Neonatal Society Spring Meeting, 14th March 2024

Royal Society of Medicine, 1 Wimpole Street, London, W1G 0AE
Meeting Virtual Link: To be emailed to delegates on 13th March 2024

Session 1
09:30. Carla L. Avena-Zampieri
Correlation of fetal lung area with MRI derived pulmonary volume

09:45. Allan Jenkinson
Chest radiographic thoracic areas and respiratory outcomes in infants with anterior abdominal wall defects

10:00. Parvaneh Adibpour
Maturation of resting-state cerebral activity in preterm infants

10:15. Morning tea/coffee break

Session 2
10:45. Alexandra Jager
Exploring clinicians’ views on the barriers to implementation of trans-anastomotic tube (TAT) feeding in babies born with duodenal atresia: A mixed methods study

11:00. George Bethell
Neonatologists’ views on the challenges and optimisation of surgical decision making in necrotising enterocolitis

11:15. Isabel Iglesias-Platas
Serum folate concentrations in preterm infants according to nutritional support pre- and post-discharge from the neonatal unit

11:30. Keynote Lecture
Professor Deena Gibbons, Professor in Early Life Immunology, KCL
‘The neonatal immune system - its importance for the neonate and the adult they become’

12:30. Lunch break (90 minutes)

Session 3
14:00. Katie McKinnon
Epigenetic scores indicate differences in the proteome of preterm infants

14:15. Rebecca Jackson
Association of antenatal or neonatal SARS-COV-2 exposure with developmental and respiratory outcomes and healthcare usage in early childhood: A national prospective cohort study
14:30. Abigail Wood
Neurodevelopment surveillance at 2-years in neonatal follow-up clinics using the INTER-NDA: A pilot qualitative study of parents’ and clinicians’ experiences

14:45. Sara Rapuc
Do cognitive assessments at 18-21 months predict cognitive outcomes at 6-8 years in children cooled for neonatal hypoxic-ischaemic encephalopathy?

15:00. Afternoon tea/coffee break

Session 4
15:30. Rising Star Annual Invited Lecture
Dr Christopher Stewart, Wellcome Trust Sir Henry Dale Fellow & Lister Institute Prize Fellow, Newcastle University
‘Diet-microbe-host interaction in infant health: Are breastmilk bioactives the missing piece of the jigsaw?’

16:00. Karen Luyt
Reducing preterm mortality and brain injury: the PERIPrem (perinatal excellence to reduce injury in premature birth) care pathway

16:15. Chris Gale
Neonatal outcomes among births occurring in or out of water following intrapartum water immersion in UK maternity services: The POOL cohort study

Session 5
16:40. Prize for best presentation by a trainee

16:45. McCance Lecture – Introduced by Professor Andy Ewer, President
Professor Manon Benders, UMC Utrecht
‘Stem cell therapy for neonatal brain injury’

17:45. Close of meeting
CORRELATION OF FETAL LUNG AREA WITH MRI DERIVED PULMONARY VOLUME

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

Carla L. Avena-Zampieri, Alena Uus, Theodore Dassios, Anna Milan, Rui Santos, Vanessa Kyriakopoulou, Daniel Cromb, Megan Hall, Alexia Egloff, Matthew McGovern, Kelly Payette, Jana Hutter, Mary Rutherford, Anne Greenough, Lisa Story

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Institution(s)
- King’s College London
- Guy’s and St Thomas’ NHS Foundation Trust

Introduction (include hypothesis)
Advanced MR techniques now enable direct evaluation of both fetal pulmonary volume and area and thus may be useful in prediction of future potential abnormalities. This study therefore aims to generate reference ranges for pulmonary volume and area in uncomplicated pregnancies, evaluate the correlation between prenatal pulmonary volume and area, as well as to assess the agreement between antenatal MRI-derived and neonatal CXR-derived pulmonary area in a cohort of fetuses that delivered prematurely as well as in a small cohort of cases with congenital diaphragmatic hernia.

Methods (include source of funding and ethical approval if required)
Fetal MRI datasets were retrospectively analysed from four ethically approved studies ([REC 16/LO/1573], [REC 19/SS/0032], [REC 21/SS/0082], [REC: 14/LO/1806]) from uncomplicated term pregnancies and a preterm cohort that delivered within 72 hours of the fetal MRI. Datasets were also analysed from seven CDH infants, with CXRs obtained between five to 125 days after MRI scans. All examinations included T2 weighted single-shot turbo spin echo images in multiple planes. In-house pipelines were applied to correct for fetal motion using deformable slice-to-volume reconstruction. An MRI-derived lung area was manually segmented from the average intensity projection images generated. Postnatal lung area in the preterm and CDH cohort was measured from neonatal CXRs within 24 hours of delivery. Pearson correlation coefficient was used to correlate MRI-derived lung volume and area. A two-way absolute agreement was performed between the MRI-derived average intensity projection lung area and CXR-derived lung area.

Funding source: Health Education England (HEE) / National Institute for Health Research (NIHR), Welcome/ESPRC Centre for Medical Engineering [WT203148/Z/16/Z], by the NIH Human Placenta Project grant 1U01HD087202 (Placenta Imaging Project (PIP)), by the Wellcome Trust, Sir Henry Wellcome Fellowship, [201374/Z/16/Z], by the UKRI: FLF/MR/T01815/1 and by the National Institute for Health Research (NIHR) Biomedical Research Centre GIST.

