid binding protein, and trefoil factor 3 (TFF-3) levels. Infants with evidence of fetal growth restriction (FGR), abnormal antenatal dopplers or significant congenital malformations were excluded. Haemoglobin was measured alongside NIRS, and three groups made: <8g/dl (group 1); 8.11.9g/dl (group 2) and ≥12g/dl (group 3). NIRS and gut biomarkers were evaluated up to 72 hours before or after RBCT and pre and post RBCT measurements compared. We used multi-level mixed effects linear regression models, nested within each infant because readings were taken over time and hence correlated within each infant. Confounding variables were included as fixed effects using STATA/SE version 15.1.

Results

Forty eight infants were recruited (median birth weight 883.5g [range 460g to 1600g], median gestational age 26.3 weeks [range 23 to 29]2; 52% were female. Using group 3 as the baseline we demonstrated no significant association between Haemoglobin and sTOI or any gut biomarker. Group 1 vs Group 3 showed a significant difference (95% CI and p value) for I-FABP, L-FABP, Calprotectin and TFF were 7% (-36% to +79%, p = 0.796), -13% (-51% to 52%, p = 0.614), -15% (-46% to 34%, p = 0.486) and -17% (-41% to 17%, p = 0.284) respectively. Group 2 vs Group 3 showed a significant difference (95% CI and p value) for I-FABP, L-FABP, Calprotectin and TFF were 61% (-206% to +337%, p = 0.351), 10% (-61% to 222%, p = 0.86), 45% (-53% to 532%, p = 0.517) and 64% (-17% to 222%, p = 0.153) respectively. Group 1 vs Group 3 and Group 2 vs Group 3 showed a significant difference (95% CI and p value) for I-FABP, L-FABP, Calprotectin and TFF were 61% (-206% to +337%, p = 0.351), 10% (-61% to 222%, p = 0.86), 45% (-53% to 532%, p = 0.517) and 64% (-17% to 222%, p = 0.153) respectively. Group 1 vs Group 3 and Group 2 vs Group 3 showed a significant difference (95% CI and p value) for I-FABP, L-FABP, Calprotectin and TFF were -15% (-46% to 34%, p = 0.486) and -17% (-41% to 17%, p = 0.284) respectively.

Conclusions

We found no association between anaemia or RBCT with gut injury in preterm infants using gut tissue biomarker levels and NIRS splanchnic tissue oxygen measurements as surrogates for gut injury. Further studies on the effect of anaemia or RBCT on gut injury in FGR infants are needed to conclusively answer the debate regarding the role of anaemia and/or RBCT in the development of NEC.

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: Prof Narendra Aladangady
The Impact of Fetal Growth Restriction on Cerebral and Gut oxygenation using Near Infrared Spectroscopy

Ceri Murphy¹, Joan Morris², Sadie Baskind¹ Terence Leung³, Simon Eaton⁴, Claire Howarth¹, Paul Fleming¹, Jayanta Banerjee⁵, Narendra Aladangady¹

Corresponding author e-mail address: Ceri.murphy1@nhs.net

Introduction (include hypothesis)
Preterm infants with fetal growth restriction (FGR) have gut hypoperfusion in-utero and are predisposed to necrotising enterocolitis; cerebral oxygenation in-utero is maintained by brain sparing. Near infrared spectroscopy may be extremely useful clinical tool in neonatal care, but first we must establish the normal values in different preterm infant groups.

Methods (include source of funding and ethical approval if required)
Splanchnic (sTOI) and Cerebral Tissue Oxygenation Index (cTOI) and CSOR were measured weekly, for 60 minutes over 6 weeks after birth. 39 preterm infants (<32 weeks gestation) were recruited into two groups: (1) FGR n=19, birthweight on <10th centile or abnormal antenatal dopplers and (2) AGA n=20, birthweight ≥10th centile. Infants who developed IVH Grade 3/4 and/or NEC were excluded. Statistical analysis performed with STATA 18 using multilevel regression. The study was approved by the Research Ethics Committee.

Results
Median (range) birthweight (FGR) 780g (693-974g), (AGA) 875g (705-1127g); gestational age (GA) (FGR) 29 (27.5-30), (AGA) 26 (24-29) weeks. Mean weekly cTOI ranged between 58.9%-69.8% in FGR and 60%-71.4% in AGA infants. Mean cTOI decreased significantly in the whole cohort with increasing postnatal age (-1.16 (-1.89, -0.42) p=0.002), Figure 1A. Mean weekly sTOI ranged between 31.5%-56.3% in FGR and 26.5%-46.8% in AGA infants. Mean sTOI significantly increased in the whole cohort with increasing postnatal age (3.43 (2.11, 4.76) p<0.0001), Figure 1B. Mean weekly CSOR ranged between 0.47-0.93 in FGR and 0.38-0.75 in AGA infants. Mean weekly CSOR increased significantly in the whole cohort with increasing postnatal age (0.07 (0.04, 0.09) p<0.0001), Figure 1C. sTOI and CSOR appear to be lower in FGR infants in weeks 2 and 3 of life, Figure 1B&1C. Confounders GA, ethnicity and feeds were associated with significantly higher sTOI and CSOR p<0.05).

Conclusions
Cerebral oxygenation decreased and splanchnic oxygenation increased during the six postnatal weeks in both FGR and AGA 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: Narendra Aladangady
Figure 1 (A) Graph depicting mean Cerebral TOI by week of life in FGR & AGA preterm infants, (B) Graph depicting mean Splanchnic TOI by week of life in FGR & AGA preterm infants, and (C) Graph depicting mean CSOR by week of life in FGR & AGA preterm infants.
ANTENATAL MAGNESIUM SULPHATE FOR FETAL NEUROPROTECTION: USE IN ENGLAND, SCOTLAND, AND WALES 2014-2022

Hannah B Edwards, Dr Carlos Sillero Rejon, Dr Christalla Pithara-McKeown, Professor Frank de Vocht, Dr Brent Opmeer, Dr David Odd, Professor Karen Luyt

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Introduction (include hypothesis)

Antenatal magnesium sulphate (MgSO4) is a neuroprotectant for premature babies. Until recently, UK use has been variable. In 2018 the National PReCePT Programme (NPP) was launched to increase uptake of MgSO4 in English maternity units. We compared trends in MgSO4 use across England, Scotland, and Wales. We hypothesised that the NPP may have led to higher or more equitable use of MgSO4 in England compared to the devolved nations.

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

We analysed pseudonymised data from the UK National Neonatal Research Database (NNRD) on babies born <30 weeks gestation. We described changes in MgSO4 uptake in England, Scotland and Wales between 2014 and 2022. Differences in uptake from before to after the NPP launch were statistically estimated with multi-level mixed-effects linear regression modelling. Cost-effectiveness was estimated and qualitative interviews with perinatal staff were conducted to understand similarities and differences between each nation’s approach to improving MgSO4 uptake. The Health Foundation funded this project and HRA approval was obtained.