Results
Datasets from 180 controls, 10 preterm fetuses and seven CDH fetuses were suitable for analysis. Mean gestational age at MRI was 28.6±4.2 for controls, 28.7±2.7 for preterm fetuses and 29.1±5.3 for the CDH fetuses. MRI-derived lung area correlated strongly with lung volumes in both lungs, left lung and right lung respectively (all p<0.001) in the control cohort, in the preterm cohort (all p<0.001) and in the CDH cohort (p=0.004, p<0.001, p=0.037). Lung volumes and lung areas were significantly smaller in the preterm cohort than in controls in both lungs, left lung and right lung respectively (volume [p=0.012, p=0.014, p=0.003]; area [p<0.001, p<0.001, p=0.008]). Lung volumes and lung areas were also significantly smaller in the CDH cohort than in controls in both lungs, left lung and right lung respectively (all p<0.001). Good agreement was found between MRI-derived fetal AIP 2D lung area and neonatal CXR-derived lung area post-delivery in both lungs, left lung and right lung respectively [0.982; 0.655; 0.764] in the preterm cohort. Agreement was found in a CDH infant postnatally imaged within 5 days of the MRI. CXR-derived lung areas were significantly lower in than the MRI-derived lung areas from controls in the preterm cohort [both lungs (p<0.001), left lung (p<0.001) and right lung (p=0.002)] and in the CDH cohort [all p<0.001]).

Conclusions
MRI-derived pulmonary area correlated well with absolute pulmonary volumes in all cohorts and there was good correlation between MRI-derived pulmonary areas and postnatal CXR-derived lung areas when delivery occurred within a few days of the MRI examination. Fetal MRI derived lung area may prove to be a useful predictor of neonatal lung areas.

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 presenting on day of meeting: Professor Anne Greenough
Introduction (include hypothesis)

Infants with anterior abdominal wall defects (AWD) can suffer from pulmonary complications. Infants born with exomphalos are reported to have worse respiratory outcomes than those of infants with gastroschisis. Our aims were to determine if the chest radiographic thoracic areas (CRTAs) on day one differed between infants with exomphalos or gastroschisis, whether this related to differing severity of outcomes and if they were lower than those of controls indicating abnormal antenatal lung growth.

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

A retrospective review of infants with exomphalos or gastroschisis born in a single surgical centre between January 2004 and January 2023 was conducted. The control group was term, newborn infants ventilated for poor respiratory drive at birth with no supplemental oxygen requirement by six hours of age. Chest radiographs were undertaken and the highest CRTA in the first 24 hours after birth for each infant were included in the analysis. Free-hand tracing of the perimeter of the left and right thoracic areas was undertaken and the CRTA calculated by the software. Outcome measures were a diagnosis of bronchopulmonary dysplasia (defined as supplemental oxygen requirement at 28 days) and requirement for inhaled nitric oxide, high frequency oscillation and/or postnatal systemic corticosteroids.

Results

A total of 319 infants were included: 62 exomphalos, 127 gastroschisis and 130 controls. Infants with gastroschisis had a lower gestational age than exomphalos infants and controls (median [IQR] 36 [35-37] weeks versus 38 [35-39] weeks versus 39.5 [38-41] weeks; both groups p<0.001). Infants with gastroschisis had a lower birthweight (median [IQR] 2380 [1905-2712] gms) than exomphalos infants (median [IQR]) 3071 [2470-3346] gms; p<0.001) and controls (3363 [2979-3687] gms; p<0.001). The CRTA was significantly related to birth weight (r=0.404, p<0.001) and type of defect (r=0.612, p<0.001), but not with gestational age at birth (r=0.088, p=0.491) or gender (r = 0.612, p=<0.001). When the CRTA was adjusted for birthweight, there were lower CRTAs in exomphalos infants versus gastroschisis infants versus controls (median [IQR] 344 [284-437] versus 406 [347-457] versus 772 [656-876] mm²; both groups p <0.001). The CRTA had an AUROC of 0.816 to predict BPD in infants with exomphalos. A CRTA of 1759 mm² had a sensitivity of 81% and specificity of 71% in predicting BPD in infants with exomphalos. No gastroschisis infant developed BPD.

Conclusions

Infants with exomphalos or gastroschisis had lower CRTAs than the controls suggesting that both groups had abnormal lung development. The CRTA was lower in the exomphalos infants who also had worse respiratory outcomes suggesting that assessment of CRTA may be a useful prognostic aid when counselling parents.

References (include acknowledgement here if appropriate)

### Title (Upper case)

**Maturation of resting-state cerebral activity 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)

Parvaneh Adibpour, Hala Nasser, Amandine Pedoux, Laurie Devisscher, Nicolas Elbaz, Elodie Hinnekens, Sara Neumane, Claire Kabdebon, Aline Lefebvre, Anna Kaminska, Lucie Hertz-Pannier, Alice Heneau Marianne Alison, Catherine Delanoë, Richard Delorme, Marianne Barbu-Roth, Valérie Biran, Jessica Dubois

### Institution(s)

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### Introduction (include hypothesis)

By interfering with the normal sequence of mechanisms serving the brain maturation, preterm birth can interfere with the child’s neurodevelopment and have long-term consequences. The early characterization of brain functioning, and maturation is thus of critical interest in preterm infants who are at high risk of atypical outcomes and could benefit from early diagnosis and interventions. Here, we aimed to characterize the maturation of the fast dynamics of the cerebral activity in preterm infants. We hypothesized that maturation result in acceleration of brain dynamics, and that preterm birth should have an adverse effect on such acceleration of brain dynamics.

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

Using Electroencephalography, we recorded resting-state brain activity in extreme and very preterm infants at the equivalent age of pregnancy term (n=44), and longitudinally 2-months later (n=33). We characterized the maturation of brain activity, while controlling for vigilance states, and by using microstate analysis (Michel & Koenig, 2018), a method to quantify the spatiotemporal dynamics of the spontaneous transient network activity. To assess the impact of prematurity on the dynamics of resting-state activity, we further compared preterms with a group of full-term born infants (n=14).

### Results

Maturation of functional networks was translated by the emergence of richer dynamics, manifested in part by the faster temporal dynamics (shorter duration of microstates) as well as an evolution in the spatial organization of the dominant microstates. The inter-individual differences in the temporal dynamics of brain activity at term-equivalent age were impacted by age at birth and sex, indicating slower microstate dynamics in boys and in infants with lower birth-age. Lower birth-age differentially impacted different network dynamics, suggesting that some networks might be more vulnerable to dysmaturation. Comparing preterms with full-terms further showed slower microstate dynamics as well as altered spatio-temporal properties of resting-state activity in preterm infants at the term-equivalent age. The impact of preterm birth was less apparent at 2 months evaluations, suggesting that maturation reduces the impact of prematurity on functional network dynamics.

### Conclusions

This work reveals maturational properties of the emerging resting-state functional networks and highlights their alterations due to prematurity, providing insights on the impact of perinatal factors on the fast dynamics of cerebral activity.

### 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: no senior author is part of neonatal society
Title (Upper case)

Exploring Clinicians’ Views on the Barriers to Implementation of Trans-Anastomotic Tube (TAT) Feeding in Babies Born with Duodenal Atresia: A Mixed Methods 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)

Alexandra Jager, Joanne Turnbull, Mark Johnson, Nigel J Hall

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Institution(s)

University of Southampton

Introduction (include hypothesis)

Following duodenal atresia repair, trans-anastomotic tubes (TATs) are used by some surgeons to provide early enteral nutrition and have been shown to reduce the need for parenteral nutrition (PN) and its associated costs and risks. However, most infants receive PN and a minority receive TATs (sometimes combined with PN). This variation is unexplained by clinical or demographic factors. We examined how clinicians plan postoperative nutrition, reasons for TAT and PN preferences, and views on barriers to (increasing) TAT feeding.

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

UK-based clinicians (neonatologists, surgeons, dietitians, and specialist nurses) completed an online mixed methods survey, interviews, and focus groups. Likert-scale replies were analysed using descriptive statistics. Open-ended survey replies were summarised thematically. Interviews were analysed inductively and deductively, facilitated by the ‘acceptability of healthcare interventions’ framework. Focus groups were used to develop interventions to increase TAT usage that were acceptable to clinicians and feasible to implement. Funder: NIHR Research for Patient Benefit (RfPB) programme. Ethical approval 78214.

Results

109 clinicians (24 neonatologists, 7 nurses, 3 dietitians, 75 surgeons) from all 25 UK neonatal surgical units completed the survey. 25 interviews and 2 focus groups (12 participants) were held. 88% of survey respondents stated that TAT use was decided solely by surgeons, driven primarily by considerations of providing appropriate nutrition and risks. Decisions about Central Venous Catheters (CVCs) were made by neonatologists (28%), surgeons (17%), jointly (48%), or ‘other’ (7%). Neonatologists and surgeons prioritised providing appropriate nutrition and risks when deciding whether to use CVCs/PN; surgeons rated a lack of supporting research and risks related to TATs as barriers to TAT usage. Costs, ethicality, resource availability, and parents’ preferences had limited influence on TAT and PN usage. Interventions to increase TAT usage include creating and disseminating further supporting clinical evidence (potentially an RCT), developing a guide to aid TAT feeding and management in the post-operative period, and training on using TATs safely.

Conclusions

Increased TAT usage requires (1) surgeons to be persuaded of TATs’ efficacy and safety; (2) neonatologist recognition that exclusive TAT feeding can provide adequate nutrition avoiding need for CVC and PN. Wider dissemination and information sharing between neonatologists and surgeons is essential to achieve this.

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:
Title (Upper case)

NEONATOLOGISTS’ VIEWS ON THE CHALLENGES AND OPTIMISATION OF SURGICAL DECISION MAKING IN NECROTISING ENTEROCOLITIS

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

George S Bethell¹, Anne-Sophie Darlington² and Nigel J Hall¹

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Institution(s)

1. University Surgery Unit, Faculty of Medicine, University of Southampton. 2. School of Health Sciences, University of Southampton.

Introduction (include hypothesis)

The decision to undertake surgery or continue medical management in necrotising enterocolitis (NEC) is often challenging and can lead to delays in undertaking surgery.¹ These challenges may be a barrier to improving overall outcomes. We aimed to understand why surgical decision making in NEC is challenging and to explore what is required to improve this.

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

Three semi-structured focus groups with 22 consultant participants (7 neonatologists, 15 neonatal surgeons) were undertaken exploring surgical decision making in NEC. Inductive thematic analysis of focus group transcripts was undertaken. This study was funding by a NIHR doctoral fellowship (NIHR302541) with institutional ethical approval (University of Southampton ref:80973).

Results

Four themes relating to challenges of surgical decision making emerged, all of which have relevance to neonatal practice. These were (i) uncertainty of NEC diagnosis, (ii) absence of objective criteria for surgery including limitations of current investigations, (iii) uncertainty of optimal timing of referral and transfer of infants and (iv) uncertainty of requirement for and the benefits of surgery.

Five themes relating to optimisation of surgical decision making were identified: (i) desire for a simple and objective decision aid, (ii) need for reduced variability in practice with promotion of a multidisciplinary approach, (iii) development of criteria for both transfer to surgical centres and referral to surgeons, (iv) expression of willingness to change practice and (v) anticipated barriers to change of practice.