Results

Preliminary results: In 2017, mean MgSO4 uptake was 69% (England), 65% (Scotland), and 66% (Wales). By 2022 this had risen to 85%, 81%, and 84% respectively. Trends were similar across nations, although in England only there was strong evidence for a step-change of around 10 percentage points (95% CI 7.47 to 12.81, p<0.001) improvement in uptake over this time-period, after adjusting for confounding factors. Variability in uptake was higher in Scotland and Wales. Uptake appeared to plateau or even slightly decline post-2020, which could be a natural ceiling effect, but also coincides with the start of the Covid-19 pandemic and UK lockdown. See Figure below. Over 48 months, at a willingness-to-pay threshold of £20,000, the NPP may have generated a societal lifetime net monetary benefit of £198,368 per maternity unit. Qualitative interviews indicate that local and national improvement initiatives were implemented in all nations over this period.

Conclusions

All three nations now have high levels of MgSO4 uptake. The NPP appears to have accelerated improvement in England, and other efforts in the devolved nations may have contributed to their improvements. Uptake may now be stabilising at a natural maximum. It is possible that the covid-19 pandemic led to a slight decrease in uptake.

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: Professor Karen Luyt
EXAMINING NEONATAL MORBIDITY AND PAEDIATRIC INTENSIVE CARE ADMISSION FOLLOWING NEONATAL DISCHARGE - USING NATIONAL LINKED DATASETS

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 Tim J van Hasselt¹, Professor Chris Gale², Dr Cheryl Battersby², Professor Elizabeth S Draper¹, Dr Sarah E Seaton¹

Corresponding author e-mail address: Tvh2@leicester.ac.uk

Institution(s)

1) University of Leicester, Department of Population Health Sciences, Leicester, United Kingdom
2) Imperial College London, School of Public Health, Faculty of Medicine, London, United Kingdom

Introduction (include hypothesis)

With increased survival following preterm birth there is a consequent increase in the number of children living with ongoing morbidity. Previous studies have identified that the number of major neonatal morbidities is associated with death and poor neurodevelopmental outcome (1,2). We aimed to investigate whether presence of multiple major neonatal morbidities was associated with unplanned admission to paediatric intensive care (PICU) in the first two years of life of children born <32 weeks, using national linked neonatal and PICU data.

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

Data from the National Neonatal Research Database (NNRD) for all neonatal admissions born <32 weeks in 2013-2018 in England and Wales were linked to PICU admissions using the Paediatric Intensive Care Network Audit (PICANet). Logistic regression models to predict unplanned PICU admission were created using: gestation, sex, birthweight <10th centile, and severe necrotising enterocolitis (NEC) requiring surgery, bronchopulmonary dysplasia requiring oxygen at 36 weeks (BPD), and brain injury. Dr Tim van Hasselt (DRF NIHR301761), and Dr Sarah Seaton (ARF NIHR300579) were funded by the NIHR. East of England REC approval (20/EE/0220) and CAG approval (20/CAG/0110) was obtained.

Results

40,789 babies born <32 weeks were discharged home, of whom 1,901 (4.7%) had unplanned admission to PICU. Children born at 23 weeks had the highest observed percentage of unplanned PICU admission (10.2%), reducing to 3.3% for children born at 31 weeks. After adjustment, babies born more preterm, and presence of major neonatal morbidities (NEC, BPD, brain injury) were associated with unplanned PICU admission. The adjusted odds ratio for gestation was 0.90 (0.87 to 0.92) per week born preterm. After categorisation of gestation and number of morbidities, the presence of 2+ morbidities was associated with the greatest increase in odds ratio (adjusted OR 2.28, 95% confidence interval 1.86 to 2.78). Model predictions matched observed data (Figure 1) for children with no or one major morbidity, however observed PICU admissions for children born 28-31 weeks with 2+ or more morbidities was greater than predicted.

Conclusions

Decreasing gestation and presence of morbidities is associated with increased risk of unplanned PICU admission after neonatal discharge home. However, further work is required to define neonatal multi-morbidity and understand how combinations of morbidities affect ongoing healthcare needs of preterm-born children.

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: Professor Chris Gale
Figure 1 – Predicted vs observed probabilities for unplanned PICU admission in the first two years of life, after neonatal discharge for children born <32 weeks, comparison by number of major neonatal morbidities.
APPRAISAL OF THE USEFULNESS OF THE 2022 NICHD BRONCHOPULMONARY DYSPLASIA OUTCOME ESTIMATOR IN AN UK SINGLE-CENTRE EXTREMELY PRETERM COHORT

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

Georgina Yan, Reena Bhatt, Jens Madsen, Howard Clark

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Institution(s)

University College London EGA Institute for Women’s Health
University College London Hospitals NHS Foundation Trust

Introduction (include hypothesis)

Bronchopulmonary dysplasia (BPD) remains a common sequelae of extreme prematurity and leads to multisystem long-term morbidity including cardiovascular impairment, poor growth, and neurodevelopmental disability. A clinical prediction model would guide prognosis counselling and may contribute towards a benefit-risk calculation of postnatal corticosteroids. We assessed the utility of the 2022 National Institute of Child Health and Human Development (NICHD) BPD estimator tool (1) for our local population.

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

Infants were identified from an observational study at University College London Hospitals (The Baby Lung Study ClinicalTrials.gov Identifier: NCT05152316). Infants were included if they were born <29 weeks gestational age without any major congenital anomalies. BPD was defined as per the 2019 classification based on the mode of respiratory support required at 36 weeks postmenstrual age (PMA). The NICHD tool calculated risk of BPD including severity, based on clinical parameters including respiratory support and oxygen requirement at a single timepoint (postnatal days 1, 3, 7, 14 or 28). Predicted risk was compared to BPD status at 36 weeks PMA.

Result

A total of 39 infants with a birth weight between 501 and 1250g were included (mean gestation at birth 26.4 weeks, mean birth weight 807g). Two infants died before 36 weeks PMA. The NICHD tool had good sensitivity for predicting risk of BPD development with 82% on Day 1 (n=35) and 100% on Day 28 (n=23) (range 77.8-100%). However, it had poor specificity with 57% on Day 1 and 0% on Day 28 (range 0-66.7%). It under-predicted severity of BPD overall and became more inaccurate over time. It did not predict Grade 3 BPD or death accurately at any timepoint. The tool did not recognise high-flow nasal cannula oxygen (HFNC) as a distinct mode of respiratory support so in subsequent analysis, infants on HFNC were entered into the tool as on continuous positive airway pressure. The sensitivity remained good with 82% on Day 1 (n=37) and 100% on Day 28 (n=30) (range 78.6-100%) but specificity for grade of BPD remained poor (Figure 1).

Conclusions

The NICHD BPD outcome estimator showed good sensitivity but poor specificity for the grade of BPD that our study infants developed. Further studies are needed to develop a tool that accounts for newer ventilation modes and other risk factors such as intrauterine growth restriction, undernutrition, and pulmonary vascular disease.