Conclusions

We have identified specific themes that illuminate the difficulties experienced by neonatologists and surgeons. Both specialties would welcome changes to current practice including standardised transfer criteria for babies with NEC and greater objectivity around several aspects of surgical decision making. This knowledge may inform future research and systems change to ultimately facilitate early and accurate decision making.

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: Nigel Hall
Title
SERUM FOLATE CONCENTRATIONS IN PRETERM INFANTS ACCORDING TO NUTRITIONAL SUPPORT PRE-AND POST-DISCHARGE FROM THE NEONATAL UNIT

Authors
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Institution(s)
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Introduction
Folate is a water-soluble B vitamin, essential for growth and cellular turnover. Adequate folate intake is required in preterm infants to support rapid growth and development. However, guidelines for supplementation (stand-alone or as a component of nutritional products) are mostly based on expert consensus due to the lack of strong evidence. Folate supplements come as part of parenteral nutrition (PN), breast milk fortifier (BMF), preterm formula or as a folic acid oral solution. We aimed to assess folate status in preterm infants at NICU discharge and in early infancy, according to exposure to folate sources and with a particular interest in those exclusively/predominantly breastfed.

Methods
A prospective, multicentre, observational cohort study was conducted in preterm infants <33 weeks' gestational age (GA) exclusively/predominantly fed human milk when approaching NICU discharge. Serum folate was determined by a chemiluminescent microparticle folate binding protein assay at: 1) timepoint 1 (T1) while inpatient near discharge home and 2) timepoint 2 (T2) at ~2-3 months corrected age (CA) during an outpatient visit. The upper limit of quantification for the method is 20 ng/mL; samples over this limit were assigned a value of 20.1 ng/mL for calculations. WHO guidelines were used to define deficiency (<3 ng/mL), possible deficiency (3-5.9 ng/mL), normal (6-20 ng/mL), and elevated folate status (>20 ng/mL). Nutritional information on type of feed and supplements was collected from hospital notes and maternal interviews. Breast milk fortifier (BMF), when used, was stopped before hospital discharge. At the time of the study, recommendations for routine oral folate supplementation (50 µg/day) in preterm infants fed unfortified breast milk had been implemented in only one centre. The study had research ethics approval (REC ref. 15/LO/1808) and parents provided written informed consent prior to entry.

Results
A first blood sample was taken from 45 infants from four UK NICUs at a median postmenstrual age of 35.4 (IQR 1.6) weeks (T1) and 37 came back for a 2nd visit at a median CA of 9.3 (IQR 11.3) weeks (T2). Thirty-two infants (71%) received PN. Twelve infants (32%) remained exclusively breastfed at T2. No infant had a serum folate concentration <6 ng/mL at either time point. Median serum folate concentrations were (T1: 17.3, IQR 3.6 ng/mL; T2: 19.0, IQR 1.8 ng/mL). A proportion of infants had elevated folate (>20ng/mL): 14 (31%) at T1, 19 (42%) at T2, and 7 (16%) at both time points. Five babies who were given folic acid oral supplements had elevated serum folate at both time points. In a multivariate regression analysis, number of days on BMF (standardized β= 0.577, p <0.001) and having received folic acid drops (standardized β= 0.381, p =0.004) were independently related to serum folate levels at T1 when adjusted for GA, PN and type of milk feeding. Folate levels at T2 were related to GA (standardised β= -0.442, p=0.002), having received PN (standardized β= -0.426, p= 0.003), and type of milk feeding at the second visit (standardized β= 0.599, p <0.001).

Conclusions
In a small cohort of exclusively breastfed preterm infants that did not receive BMF or extra folic acid drops, and based on serum folate concentrations, none had evidence of confirmed/possible folate deficiency at discharge or on follow up. Babies that had been fed fortified breastmilk or formula pre-discharge had higher serum folate concentrations, both at T1 and T2, and more than a third had elevated concentrations. These findings suggest that the provision of extra folate supplement drops to breastfed preterm infants may be superfluous. Further studies are needed to confirm these findings and to clarify if high folate status can result in an imbalance of folate and vitamin B12, as these vitamins work in synergy and vitamin B12 deficiency in infancy is very common.

References
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. Paul Clarke
EPigenetic Scores indicate differences in the Proteome of Preterm Infants

Katie McKinnon1, Eleanor L.S. Conole2, Kadi Vahe1,4, Robert F. Hillary3, Danni A. Gadd3, Justyna Binkowska1, Gemma Sullivan4, Anna J. Stevenson3, Amy Corrigan1, Lee Murphy5, Heather C. Whalley4, Hilary Richardson6, Riccardo E. Marion3, Simon R. Cox2, James P. Boardman1,4

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Title (Upper case)

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

Epigenetic scores (EpiScores), reflecting DNA methylation (DNAm)-based surrogates for complex traits, have been developed for multiple circulating proteins1,2,3,4. EpiScores for pro-inflammatory proteins, such as C-reactive protein (DNAm CRP), are associated with brain health and cognition across the lifespan, and with inflammatory comorbidities of preterm birth in neonates5. Social disadvantage can become embedded in child development through inflammation, and deprivation is over-represented in preterm infants. We tested the hypotheses that preterm birth and socioeconomic status (SES) are associated with alterations in a set of EpiScores enriched for inflammation-associated proteins.

Epigenetic scores (EpiScores) were derived from saliva samples of 323 neonates born at gestational age (GA) 22+1 to 42+1 weeks. Participants were born at the Royal Infirmary Edinburgh and recruited to a longitudinal cohort study (2012-2021). Saliva sampling was between 36+4 and 47+1 weeks. We built linear regression models for each EpiScore, examining the relationship with birth GA, SES (as either the Scottish Index of Multiple Deprivation, maternal education, or maternal occupation), and a birth GA*SES interaction, adjusting for sampling GA, sex, and methylation processing batch. In a preterm sub-group (n=217, median [range] GA 22+2 weeks [22+1 to 33+0 weeks]), we additionally adjusted for inflammatory exposures (sepsis, bronchopulmonary dysplasia, necrotising enterocolitis, and histological chorioamnionitis). We used principal component analysis for data-driven correction for multiple comparisons. Ethical approval: NRES, South-East Scotland REC (11/55/0061, 13/SS/0143, 16/SS/0154), and NHS Lothian Research and Development (2016/0255). Funding: Theirworld, UKRF MRC Programme Grant (MR/X003434/1).

Results

Forty-three (41%) EpiScores were associated with low GA at birth (standardised estimates [0.14-0.88], Bonferroni-adjusted p-value <8.3x10^-9, Figure 1). These included EpiScores for chemokines, growth factors, proteins involved in neurogenesis and vascular development, cell membrane proteins and receptors, and other immune proteins. Three EpiScores were associated with SES, or the interaction between birth GA and SES: afamin, intercellular adhesion molecule 5 and hepatocyte growth factor-like protein (standardised estimates [0.06-0.13], Bonferroni-adjusted p-value <8.3x10^-9). In the preterm sub-group, SES-EpiScore associations did not remain statistically significant after adjustment for inflammatory exposures.

Conclusions

Low birth GA is substantially associated with a set of EpiScores. The set was enriched for inflammatory proteins, providing new insights into immune dysregulation in preterm infants. SES had fewer associations with EpiScores; these tended to have small effect sizes and were not statistically significant after adjusting for inflammatory comorbidities. This suggests that inflammation is unlikely to be the primary axis through which SES becomes embedded in the development of preterm infants in the neonatal period.

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: x

Senior author supporting presentation on day of meeting: Prof James P Boardman
EpiScores associated with gestational age in regression models adjusted for socioeconomic status

Figure 1. EpiScores associated with gestational age in regression models with (A) Scottish Index of Multiple Deprivation, (B) maternal education, and (C) maternal occupation. Figure 2A (n=331) shows 39 associations, Figure 2B (n=323) shows 35 associations, and Figure 2C shows (n=328) shows 39 associations. Points and bars represent standardised beta and 95% confidence intervals, with red indicating positive and blue negative associations. Covariates included in all models: age at sample, birthweight z-score, sex, and methylation processing batch. Bonferroni-adjusted p-value <8.3x10^{-3}.

ASSOCIATION OF ANTENATAL OR NEONATAL SARS-CoV-2 EXPOSURE WITH DEVELOPMENTAL AND RESPIRATORY OUTCOMES AND HEALTHCARE USAGE IN EARLY CHILDHOOD: A NATIONAL PROSPECTIVE COHORT STUDY

Authors
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Introduction (include hypothesis)
Perinatal exposure to SARS-CoV-2 may adversely affect child development before 12 months of age. However, knowledge of its impact on longer term developmental outcomes is lacking¹. Further, SARS-CoV-2 is primarily a respiratory virus and the relationship between exposure and early childhood respiratory symptoms is unknown. We therefore aimed to investigate whether antenatal or neonatal SARS-CoV-2 exposure is associated with developmental and respiratory outcomes, and general health care usage in early childhood.

Methods (include source of funding and ethical approval if required)
A prospective national population-based study of children with and without antenatal or neonatal exposure to SARS-CoV-2 infection. Children were assessed at 21-32 months of age via parent questionnaires: Ages and Stages Questionnaire 3rd Edition (ASQ-3), Ages and Stages Questionnaire Social-Emotional 2nd Edition (ASQ:SE-2), Liverpool Respiratory Symptom Questionnaire (LRSQ), and health care usage questionnaire (unvalidated). The primary outcome was total ASQ-3 z-score. Secondary outcomes: ASQ:SE-2 z-scores; risk of delay in ASQ-3 domains (communication, gross motor, fine motor, problem solving, personal-social); total LRSQ scores. and health care usage.

Results
Data were collected from 339 children (exposure cohort=96; comparison cohort=243) between October 2021 and January 2023. The mean total ASQ-3 z-score did not differ between the exposed and comparison cohort when adjusted for children’s age, sex, maternal ethnicity, parental education and index of multiple deprivation (-0.2 (-0.5, 0.03)). However, early SARS-CoV-2 exposure was associated with an increased risk of delayed personal-social skills (odds ratio 3.81; 95% CI, 1.07 to 13.66), higher ASQ:SE-2 total scores (mean difference in z-score 0.4; 95% CI, 0.2 to 0.6, indicating poorer outcomes) and higher risk of delayed social-emotional development (OR 3.58, 95% CI, 1.30 to 9.83). The exposed cohort also had a higher mean square root total LRSQ score (difference in mean square root of total score = 0.6 95%, CI: 0 to 1.1) and higher inpatient (38% vs. 21%, p<.001), outpatient (38% vs. 30%, p=.009), and General Practitioner appointments (60% vs. 50%, p=.02) than the comparison cohort. No differences in other secondary outcomes were identified between the exposed

Conclusions
SARS-CoV-2 exposure in the antenatal or neonatal period may impact social-emotional development, respiratory symptoms and healthcare utilisation in early childhood. Longer term follow-up of children exposed to SARS-CoV-2 is needed to determine if effects persist and to identify those in need of intervention.