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: Professor Howard Clark
<table>
<thead>
<tr>
<th>Actual outcomes</th>
<th>No BPD</th>
<th>Grade 1 BPD</th>
<th>Grade 2</th>
<th>Grade 3 BPD</th>
<th>Death</th>
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<tbody>
<tr>
<td>Day (n)</td>
<td>D1(9)</td>
<td>D1(6)</td>
<td>D1 (19)</td>
<td>D1(3)</td>
<td>D1(2)</td>
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<tr>
<td>Death</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Grade 3 BPD</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Grade 2 BPD</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>10.5%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Grade 1 BPD</td>
<td>22.2%</td>
<td>80%</td>
<td>66.6%</td>
<td>52.6%</td>
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<td>78.8%</td>
<td>20%</td>
<td>33.3%</td>
<td>36.8%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Figure 1: The NICHD BPD outcome estimator tool’s most likely predicted BPD grade compared to actual outcome. Infants on high-flow nasal cannula oxygen have been included.
THE CONTRIBUTOR AND CAUSES OF DEATH AFTER NEONATAL ILLNESS

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

David Odd¹,², Tom Williams¹, Sylvia Stoianova¹, Grace Rossouw¹, Peter Fleming¹, Karen Luyt¹

Corresponding author e-mail address: Karen.Luyt@bristol.ac.uk

Institution(s)
1. National Child Mortality Database, Bristol Medical School, University of Bristol, UK
2. School of Medicine, Division of Population Medicine, Cardiff University, UK

Introduction (include hypothesis)

While the immediate impact of neonatal illness is well recognised, the wider, and longer term, impact on childhood mortality and the role and impact of specific pathologies across childhood is unclear. The aim of this work was to investigate how many deaths in childhood are associated with neonatal illness, what consequences they had, and the reasons the children died.

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

We included all deaths of children before their 10th birthday reported to NCMD, that occurred between 1st April 2019 and 31st March 2021 (24 months), after being born at, or after 22 weeks, gestation. Data was linked to any BadgerNet or HES record available. Baseline data and cause of death were identified from the death notification. Exposure was receiving care in a neonatal unit after birth, plus those who died in the first day of life, prior to admission; or specific neonatal pathologies. Main outcomes were risk of co-morbidities seen in these children and the perinatal contributors to their deaths. Risks were calculated and compared using a Poisson model.

Results

A total of 4829 children died before their 10th birthday, with 71.6% of deaths having evidence of likely neonatal illness. Children who died before 10 years, with preceding neonatal illness had (after adjustment for age of death), higher risks of behavioural or developmental disorders (OR 3.31 (2.47-4.42)), and chronic neurological (OR 3.00 (2.51-3.58)) and respiratory disease (OR 3.01 (2.43-3.73)) than children without neonatal admissions or illness. A similar profile was seen for children born preterm, those with HIE and those with congenital abnormalities. Overall, preterm birth (33.4%), congenital abnormalities (25.5%) and HIE (7.8%) were the most common perinatal factors reported as causes, or contributors, to all-cause mortality. In children over 1 year of age congenital abnormalities (21.6%) and HIE (4.6%) remained important contributors (Table).

Conclusions

The impact of neonatal illness continues long after discharge from the neonatal unit, with increased prevalence’s of developmental disorders, neurological disease and respiratory disease. Infant mortality was strongly associated with preterm birth, but with substantially reduced impact for deaths after 1 year of age. Congenital abnormalities and HIE remained strongly associated with deaths in both the first year of life, and between 1 and 9 years.

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: Karen Luyt
Table. Recorded causes and contributors to childhood death before 10 years of age; split by neonatal conditions (n=4829)

<table>
<thead>
<tr>
<th>Age</th>
<th>n</th>
<th>Preterm</th>
<th>Hypoxic-Ischaemic Encephalopathy</th>
<th>Congenital Abnormality</th>
<th>Intracranial Haemorrhage</th>
<th>Chorio-amnionitis</th>
<th>Necrotising Enterocolitis</th>
<th>Perinatal Lung Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Deaths</td>
<td>4829</td>
<td>1614 (33.4%)</td>
<td>376 (7.8%)</td>
<td>1233 (25.5%)</td>
<td>215 (4.5%)</td>
<td>154 (3.2%)</td>
<td>277 (5.7%)</td>
<td>147 (3.0%)</td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>3730</td>
<td>1596 (42.8%)</td>
<td>326 (8.7%)</td>
<td>996 (26.7%)</td>
<td>192 (5.2%)</td>
<td>154 (4.1%)</td>
<td>256 (6.9%)</td>
<td>-a</td>
</tr>
<tr>
<td>1-9 years</td>
<td>1099</td>
<td>18 (1.6%)</td>
<td>50 (4.6%)</td>
<td>237 (21.6%)</td>
<td>23 (2.1%)</td>
<td>0 (0.0%)</td>
<td>21 (1.9%)</td>
<td>-a</td>
</tr>
</tbody>
</table>

Numbers are n(%)  
 a. Small number (below 6) are suppressed to prevent identifiability
IMPAIRED ATTENTIONAL ANTECEDENTS OF EXECUTIVE FUNCTIONS IN TODDLERS WITH CONGENITAL HEART DISEASE: AN EYE-TRACKING STUDY

Alexandra F Bonthrone1, Vanessa Kyriakopoulou1, Luke Mason2, Andrew Chew1, Shona Falconer1, Christopher J Kelly1, John Simpson3, Kuberan Pushparajah3, Mark Johnson4,6, A David Edwards1, Chiara Nosarti1,5, Emily JH Jones6*, Serena J Counsell1*

Corresponding author e-mail address: alexandra.bonthrone@kcl.ac.uk

Introduction (include hypothesis)

Executive function (EF) impairments are common in children and adolescents with Congenital Heart Disease (CHD). However no study to date has assessed these in toddlers, in part due to the challenge of separating EF from non-executive skills such as language and motor abilities at this age. We hypothesised that toddlers with CHD would show impaired attentional antecedents of EF measured with eye-tracking when compared to typically developing controls.

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

The project was approved by the National Research Ethics Service West London committee (CHD 07/H0707/105; Controls 14/LO/1169). Participants with CHD were recruited at birth and invited to attend a 22-month eye-tracking assessment at St Thomas’ Hospital. Inclusion criteria were (i) diagnosis of CHD requiring cardiac surgery or intervention by catheterisation at <1 year and (ii) no known genetic disorder. A subset of typically developing toddlers from the Developing Human Connectome Project assessed at ≥21 months corrected age was included as controls. Gaze behaviours were tracked during a series of tasks designed to assess attentional antecedents of EF. The difference between CHD and controls was assessed using analyses of covariance adjusting for gestational age at birth, cognitive abilities and any additional covariates associated with gaze behaviours (p<0.1). This research was funded by the Medical Research Council UK (MR/L011530/1; MR/V002465/1), the British Heart Foundation (FS/15/55/31649) and Action Medical Research (GN2630). Control data was collected as part of the Developing Human Connectome Project, funded by the European Research Council under the European Union’s Seventh Framework Program (FP7/20072013)/European Research Council grant agreement no. 319456.

Results

When compared to controls [N=66, 36 male, median (IQR) corrected age at assessment 22 (21.5-23.8) months], toddlers with CHD [N= 30, 19 male, corrected age at assessment 22.2 (22-23.1) months] were less accurate when switching locations during a set-shifting task [accuracy CHD 79%, (28-100) control 100% (86-100), pFDR=0.032], had slower reaction times during selective [CHD 1.243 seconds (0.986-1.786), control 1.065 (0.851-1.397), pFDR<0.001] and exogenous attention tasks [CHD 0.312 seconds (0.279-0.358), control 0.289 (0.249-0.331), pFDR=0.032] and had less mature endogenous attention (prolonged looks at facial stimuli in seconds median (IQR) CHD 0.670 (0.518-0.885), control 0.500 (0.250-0.625), pFDR=0.006). Importantly, these results survived correction for general cognitive abilities and were unrelated to socioeconomic status measured with the index of multiple deprivation 2015.

Conclusions

Attentional antecedents of EF were impaired in toddlers with CHD; crucially these results were significant when adjusting for cognitive abilities. These metrics may represent clinically feasible, early objective measures of impaired attention and executive functions development in CHD.

References (include acknowledgement here if appropriate)
We would like to thank the families who participated in this study. We also thank colleagues from St Thomas’ Neonatal Intensive Care Unit; the Evelina London Children’s Hospital Fetal and Paediatric Cardiology Departments; the Evelina London Paediatric Intensive Care Unit and the Centre for the Developing Brain at King’s College London.

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: A. David Edwards
**Title** (Upper case)

**MELATONIN REDUCES BRAIN INJURY FOLLOWING INFLAMMATION-AMPLIFIED HYPOXIA ISCHAEMIA IN A NEWBORN PIGLET MODEL RELEVANT TO LOW RESOURCE SETTINGS**

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

Raymand Pang¹, Christopher Meehan¹, Katie Tucker¹, Ellie Campbell¹, Alison Mintoft¹, Francisco Torrealdea², Alan Bainbridge², Xavier Golay³, John Barks⁴, Nicola J Robertson¹,⁵

**Corresponding author e-mail address:** r.pang@ucl.ac.uk

**Institution(s)**

¹Institute for Women’s Health, UCL, ²Department of Medical Physics, University College London Hospital NHS Trust, ³Institute of Neurology, UCL, ⁴Department of Paediatrics, University of Michigan, ⁵Centre for Clinical Brain Sciences, University of Edinburgh

**Introduction (include hypothesis)**

Infection and inflammation are independent risk factors for neonatal encephalopathy (NE) in Sub-Saharan Africa (1). There are safety and efficacy concerns of therapeutic hypothermia (HT) in some LMICs (2) and alternative therapies are needed. Brain injury is more severe following inflammation-amplified hypoxia-ischaemia (IA-HI) in newborn piglets and HT is not protective (3). We hypothesised that melatonin (in 5% ethanol) (20mg/kg IV at 1h + 10mg/kg every 12h between 24-60h) is safe and reduces brain injury in piglets following IA-HI.

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

This study was powered to detect a difference in Log10 Lac/NAA of 0.5 with SD 0.4 based on previous studies. Newborn piglets (male and female) underwent IA-HI by carotid artery occlusion and reduction in FiO2 to 6% at 4h into E. coli lipopolysaccharide sensitisation (2mcg/kg bolus + 1mcg/kg/h 12h infusion). At 1h after HI, piglets were randomised to receive saline (n=12) or melatonin (n=11). Continuous electroencephalogram (aEEG/EEG) was recorded and magnetic resonance spectroscopy was acquired at 60h. Piglets were euthanised at 65h and brain dissected for immunohistochemistry. This study was funded by the Bill and Melinda Gates Foundation.

**Results**

There were no differences in baseline insult severity between the two groups. Target melatonin levels of 15-30mg/L were achieved within 3h after IA-HI. Blood alcohol levels were below 0.25g/L and no hypotension was observed. On 1H MRS, melatonin treatment was associated with a reduction in Lac/NAA in the BGT voxel (0.197 Log10 units, 95% CrI (-0.366 to -0.028, see Fig)). Bayesian analysis with noninformative priors shows a probability of treatment superiority (Psup) of 98.8%. No treatment benefit was observed in WM Lac/NAA. On 31P MRS, melatonin was associated with higher PCr/Epp ratio (PSup 97.6%) vs control, suggesting preserved cerebral energy metabolism (see Fig). On EEG/aEEG, melatonin was associated with earlier recovery of background electrical activity from 19-24h (Psup 95.4%, See Fig). On immunohistochemistry, melatonin was associated with a significant reduction in TUNEL positive cells in the putamen and hippocampus (see Fig).

**Conclusions**

This study adds to the body of evidence supporting the benefit of melatonin for NE. In this IA-HI piglet model, where HT is not protective, melatonin monotherapy improved cerebral energy metabolism, EEG/aEEG recovery and reduced cell death in 2 regions. The translation of melatonin to early phase clinical trials is urgently needed.

**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 N Robertson
Figure 1 Neurological outcomes in animals treated with melatonin (orange) vs control (red). Bayesian statistical analysis performed using a non-informative prior (probability of treatment superiority shown) BGT: Basal ganglia and thalamic, Lac/NAA: lactate to N-acetylaspartate ratio, TUNEL: Terminal deoxynucleotidyl transferase dUTP nick end labeling
Title (Upper case)

IMPACT OF ANTENATAL SARS-COV-2 EXPOSURE ON DEVELOPMENTAL OUTCOMES WITHIN 12 MONTHS OF AGE: A META-ANALYSIS

Authors

Jackson B1, Woodward K1, Ireland M1, Larkin C2, Kurinczuk J3, Knight M2, Gale C3, Johnson S4, Cornish R5, Chakkarapani E1.

Corresponding author e-mail address: ela.chakkarapani@bristol.ac.uk

Institution(s)

1 Translational Health Sciences, Bristol Medical School, University of Bristol. 2 NPEU, University of Oxford. 3 Neonatal Medicine, School of Public Health, Imperial College London. 4 Department of Population Health Sciences, University of Leicester. 5 Population Health Sciences, Bristol Medical School, University of Bristol.

Introduction (include hypothesis)

Previous meta-analysis suggested that antenatal exposure to SARS-CoV-2 may increase the risk of delayed fine motor development before 12 months of age.[1] However, we do not know whether antenatal SARS-CoV-2 exposure has different effects in preterm vs term born infants and in different developmental domains. Therefore, we conducted a systematic review examining the impact of antenatal SARS-CoV-2 exposure in preterm and term born infants on developmental test scores and risk of developmental delay by 12 months of age.