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: Dr Ela Chakkarapani

Figure 1.
Title (Upper case)

NEURODEVELOPMENT SURVEILLANCE AT 2-YEARS IN NEONATAL FOLLOW-UP CLINICS USING THE INTER-NDA: A PILOT QUALITATIVE STUDY OF PARENTS’ AND CLINICIANS’ EXPERIENCES

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

Wood A1, Fernandes M1,2,3, Lima R1, Johnson M1,4, Dorling J1,4

Corresponding author e-mail address: Aw4g21@soton.ac.uk

Institution(s)

1Department of Neonatology, Princess Anne Hospital, University Hospital Southampton NHS Foundation Trust
2MRC Lifecourse Epidemiology Centre, Faculty of Medicine, University of Southampton
3Nuffield Department of Women’s and Reproductive Health, University of Oxford
4NIHR Southampton Biomedical Research Centre, University of Southampton

Introduction (include hypothesis)

The INTER-NDA is an open-source, rapid, standardized developmental assessment for children aged 22 to 30 months; its norms are the first international standards of early child development. A large number of NICU graduates, who do not meet NICE2, NNAP3 and Trust criteria for standardised developmental assessments at age 2, may benefit from a standardised assessment on the INTER-NDA. The aim of this study was to assess parental and clinician perspectives about the use of the INTER-NDA for the neurodevelopmental surveillance of NICU graduates.

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

This cross-sectional, qualitative study was conducted as part of a larger feasibility study (INTER-NEO) between June and December 2023, at the neonatal clinics at University Hospitals Southampton. Fifteen 2-year-olds not meeting Trust, NICE or NNAP criteria for standardised developmental testing but attending neonatal out-patient appointments were administered the INTER-NDA. Parent and clinician experiences were collected using the Experience of Services Questionnaire and Parent Experiences Questionnaire, and Clinician Experiences Questionnaire, respectively. Experience scores were compared between the INTER-NDA and standard of care (SOC) using the Wilcoxon Signed-Rank Test; qualitative data was thematically analysed. Ethics IRAS ref: 327510; ERGO ref: 87744; funding: NIHR.

Results

All parents (n=15) reported high levels of satisfaction with the INTER-NDA and that it met their expectations. They reported that their children enjoyed the INTER-NDA (75%) more than SOC assessments (58.33%). Parents significantly ranked the INTER-NDA and developmental assessments performed by doctors above both SOC parent-reported questionnaires [ASQ-3 (0.040) and PARCA-R (0.010)]. All parents reported it would be valuable to use the INTER-NDA to assess neurodevelopment in neonatal outpatients at children’s two-year follow-up. Thematic analysis identified four themes; interactive, enjoyable, 1:1 nature and good resources. Clinicians (n=2) found the INTER-NDA report easy to interpret and helpful to have ahead of the child’s appointment. Clinicians and parents reported no disadvantages or areas of concern relating to the INTER-NDA.

Conclusions

Parents and clinicians reported high levels of satisfaction with the INTER-NDA for the developmental assessment of NICU-graduates at their 2-year follow-up as compared to SOC. Larger samples would provide further insights with a higher degree of accuracy: data collection (including for feasibility and health economics aspects) is on-going.

References (include acknowledgement here if appropriate)


Check box if presenting author is a trainee: Medical Student

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 Jon Dorling
**Title (Upper case)**

DO COGNITIVE ASSESSMENT AT 18-21 MONTHS PREDICT COGNITIVE OUTCOMES AT 6-8 YEARS IN CHILDREN COOLED FOR NEONATAL 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)**

Sara Rapuc1, Sally Jary1, Ross Vanderwert2, David Odd3, Ela Chakkarapani1,4.

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

**Institution(s)**

1Translational Health Sciences, Bristol Medical School, University of Bristol; 2Cardiff University Centre for Human Developmental Science (CUCHDS), School of Psychology, Cardiff University; 3School of Medicine, Division of Population Medicine, Cardiff University; 4Neonatal Intensive Care Unit, St Michael's Hospital, UHBW.

**Introduction (include hypothesis)**

Children who undergo therapeutic hypothermia for hypoxic-ischaemic encephalopathy (HIE) are at a significant risk of cognitive deficits at early school-age1. Early identification of these children for targeted support is crucial. Given that the cognitive and language scores at 18-22 months and 6-7 years are correlated in preterm-born children2, we hypothesised that, in children cooled for HIE, cognitive and language scores at 18-21 months will predict cognitive scores at 6-8 years.

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

This study included 48 children without cerebral palsy, cooled for HIE, who were part of the CoolMRI project (ethics approval: 15/SW/0148). Cognitive and language skills were assessed using Bayley-III scales at 18-21 months and full-scale IQ assessed using WISC-IV scale at 6-8 years of age. Both scales have a mean (SD) of 100 (15) for composite scores. The associations between Bayley-III cognitive/language/average of cognitive and language composite scores and WISC-IV FSIQ/domain composite scores were first estimated and then adjusted for covariates including clinical and socioeconomic variables using linear regression models.

**Results**

The results of the unadjusted and adjusted analyses are presented in Table 1. Bayley-III average cognitive and language composite scores were associated with WISC-IV FSIQ (Coef 0.40 (0.13-0.66), R² adjusted 27%) and verbal comprehension (Coef 0.34 (0.07, 0.61), R² adjusted 21%) scores, but less evidence of an association with perceptual reasoning (Coef 0.28 (-0.01, 0.57), R² adjusted 12%) and processing speed (Coef 0.32 (-0.15, 0.79), R² adjusted 12%) (all adjusted estimates).

Most children had a Bayley-III average cognitive and language composite of 85-100 (16 [34.0%]) or above 100 (29 [61.7%]) at 18 months of age, with two (4.2%) children having a score below 85. Children with a Bayley-III average cognitive and language composite between 85-100 had a range of FSIQ with 37.5% below 85, 43.8% between 85-100 and 18.8% above 100. Children with a Bayley-III average cognitive and language composite above 100 had a range of FSIQ with 3.4% below 85, 48.3% between 85-100 and 48.3% above 100.

**Conclusions**

Bayley-III demonstrated limited predictive validity for school-age cognitive outcomes in our cohort of children with HIE and mostly favourable outcomes. Furthermore, among children with Bayley-III scores within the normal range, FSIQ was more variable, emphasizing the difficulty in identifying subtle cognitive deficits. These results highlight the importance of longitudinal monitoring of children at risk of cognitive deficits into 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 secretaries, and the abstract has not been presented previously: ✗

Senior author supporting presentation on day of meeting: Ela Chakkarapani
Table 1. Regression models of WISC-IV scores at 6-8 years by Bayley-III composite scores at 18-21 months.

<table>
<thead>
<tr>
<th></th>
<th>Full-Scale IQ</th>
<th>Verbal Comprehension</th>
<th>Perceptual Reasoning</th>
<th>Working Memory</th>
<th>Processing Speed</th>
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<tbody>
<tr>
<td><strong>Bayley-III</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cognitive composite</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coefficient</td>
<td>0.36</td>
<td>0.31</td>
<td>0.23</td>
<td>0.27</td>
<td>0.36</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(0.09, 0.62)</td>
<td>(0.05, 0.57)</td>
<td>(-0.06, 0.51)</td>
<td>(-0.05, 0.60)</td>
<td>(-0.06, 0.78)</td>
</tr>
<tr>
<td>p value</td>
<td>0.009</td>
<td>0.020</td>
<td>0.112</td>
<td>0.094</td>
<td>0.088</td>
</tr>
<tr>
<td>$R^2_{\text{adjusted}}$</td>
<td>0.12</td>
<td>0.09</td>
<td>0.03</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Language composite</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coefficient</td>
<td>0.31</td>
<td>0.29</td>
<td>0.21</td>
<td>0.21</td>
<td>0.27</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(0.09, 0.54)</td>
<td>(0.07, 0.51)</td>
<td>(-0.02, 0.45)</td>
<td>(-0.06, 0.48)</td>
<td>(-0.06, 0.60)</td>
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<tr>
<td>p value</td>
<td>0.006</td>
<td>0.012</td>
<td>0.071</td>
<td>0.122</td>
<td>0.109</td>
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<tr>
<td>$R^2_{\text{adjusted}}$</td>
<td>0.14</td>
<td>0.11</td>
<td>0.05</td>
<td>0.03</td>
<td>0.04</td>
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<tr>
<td><strong>Average composite</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coefficient</td>
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<td>0.38</td>
<td>0.30</td>
<td>0.32</td>
<td>0.40</td>
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<tr>
<td>(95% CI)</td>
<td>(0.17, 0.70)</td>
<td>(0.12, 0.64)</td>
<td>(0.01, 0.58)</td>
<td>(0.00, 0.64)</td>
<td>(-0.03, 0.82)</td>
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<tr>
<td>p value</td>
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<td>0.18</td>
<td>0.14</td>
<td>0.07</td>
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**Adjusted models**

<table>
<thead>
<tr>
<th></th>
<th>Full-Scale IQ</th>
<th>Verbal Comprehension</th>
<th>Perceptual Reasoning</th>
<th>Working Memory</th>
<th>Processing Speed</th>
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</thead>
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<tr>
<td><strong>Cognitive composite</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Coefficient</td>
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<td>0.20</td>
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<td>0.32</td>
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<tr>
<td>(95% CI)</td>
<td>(0.05, 0.57)</td>
<td>(0.00, 0.52)</td>
<td>(-0.09, 0.49)</td>
<td>(-0.08, 0.54)</td>
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<tr>
<td>$R^2_{\text{adjusted}}$</td>
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<td>0.17</td>
<td>0.09</td>
<td>0.19</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Language composite</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coefficient</td>
<td>0.30</td>
<td>0.27</td>
<td>0.22</td>
<td>0.25</td>
<td>0.19</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(0.07, 0.53)</td>
<td>(0.04, 0.50)</td>
<td>(-0.03, 0.46)</td>
<td>(-0.02, 0.51)</td>
<td>(-0.19, 0.57)</td>
</tr>
<tr>
<td>p value</td>
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<td>0.025</td>
<td>0.113</td>
<td>0.021</td>
<td>0.579</td>
</tr>
<tr>
<td>$R^2_{\text{adjusted}}$</td>
<td>0.24</td>
<td>0.20</td>
<td>0.11</td>
<td>0.21</td>
<td>-0.03</td>
</tr>
<tr>
<td><strong>Average composite</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coefficient</td>
<td>0.40</td>
<td>0.34</td>
<td>0.28</td>
<td>0.32</td>
<td>0.32</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(0.13, 0.66)</td>
<td>(0.07, 0.61)</td>
<td>(-0.01, 0.57)</td>
<td>(0.01, 0.64)</td>
<td>(-0.15, 0.79)</td>
</tr>
<tr>
<td>p value</td>
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<td>0.020</td>
<td>0.090</td>
<td>0.016</td>
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<tr>
<td>$R^2_{\text{adjusted}}$</td>
<td>0.27</td>
<td>0.21</td>
<td>0.12</td>
<td>0.22</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

The regression coefficients were adjusted for sex, birth weight, and gestational age, HIE grade, maternal educational level, and social deprivation index.
REDUCING PRETERM MORTALITY AND BRAIN INJURY: THE PERIPREM (PERINATAL EXCELLENCE TO REDUCE INJURY IN PREMATURE BIRTH) CARE PATHWAY

Karen Luyt on behalf of the PERIPrem Steering Group

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Institution(s)

Bristol Medical School, University of Bristol, Bristol, UK

Introduction (include hypothesis)

NHS England policy is to reduce neonatal mortality and brain injury by 50% by 2025. In 2020, the PERIPrem project was launched in South-West (SW) England. The aim was to reduce preterm mortality and brain injury. PERIPrem is a perinatal care bundle of 11 evidence based interventions to reduce mortality and brain injury (1), including prophylactic low dose dexamethasone and multi-strain probiotics, implemented using Quality Improvement (QI) methodology. We performed quantitative, as part of a mixed methods evaluation, to study the changes in clinical outcomes following the introduction of PERIPrem.