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

This systematic review followed PRISMA guidelines and was registered in PROSPERO (CRD42022314063). SARS-CoV-2 exposure was defined as detection of SARS-CoV-2 using nucleic acid amplification or antigen tests during any gestation of pregnancy. Comparison cohorts included unexposed infants born during the same period. Embase, Ecmare, MEDLINE, PsycINFO and Web of Science databases were searched (completed 4-May-23). Outcomes assessed: continuous developmental scores, risk of developmental delay.

Results

A total of 828 studies were screened for eligibility, resulting in 4 studies selected for inclusion. Developmental outcomes were assessed using the Ages and Stages Questionnaire 3, Denver Developmental Screening Test and Developmental Assessment of Young Children-2nd Edition. Overall, 852 infants were screened for developmental delay (n=315 exposed; n=537 non-exposed) between 3 and 11 months of age. In term born infants, there was evidence for an increased risk of fine motor delay (risk difference: 0.04 (95% CI: 0.01 to 0.07)). There was no evidence of increased risk of delay in other domains (communication, gross motor, problem solving and personal social). Mean scores in term born infants were slightly lower in the exposed cohorts in problem solving (difference in means: -0.12 (-0.27, 0.04)) and personal social domains (-0.18 (-0.39, 0.04)) and slightly higher in the fine motor domain (0.13 (-0.03, 0.29)); however, estimated differences were imprecise with confidence intervals crossing zero (Figure 1). In preterm born infants, the number of infants in the exposed (n=30) and comparison cohorts (n=33) were too small to report meaningful comparisons.

Conclusions

Antenatal exposure to SARS-CoV-2 may result in a slightly increased risk of delayed fine motor development up to 12 months of age among term-born infants but based on a small number of studies there is no evidence of delayed development in other domains. Larger cohorts of preterm infants are needed, as are developmental outcomes later in childhood.

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: ☒
Figure 1. Forest plot of continuous developmental scores and risk of developmental delay in term born infants with exposure to SARS-CoV-2 maternal infection in pregnancy compared to nonexposed infants up to 12 months of age.

### Communication

<table>
<thead>
<tr>
<th>Study</th>
<th>Exposed</th>
<th>Unexposed</th>
<th>SMD with 95% CI</th>
<th>Weight (%)</th>
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<tbody>
<tr>
<td>Shuffrey et al. 2022</td>
<td>107</td>
<td>37.7 8.0 131</td>
<td>48.1 9.8</td>
<td>0.04 [-0.30, 0.21]</td>
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<td>Wu et al. 2021</td>
<td>45</td>
<td>46.8 10.3 56</td>
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<td>Firestein et al. 2023</td>
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<td></td>
<td>0.04 [-0.11, 0.20]</td>
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</tbody>
</table>

Heterogeneity: $I^2=33\%$, $p=0.2$

### Gross motor

<table>
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<tr>
<th>Study</th>
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<td>-0.08 [-0.24, 0.08]</td>
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Heterogeneity: $I^2=33\%$, $p=0.21$

### Fine motor

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<td>46.0 11.1</td>
<td>0.01 [-0.25, 0.26]</td>
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Heterogeneity: $I^2=51\%$, $p=0.01$

### Problem solving

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<td>47.8 12.3</td>
<td>-0.04 [-0.26, 0.18]</td>
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<td>Wu et al. 2021</td>
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<td>115.8 13.5 252</td>
<td>116.1 14.1</td>
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<td>-0.12 [-0.27, 0.04]</td>
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Heterogeneity: $I^2=50\%$, $p=0.09$

### Personal social

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<td>Shuffrey et al. 2022</td>
<td>107</td>
<td>48.7 11.8 131</td>
<td>46.0 11.5</td>
<td>0.09 [-0.16, 0.32]</td>
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<tr>
<td>Wu et al. 2021</td>
<td>45</td>
<td>49.9 9.5 56</td>
<td>46.6 9.9</td>
<td>-0.77 [-1.17, -0.37]</td>
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<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td>-0.18 [-0.38, 0.02]</td>
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</tbody>
</table>

Heterogeneity: $I^2=51\%$, $p=0.01$

Note: sample (N), standard deviation (SD), standard mean difference (SMD), risk difference (Risk diff.), 95% confidence interval (95% CI).
THE ECONOMIC IMPACT OF ANTENATAL MAGNESIUM SULPHATE FOR FETAL NEUROPROTECTION: USE IN ENGLAND, SCOTLAND, AND WALES 2014-2022

Carlos Sillero-Rejon, Hannah B Edwards, Christalla Pitkara-McKeown, David Odd, Professor Karen Luyt, Hugh McI

Corresponding author e-mail address: Carlos.sillerorejon@bristol.ac.uk

University of Bristol; University Hospitals Bristol and Weston NHS Foundation Trust

Introduction (include hypothesis)

Antenatal magnesium sulphate (MgSO₄) is an effective and cost-effective treatment for neuroprotection for premature babies. However, the uptake of MgSO₄ treatment has been slow with high variability between maternity units. The impact of suboptimal implementation on health and outcomes can be measured in monetary terms. We estimate the net monetary loss due to suboptimal implementation of MgSO₄ over time in England, Scotland and Wales. We also explore the impact of potential targeted implementation interventions to increase MgSO₄ uptake in these nations, assuming they achieved similar results to the Prevention of Cerebral Palsy in Preterm labour (PReCePT) [1].

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

The net monetary benefit of MgSO₄ treatment from a lifetime and societal perspective was estimated from the literature [2]. We analysed pseudonymised data from the UK National Neonatal Research Database on babies born <30 weeks gestation to estimate the changes in MgSO₄ uptake in England, Scotland and Wales between 2014 and 2022. We used our framework for the economic evaluation of implementation initiatives [3] to estimate and visualise the net monetary loss due to suboptimal implementation (the difference between the value of MgSO₄ uptake as the accumulative net monetary benefit for babies who received MgSO₄ and the value of MgSO₄ implemented ‘perfectly’ (i.e., 95% uptake). We also estimated the net monetary benefit of potential implementation interventions to increase MgSO₄ uptake in English, Scottish and Welsh units, assuming they achieved similar results to the PReCePT (6 percentage point MgSO₄ increment, £6,000 costs per unit and one-year duration).

Results

MgSO₄ treatment has increased over time in England, Scotland and Wales, generating a positive economic impact (illustrated by the decrease in the red areas over time; Figure 1). However, there is still room for improvement as the net monetary loss due to suboptimal implementation was from £100k to £2M across the three nations from Jun21 to Jun22. A further targeted implementation intervention would likely be cost-effective, as if on average two additional babies per unit received MgSO₄ a net monetary benefit from £30,000 to £56,000 per unit would be generated.

Conclusions

There is a cost associated with delayed adoption of MgSO₄ for fetal neuroprotection into clinical practice. MgSO₄ uptake in the three nations shows how the extent of implementation of a cost-effective treatment has important measurable economic implications. Further effort is required to achieve ‘perfect’ treatment implementation. Our analysis should encourage investment in further targeted interventions to speed up MgSO₄ uptake in all three nations.

Acknowledgements: The Health Foundation funded this project. HRA approval was obtained.

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: Professor Karen Luyt
Figure 1. Net monetary benefit of MgSO₄ implementation in England, Scotland and Wales (2014-2022)

light green: the net monetary benefit of MgSO₄ uptake achieved
dark green: the net monetary benefit of perfect MgSO₄ implementation (95% uptake)
red area, the net monetary loss of suboptimal implementation: the difference between the net monetary benefit of current uptake and the net monetary benefit of perfect uptake
Willingness to pay = £20,000 per quality-adjusted life-year (QALY) gained
Establishing the safety of waterbirth for mothers and babies: The POOL observational cohort study

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

Sanders J1, Milton R1, Barlow C1, Brockehurst P2, Cannings-John R1, Channon S1, Gale C3, Cutter J4, Hunter B1, Paranjothy S5, Lugg-Widger FV1, Milosevic S1, Morantz L6, Plachcinski R6, Nolan M7, Robling M1

Corresponding author e-mail address: Christopher.gale@imperial.ac.uk

Institution(s)


Introduction (include hypothesis)

It is estimated there are approximately 60,000 waterbirths in the United Kingdom annually, ~9/100 births. Women commonly use a pool during labour for pain relief, with some remaining in the pool for birth. There has only been limited data on the impact of birth in water on maternal and neonatal outcomes. The aim of the POOL study was to establish whether in low risk women, waterbirth, compared to using water immersion during labour but leaving a pool prior to birth, is as safe for mothers and infants.

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

In this observation study prospective and retrospective data were extracted from National Health Service electronic maternity records at 26 participating sites in England and Wales, relating to births between January 2015 and June 2022. For babies admitted to a neonatal unit, data were also extracted from the National Neonatal Research Database (NNRD). The primary neonatal outcome was a composite of ‘adverse infant outcomes or treatment’ which included neonatal unit admission for respiratory support, antibiotic administration within 48 hours of birth and intrapartum stillbirth or death prior to neonatal discharge. Primary analysis was a non-inferiority analysis using logistic regression with adjustment for potential confounders. To ensure a complete cohort, the study used an opt-out model, for which ethical approval was granted (REC 18/WA/0291; CAG 18CAG0153). Funding: NIHR HTA 16/149/01. Protocol published and registered ISRCTN13315580.

Results

Between January 2015 and June 2022 871,829 birth records were extracted from 26 sites; 87,040 (10%) used a pool during labour for analgesia (range by site 1.6% to 22.9%) and 46,283 (5.3%) had a waterbirth (range by site 1.1% to 13.4%); there was a reduction in pool use (10.2% to 7.7%) and waterbirth (5.5% to 4.0%) over the study period. Women who used a pool during labour or delivery were predominantly of white ethnicity (81%) and more commonly from less deprived quintiles (21% from least deprived decile vs 14% from most deprived). 13,811 (15.9%) of women using a pool during labour had risk factors at the time of pool use: 6% induction of labour, 2.3% GBS carriage, 1.5% booking BMI >35, 1% prolonged rupture of membranes >36 hours. There was an increase in the proportion of women who used a pool during who had risk factors over the study period (12.1% in 2015, 23.2% in 2022).

Conclusions

Use of water during labour and birth in water are both common in the United Kingdom but appear to be decreasing. An increasing proportion of women using a pool during labour and at birth were considered high risk at the time of pool use.

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:
Title (Upper case)
DETECTION AND QUANTITATIVE ANALYSIS OF PATIENT-VENTILATOR INTERACTIONS IN VENTILATED INFANTS BY CONVOLUTIONAL NEURAL NETWORKS

Authors (Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)
David Chong, Lakshana Gunathilagan, Gusztav Belteki

Corresponding author e-mail address: chondtwdavid94@gmail.com

Institution(s)
Cambridge University Hospitals NHS Foundation Trust, Cambridge, The Rosie Hospital

Introduction (include hypothesis)
Mechanical ventilation is still frequently used in extremely preterm or critically ill1. In adults and children adverse patient-ventilator interactions (PVI) occur frequently, cause discomfort and are associated with increased duration ventilation and increased mortality2. Their clinical significance in newborns in not known. To support a systematic study of neonatal PVIs, we surveyed their prevalence in ventilated babies and developed deep learning models for their automatic detection.

Methods (include source of funding and ethical approval if required)
We performed an observational study of 23 neonates randomly selected from 170 neonates who were mechanically ventilated using the Dräger Babylog VN500 ventilator in SIPPV-VG, SIMV-VG, or PSV-VG modes. Pressure and flow waveform data were downloaded at 100 Hz sampling rate and pre-processed with Ventiliser3 to segment into individual breaths. 11,500 breaths were manually labelled for PVIs according to a recent classification scheme and a multiscale Convolutional Neural Network model was trained using Pytorch for PVIs with prevalence >1% using a training and test set consisting of breaths from 18 and 5 neonates respectively.

Results
The Asynchrony Index (AI) across the 11,500 breaths was 52.5%. The PVIs with prevalence of more than 1% were Expiratory Work (31.2%), Late Cycling (9.9%), Late Triggering (5.9%), Failed Triggering (4.3%), Multiple Triggering (1.3%), Early Triggering (1.2%), and Early Cycling (1%). Approximately 25% of breaths with PVI had 2 or more PVIs occurring simultaneously. The Convolutional deep learning binary classifiers developed for each PVIs demonstrated F1 scores > 0.9 on out of sample testing except for Early Triggering where it was 0.809.

Conclusions
PVIs occur frequently in neonates undergoing conventional mechanical ventilation with a significant proportion of breaths containing multiple PVIs. We have developed models with good specificity for 7 different PVIs to facilitate automated detection and further evaluation of the clinical significance of these PVIs in neonates.

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: Gusztav Belteki
Title (Upper case)

NETWORK VARIATION OF POSTNATAL DEXAMETAHSONE USE AND BPD SEVERITY ACROSS ENGLAND AND WALES IN INFANTS BORN <28 WEEKS OF GESTATION: A POPULATION-BASED STUDY

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

T'ng Chang Kwok, Don Sharkey.

Corresponding author e-mail address: tng.kwok@nottingham.ac.uk

Institution(s)

Centre of Perinatal Research, School of Medicine, University of Nottingham, Nottingham, UK.

Introduction (include hypothesis)

Postnatal dexamethasone (PND) is used in preterm infants to facilitate extubation and prevent bronchopulmonary dysplasia (BPD). NICE guidance suggests consideration of PND in high-risk infants from the second week of life. There may be subjectivity in how high-risk infants are identified and anxieties about side-effects. PND use has increased on a backdrop of increasing BPD rates. Hypothesis: Identifying infants at risk of death or severe BPD for treatment with PND is difficult resulting in variation with PND use. Aims: to explore (1) variation in PND use and severe BPD, and (2) difference in infant characteristics based on PND use.

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

Routinely collected data from infants born <28 weeks gestation who survived the first week of life from 2010 to 2020 in England and Wales were extracted. PND was defined as ≥3 consecutive days of treatment. Variation in PND use across 13 neonatal networks was explored using Cochran’s Q statistic derived from the caterpillar package in STATA. Among infants requiring respiratory pressure support (severe BPD) or death at 36 weeks corrected, characteristics of infants receiving PND was compared with infants not receiving PND. Ethical approval granted by the Sheffield Research Ethics Committee. University of Nottingham funded the study.

Results

22,527 infants were included. 3,777 (17%) infants received PND. There is variation in severe BPD or death rates at 36 weeks corrected (range 40-54%) and PND use (range 2-31%) across the 13 neonatal networks (p<0.0001) (Figure). Of the 10,133 infants with severe BPD or death at 36 weeks corrected, characteristics of infants receiving PND was compared with infants not receiving PND. Compared to infants receiving PND, infants that did not receive PND were born at higher gestation (median 25+5 vs 25+0 weeks) and birthweight (754g vs 690g) with shorter invasive ventilation (20 vs 40 days) and hospital stay durations (110 vs 130 days) in survivors to discharge and less likely to require respiratory support at discharge (51% vs 73%) (all p<0.0001).

Conclusions

There is wide variation in PND use across England and Wales with a large proportion of infants with poor respiratory outcomes not receiving PND. It is unclear if anxieties around PND treatment with long-term development is a factor. A more objective personalised approach is needed to aid identification of high-risk infants for PND treatment and what is the optimal treatment timing and course based on this assessment.

References (include acknowledgement here if appropriate)

We are grateful to the United Kingdom Neonatal Collaborative and Neonatal Data Analysis Unit. 1. NICE (NG124) guideline 2019. 2. Yao et al BMJ Open 2022. 3. von Hoxel et al Econ Education Review

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: Professor Don Sharkey
UNEXPECTED AND UNEXPLAINED DEATHS IN EX-PRETERM INFANTS: HOW EFFECTIVELY ARE WE GETTING PARENTS TO IMPLEMENT SAFE SLEEP PRACTICES?

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)

National Child Mortality Database, University of Bristol

Introduction (include hypothesis)

Preterm infants are at increased risk of unexpected and unexplained deaths in infancy and continue to be over-represented amongst such deaths. Previous studies have shown that unsafe sleep environments were more common amongst ex-preterm infants than term infants¹, and we hypothesised that a reduction of such potentially modifiable environmental factors might lead to a reduction of risk for ex-preterm infants.

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

The National Child Mortality Database, (funded by NHS England via HQIP), collects detailed information on all child deaths (birth to 17 years) in England, with statutory notification required within 48 hours. As part of an investigation into factors contributing to unexpected deaths in childhood, we reviewed all unexpected, unexplained infant deaths in England in 2020 to assess the significance of unsafe sleep environments amongst ex-preterm infants who died in this way.

Results

During 2020 we identified 361 unexpected deaths of infants aged less than 1 year in England, for which the child death review process had been completed for 249 (77%). For 120 deaths a full explanation was found (e.g., infection, previously unrecognised congenital abnormality, metabolic abnormality) and for 129 no explanation was found. Of the unexpected unexplained deaths, 28% had been born before 37 weeks gestation. Of the ex-preterm infants 59% died whilst bedsharing, all in hazardous circumstances (e.g., with an adult who smoked, had drunk alcohol, or taken drugs, or on a sofa). For one third of the unexpected unexplained deaths of ex-preterm infants the infant had been put down to sleep in the prone or side position.

Conclusions

Preterm infants are at increased risk of unexpected unexplained infant deaths, and the high prevalence of hazardous sleep environments in such infants has changed little in the past 30 years. This emphasises the need for working with parents to ensure they understand the importance of safe sleep practices.

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:
Timing of Stoma Closure in Neonates (ToSCiN)- a mixed methods feasibility study

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

Nick Lansdale,1,2,* Kerry Woolfall,1 Elizabeth Deja,3 Tracy Mitchell,3 Graciaa Singhal,4 Raphael Goldacre,5,6 Rema Ramakrishnan,7 Nigel Hall,8 Cheryl Battersby,9 Chris Gale,9 Gareth Penman,10 Marian Knight,7 Kayleigh Stanbury,11 Madeleine Hurd,11 David Murray,11 Louise Linsell,11 Pollyanna Hardy.11

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Institution(s)
See overleaf

Introduction (include hypothesis)

Neonates undergoing abdominal surgery frequently require a stoma; closing this stoma is an essential part of recovery. Timing of closure varies. Optimal timing is unclear and would be best resolved with a randomised controlled trial: such a trial is likely to be challenging. ToSCiN’s aim was to determine if it is feasible to conduct a clinical trial comparing ‘early’ and ‘late’ stoma closure.

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

Mixed methods study (2019-2022) in UK specialist centres, comprising: clinician survey, prospective cohort study, parent interviews, focus groups, database analyses and consensus meeting. Data are presented as median [range]. Funded by the National Institute for Health Research (NIHR) HTA programme. Research ethics Committee reference 20/Lo/1227.

Results

A total of 166 professionals completed the clinician survey. 56 infants were enrolled in the cohort study from eight centres. Infants were mostly preterm (44/56) and low birthweight (961g, [415-3962]) with NEC or perforation (37/56). At six weeks (possible intervention time), weight was 2024g [795-4460] and nine remained. By 12 weeks, weight was 2548g [1170-5480] and four were ventilated. 24 parents were interviewed and 36 staff (from 5 of 8 sites) took part in 6 focus groups. 52 key stakeholders attended an online consensus meeting. Most parents and professionals considered the proposed trial acceptable. Professionals identified extreme preterm gestation and clinical condition as reasons for not wanting to randomise. Parents and professionals stated that the timing of comparator arms needed more flexibility. Analysis of existing UK databases revealed variation in timing of stoma closure and identified approximately 300 infants per annum eligible for a trial. Consensus meeting attendees favoured: (i) including all infants with stomas in a trial (83%); (ii) comparing closure at six weeks with expectant management (58%); and (iii) weight gain/growth (38%) or length of stay (32%) as primary outcomes.

Conclusions

A trial appears feasible and is important to key stakeholders. The population of trial-eligible babies is sufficient. Challenges centre around lack of equipoise in extremely preterm infants; waiting too long for stoma closure in the ‘late’ comparator; and logistical issues in closing a stoma at a trial-allocated time.

References (include acknowledgement here if appropriate)

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

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8. University Surgery Unit, University of Southampton, Southampton, UK
9. Neonatal Medicine, School of Public Health, Imperial College London, London, UK
10. Department of Neonatology, St Mary’s Hospital, Manchester, UK
11. National Perinatal Epidemiology Unit Clinical Trials Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK
TRANSFER: ThReatened preterm birth, Assessment for in utero transfer; 22+0-23+6 weeks’ gestation

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

Smith-Collins APR, Griffin MJ on behalf of the TRANSFER project collaborative UK

Introduced to the Society by Dr E. Chakkarapani

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Institution(s)

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Introduction (include hypothesis)

Updated guidance from the British Association of Perinatal Medicine on decision making and management of threatened preterm birth between 22+0 and 23+6 weeks gestation has significant implications for practice and clinical service planning for both neonatal and maternity services. Optimising outcomes requires birth in maternity services co-located with tertiary NICU facilities, and close neonatal and obstetric input before as well as after birth. There is a lack of UK data on the scale of demand and resource required to optimise services.

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

TRANSFER was established as a UK-wide collaborative to undertake a multicentre prospective service evaluation of care for women presenting with threatened preterm birth between 22+0-23+6 weeks gestation. Ninety UK maternity units were recruited as contributing members of the collaborative, providing data over a 58 week period from May 2021-June 2022. Data on all cases were entered on a centrally developed Redcap form. Key outcomes from the study included number of presentations; number presenting at maternity units without tertiary NICU; number opting for active management; number of in utero transfers; number of births before 24+0

Results

1. 511 women presented with threatened preterm birth to obstetric units in England, Wales, Scotland and NI between 22+0-23+6 weeks’ gestation during the study period
2. 294 (58%) women presented to obstetric units without level 3 NICU
3. 349 (68%) of women opted for active/survival-focussed management
4. 235 (46%) of all women required transfer for optimal management (obstetric care or active neonatal pathway) – this was achieved in 219 cases (93%)
5. 283 (55%) women gave birth during the recorded admission. 46 (9%) women did so in a unit without a Level 3 NICU
6. 187 babies born alive between 22+0-23+6 weeks gestation. 108 (58%) survived to NICU admission
7. Average length of antenatal stay was 5.32 days in maternity centres with co-located NICU

Conclusions

Updated national guidance has seen significant shifts in practice with active obstetric and neonatal management offered to increasing numbers of women with threatened preterm birth before 24 weeks gestation. Service planning for optimal outcomes requires accurate data but neonatal systems capture a minority (~20%) of cases. This multicentre collaborative identified ~2000 bed days p.a. of tertiary obstetric need for this patient group.

References (include acknowledgement here if appropriate)


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

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

NOVEL POLYMER COATING OF NASOGASTRIC TUBES TO INHIBIT MICROBIAL BIOFILM FORMATION IN AN IN-VITRO MODEL

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)

We have previously reported\(^1\) that 76% of neonatal nasogastric tubes (NGTs) become colonised with biofilms from a range of pathogenic organisms potentially causing late-onset infection (LOI) in preterm infants\(^2\). LOIs are associated with significant morbidity and mortality along with long-term neurodevelopmental impairment\(^3\). Previously we demonstrated Candida biofilm resistance (NNS 2022). Using our rapid, high-throughput polymer discovery platform\(^4\), we aimed to coat neonatal NGTs with candidate polymer coatings to explore broader biofilm-inhibition of common neonatal pathogens.

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

NGTs were coated with six candidate polymers combinations (DPEA, TEGMA, DEGMA, CyDMA and iBNA) and then exposed to term formula milk for 30mins or no-milk. Uncoated (control, n=5) and coated (n=5/polymer) sections then underwent 24hr incubation with Staphylococcus epidermidis, Pseudomonas aeruginosa and Candida albicans followed by biofilm biomass quantification with confocal fluorescent microscopy. One-way ANOVA with Dunn's multiple comparisons analysis compared controls to polymers.

Results

All organisms had significantly higher rates of biomass formation when exposed to milk (**P<0.01 all**). All six polymer combinations significantly (P<0.0001) reduced biomass (µg/cm\(^2\)) with some almost inhibiting growth by >99% (table) compared to uncoated control NGTs.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Milk</th>
<th>Control</th>
<th>P 1</th>
<th>P 2</th>
<th>P 3</th>
<th>P 4</th>
<th>P 5</th>
<th>P 6</th>
</tr>
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<tr>
<td>S epidermidis</td>
<td>N</td>
<td>30.8±4.1</td>
<td>16.5±2.0</td>
<td>2.1±0.7</td>
<td>&lt;0.1±0.0</td>
<td>&lt;0.1±0.1</td>
<td>13.6±3.2</td>
<td>20.7±3.8</td>
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<tr>
<td></td>
<td>Y</td>
<td>42.7±3.4*</td>
<td>13.8±3.7</td>
<td>7.2±2.7</td>
<td>&lt;0.1±0.0</td>
<td>&lt;0.1±0.0</td>
<td>16.5±4.2</td>
<td>31.0±4.1</td>
</tr>
<tr>
<td>P aeruginosa</td>
<td>N</td>
<td>19.8±2.6</td>
<td>8.1±2.6</td>
<td>3.2±1.2</td>
<td>1.0±0.4</td>
<td>1.0±0.3</td>
<td>4.9±1.4</td>
<td>8.5±2.6</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>38.5±3.6*</td>
<td>22.0±3.5</td>
<td>5.1±1.9</td>
<td>0.4±0.1</td>
<td>0.4±0.2</td>
<td>6.2±1.8</td>
<td>8.1±1.8</td>
</tr>
<tr>
<td>C albicans</td>
<td>N</td>
<td>15.3±1.6</td>
<td>11.1±1.0</td>
<td>1.6±0.7</td>
<td>4.3±1.3</td>
<td>3.9±1.3</td>
<td>0.2±0.1</td>
<td>0.7±0.4</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>26.8±3.1*</td>
<td>19.3±2.6</td>
<td>15.1±2.7</td>
<td>6.4±1.9</td>
<td>4.7±1.6</td>
<td>0.4±0.3</td>
<td>1.7±0.5</td>
</tr>
</tbody>
</table>

Conclusions

The presence of formula milk enhances biofilm formation on NGTs. Using rapid polymer discovery, we've identified polymer combinations capable of significantly reducing biofilm formation against common neonatal pathogens. Scaling polymer coated NGT production would allow clinical studies to explore their utility at reducing LOI and other morbidities, such as BPD and necrotising enterocolitis, in this high-risk population.

References (include acknowledgement here if appropriate)

\(^1\)Hurrell et al BMC Infect Dis 2009. \(^2\)Gross et al Arch Dis Child 2019. \(^3\)Hook et al Nature Biotechnology 2012
\(^4\)Singh et al Biomaterials 2020.

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

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Senior author supporting presentation on day of meeting: Don Sharkey