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

Setting: 12 Perinatal Units. Routinely collected SW Vermont Oxford Network (VON) data for all very low birthweight infants (<1500g) were utilised to compare proportions for the cohorts preceding (2014-2019) and following (2020-2022) PERIPrem implementation. The cohorts included infants of 22 and 23 weeks' gestation and delivery room deaths. Primary outcome was mortality. Secondary outcomes were intraventricular haemorrhage (IVH; all grades), severe preterm brain injury (cystic PVL, Grade 3 or 4 IVH). Aggregate UK VON outcome data, grouped by the same cohorts are described as counterfactual. Chi-squared test was used to compare proportions. P<0.05 was considered statistically significant.

Results

Baseline (2014-2019) cohort n=2,329. PERIPrem cohort (2020-2022) n=860. There was a 3% absolute and 30% relative reduction in mortality following the introduction of PERIPrem in SW England (9.9% in 2014-2019 cohort; 6.9% in 2020-2022 cohort; p<0.008; Table 1). The VON UK counterfactual for mortality over the same period remained unchanged (15% in 2014-2019 cohort; 15.4% in 2020-2022 cohort; p=0.550). There was a 5% absolute and 17% relative reduction in IVH following the introduction of PERIPrem in SW England (30.6% in 2014-2019 cohort; 25.4% in 2020-2022 cohort; p<0.006; Table 1) and a small non-significant reduction in severe brain injury (10.1% in 2014-2019 cohort; 8.4% in 2020-2022 cohort; p<0.157; Table 1). The VON UK counterfactual for IVH and severe brain injury over the same period remained unchanged (Table 1).

Conclusions

Implementation of PERIPrem, delivered by a large regional perinatal QI collaborative, was associated with an improvement in preterm mortality and brain injury in very low birthweight infants. Preterm mortality and brain injury remained unchanged in the UK over the same period.

References (include acknowledgement here if appropriate)


PERIPrem was funded by the West of England and South West Health Innovation Networks and supported by the SW ODN.

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
Table 1

<table>
<thead>
<tr>
<th></th>
<th>South West VON Network</th>
<th>UK VON Network</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>9.9% (231/2329) 6.9% (59/860)</td>
<td>15.0% (1186/7912) 15.4% (544/3527)</td>
</tr>
<tr>
<td>IVH (All grades)</td>
<td>30.6% (669/2188) 25.4% (208/818)</td>
<td>30.7% (2232/7263) 32% (1057/3302)</td>
</tr>
<tr>
<td>Severe Brain Injury (cPVL+ sIVH)</td>
<td>10.1% (222/2203) 8.4% (70/835)</td>
<td>10.6% (774/7334) 10.3% (343/3333)</td>
</tr>
</tbody>
</table>

*Chi-squared test (p<0.05 considered statistically significant).
Title (Upper case)

Neonatal outcomes among births occurring in or out of water following intrapartum water immersion in UK maternity services: The POOL 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)

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

Institution(s)

1. Cardiff University; 2. University of Birmingham; 3. Imperial College London; 4. Cardiff and Vale University Health Board; 5. Royal College of Midwives, London; 6. University of Aberdeen; 7. PPI representative

Introduction (include hypothesis)

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. This cohort study aimed to establish whether, among women using intrapartum water immersion analgesia, waterbirth is as safe for them and their babies as leaving the water before birth.

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

In this observational cohort study prospective and retrospective data were extracted from National Health Service electronic maternity records at 26 participating sites in England and Wales, for births between January 2015 and June 2022. For babies admitted to a neonatal unit, data were 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 consent model, for which ethical approval was granted (REC 18/WA/0291; CAG 18/CAG0153). Funding: NIHR HTA 16/149/01. Protocol published¹ and registered ISRCTN13315580.

Results

Between January 2015 and June 2022 869,744 birth records were extracted from 26 sites; 87,040 (10%) used a pool during labour for analgesia and 46,283 (5.3%) had a waterbirth. 60,402 birth records relating to women without antenatal or intrapartum risk factors were eligible for the primary analysis: 39,627 (65.6%) were waterbirths and 20,775 (34.4%) were births out of water. The composite adverse outcome among babies was rare in both groups and rates of the primary outcomes were no higher among waterbirths compared to births out of water. Similar patterns were seen for each of the individual components within the composite infant primary outcome, rates were no higher among waterbirths compared to births out of water. Infant secondary outcomes were similar across groups, apart from a higher rate of the umbilical cord snapping before it was clamped among births in water compared to births out of water, although this was rare in both groups; no babies with a snapped cord died, received therapeutic hypothermia for treatment of neonatal encephalopathy or a blood transfusion.

Conclusions

The study found that among women without pregnancy or intrapartum risk-factors who used water immersion during labour, giving birth in water was as safe as giving birth out of water, with no increase in the incidence of adverse neonatal outcomes.

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: