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Book of Abstracts

Abstracts are arranged alphabetically
by first author's surname

Contents

Karel Allegaert: Aminoglycoside target exposure in neonates: peak, trough and/or area under the curve.

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Background
Interestingly, there is no consensus about the optimal pharmacokinetic (PK)/pharmacodynamic (PD) target for aminoglycoside, like amikacin. In current clinical care, the peak or C_{max}/minimum inhibitory concentration (MIC) ratio (for amikacin, ratio >8-10) is typically used as a PK/PD index for aminoglycoside efficacy, while the trough (C_{min}) generally related to toxicity. The evidence to support this approach is limited, while more recently, the use of the area under the concentration-time curve (AUC)/MIC ratio has also been re-suggested as target. This EUCAST recommendation is recent, and not specific to neonates. A relationship between the AUC/MIC ratio and clinical outcome has been shown for aminoglycosides, primarily derived from clinical data on tobramycin use in cystic fibrosis. More recently, recommendations from EUCAST (2024) and The United States Committee on Antimicrobial Susceptibility Testing (USCAST) have shifted to using the AUC/MIC ratio for amikacin, a concept which has not been validated in neonates but is increasingly used as PK/PD target in neonatal studies. Employing the AUC/MIC ratio as a PK/PD target necessitates the use of an appropriate population PK model tailored to this population.

Methods
Using retrospectively collected data from neonates from two centers, PK/PD target attainment of a complex amikacin model-derived dosing regimen and a simplified dosing regimen was assessed, applying the different targets (conventional, or AUC) in a modelling and simulation effort (nonmem).

Results
In total, 366 neonates (768 concentrations) and 579 neonates (1,195 concentrations) received the simplified and complex dosing regimen, respectively. Both regimens achieved target attainment of 100% for C_{max}≥ 15 mg/L, C_{min}≤ 5 mg/L, AUC/MIC for bacteriostasis, and AUC/MIC for 1-log reduction up to a MIC of 2 mg/L with the simplified and complex amikacin dosing regimen.

Conclusion
Conventional targets, such as C_{max}≥ 15 mg/L and C_{min}≤ 5 mg/L, were successfully reached in ≥90% of patients with either the simplified or complex dosing regimen. Clinicians can choose one of both depending on their local circumstances. However, AUC/MIC targets (MIC > 2 mg/L) for a 1-log 10 CFU/mL reduction across the entire wild-type MIC distribution of were not met with either regimen. Bacteriostasis targets were reached, which may be acceptable if amikacin is used as part of combination therapy. Further research is needed to determine the optimal PK/PD target for treating neonatal sepsis when amikacin is used in combination therapy.

Jacob Aranda: Caffeine and/or Ibuprofen Effects on Biomarkers of Alveolarization and Microvascular Maturation in Neonatal Rat Lungs in the Saccular Stage of Development.

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Background

Caffeine citrate (Caff) and Ibuprofen lysine (Ibu) are used for apnea of prematurity and closure of a symptomatic PDA, respectively. Both have anti-inflammatory and antioxidant properties and caffeine exerts protective effects on lungs. Alveolarization and microvascular maturation are major processes in lung development that are regulated by matrix metalloproteinases (MMPs) and vascular endothelial growth factor (VEGF), respectively. We tested the hypothesis that early postnatal treatment with Caff and/or Ibu protects the immature lungs in the saccular stage of development against oxidative injury, and improve biomarkers of alveolarization and microvascular maturation.

Materials/Methods

Neonatal rats (n=18/group) were exposed to intermittent hypoxia (IH), hyperoxia (Hx) only (50% O2), or room air (RA), from the first day of life (P0) to P14, during which they received: 1) Caff (20 mg/kg loading IP) on P0; and 5 mg/kg/day on P1- P14; 2) Ibu (10 mg/kg loading IP) on P0; and 5 mg/kg/day on P1 and P2; 3) Caff+Ibu; or 4) placebo saline (Sal) on P0-P14. Lungs were examined at P14 and P21 for histopathology; hypertension; apoptosis; biomarkers of alveolarization and angiogenesis. Data are mean ± SEM.

Results

Hx and IH resulted in significant damage in the Sal groups with reductions in secondary crest formation (Hx:16.2±1.2; IH: 12.5±1.5 vs. RA: 22.1±1.8, p<0.01). Radial alveolar counts and medial wall thickness increased in Hx (3.2±0.17 and 0.34±0.02, respectively, p<0.01) and IH (3.2±0.21 and 0.35±0.02, respectively, p<0.01) vs. RA (4.3±0.3 and 0.23±0.02), effects that were improved with all treatments, although hemorrhage was noted with Ibu. Apoptosis was increased with Hx (1550.2±192.5, p<0.01) and IH (2898.3±181.5, p<0.01) vs. Sal (769.7±100.9), and only Ibu effectively reduced it (Hx: 624.3±44.7; IH: 515.0±74.2, p<0.01). MMP-2 and -8 were decreased in Hx and IH, but MMP-9 was elevated in the Sal group. All treatments reversed these effects. Angiogenesis biomarkers were decreased with Sal in Hx and increased in IH, and only Ibu reversed those effects.

Conclusions

The immature lung in the saccular stage of development is highly vulnerable to oxidative damage. Improvements in lung architecture and pulmonary outcomes with Caff may be due to its effects on matrix metalloproteinases (MMPs) and vascular endothelial growth factor (VEGF during development and in organ remodeling. While Ibu improved apoptosis and angiogenesis biomarkers, hemorrhage is a cause for concern.

Supported by NIH/NICHD U54 grant #1U54HD071594.

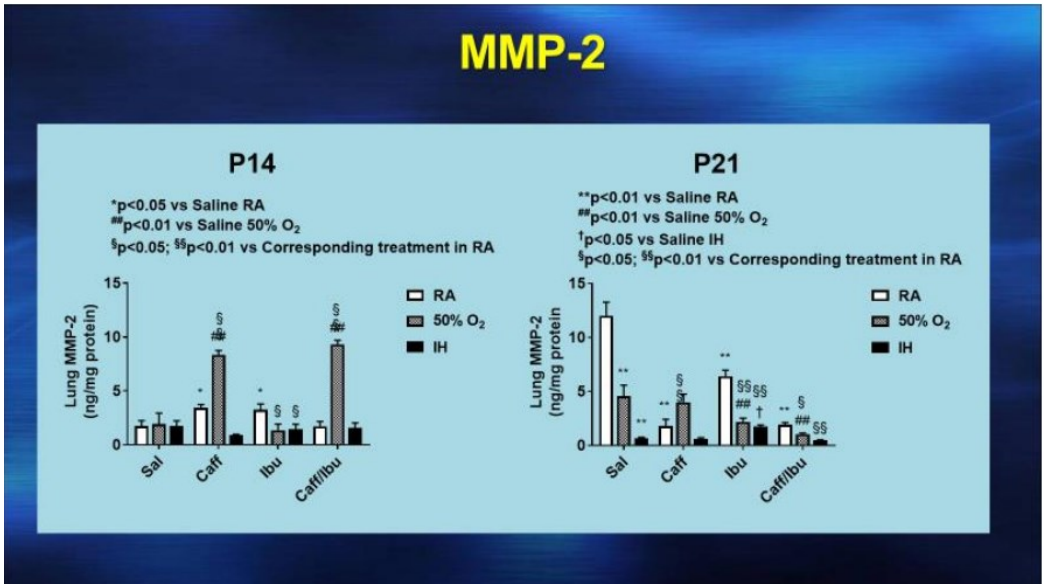

FIGURE 1: Effects of Caffeine and Ibuprofen on Metalloproteinase -2 (MMP-2) under Room Air, Hyperoxia (50% Oxygen) and Intermittent Hypoxia

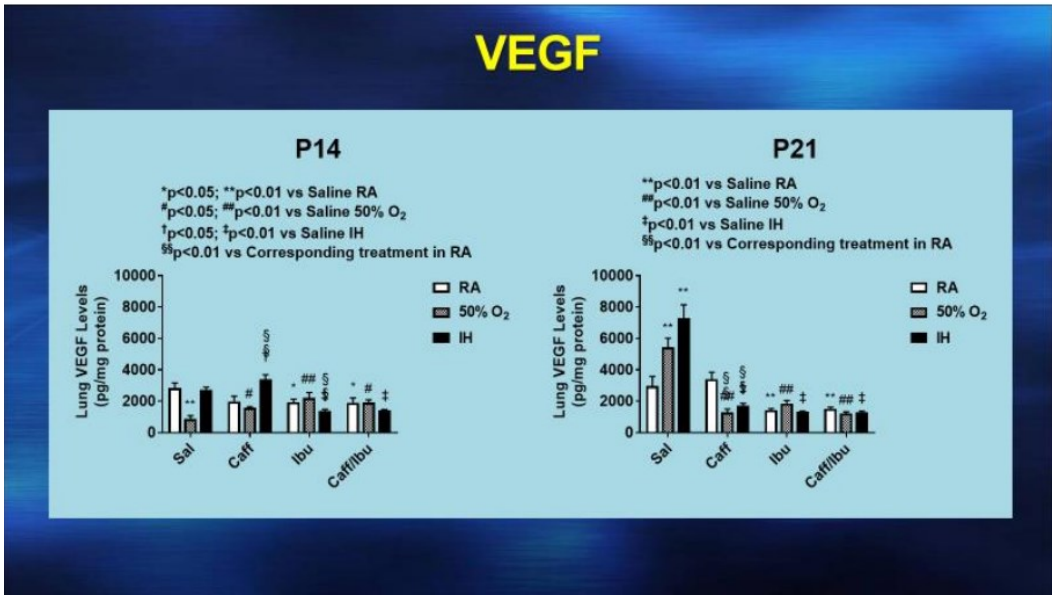

FIGURE 2: Effects of Caffeine and Ibuprofen on VEGF under Room Air, Hyperoxia (50% Oxygen) and Intermittent Hypoxia

Virginia Beretta: Neonatal autonomic and adrenocorticotropic features in newborns of mothers with gestational diabetes

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Background

Gestational diabetes mellitus (GDM) affects intrauterine glucose regulation, potentially impacting heart rate variability (HRV), a marker of autonomic function, and cortisol levels, a marker of hypothalamic-pituitary-adrenal function, in newborns. HRV and cortisol changes can highlight stress-related burden in newborns. Aim: To assess HRV and cortisol levels in newborns from healthy (control) and GDM mothers during the first 24 hours of life. A secondary aim was to compare HRV and cortisol levels between male and female newborns.

Materials and methods

A total of 59 newborns (38 GDM, 21 controls) were monitored for heart rate (HR) and HRV from the 6th hour of life. Salivary cortisol was measured 3-6 hours (T1) and 20-24 hours (T2) after birth. HRV parameters included the root mean square of successive differences (RMSSD), the high (HF) and low (LF) band power of HRV, and the LF/HF ratio.

Results

GDM newborns exhibited significantly lower HR values, higher values of RMSSD and lower values of LF/HF compared to CTRs (Figure 1). Specifically, GDM females exhibited significantly lower values of HR compared to CTR females and GDM males had higher RMSSD and HF values compared CTR males (Figure 2). Saliva cortisol concentrations significantly decreased between T1 and T2 ($F_{(1,50)}$ =16.90; p = < 0.001), with no significant differences between GDMs and CTRs.(FIGURE 1)

Conclusions

Newborns from GDM mothers exhibited lower HR and higher cardiac vagal modulation, with sex-specific differences. GDM females showed a decrease in HR without changes in HRV, whereas GDM males showed an increase in vagally-mediated HRV without changes in HR. GDM does not seem to affect cortisol levels in newborns. These findings highlight sex-specific cardiac autonomic responses to birth stress in GDM-exposed newborns across the first day of life which might play an important role in shaping different behavioural, resilience, and well-being trajectories in early life stages.

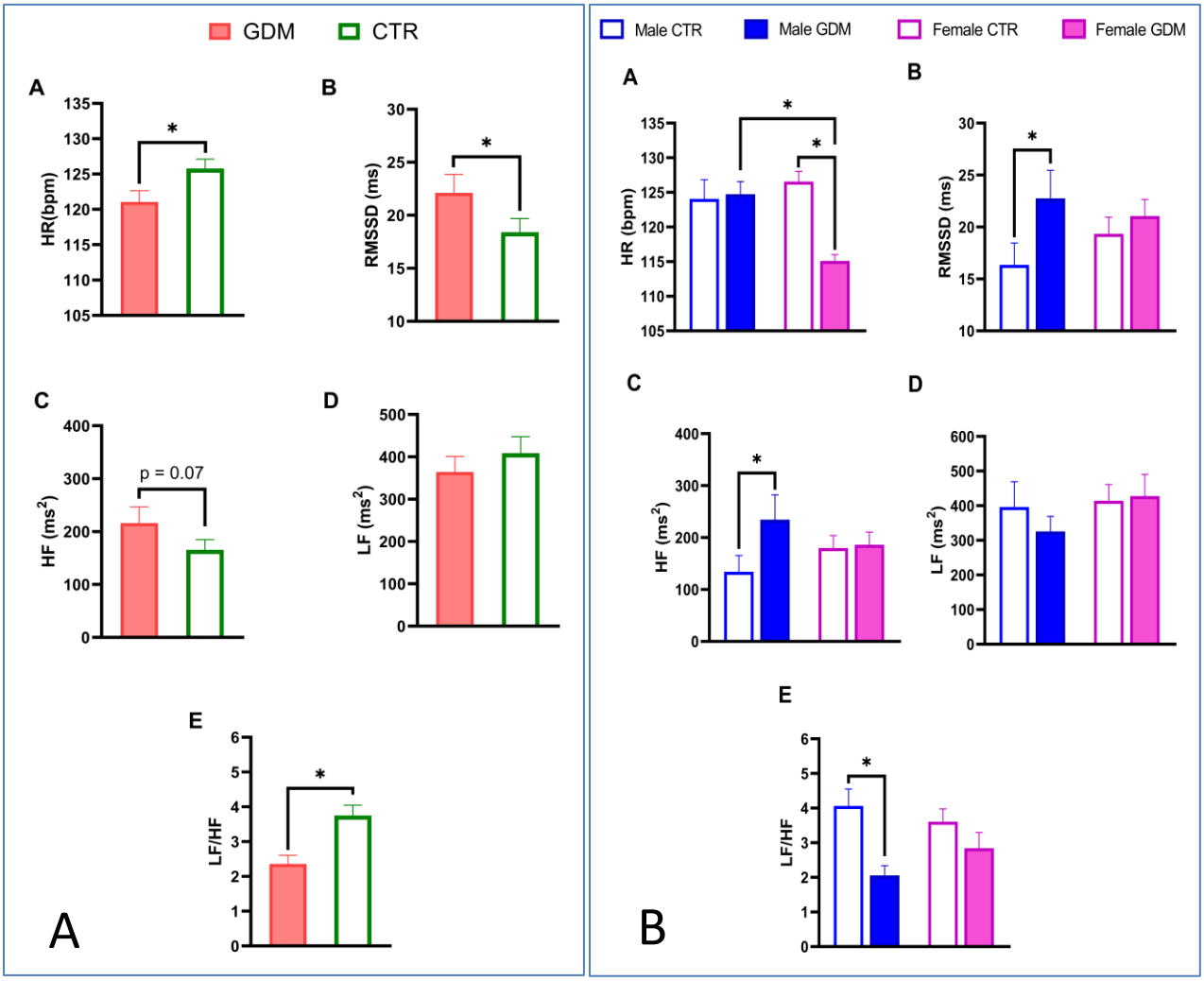

FIGURE 1: A Heart rate and heart rate variability values in GDM and CTR (newborns. Data are reported as mean ± standard error. B Heart rate and heart rate variability values in GDM (n=13) and CTR (n=12) males and GDM (n=8) and CTR (n=26) females. Data are reported as mean ± standard error. * Indicates a significant difference ($p<0.05$).

Matteo Bruschettini: The JACK Study: Justified Administration of Caffeine for preterm Kids

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Background
Caffeine is one of the most widely used pharmacological interventions in preterm infants to improve respiratory function. Despite its widespread use, there remains uncertainty regarding optimal strategies for caffeine initiation, dosing and administration, and discontinuation. Understanding the benefits and potential harms of these approaches is essential to guide evidence-based neonatal care.

Methods
We conducted three complementary systematic reviews according to Cochrane methodology. We searched MEDLINE, Embase, CENTRAL, PubMed, and major trial registries without language restrictions. We included randomized controlled trials (RCTs) assessing 1) timing and indication for caffeine initiation, 2) different strategies of administration (intravenous vs. oral, once- vs. twice-daily dosing, higher vs. standard doses, adjusted vs. fixed regimens, caffeine with vs. without adjunctive drugs), and 3) timing and strategy for caffeine discontinuation. Fixed-effect meta-analyses were performed, and certainty of evidence was evaluated using GRADE.

Results
Nineteen RCTs were included. 1) Initiation strategies: Eleven RCTs (774 infants) evaluated different initiation timings. Early initiation (within 2 hours vs. later in the first day, or within 72 hours vs. after 72 hours) showed very uncertain effects on mortality, chronic lung disease (CLD), mechanical ventilation, and apnea, with consistently low- to very low-certainty evidence. Initiation within the first three days in asymptomatic infants, compared to treatment of symptomatic infants only, likely reduced CLD (moderate-certainty evidence) but showed little or no effect on mortality or adverse events. Initiation during mechanical ventilation, compared to at extubation, likely reduced CLD and may shorten ventilation duration. 2) Administration strategies: Three RCTs (210 infants) compared alternative regimens. Intravenous administration versus oral showed very uncertain evidence, with a possible reduction in mortality but longer hospitalization. Twice-daily dosing compared to once-daily may shorten hospital stay but had little to no effect on mortality or ventilation duration. No studies were available for higher vs. standard doses, adjusted vs. fixed regimens, or combination strategies. Two trials are ongoing. 3) Discontinuation strategies: Five RCTs (1389 infants) explored different cessation strategies, although findings from one of these RCTs have not been published yet, and thus are not included in this review. Early discontinuation before 35 weeks' postmenstrual age increased intermittent hypoxemia within seven days (low-certainty evidence) but had little or no impact on mortality. Discontinuation based on symptom resolution, compared to predetermined PMA, likely increased intermittent hypoxemia without affecting apnea or mortality. Stopping caffeine at discharge versus afterwards had little to no effect on mortality, neurodevelopmental disability, or common adverse events. Four trials are ongoing. We are currently preparing GRADE guidelines based on these three reviews (preliminary findings are not included here).

Conclusion
Evidence from RCTs suggests that caffeine initiation within the first three days of life may reduce CLD in preterm infants, particularly when started during mechanical ventilation. Evidence regarding administration strategies is sparse and inconclusive. Early discontinuation of caffeine may increase intermittent hypoxemia. Further high-quality, adequately powered RCTs are urgently needed to clarify optimal initiation, administration, and discontinuation strategies, and to assess long-term neurodevelopmental outcomes. GRADE recommendations, either strong or conditional, will be soon available for each clinical question.

Summary of findings:

Caffeine initiated on the first three days of life compared to caffeine treatment of symptomatic infants in high-risk preterm infants

Patient or population: high-risk preterm infants
Setting: neonatal units (Egypt, China)
Intervention: Caffeine initiated on the first three days of life
Comparison: caffeine treatment of symptomatic infants

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with caffeine treatment of symptomatic infants	**Risk with Caffeine initiated on the first three days of life**				
All-cause mortality until hospital discharge	164 per 1000	**156 per 1000** (77 to 316)	**RR 0.95** (0.47 to 1.92)	163 (1 RCT)	⨁⨁◯◯ Low[a]	Caffeine initiated on the first three days of life may result in little to no difference in all-cause mortality until hospital discharge compared to caffeine treatment of symptomatic infants.
Chronic lung disease (CLD/BPD) 36 weeks' postmenstrual age, defined as need for oxygen or respiratory support	204 per 1000	**100 per 1000** (53 to 192)	**RR 0.49** (0.26 to 0.94)	219 (2 RCTs)	⨁⨁⨁◯ Moderate[b,c]	Caffeine initiated on the first three days of life likely reduces chronic lung disease (CLD/BPD) 36 weeks' postmenstrual age, defined as need for oxygen or respiratory support compared to caffeine treatment of symptomatic infants.
Any adverse event leading to caffeine cessation until hospital discharge	14 per 1000	**4 per 1000** (0 to 90)	**RR 0.27** (0.01 to 6.56)	163 (1 RCT)	⨁⨁◯◯ Low[a]	Caffeine initiated on the first three days of life may result in little to no difference in any adverse event leading to caffeine cessation until hospital discharge compared to caffeine treatment of symptomatic infants.
Duration of mechanical ventilation until hospital discharge	The mean duration of mechanical ventilation until hospital discharge was **10** days	MD **0.81 days fewer** (1.89 fewer to 0.27 more)	-	56 (1 RCT)	⨁◯◯◯ Very low[c,d]	The evidence is very uncertain about the effect of caffeine initiated on the first three days of life on duration of mechanical ventilation until hospital discharge compared to treatment of symptomatic infants.
Duration of hospital stay until hospital discharge	The mean duration of hospital stay until hospital discharge was **43.7** days	MD **1.43 days fewer** (4.9 fewer to 2.04 more)	-	56 (1 RCT)	⨁◯◯◯ Very low[c,d]	The evidence is very uncertain about the effect of caffeine initiated on the first three days of life on duration of hospital stay until hospital discharge compared to treatment of symptomatic infants.
Apnea: number of infants with at least one episode (defined as interruption of breathing for more than 20 seconds) until hospital discharge - not reported	-	-	-	-	-	
Intermittent hypoxemia (IH): number of infants with at least one episode until hospital discharge - not reported	-	-	-	-	-	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]downgraded two levels for very serious imprecision due to very wide CI
[b]not downgraded due to risk of bias as the Kou 2020-study (with overall high risk of bias) only contributes 12% to the overall weight of the meta-analyses estimate, and that the results do not substantially change when doing a sensitivity analysis excluding this study.
[c]downgraded one level for serious imprecision due to wide CI
[d]downgraded two levels for overall high risk of bias

Frances Callaghan: The relationship between arginine/ADMA ratio and mortality in postoperative neonates: a narrative review based on a systematic search strategy

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Background
Nitric oxide (NO) is synthesised from L-arginine by nitric oxide synthase (NOS) and plays a key role in vasodilation within the cardiovascular, respiratory, and gastrointestinal systems. Asymmetric dimethylarginine (ADMA), a by-product of protein catabolism, acts as a competitive inhibitor of NOS, thereby limiting NO production. The arginine/ADMA ratio has been implicated in the pathophysiology of multi-organ dysfunction and adverse clinical outcomes in both paediatric and adult critical illness. This review sought to address the question: "In post-operative neonates, is a lower arginine/ADMA ratio associated with increased mortality risk?"

Methods
A systematic search strategy, pre-registered with PROSPERO (CRD42024539298), was employed to identify studies that measured arginine and ADMA concentrations in neonates requiring surgical intervention. Searches were conducted across multiple electronic databases (Pubmed, Scopus, Web of Science, Cochrane, CINAHL, ISRCTN register and Google scholar). Data from relevant articles was obtained using a data extraction checklist written for the purpose of this review.

Results
No study fully met the pre-specified inclusion criteria. However, four studies were judged to be highly relevant to the research question, and their findings were synthesised narratively. In both neonatal and paediatric populations undergoing congenital heart surgery, reduced arginine concentrations and elevated ADMA levels were linked with prolonged intensive care and hospital admission, persistent post-operative hypoxaemia, extended mechanical ventilation, and the development of low cardiac output syndrome. In neonates diagnosed with necrotising enterocolitis (NEC), lower arginine concentrations and lower arginine/ADMA ratios were associated with higher mortality rates.

Conclusions
Although no directly eligible studies were identified, the reviewed literature indicates that alterations in arginine and ADMA metabolism may serve as markers of disease severity and potential targets for intervention in critically ill neonates and children. Optimising arginine bioavailability, either through supplementation or via strategies to reduce ADMA, could offer a means of improving post-operative outcomes. Measurement of the arginine/ADMA ratio may also have utility in pre-operative risk stratification. These hypotheses warrant further investigation through prospective, targeted clinical studies.

Antonia Charitou: Cardiac dysfunction in neonates of diabetic mothers due to marked hypertrophy of their right ventricle

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Background

Pregnancies complicated by Diabetes Mellitus (DM) either in the form of insulin dependent (DMI), gestational DM(GDM) or insulin resistant (DMII), have been shown to be related to a higher-than-normal incidence of fetal cardiovascular involvement. Among the most frequent are a variety of simple complex congenital heart diseases and a transient form of asymmetric hypertrophic cardiomyopathy. This condition can be seen by up to 30% of all neonates related to pregnancies involving any of the form of maternal MD. This condition is seldomly asymptomatic and normalizes in the first year of the life of the newborn.

Methods

Aim: To present two cases of extreme form of right ventricle (RV) hypertrophy leading to diastolic dysfunction of the RV and presenting as respiratory distress needing additional to hypoglycemic episodes, respiratory support and medicine treatment to improve the diastolic and systolic function. Population-Methods: Case I: Female term baby 38/40 +5 Days of Gestational Age. Cesarian Section (CS). Apgar scores 7/8. Birthweight:4.650Kg. Mother suffering from GDM, poorly treated by insulin due to patient compliance. Recent HbA1c was 9.5%. Apgar Score: 7/8 Case II: Female term baby 39/40 +2 Days of Gestational Age. CS. Apgar scores 8/8. Birthweight:4.350Kg. Mother suffering from DM II, poorly managed due to patient compliance. Recent HbA1c 8.2%.

Results

Both neonates presented with respiratory distress and needed non-invasive ventilation with FiO_2 of 65% for the first 5 days for case I and 50% for case II for 3 days. A cardiac evaluation by Echo-2D in both neonates revealed hypertrophic RV, diastolic on Tissue Doppler Imaging (TDI) and systolic dysfunction by Tricuspid Annulus Plane Systolic Excursion (TAPSE). Additional to basic neonatal support, b-blocker and furosemide to establish volume, preload management and rate control were used. Case I required a 14-day and Case II 9-day hospitalization.

Conclusion

To our knowledge these are among the rarest cases of symptomatic neonates of pregnancies complicated by DM presenting with both diastolic and systolic dysfunction in need for cardiac medicine treatment.

David Corcoran: Reliability of Radiometer Gas Analyzer for Neonatal Hyperbilirubinaemia

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Background/Aim
To assess the accuracy of capillary gas bilirubin (Radiometer TBiL) compared to venous total plasma bilirubin (Roche TPB), and to evaluate the reliability of Radiometer TBiL in neonatal hyperbilirubinaemia.

Methods
A prospective study was conducted at a tertiary neonatal centre in Dublin, Ireland between December 2023 and May 2025. Paired Radiometer TBiL and Roche TPB measurements were obtained from 97 neonates requiring bilirubin assessment.

Results
Radiometer TBiL demonstrated high correlation with Roche TPB ($r = 0.967$, $p < 0.0001$), although Radiometer TBiL showed an overestimation, especially at bilirubin levels between 150 to 230 µmol/L. Bland-Altman analysis revealed a mean difference of -16.6 µmol/L with wide limits of agreement (-63.6 to 30.4 µmol/L).

Conclusion
Radiometer TBiL offers a rapid and less invasive alternative for bilirubin screening a in neonates, with high correlation to standard laboratory measurements. While a tendency to overestimate bilirubin levels may lead to overtreatment, our study suggests Radiometer TBiL is a safe tool for clinical decision-making. Larger studies are warranted to validate these findings and refine clinical thresholds.

Theodoros Dassios: Prone positioning and Respiratory Function in Ventilated Newborn Infants

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Background

Prone positioning has been associated with improved oxygenation in ventilated newborn infants but the physiological basis of this improvement has not been previously studied. We aimed to test the hypothesis that respiratory function measured by composite physiological indices would be improved in the prone compared to the supine position.

Methods

Prospective observational study of ventilated newborns in a tertiary neonatal unit studied prone and supine at random order. The ventilation to perfusion ratio (V/Q) and right to left shunt were non-invasively calculated using the oxyhemoglobin dissociation curve method. The gradient of the arterial to end tidal carbon dioxide (PaCO2 – EtCO2 gradient) was calculated to describe changes in the alveolar dead space.

Results

Forty-six (26 male) infants with a median (IQR) gestational age of 34.8 (33.1–36.3) weeks and birth weight of 2.34 (1.77–2.87) kg were studied after 5 (2–10) hours of invasive ventilation. The V/Q was significantly higher in the prone position [0.57 (0.52–0.63)] compared to supine [0.53 (0.46–0.62), p = 0.001]. Right to left shunt was significantly lower in prone [7 (0–12) %] compared to supine [9 (1–16) %, p = 0.003]. The PaCO2 – EtCO2 gradient was significantly lower in prone [6.3 (3.8–8.4) mmHg] compared to supine [12.1 (7.1–16.0) mmHg].

Conclusions

The prone position in ventilated neonates was associated with improved ventilation to perfusion matching and lower intrapulmonary shunting and alveolar dead space compared to supine.

Gabriel Dimitriou: From the Brink of Collapse to Survival: A Critically ill Neonate with Overwhelming Multisystem Dysregulation - Unraveling the Unknown

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Background

Critical illness in neonates remains a challenge for healthcare professionals. Approach to the critically ill neonate is well established and requires a structured and coordinated effort. However, uncommon causes of hemodynamic instability should be addressed early and treated aggressively in order to reduce morbidity and mortality in this vulnerable population.

Case presentation / Results

A male neonate, delivered at 37+2 weeks of gestation, following an uncomplicated pregnancy, was transferred to our neonatal intensive care unit with gradually progressive respiratory distress, requiring mechanical ventilation. Due to persistent pulmonary hypertension, he required inhaled nitric oxide, sedation and inotropic support. He received broad spectrum antibiotics for suspected sepsis. On the third day of life (DOL), *Pseudoescherichia vulneris* was isolated in the blood culture, and antibiotics were appropriately modified. During DOL 3-5, he was critically ill requiring high-frequency ventilation, inotropic support, inhaled nitric oxide, multiple blood transfusions, and fresh frozen plasma administration. In the next days he developed capillary leak syndrome, anasarca and oliguric renal failure. He was treated as per protocol of neonatal capillary leak syndrome, with diuretics and fluid restriction, albumin, fresh frozen plasma, aminophylline, methylprednisolone and intravenous immunoglobulin (IVIG, total 2gr/kg), resulting in gradual clinical improvement (DOL 7-8). On the 11th DOL, high IgG COVID-19 antibody titers were detected (6 times greater than the mother's), followed by echocardiography that revealed coronary artery aneurysms (z scores >2.5), not present previously, and at this point the diagnosis of Multisystem Inflammatory Syndrome in Neonates (MIS-N) was confirmed. He tested negative for SARS-CoV-2 antigens. He received a second course of IVIG (2gr/kg) and continued methylprednisolone. Due to hemodynamic instability in the next 48 hours, despite maximum respiratory and cardiovascular support, his treatment escalated to anakinra (an interleukin-1 receptor antagonist at a dose of 1mg/kg x2, increased to 1.5mg/kgx2) with subsequent clinical improvement. Due to elevated liver enzymes (4-fold), anakinra was weaned and finally discontinued by DOL 37 with rapid recovery of the liver enzymes (within 48 hours). He was discharged on DOL 52.

Conclusion

MIS-N is an extremely rare neonatal disease associated with high morbidity and must be considered in critically ill neonates presenting with multisystem involvement. Early recognition and prompt management are essential to improve outcomes in these difficult situations.

Vineta Fellman: Neonatal auditory event-related potentials do not predict long-term outcome in very preterm infants

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Background

Auditory event-related potentials (AERPs) are neurophysiological correlates of cortical activity related to sound processing and discrimination. Acoustic stimuli elicit obligatory AERPs, which represent sound detection and processing of acoustic characteristics of the sound and are dependent on the integrity of the primary auditory pathway. Higher order neural responses, such as change detection can be assessed with the mismatch negativity (MMN) response. In adults, MMN is a frontocentral negativity between 150-250 ms in the difference waveform obtained by subtracting the average response to a frequent (standard) stimulus from that recorded to a rare (deviant) stimulus. In infants, the mismatch response (MMR) can be either positive or negative. AERPs are different in preterm infants compared to healthy full-term infants at term and during development. We hypothesized that neonatal AERPs as an early measure of brain function have prognostic value for neurocognitive development in preterm infants.

Methods

We studied 41 very preterm infants (26.5±2.0 gestational weeks, gw) at term equivalent age. As auditory stimuli we used an oddball paradigm consisting of a standard 1000 Hz pure tone randomly replaced by one of two deviants differing in either duration or frequency. Obligatory AERPs and change-related MMRs were recorded using the NeuroScan 4.3 system. Neurocognitive outcome was assessed at 2 years of corrected age with Bayley Scales of Infant Development 2nd Edition. At 12 years of age, the subgroup of children born before 27 gw (n=18, 25.1±1.1 gw) were assessed with Wechsler Intelligence Scale for Children (WISC-V), and three language tests (CELF-4, Reading speed, and TOWRE-2).

Results

At 2 years of age, 16 of 41 children had suboptimal test results. In univariable analysis, higher Bayley scores were associated with larger negative AERP amplitudes after 250 ms from stimulus onset to the standard and a negative rather than positive MMR to the frequency deviant. After adjustment for perinatal factors only the duration MMR was associated with mental developmental index. The WISC-V index in the 18 tested children was 92±17 (reference value100±15), and the additional tests were lower than reference values. AERPs were not predictive of WISC-V index. The neonatal morbidity (defined as ventilatory support duration, (FIGURE 1 B) was associated with WISC-V, and affected the relationship between standard response and WISC-V (FIGURE 1 D). An association between standard response and Reading speed score was found (FIGURE 1 G). No significant relationship was found between MMR and outcome.

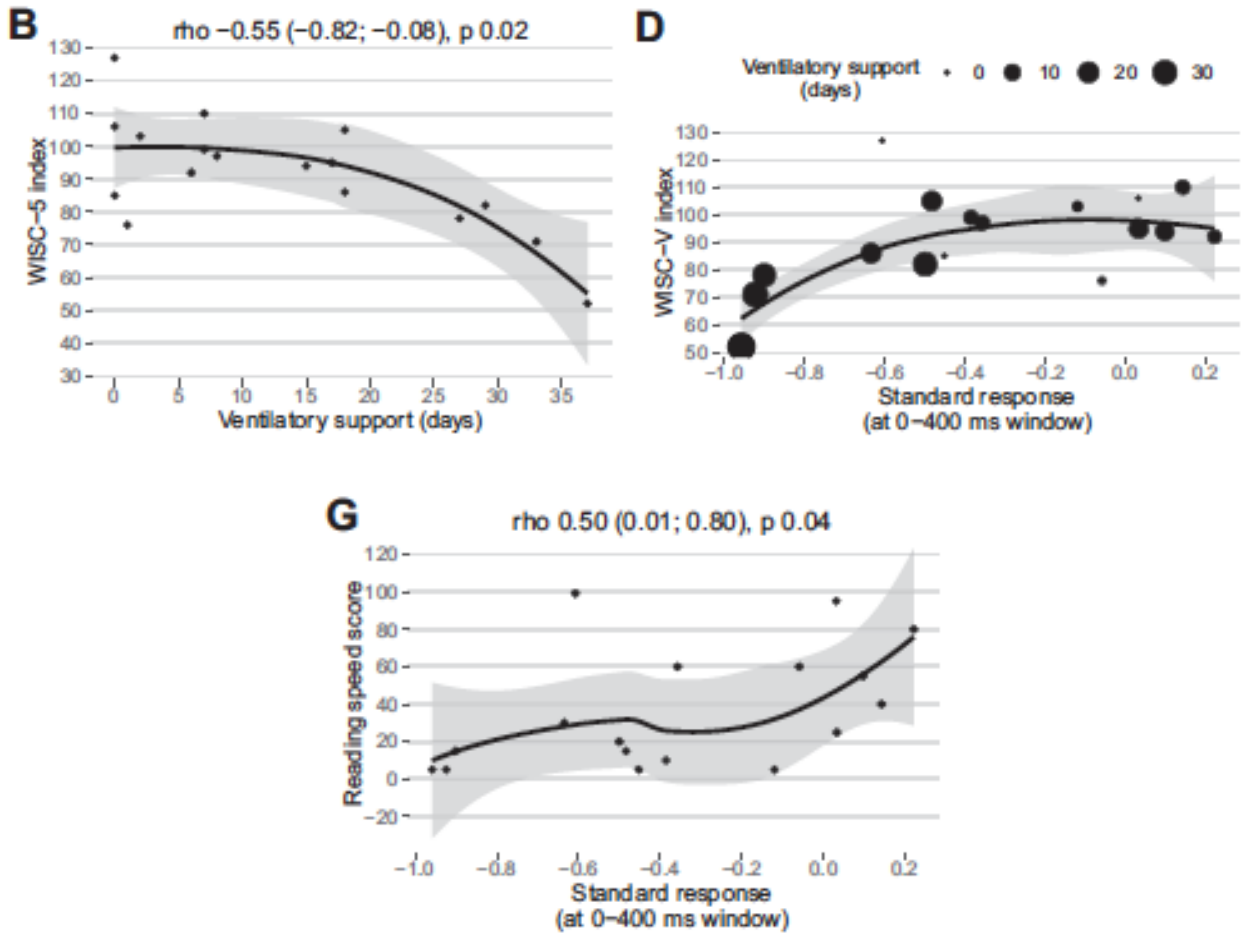

FIGURE 1 Associations among neonatal morbidity, neurocognitive outcomes, and reading performance. (B) Neonatal morbidity, operationalised as duration of ventilatory support, was associated with WISC-V performance. (D) Neonatal morbidity moderated the association between Standard Response and WISC-V. (G) Standard Response was associated with Reading Speed score.

Conclusions

Despite that some relationships between obligatory responses and outcome were found at 2 years of age, no significant association was found with WISC-V at 12 years of age. Thus, AERPs at term in very preterm infants do not predict long-term outcome and are not useful as an early clinical prognostic measure.

André Graça: Neuroprotection and repair in perinatal brain injury

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Background
Perinatal brain injury is a leading cause of long-term neurodevelopmental impairment. Despite major improvement in neonatal survival brought by advances in neonatal intensive care, encephalopathy of prematurity and neonatal encephalopathy at term continue to result in significant cognitive, behavioural, and motor sequelae.
During this talk, I aim to summarize clinical definitions, epidemiology, mechanisms, and therapeutic strategies related to neuroprotection and repair in perinatal brain injury.

The presentation reviews the spectrum of neonatal brain injury. In preterm infants, encephalopathy of prematurity and intraventricular haemorrhage predominate, whereas at term, hypoxic-ischemic encephalopathy and perinatal stroke are more frequent. In both gestational age groups, pathophysiology involves excitotoxicity, oxidative stress, inflammation, and disruption of brain development, but expression of injury can be substantially different in its clinical presentation and outcomes. Conventional neuroimaging has an important role for prediction outcome in term infants with brain lesions but remains limited in predicting outcomes in very preterm infants with encephalopathy of prematurity.

Current and emerging neuroprotective strategies include therapeutic hypothermia, pharmacological approaches targeting inflammation and oxidative stress, stem-cell based therapies, and interventions to enhance neural plasticity, and are being used or trialled in different ways for term and preterm infants with brain injury.

Conclusion
Understanding the interplay between destructive and developmental disturbances is essential for designing effective interventions. Translational research combining clinical, imaging, and molecular insights is crucial to optimize neuroprotection and promote repair, aiming to reduce long-term disability.

Eleftheria Hatzidaki: Breastmilk melatonin and neurodevelopmental outcomes in preterm infants at nine months' corrected age. Evidence from adjusted regression models in the ProMote Study

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Background
Preterm neonates are exposed to a prolonged period of circadian melatonin deprivation due to delayed onset of endogenous production. During this vulnerable phase, breastmilk provides their only source of melatonin. Melatonin is implicated in neurodevelopmental processes, but evidence linking breastmilk melatonin directly to developmental outcomes remains scarce. This study investigated associations between breastmilk melatonin concentrations during the neonatal period and neurodevelopmental outcomes at nine months' corrected age.

Methods
This study within the ProMote project included 56 mother–preterm infant pairs (<37 weeks' gestation). Fifty-six mother–preterm infant pairs (<37 weeks' gestation) from the ProMote study provided nighttime breastmilk samples (01:00–05:00 h) at three postnatal stages: colostrum (M1, days 3–5), transitional milk (M2, days 10–14), and mature milk (M3, days 20–28). Samples were frozen at –80°C and analysed by ELISA. Neurodevelopment at nine months' corrected age was assessed with the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III), by neonatologists blinded to melatonin results. Associations between $\log_2$-transformed melatonin concentrations and Bayley composite scores (cognitive, language, motor) were analysed with linear regression, unadjusted and adjusted for sex, gestational age, maternal age and education, and maternal depression and anxiety.

Results
Mean composite scores were: cognitive 94.9 (SD 9.7), language 102.5 (SD 9.2), and motor 93.2 (SD 11.8). Unadjusted analyses: Higher colostrum melatonin was associated with increased motor scores (B = 3.0, 95% CI 0.3–5.7, p = 0.032) (FIGURE 1). No significant associations were observed for language or cognitive scores. Minimally adjusted models (sex, gestational age): The motor association with colostrum melatonin strengthened (B = 3.2, 95% CI 0.3–6.0, p = 0.029). Fully adjusted models (sex, gestational age, maternal age and education, depression, anxiety): The relationship became stronger and more robust: colostrum melatonin predicted higher motor scores (B = 4.5, 95% CI 1.0–7.9, p = 0.013). Associations with cognitive and language outcomes remained non-significant, although a trend was observed for mature milk melatonin and cognitive scores (B = 2.3, 95% CI –0.1–4.7, p = 0.064).

Conclusion
Breastmilk melatonin concentrations in colostrum are significantly and robustly associated with motor development at nine months' corrected age in preterm infants, with associations strengthening after adjustment for key confounders. These preliminary findings suggest that early postnatal exposure to higher melatonin concentrations in breastmilk, particularly colostrum, may positively influence motor development in preterm infants. Breastmilk melatonin may thus represent a novel and early biomarker of neurodevelopmental potential in this vulnerable population. Larger longitudinal studies are needed to confirm these associations and to explore clinical applications in neonatal nutrition and care.

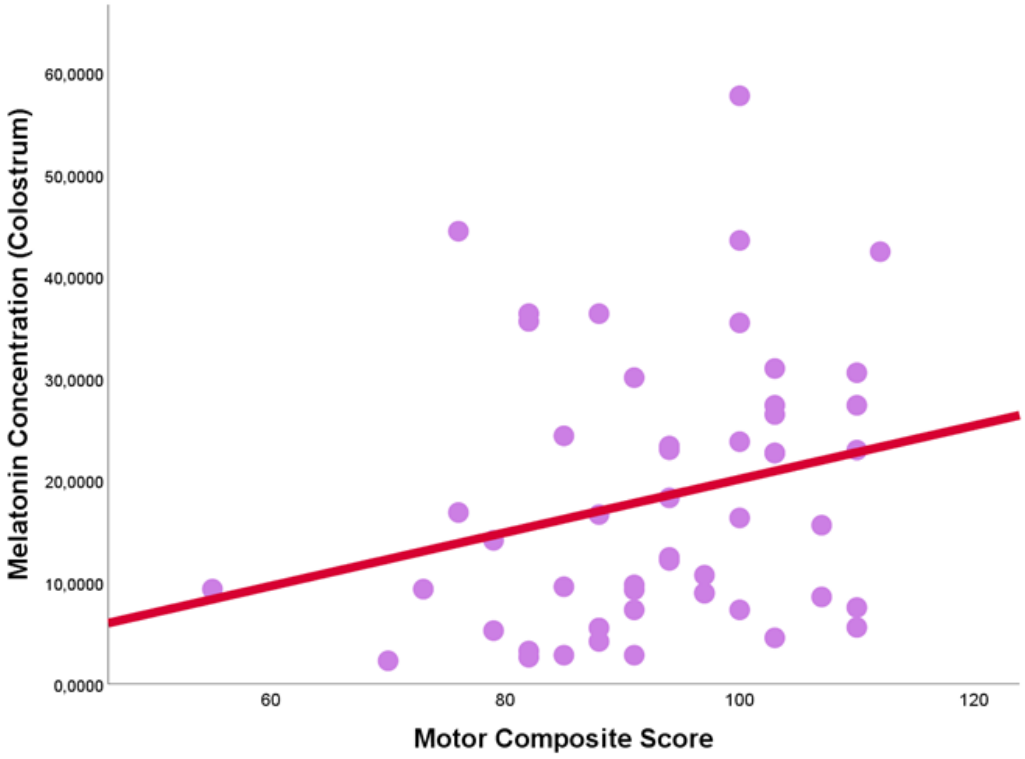

FIGURE 1. Higher colostrum melatonin was associated with increased motor scores

Breda Hayes: The Placenta In HIE

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The Rotunda Hospital Dublin

Background
Peripartum Sentinel Events are evident in approximately 25- 40% of cases of Hypoxic Ischaemic Encephalopathy (HIE). Unanswered questions as to the aetiology remain in 60-75% of cases. Understanding how the placenta may impact the type of brain injury and how this injury may manifest in later life opens opportunities for injury prevention and/or modulation. This study hypothesised that placental pathology abnormality is more common in cases with HIE than healthy controls and cardiotocography (CTG) abnormalities are associated with presence of placental pathology.

Methods
Retrospective single site case-control study. Cases: Moderate/Severe HIE ≥36+0 weeks gestation born 2006 – 2021. Controls: Healthy infants ≥36+0 weeks gestation with a normal neurological status, born January 2022-January 2023. Controls had no clinical indication for placental analysis. Placental histology was reviewed by a perinatal pathologist. CTG was reviewed by an obstetrician.

Results
140 cases [Moderate HIE 66%; Sentinel Event 39%; Therapeutic hypothermia 72%] and 98 controls. Placental histology was available for 76 cases. Intrapartum CTG was available for 90 cases. Placental histology and intrapartum CTG was available for all controls.
Fetal vascular malformation, delayed villous maturation and chorioamnionitis especially with fetal inflammatory response were associated with HIE. Although placental pathology increased risk of HIE it was not associated with grade of encephalopathy. However, babies with any placental pathology and not treated with therapeutic hypothermia had more white matter injury on MRI. In addition, babies with placental pathology and no history of a sentinel event had higher cortical injury scores. Placental pathology was also associated with numerous summary CTG characteristics however; on logistic modelling to predict placental pathology, CTG abnormalities performed poorly.

Conclusions
Placenta pathology reduces labor tolerance and increases the risk for HIE even in children with a known sentinel event. Placental pathology potentially influences brain development and maturation. This is particularly true of chorioamnionitis where inflammation plays a key role. There is no accurate way of identifying this in the peripartum period at present. Better modalities of intrapartum monitoring of the maternal placental fetal triad are needed. The placenta performs very diverse and important functions in utero. Large cohorts with detailed neurodevelopmental follow up are required to assess the effects of placental dysfunction in the setting of HIE on longer term school age outcomes.

Egbert Herting: Lung function following premature birth until the age of 12 years

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Background
Adults born preterm have poor lung function measures and a high risk of Chronic Obstructive Pulmonary Disease (COPD). It is yet unclear if this is dependent on the initial injury or a consequence of the capacity for regeneration during childhood.
Objectives. Analyses of longitudinal spirometry follow-up data of a large cohort of children born preterm.

Methods
Spirometry at ages 5 and 11 years in children born at term and preterm was performed by a trained study team of the GNN with identical lung function testing devices and personell of the German Neonatal Network (GNN) study team. Polygenic risks for COPD were calculated based on single nucleotide polymorphism array data. FEV_1 z-scores at 5 and 11 years were analyzed with paired t-test and multiple linear regression models.

Results
Sixty children born at term and 585 children born preterm were studied. Between 5 and 11 years, mean FEV_1 z-scores were constant in children born at term (-0.44 ± 1.0 vs. -0.48 ± 1.0) and improved in children born preterm (-1.37 ± 1.1 vs. -1.07 ± 1.1, p for time x group interaction=0.021). In children born preterm the effect size of each additional polygenic COPD score decile on FEV_1 z-scores was -0.06 ± 0.015 ($p=9.0 \times 10^{-5}$) at age five years and -0.07 ± 0.015 ($p=3.7 \times 10^{-6}$) at age 11 years. Preterm children with a higher polygenic COPD risk had lower changes in FEV_1 z-scores from age 5 to age 11 years (-0.04 ± 0.01 per additional decile, p=0.005).

Conclusions
Lung function of children born preterm has the capacity to regenerate between 5 and 11 years along their genetic COPD profiles.

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Stanislava Hitrova-Nikolova: Neonatal outcome in newborns of mothers with diabetes mellitus

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Background
Maternal diabetes mellitus can adversely influence fetal development and cause an increased risk of neonatal and long-term complications in the offspring. The aim is to establish a correlation between the serum insulin levels of umbilical cord blood and glycated hemoglobin in mothers. To evaluate a relationship between glycated hemoglobin and some complications in the early neonatal period (pulmonary morbidity, oxygen therapy, infections, etc.).

Methods
This prospective study was conducted in the University Hospital of Obstetrics and Gynecology "Maichin dom," Sofia, from August 2020 to November 2023. The study included 59 newborns and their mothers with diabetes. Umbilical cord blood was collected immediately after delivery, and insulin levels were measured by using an automated chemiluminescent immune assay (Roche, Germany). Hyperinsulinemia was defined as serum insulin levels ≥13.0 µU/ml. Abnormal glycated hemoglobin (HbA1C%) before delivery was defined as values above 7%. The evaluated neonatal outcomes were low birth weight, macrosomia, Apgar at 1 and 5 min, respiratory morbidity, and infections.

Results
A total of 59 newborns were enrolled with a mean gestation week of 36 weeks (31-41) and a birth weight of 3213 grams (980-4546), respectively. The mean cord blood insulin levels were 45.1±13 µU/ml (0.6-636), and the mother's mean HbA1C levels were 6.4±1.5 (4-13). The study results showed the following rates of low birth weight (8.9%), macrosomia (7.8%), respiratory morbidity (64.4%), and infections (25.4%). A positive linear correlation was demonstrated between maternal glycated hemoglobin levels and cord blood insulin (r=+0.303, p=0.023). The study indicated that only newborns of mothers with type 1 diabetes had lower Apgar scores at 1 minute (χ^2=7.881, p=0.005). A statistically significant relationship was found between high glycated maternal hemoglobin (HbA1C > 7%) and respiratory morbidity (χ^2 = 7.342, p = 0.007) and, respectively, the need for oxygen therapy in newborns (Fisher = 5.684, p = 0.012). No difference was found in the frequency of newborns with infection depending on the mother's glycated hemoglobin.

Conclusions
Hyperinsulinemia in newborns and high maternal glycated hemoglobin are predictive factors for expected neonatal morbidities. Strict glycemic control in the mother and neonatal monitoring are required to prevent morbidity in infants of diabetic mothers.

Michel Holger: Pulse wave transit time measurement in neonates for estimation of cardiac output changes and non-invasive haemodynamic monitoring

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Background
In neonates, estimation of cardiac output (CO) is essential for hemodynamic treatment. Studies in adults have shown that CO can be derived non-invasively from pulse wave transit time (PWTT). Data on neonates is scarce. The goal of this study was to evaluate the influence of cardiac output changes on PWTT in neonates in different haemodynamic situations.

Methods
In this study, we performed 198 PWTT measurements in 55 neonates with simultaneous echocardiographic evaluation of shortening fraction, stroke volume, cardiac output, ductus arteriosus (DA) size and signs of pulmonary hypertension (eccentricity index). PWTT recording was performed using a LifeScope TR Monitor from Nihon Kohden by measuring real-time values derived from ECG and pulsoxymetry. PWTT was measured at the right wrist and one foot for one hour and the mean values were calculated and normalized for body surface area (BSA) and body-length.

Results
Correlation analysis confirmed a strong negative correlation between the left ventricular cardiac output, the cardiac index and the PWTT values normalized by BSA, with a large influence of the infant's physical characteristics. When we corrected for this influence in a partial correlation analysis, a less pronounced but significant (p 0.03) negative correlation was found between the cardiac index and the PWTT. Increasingly large patent DA was associated with an increase in LV stroke volume and led to a significant (p = 0,017) decrease in PWTT. Increasing signs of pulmonary hypertension led to a decrease in PWTT with a significant positive correlation (p= 0,009) between the PWTT and the eccentricity index in echocardiography.

Conclusion
In our study, typical hemodynamic changes in neonates had a significant influence on the PWTT. Therefore, its measurement might be a tool for non-invasive hemodynamic monitoring in neonates. Further studies are needed to evaluate this tool.

Nicoletta M. Iacovidou The effect of neonatal asphyxia on the ovarian histology of newborn piglets: an experimental study.

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Background
Perinatal asphyxia (PA) is characterized by severe impairment of oxygen and nutrient supply to the newborn's tissues, due to peripartum or antenatal/postnatal factors. The impact of PA on organs and systems, such as the CNS, CV, and renal system has been repeatedly studied. However, little is known about the effect of PA on the ovaries. As several traits of the adult female reproductive system have been associated with perinatal conditions, it is reasonable to speculate that a severe hypoxic incident during perinatal period might affect the ovaries. Furthermore, PA has "gender-dependent" effect on some of the affected systems, and this differentiation might be partly mediated by alterations of the gonads.
We aimed at investigating the potential histological alterations of the ovaries of newborn piglets subjected to severe hypoxia with or without resuscitation.

Methods:
26 female Large White/ Landrace piglets, aged 1-4 days, randomly distributed in 3 groups were the study subjects. In Group A(control) the animals underwent no further manipulations except for the initial preparation and mechanical ventilation prior to the surgical removal of the ovaries. In Group B(asphyxia) and group C(asphyxia/ resuscitation) the animals were subjected to severe hypoxia until bradycardia or severe hypotension occurred. Following that time-point, group B animals had their ovaries surgically removed, while group C animals were resuscitated as per the NLS guidelines. Following ROSC the latter were stabilized for 30 minutes, prior to the removal of the ovaries and the termination of the experiment.
The ovaries were then preserved and examined by the pathologists, who assessed them with regards to 4 histological parameters: presence of balloon cells, apoptosis, vacuoles in oocytes and stroma cells. The above-mentioned parameters were graded from 0 (absence) to 3 (abundant presence).

Results:
Balloon cells and apoptosis were more prominent in samples from asphyxiated animals (groups B&C) vs that of the control group(A) (p value: 0.0487 and 0.036 for balloon cells and apoptosis respectively). Marked differentiation was noted in the samples from the asphyxiated animals (with or without resuscitation) with regards to the higher gradings (2-3) of balloon cells (p value: 0.0214, OR: 9, 95% CI:1.39–58.4). Regarding the rest of the histological parameters, there was no statistically significant difference noted between the study groups. However, upon investigating the potential effect of the duration of asphyxia or resuscitation on the histological findings, it is worth mentioning that the duration of asphyxia appeared to have a negative correlation with the grade of vacuoles in oocytes ($r = -0.54$, $p = 0.039$).

Conclusion
In conclusion, this experimental study suggests that PA leads to alterations of the neonatal ovarian histology. Further research is required in order to investigate the clinical impact and significance of the above findings, as well as the potential correlation with other systemic or biochemical alterations.

Nelly Jekova: Outcome of newborn infants with non-immune fetal hydrops – clinical challenges

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Background
Nonimmune hydrops fetalis (NIHF) is the pathological accumulation of fluids in the fetal compartments, without maternal alloimmunization. It accounts for 85% to 95% of hydrops cases and arises from various conditions that disrupt fluid regulation in the fetus. Prenatal interventions are used to alleviate fluid collections, but the outcome is uncertain because the underlying causes of NIHF vary. We aimed to investigate the survival rate of infants with hydrops fetalis after fetal interventions and neonatal intensive care.

Methods
We reviewed the medical records of patients diagnosed with hydrops fetalis from January 2021 to May 2025, born at the University Hospital “Maichin dom”. All cases exhibited abnormal fluid accumulation in at least two body compartments during both pre- and postnatal examinations. The primary outcome measure was the mortality rate. We also collected information regarding disease etiology, maternal history, initial diagnosis of hydrops fetalis, fetal intervention, Apgar score, gestational age at birth, initial albumin and pH levels, and neonatal intensive care treatment.

Results
Of the 7 cases enrolled, 2 survived and 5 died; the mortality rate was 71,4%. The diagnosis of NIHF was identified between 31 and 36 weeks of gestation. Only two of the infants received fetal intervention, while five of them did not. The survival rate was associated with gestational age at birth, time of initial diagnosis, birth weight, Apgar score, initial albumin, and pH levels. The most common aetiologies were severe intrauterine infections: congenital syphilis (4/7), congenital Parvovirus B19 infection (1/7), and intrauterine peritonitis with intestinal perforation (1/7). One of the cases was caused by a congenital cardiovascular disorder (1/7). All infants underwent thoracocentesis and drainage of ascites along with specific antibiotics and neonatal intensive treatment.

Conclusions
Overall, hydrops fetalis was diagnosed late, and fetal intervention was performed in a few cases. Preterm births were more frequent, and birthweight was lower in the cases that underwent fetal intervention than in those that did not, but there was no significant difference in mortality. The initial diagnosis time, gestational age at birth, birthweight, Apgar score, and first albumin and pH levels were independently associated with mortality.

Ursula Kiechl-Kohlendorfer6: Transition to home: improving outcomes of very preterm infants and families – a systematic review

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Background:
The transition to home is a sensitive and critical process for both preterm infants and their parents. However, there is limited overview of existing transition interventions and comparison of their effectiveness. We systematically reviewed the literature on interventions aimed at improving the transition from hospital to home for very preterm-born infants and their parents, and meta-analyzed their efficacy.

Material and Method
We analyzed peer-reviewed studies published between January 1, 1990, and April 5, 2023, from biomedical databases (Cochrane, Medline, CINAHL, EMBASE, PsycINFO on transition-to-home interventions for very preterm-born infants These included randomized controlled trials, observational studies, case-control studies, and systematic reviews. Case series with fewer than ten cases, conference abstracts, and preprints were excluded.

Results
2,670 studies were identified, of which 42 were included in this review. Median gestational age was 28.1 (interquartile range 27.2, 28.0 weeks, median birth weight was 1042.2 (1018.9, 1152.5 grams. Intervention categories included parental counselling, sensory interventions, developmental stimulation, breastfeeding promotion, physiotherapy, and other. Most studies assessed developmental outcomes, but also measured parent-child interaction, parental mental health and satisfaction, breastfeeding rates, anthropometric parameters, and hospital readmission rates. Sensory interventions had the largest effect size at 12 months (SMD: 0.944, 95% CI: -0.154 to 2.042, while developmental stimulation had a moderate effect (SMD: 0.392, 95% CI: -0.011 to 0.796. Parental counselling showed a small but consistent benefit.

Conclusion
Our findings suggest that sensory and developmental stimulation are most effective in supporting the transition to home process for very preterm-born infants and their parents. This systematic review provides a basis for healthcare professionals and researchers aiming to improve the transition to home process for this population.

Esin Koç: Evaluation of the Frequency, Risk Factors, and Outcomes of ROP in Preterm Infants with a BW >1500 grams or GA>32 weeks in Turkiye (TR-ROP 2) and Medico-legal Fears: A Turkish Neonatal Society Multicentre Study

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Background

This study aimed to evaluate the prevalence and risk factors of ROP in preterm infants with a birth weight (BW) >1500 grams or gestational age(GA) >32 weeks in Turkiye.

Methods

A prospective cohort study (TR-ROP 2) was conducted in 80 neonatal intensive care units between September 30, 2023, and November 1, 2024. Infants with a BW >1500 grams or GA >32 weeks who had an unstable clinical course or were deemed at risk for ROP were included. The effect of medicolegal concerns on decision to screen was also evaluated.

Results

The study included 4140 infants at risk for ROP development; 242 (5.8%) developed any stage of ROP, and 17 (0.4%) developed severe ROP requiring treatment. Risk factors independently associated with ROP included lower GA and BW, small for gestational age status, red blood cell transfusion, oxygen therapy >5 days, mechanical ventilation >1 day, early neonatal sepsis (ENS) with comorbidities, or presence of ≥3 comorbidities (excluding ENS). The highest BW and GA among treated infants were 2400 g and 35 weeks. Of those with BW >2000 g, 31.4% were screened for medicolegal reasons; 2.2% developed ROP, but none had severe ROP.

Conclusions

ROP in mature infants is rare but can occur in the presence of multiple risk factors. Medicolegal concerns may contribute to overscreening. Developing evidence-based, risk adapted screening guidelines is essential to ensure appropriate care without unnecessary interventions.

Helmut Küster: Comparison of outcome using different drugs to treat Neonatal Abstinence Syndrome

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Background
Neonatal Abstinence Syndrome (NAS) due to maternal drug abuse is a condition affecting up 22 % of infants in the Medicaid population and increased in the US by 333 % from 1999 to 2014. No consensus exist regarding the pharmacological treatment of the newborn infant. Our aim was to compare the treatment schemes for NAS at our institution during the last decades.

Methods
In a prospective single-center study at the level IV Perinatal Center at Göttingen University, Germany, charts of all patients diagnosed of having NAS were analyzed retrospectively. Eligible were all inborn infants and those admitted within a few hours after birth.

Results
During the study period of 15 years 13177 infants were born of whom 100 had the diagnosis of NAS (ICD-10: P96.1). Mean gestational age was 39.2 (32.2 - 42.0) weeks, mean birth weight 2895 g (1270 - 3303), 50 % were male, 33 % SGA. This period contained two-time frames of 6 years each when the only drug used to treat NAS was tinctura opii (morphin) and levomethadone, respectively. The substances used by the mothers were levomethadone (49), Buprenorphine (26), Methadone (16), Heroin (13), THC (14), Cocaine (4), Amphetamine (2), and Opoids (2). 86 mothers had been supervised in a substitution program and thereby were on levomethadone. Of the 100 infants, 76 had a drug screening in urine, 17 in meconium with both tests about 60 % consistent with the substance claimed to be used during pregnancy. Of these infants, 27 received non-pharmacological care only, 46 tinctura opii, 20 levomethadone, 7 other drugs and 10 a combination of several drugs. Comparing the two treatments used most frequently the median duration of therapy was 22 days (IQR 15 - 31 days) with tinctura opii only versus 25 days (IQR 15 - 38 days) with levomethadone only (non-significant). The length of stay was significantly different with 30 days (IQR 24 - 37 days) versus 34 days (IQR 21 - 53 days), respectively. Using the Finnegan score to assess the treatment effect infants on tinctura opii had a median score of 8 - 5 - 5 on day 2 - 12 - 24 compared to 12 - 7 - 6.5 for those on levomethadone. Weight gain was 24 g / day (IQR 18 - 28 g/day) in the tinctura opii group versus 20 / g/day (IQR 4 - 25 g/day) in the levomethadone group.

Conclusions
Our study showed that using levomethadone compared to tinctura opii to treat NAS seems to be more effective in controlling clinical symptoms of drug withdrawal but leads to longer duration of treatment. The latter might be due to underestimation of positive effects of very small doses of levomethadone by physicians and nurses at the end of its down titration. We postulate that a more individualized therapy of NAS using the substance the infant has adapted himself to as a fetus may be more appropriate for postnatal treatment - if long term outcome proves to be identical.

Verena Lehnerer: Early life serum NfL and GFAP as brain damage biomarker in perinatal asphyxia

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Background
Neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) are emerging serum biomarkers of neuro-axonal damage and glial activation in various neurologic diseases. Whether NfL and GFAP may indicate brain damage in perinatal asphyxia at an early stage is largely unknown.

Methods
We performed a prospective single-center study in 2022 and 2023 (BioAsS trial) in neonates with more than 35 weeks gestation and the following conditions, i) asphyxia with moderate to severe hypoxic-ischemic encephalopathy (HIE, n=16), ii) perinatal acidosis or asphyxia without HIE (n=23) and iii) neonates without birth acidosis (n=20). Cerebral ultrasonography (US) was performed in all patients, magnetic resonance imaging (MRI) only in those with HIE. Serum NfL and GFAP concentrations were assessed at birth, day of life (DOL) 2-3 and DOL 5 and were measured using ultrasensitive single-molecule array (Simoa) assays.

Results
Serum NfL was significantly higher in neonates with moderate-severe HIE at birth, DOL 2-3 and DOL 5 as compared to neonates without birth acidosis, whereas serum GFAP was higher only at DOL 5. The predictive ability of NfL for brain damage detected by US or MRI was at birth 0.816 AUC of the ROC curve (95% CI 0.618-0.870), at DOL 2-3 0.801 (0.650-0.953) and at DOL 5 0.841 (0.708-0.974). Albeit AUC of GFAP was less good, a combination of both NfL and GFAP increased slightly performance at birth and DOL 5.

Conclusion
Serum NfL reflects cerebral damage already shortly after perinatal asphyxia and may serve as an early predictor of unfavourable outcome.

Lars Mense: Surfactant administration during endotracheal CPAP (DD-SURF): feasibility, risk factors and short-term outcome

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Background

Although there is agreement that surfactant should be administered without mechanical ventilation, there is still a debate concerning the optimal method. DD-SURF combines the benefits of INSURE and thin-catheter surfactant (TC-Surfactant) administration: CPAP is applied via a T-piece device attached to an endotracheal tube (ETT) with surfactant side-port after the ETT is placed in a nasopharyngeal position. The ETT is advanced into an endotracheal position and the surfactant is administered during spontaneous breathing while CPAP is continued. No positive pressure ventilation is routinely performed but can be applied in case of severe apnea. Subsequently, the newborn is extubated and binasal CPAP initiated.

Methods

Retrospective cohort study of all preterm newborns below 300/7 weeks gestational age admitted to the neonatal intensive care unit. Data on surfactant therapy, respiratory support during the first 96 h of life and neonatal morbidities until hospital discharge were collected from the electronic patient charts to evaluate the efficacy and safety of our approach.

Results

In total, 222 newborns met the inclusion criteria; 174 (78%) received surfactant in the delivery room by the DD-SURF procedure and 21 infants (10%) were not extubated after surfactant administration (Surf-and-vent group). After DD-SURF, 75% of patients did not require reintubation. Intraventricular haemorrhage and bronchopulmonary dysplasia occurred more often in infants after DD-SURF failure than after successful DD-SURF.

Conclusion

DD-SURF potentially combines the benefits of INSURE and TC-Surfactant and represents a useful alternative of surfactant delivery with comparable success rates to TC-Surfactant administration.

Colin Morgan: Evaluating complex clinical interventions: using bioelectrical impedance to support fluid management in sick term and preterm infants

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Background
Bioelectrical Impedance Analysis (BIA) is a non-invasive method of measuring body composition. Recent changes in technology and licencing agreements allow use in preterm infants down to 23 weeks gestation. BIA produces a large complex dataset describing fluid distribution across extracellular, intracellular and intravascular compartments. Our recent European survey found most respondents (90%) did not use body composition measurements in clinical practice, with most (71%) unaware that BIA could be used in infants as small as 23/40 weeks. This indicated that developing a randomised controlled trial protocol to investigate whether BIA data could improve neonatal fluid management would require both an educational package, qualitative evaluation and a focussed BIA dataset to allow effective interpretation in the clinical environment.

Methods
Setting: Large level 3 UK neonatal service: >1000 admissions per year; 20 consultant neonatologists, 55 resident doctors or advanced neonatal nurse practitioners, 173 neonatal nurses. **Education package**: A mixed methods approach was used to assess the impact of an education package for the multidisciplinary team (MDT) working in the Neonatal Intensive Care Unit (NICU) regarding the use of bioelectrical impedance analysis (BIA). knowledge acquisition was assessed and feedback sought regarding the content, format and delivery of the teaching. **Protocol development:** Previously unpublished plasma sodium data from 150 preterm infants (recruited to the SCAMP nutrition study in this centre) born <29 weeks was used to calculate a plasma sodium perturbation index: cumulative deviations in plasma sodium (mmol/l) outside the normal range (133-143mmol/l) over the first 14 days of life. Similarly, PAINT18 study data (n=26) were used to characterise the most useful BIA assessments using physiological and biochemical data together with a clinician opinion on clinical utility.

Results
Education package: There were initially 106/273 (39%) pre-education survey responses (Survey A) and 64/100 (23%) post-education survey (survey B). There was a significantly improved change in mean knowledge scores from 1.75 to 2.8 /5 after the education programme (p=<0.001). **Protocol development:** Single centre, randomised controlled trial (non-blinded; opt-out). i) Population: neonates expected to require >7 days intravenous fluids ii) Intervention: standard care augmented with daily BIA with a screenshot of the most valuable dataset: providing absolute, relative and trend data of fluid distribution across the body compartments to inform fluid management decisions during key clinical decision making periods (usually the NICU ward round); iii) Control group receives standard care; iv) Outcome: 170 infants (85 each arm) are required to detect a difference of >5mmol/l in the 14 day plasma sodium perturbation index (power: 80%; significance level: 0.05). The secondary outcomes include growth, biochemical and nutritional biomarkers and neonatal morbidities. An embedded qualitative element utilises semi-structured observational and interview data to assess clinical utility and acceptability.

Conclusions
BIA is a potentially useful tool in neonatal fluid management but evaluating the added value of large datasets in day-to-day decision making requires a complex mix of qualitative and quantitative research methods. These include education and training packages, identifying the clinically useful datasets and short-term biochemical outcomes. This will allow effective design of future RCTs powered for long-term clinical outcomes.

Britt Nakstad: Extreme Heat Impacts on Neonatal Health and Wellbeing. Awareness of Neonatal Health in the Global South

Nakstad B

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Background

Extreme heat impacts on child health and wellbeing due to immature thermoregulation, less sweating and a high surface-to-body mass ratio that make them more vulnerable to heat-related illness. Severe dehydration, especially if struggling with breastfeeding, renal failure and electrolyte imbalance, neurological and cardiorespiratory failure may result.

This late preterm was born healthy during a heatwave and developed lethargy and minimal responsiveness from day-of-life (DOL) 5, developed seizures at DOL 12, then demised at DOL 20. All hospitals involved in the diagnostic work-up and treatment presumed severe sepsis and treated accordingly. However, microbiology results were always negative. In infants, especially if preterm, it is challenging to distinguish septic shock from heat-related illness, as well as other neonatal diagnoses.

Conclusions

Medical history including risk factors for infection and heat-related disease must be thoroughly explored.
It is important for health care workers and the public to be aware of potentially fatal neonatal heat-related illness.

Sally Ogden: Using simulation to influence design of a new departmental major haemorrhage policy.

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Background
Liverpool Women's Hospital specialises exclusively in the health of women and their babies with a large tertiary level neonatal intensive care unit. It is an isolated hospital away from other acute services and notably doesn't have laboratory services including for blood transfusion. The blood bank is provided by the nearby tertiary children's hospital requiring blood products to be transferred across the city. We developed a new major haemorrhage policy and used transformative simulation to test the policy and identify practical changes before implementation to improve safety in this emergency scenario.

Methods
We initially performed a tabletop simulation followed by a MDT simulation in real time of the new major haemorrhage scenario within our unit. Following the simulation and debrief we identified areas within the policy that could be developed and improved before finalising the policy. To assess this process, I undertook questionnaires both pre and post simulation to assess how staff found simulation to be used for developing policy design. This was backed up by semi structured interviews with participants analysing both the process and the simulation.

Results
From the initial simulation debrief we identified 16 primary issues with the new policy and 28 action points. From this information we developed additional tools for managing an major haemorrhage emergency on the unit and improved the policy for a more functional use if a haemorrhage were to occur. The simulation was then repeated with these new changes in place. To research the use of simulation in this way the 13 participants agreed to complete pre and post simulation questionnaire with 5 also taking part in semi-structured interviews to assess the process. The results of the questionnaires are shown in the table below (TABLE 1). These questionnaires showed that teaching staff about a new policy through simulation was an effective method for improving knowledge particularly for rarely seen emergencies.
From the semi-structured interviews, I was able to identify several recurrent themes regarding the simulation process. These were that the level of confidence about the new policy increased following the simulation compared to routine policy changes. That the simulation was less stressful when assessing policy changes as staff felt empowered to help develop the policy changes in the department and that this increased interprofessional working. Overall staff found simulation to be effective as a tool for policy design and implementation.

Conclusions
We found simulation to be an effective tool for developing and implementing complex new policies particularly relating to infrequent but emergency protocols. In addition to increasing staff knowledge and confidence in the policy we demonstrated that you can use simulation to improve the policy itself by identifying otherwise unanticipated issues prior to ratification.

TABLE 1. Results from the combined pre and post simulation surveys.

Question	Response	Pre-simulation results	Post-simulation results	P value
Are you aware of the new major haemorrhage protocol being introduced in the department?	Yes	13 (87%)	13 (100%)	0.17
	No	2 (13%)	0	
Would you know when to trigger the major haemorrhage protocol?	Yes	9 (60%)	13 (100%)	0.01
	No	6 (40%)	0	
Do you know how to trigger the major haemorrhage protocol?	Yes	8 (53%)	13 (100%)	0.004
	No	7 (47%)	0	
Do you know what blood products come as part of the major haemorrhage bundle?	Yes	8 (53%)	13 (100%)	0.004
	No	7 (47%)	0	
Would you know how to store and administer the blood products that arrive as part of the major haemorrhage bundle?	Yes	6 (40%)	12 (92%)	0.003
	No	9 (60%)	1 (8%)	
Do you know which staff groups need to be informed when the major haemorrhage protocol is triggered?	Yes	9 (60%)	13 (100%)	0.01
	No	6 (40%	0	

Livia Ognean: Vitamin D status at birth in very preterm infants in Romania.

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Background
Recently, vitamin D deficiency (VDD) has been described as a pandemic, affecting all groups of population. Very preterm infants (VPIs) are particularly vulnerable to vitamin D deficiency. Objectives: We aimed to evaluate the maternal and neonatal vitamin D and to identify the risk factors for neonatal VDD and vitamin D insufficiency (VDI) in VPIs.

Methods
The prospective observational study was conducted in the regional level III maternity of the Clinical County Emergency Hospital Sibiu and included all VPIs delivered at ≤32 weeks of gestation between 1 March 2022 and 28 February 2025. Maternal and neonatal data were collected from medical records. 25-hydroxy vitamin D levels were measured from blood using immunochromatography technology within the first 12 hours of life in VPIs and within 48 hours after birth in the mothers. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 23.0.

Results
A total of 164 VPIs born (median gestational age 30 [27-31] weeks and birth weight 1200 [900-1527] g) and 146 mothers (median (IQR) age 30 [24-35] years) were included in the study. Severe VDD (<10 ng/mL) was found in 16.46% of the infants, VDD (<20 ng/mL) occurred in 58.53% cases while 25.61% of the infants presented VDI (20-29 ng/ml). A significant correlation was found between the maternal and neonatal status (r=0.684, r2=0.468, p<0.001, B=0.62, meaning that for each 1 ng/mL increase in the maternal 25(OH)D levels, the neonatal level increases by 0.62 ng/mL. Both maternal and neonatal vitamin D status were correlated with the vitamin D duration and dose used for supplementation during pregnancy.

Conclusions
Our findings revealed a worrisome prevalence of severe VDD, VDD, and VDI in VPIs and in their mothers. The maternal and neonatal vitamin D status are strongly correlated. Additionally, less than half of the mothers in the study used vitamin D supplements during pregnancy despite the national recommendations. The professionals involved in carrying pregnant women and the policymakers should find solutions to improve the vitamin D status in these vulnerable groups of population.

Thalia Papadouri: Provision of Health Care Services in the Neonatal Intensive Care Unit Archbishop Makarios III Hospital-NAM III-OKYPY, Nicosia, Cyprus

Papadouri T

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Background
This presentation provides a comprehensive overview of the healthcare services offered to neonates in Cyprus, with a focus on the Neonatal Intensive Care Unit (NICU) of the Archbishop Makarios III Hospital (NAM III), the only Level III NICU operating nationwide under the State Health Services Organization (OKYPY). It outlines critical demographic trends in Cyprus, including birth rates, prematurity, and cesarean section prevalence, and highlights the increasing complexity and volume of neonatal cases requiring intensive care.

The NICU at NAM III functions as the national referral center, supporting both public and private sectors, as well as British military bases, and occasionally admitting neonates from territories outside government control. Key statistics are presented regarding staffing, bed capacity, and high-risk admissions, including neonates born before 32 weeks' gestation or with extremely low birth weights.

The presentation emphasizes the NICU's advanced capabilities, such as mechanical respiratory support, therapeutic hypothermia, administration of inhaled nitric oxide, and specialized surgical and developmental care. It also details screening programs, neuroprotective practices, and interdisciplinary collaborations that ensure comprehensive care from delivery through post-discharge follow-up up to two years of age.

Conclusion
Ongoing efforts to renovate and expand the facility are aligned with international standards, aiming to improve patient outcomes, reduce complications, shorten hospitalization durations, and promote neurodevelopmental health. The unit's objectives reflect a commitment to minimizing neonatal morbidity and mortality while supporting family-centered care and professional training.

Serafina Perrone: Newborn Bone Health Assessment Using REMS: Initial Validation of a Novel Approach

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Background
Skeletal growth during early life is a dynamic process influenced by genetic, nutritional, and environmental factors, with long-term consequences for bone health. Currently, dual-energy X-ray absorptiometry (DXA) is the standard method for neonatal bone assessment, but its limitations—such as ionizing radiation exposure and motion artifacts—hinder its use in longitudinal studies. The radiofrequency echographic multi-spectrometry (REMS) technique is widely used for assessing bone mineral density (BMD) in adults to diagnose and prevent osteoporosis. However, its potential application in early infancy remains unexplored. Aim This study aims to apply a REMS-based approach in early infancy to establish a model for femoral growth assessment, developing a ranking system that remains consistent over time (at 3 and 6 months of age), using weight as a target.

Methods
We enrolled 64 healthy term newborns (mean gestational age at birth: 39.5 + 1.5 weeks and mean birth weight 3.5 + 0.6) and performed REMS scans at 3 and 6 months of age. Since no existing algorithm apply REMS technology to neonatal bone assessment, a novel approach tailored to early infancy was developed including the following key steps: 1) Identification of the femoral region of interest (ROI) through a precise localization of the anatomical structures of interest; 2) Frequency-based analysis using the Fast Fourier Transform (FFT) to obtain averaged spectral signatures, facilitating the extraction of key bone characteristics; 3) Predictive Ranking Model Development using Partial Least Squares (PLS) regression, with neonatal weight as the target variable; 4) Validation of Ranking Consistency by verifying the consistency of the ranking model at 3 and 6 months of age, ensuring that the predictive framework remained stable over time.

Results
The PLS model demonstrated a consistent ranking of infants' BMD as assessed with REMS over time (Spearman's rank correlation: 0.53, p = 0.014; Kendal-Tau: 0.37, p = 0.021) (Figure 1). The average power spectrum for subjects categorized by weight showed distinct spectral differences between the extreme tertiles (Figure 2)

Conclusions
The findings suggest that REMS-derived spectral features may provide relevant physiological insights. While further validation is required, this study represents a pioneering effort to extend REMS technology to infancy, offering a potential alternative to DXA for early bone assessment and skeletal health monitoring Keywords: Radiofrequency Echographic Multi-Spectrometry (REMS); Bone Mineral Density (BMD); Neonatal Bone Assessment; Skeletal Growth; Osteoporosis Prevention.

Acknowledgements PNNR-MAD-2022-12376819 Project funded under the National Recovery and Resilience Plan (NRRP, M6/C2_CALL 2022 Italian Ministry of Health funded by the European Union – NextGenerationEU)

Scatterplot showing ranking consistency at 3 and 6 months based on median frames for each infant (Spearman's rank correlation: 0.53, p = 0.014; Kendal-Tau: 0.37, p = 0.021)

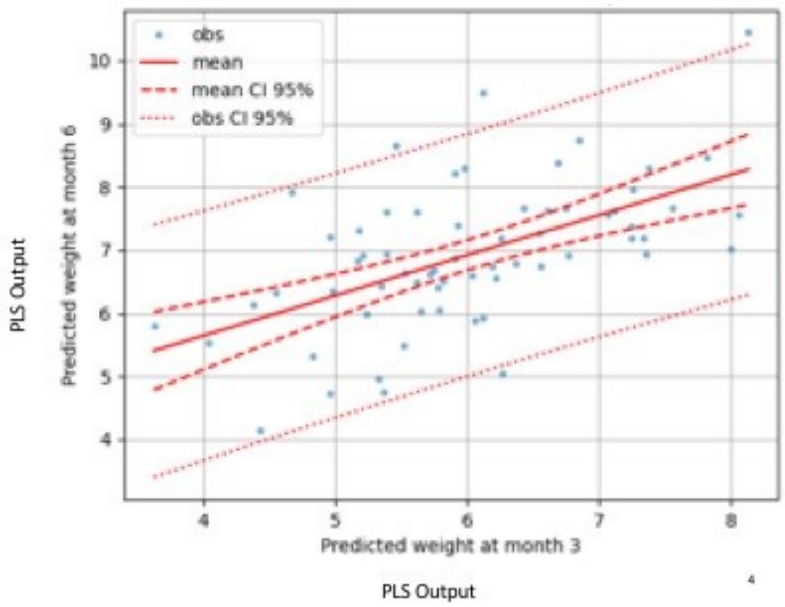

FIGURE 1. Ranking of infants' BMD as assessed with REMS over time

Mean power spectrum comparison of first and third weight tertiles: observed spectral separation is consistent with previously reported findings on adults (Convesarno F et al, Ultrasound Med Biol, 41:281–300, 2015

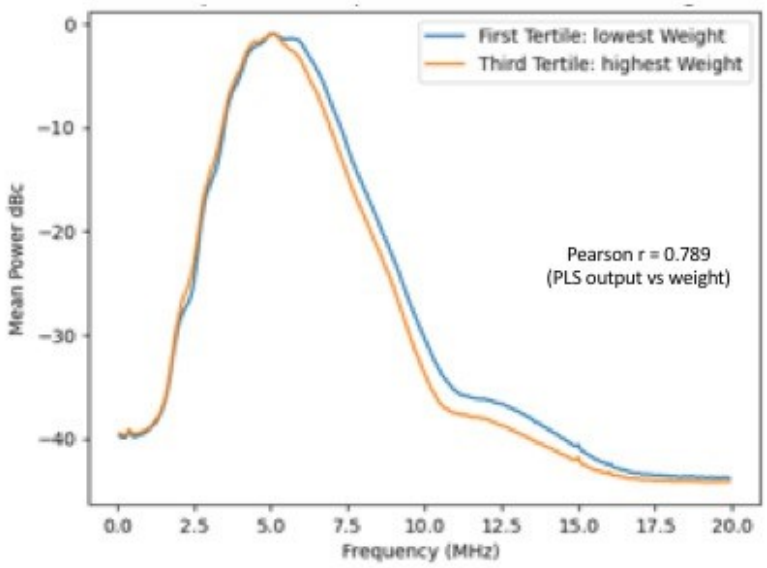

FIGURE 2. Mean power spectrum for subjects categorized by weight

Olga Romantsik: Devices to improve success of peripheral vascular catheterization in newborn infants – a systematic review and meta-analysis

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Background
Peripheral intravenous catheterization is essential in sick neonates but often challenging due to their small vessel size, leading to repeated attempts and complications. Device-assisted techniques—such as near-infrared light, ultrasound, and augmented reality—may improve success rates and reduce pain. This review assesses the benefits and harms of device-assisted techniques compared with standard technique.

Methods
We searched MEDLINE, Embase, CENTRAL, Cochrane Database of Systematic reviews, WHO ICTRP, and ClinicalTrials.gov (October 2024) for randomized controlled trials (RCTs) and quasi-RCTs. Data collection and analysis were conducted in accordance with standard Cochrane methodology.

Results
We included 12 RCTs (1251 neonates). Devices were used for placement in 5 studies (417 neonates) and tip confirmation in 6 studies (740 neonates). One study used ultrasound for both PICC placement and tip confirmation (94 neonates). Devices may increase first-attempt success compared to standard technique: RR 1.18, 95% CI 1.04 to 1.33 for placement and RR 1.20, 95% CI 1.10 to 1.30 for tip confirmation, however the certainty of evidence was low. Six studies (528 neonates) reported a shorter time to successful catheterization (moderate certainty of evidence). Of note, we were unable to conduct the meta-analysis due to missing account for censoring time-to event data. Devices likely reduce hematoma (RR 0.32, 95% CI 0.13 to 0.75; moderate certainty of evidence), bleeding (MD -0.68, 95% CI -0.83 to -0.53; low certainty of evidence), and phlebitis (RR 0.19, 95% CI 0.06 to 0.58; low certainty of evidence). Evidence was of very low certainty for thrombosis for placement (RR 0.33, 95% CI 0.01 to 7.99) and tip confirmation (RR 0.25, 95% CI 0.05 to 1.16), catheter-related bloodstream infection (RR 1.25, 95% CI 0.34 to 4.58), and arrhythmia (RR 0.09, 95% CI 0.01 to 0.70). Only one study reported the pain score (MD 0.25, CI95% -0.08-0.57, 90 neonates).

Conclusion
Device-assisted peripheral vascular catheterization may improve first-attempt success rates and reduce catheterization time in neonates. The evidence on pain reduction and complications is limited and requires further research. Given the variability in study methodologies and outcome reporting, high-quality RCTs with standardized outcome measures are needed to confirm these findings.

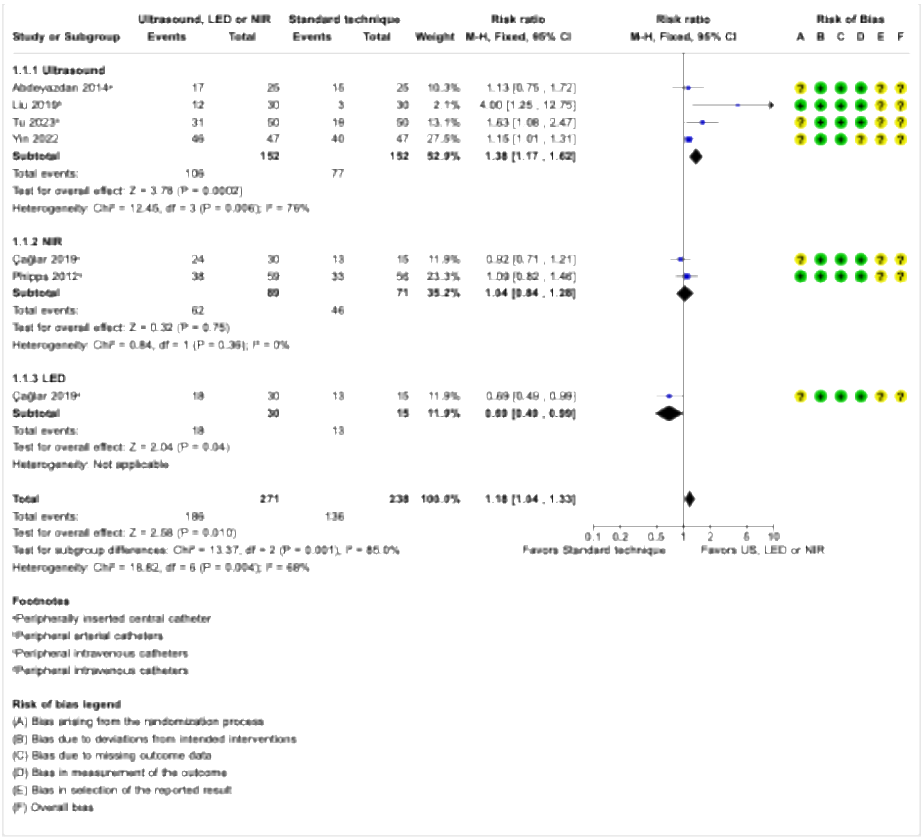

FIGURE 1. Forest plot of the outcome success at first attempt for the comparison: device-assisted catheter placement vs standard technique.

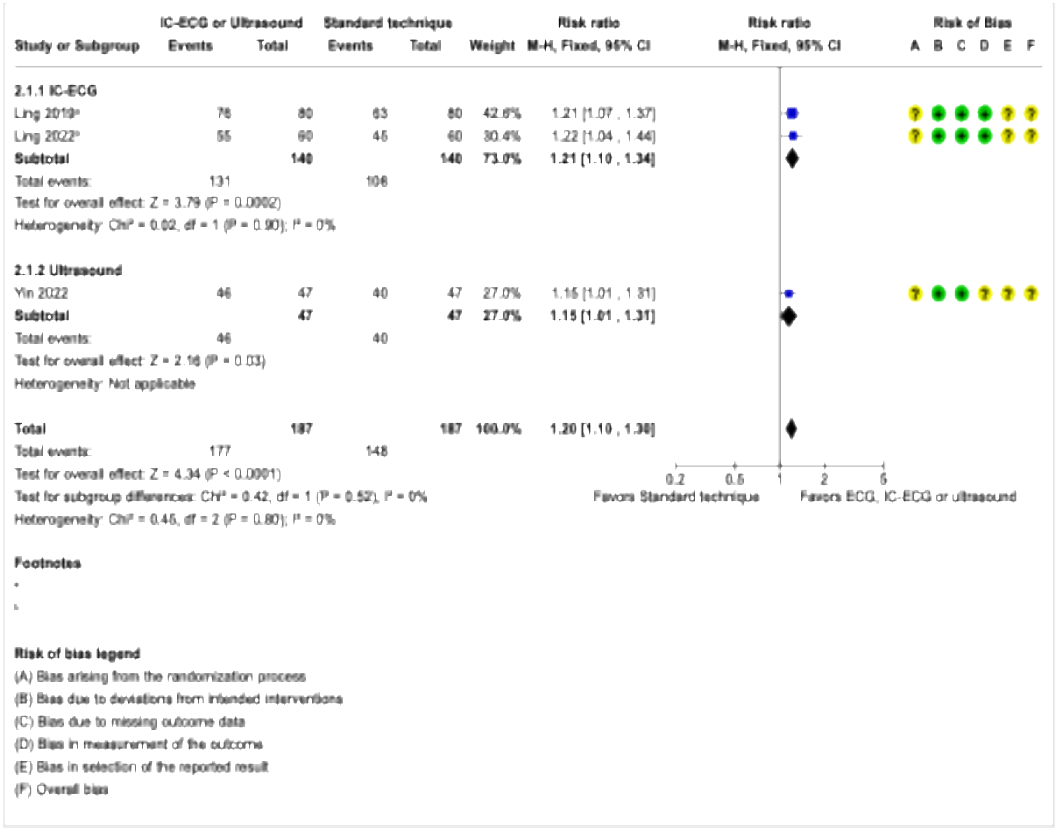

FIGURE 2. Forest plot of the outcome success at first attempt for the comparison: device-assisted confirmation of catheter tip position vs standard technique.

Kosmas Sarafidis: A case–control study of gastric fluid metabolomics to predict the need for surfactant therapy in very preterm infants

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Background
Respiratory distress syndrome (RDS) is a leading cause of morbidity in premature infants. However, predicting its progression and, in particular, the need for exogenous surfactant replacement after birth remains challenging. Current approaches to guide treatment, such as assessing oxygen requirements during non-invasive ventilation, using lung ultrasound and evaluating surfactant activity in amniotic or gastric fluid, offer relatively limited accuracy. In this study, we investigated whether targeted metabolomic analysis of gastric fluid collected shortly after birth could improve the prediction of surfactant therapy needs in very preterm neonates.

Methods
This was a prospective, single-center study conducted in preterm infants born at <32 weeks' gestational age. Data were collected on neonatal-perinatal characteristics and the administration of exogenous surfactant for the treatment of RDS. Metabolomic analysis was performed using gas chromatography–mass spectrometry (GC-MS).

Results
A total of 43 infants with RDS who required surfactant therapy (cases) were compared with 30 infants with mild or no RDS who did not receive surfactant (controls). Significant differences in gastric fluid metabolites -including L-proline, L-glycine, L-threonine, and acetyl-L-serine- were observed between the groups. However, no single metabolite alone could accurately predict the need for surfactant. Univariate analysis identified several significant predictors of surfactant administration, such as gastric fluid metabolites (L-glycine and acetyl-L-serine) and clinical parameters (gestational age, Apgar scores, and intubation in the delivery room). Two multivariable models were developed: (a) one including only significant clinical variables, and (b) another combining clinical variables with gastric fluid metabolites. The area under the curve (AUC) for the first model was 0.69 (95% CI: 0.57–0.81), while the second model yielded an AUC of 0.76 (95% CI: 0.64–0.86). In the latter, acetyl-L-serine and intubation in the delivery room emerged as significant predictors of surfactant therapy.

Conclusion
This study adds to the growing body of evidence on biomarkers predictive of the need for surfactant therapy in very preterm infants with RDS. However, further research is necessary to validate the clinical utility of gastric fluid metabolomics in this context.

Christos Tsakalidis: Early markers of neonatal sepsis

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Background

Neonatal sepsis is a bacterial infection of the circulation that causes severe symptoms that are often linked to death or permanent, irreversible impairments. In the first 72 hours following birth, neonatal sepsis is classified as early onset sepsis (EOS); if it is discovered later, it is classified as late onset sepsis (LOS). On the basis of clinical symptoms, diagnosing newborn sepsis—especially EOS—can be extremely challenging. Currently, there is a lack of a clear definition for sepsis in neonates, and a number of scientific organizations have proposed particular standards for correct diagnosis. The risk calculator used to determine which children should receive treatment is often prepared by taking into account a number of maternal factors, area epidemiology, GA, and other specific parameters in addition to the clinical signs. The availability of biomarkers that could help diagnose the condition early could enhance the short- and long-term outcomes of cases of true sepsis and lessen the harmful and indiscriminate use of preventative antibiotics. An optimal marker is known to rise quickly following the commencement of the disease and fall just as quickly once the infection has been eradicated. Although blood cultures are still the gold standard for diagnosing newborn sepsis, their relatively low sensitivity and other drawbacks prevent them from being routinely used as the only indicator of neonatal sepsis in clinical practice. Over the past three decades, numerous attempts have been undertaken to identify more trustworthy alternatives in order to address this issue. Unfortunately, none of the suggested markers meet all the requirements to be considered excellent markers. The accuracy of white blood cell count and differential count in detecting sepsis in neonates is quite low. The most often utilized indicators are acute phase reactants, such as PCT and CRP. They are both limited in a number of ways. It is highly challenging to determine precise cut-off levels for them, especially CRP, due to their non-ideal kinetic features and substantial prenatal, perinatal, and postnatal influences. Although there is a lack of solid evidence about the influence of certain prenatal and postnatal factors on blood levels and no clear cut-off levels for this marker, interleukins and other acute phase biomarkers may give some benefit. Pancreatic stone protein (PSP), among other biomarkers, is a globular polypeptide that contains domains of calcium-dependent glycan-binding proteins called C-type lectins. These proteins stimulate adhesion and signaling receptors during homeostasis and innate immune activation, causing pro-inflammatory activity. It has been noted that PSP levels rise before to sepsis and continue to rise throughout septic shock.

Methods

In an ongoing prospective study, we evaluated PSP values in 30 extremely preterm neonates during the first 10 days of life.

Results

Our results indicate that PSP increases up to 24h earlies than CRP in preterm neonates with EOS. Interestingly, a significant increase in PSP was noted in neonates with NEC, 24h prior of the onset of symptoms.

Conclusion

PSP might be a promising biomarker of EOS and NEC in extremely preterm neonates.

Madalena Tuna: Newborn Screening for Congenital Cytomegalovirus – a New Approach - ENROL cCMV6

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Background
Congenital cytomegalovirus (cCMV) infection is the most prevalent congenital infection and an important public health concern. It is a leading cause of hearing loss and cognitive impairment, with significant lifelong costs. Early diagnosis is challenging because most congenitally infected newborns are asymptomatic at birth. Recently, interest in newborn screening for cCMV has increased, but the reference standard for diagnosis is costly and impractical for large-scale screening programs. A simpler, affordable, yet reliable screening method is needed. The aim of this study is to evaluate whether pooled testing of Guthrie card samples—dried saliva spots (DSS) and dried urine spots (DUS)— achieves diagnostic accuracy comparable to the reference standard individual fresh urine PCR testing used for diagnostic purposes, as a strategy to improve feasibility for large-scale cCMV screening.

Methods
This observational, analytical, prospective cohort study is conducted in three phases. Phase 1, initiated in February 2023, evaluates the accuracy of two methodologies based on PCR analysis: (i) dried saliva spots (DSS) collected on Guthrie cards, tested in pools of four, and (ii) dried urine spots (DUS) collected on Guthrie cards, also tested in pools of four, for cCMV screening. Phase 2, initiated in March 2024 and currently ongoing, involves the implementation of both methods in two Portuguese hospitals. Phase 3, dependent on the outcomes of Phases 1 and 2, will extend the implementation to a hospital in São Tomé and Príncipe. The cohort included newborns screened within the first 3 weeks of life in the two Portuguese hospitals and was further enriched with samples from newborns with confirmed cCMV. In Phase 1, for each newborn, one urine sample (DUS) and one saliva sample (DSS) were collected on Guthrie cards. A fresh urine sample was also obtained for comparison by gold-standard testing. Saliva pools were assembled by combining four DSS from different newborns (4-pool), and urine pools were assembled similarly with four DUS samples (4-pool). Both pooled and individual samples were tested by nested PCR, and RT-PCR was used for viral load quantification in positive samples. Sensitivity and specificity were calculated with 95% confidence intervals (CI) for both saliva and urine.

Preliminary results
In Phase 1, a total of 584 newborns were enrolled to evaluate the accuracy of both methods, corresponding to 1,168 individual samples and 292 pools. Congenital CMV infection was confirmed in 23 newborns by the reference standard. For urine samples, individual dried urine spots (DUS) demonstrated a sensitivity of 91.3% (21/23; 95% CI: 72.0–98.9) and a specificity of 100% (561/561; 95% CI: 99.3–100). Pooled dried urine spot samples (DUS pool) showed slightly lower sensitivity, 86.9% (20/23; 95% CI: 66.4– 97.2), with specificity remaining at 100% (123/123; 95% CI: 97.1–100). For saliva samples, individual dried saliva spots (DSS) achieved a sensitivity of 100% (23/23; 95% 2 CI: 85.2–100) and a specificity of 100% (561/561; 95% CI: 99.3–100). Pooled saliva samples (DSS pool) showed identical results, with 100% sensitivity (23/23; 95% CI: 85.2– 100) and 100% specificity (123/123; 95% CI: 97.1–100).

Conclusion
Saliva collected on Guthrie cards appears to be an accurate and feasible approach for large-scale cCMV screening, with practical advantages and reliable performance even in pooled testing. Urine-based methods demonstrated high specificity but slightly lower sensitivity. Although the number of infected newborns was limited, leading to wide Cis for sensitivity, these preliminary findings are promising. Given the low estimated prevalence of cCMV (around 0.5% in Portugal), population-based studies are required to obtain precise accuracy estimates.

Zeynep Alp Ünkar: Early Prediction of ROP in Preterm Infants: Diagnostic Utility of 6PTC as a Biomarker of Oxidative Stress

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Background
Retinopathy of prematurity (ROP) continues to be one of the most preventable yet serious causes of visual impairment in preterm infants. While current screening methods rely heavily on clinical risk factors and postnatal oxygen exposure, there remains a critical unmet need for early, reliable, and non-invasive biomarkers to predict ROP development before fundoscopic findings emerge.

Methods
In this exploratory prospective pilot study, we employed a targeted metabolomics approach to evaluate the predictive potential of 6-hydroxymethylpterin (6PTC), a pteridine-derived oxidative stress biomarker. Plasma samples were collected from 18 preterm infants (<32 weeks gestation or <1500 g birth weight) on the 14th postnatal day. Quantification was performed using a validated LC-MS/MS protocol. Associations between 6PTC levels and subsequent ROP diagnosis were assessed using appropriate statistical methods, including ROC curve analysis.

Results
Infants who developed ROP (n=5) exhibited significantly higher plasma 6PTC levels compared to those without ROP (p=0.034). Receiver operating characteristic (ROC) analysis demonstrated strong discriminative performance with an AUC of 0.831 (95% CI: 0.640–1.000). The optimal cut-off value (22.45 ng/mL) provided 100% sensitivity and 69% specificity.

Conclusions
Our findings suggest that elevated 6PTC levels on postnatal day 14 may serve as a novel early biomarker for ROP risk stratification. Given the exploratory nature and sample size limitations of this pilot study, these results should be interpreted with caution. Nevertheless, they offer compelling rationale for expanded, multicenter investigations incorporating longitudinal sampling and multimodal predictive modeling. A larger validation study is currently underway.

Heili Varendi: Enteral feeding of very preterm infants – results from the national registry of preterm infants in Estonia

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Background
Early initiation of enteral feeding and rapid progression to full enteral nutrition is one of the priorities in the management of very low gestational age newborns (VLGAN) that reduces the need for central venous catheters, occurrence of nosocomial invasive infections, and the duration of hospitalization.
So, the aim was to analyze enteral feeding in VLGAN in Estonia in 2020–2023: to assess the implementation of the national guideline recommendations (2019), and compare the results with the target values of feeding indicators established during the pre-guideline clinical audit.

Methods
This study used prospectively collected data from the Estonian Health Development Institute's Pregnancy Information System, specifically from the Preterm Infant supplementary Registry, covering all births in Estonia that occurred from 22 and before the end of the 32nd gestational week (GW) in 2020–2023 (a total of 358 VLGA live births) that describe the conditions, investigations, and treatments of these infants until death, discharge, or up to 44 postmenstrual weeks (PMW). Infants with gastrointestinal surgical diseases and malformations that could affect the initiation and progress of enteral feeding were excluded from the analysis. The study assessed the timing of initiation of enteral feeding and the time to reach a volume of 10 ml/kg/24h; the choice of the first feed; the age at achieving full enteral nutrition (defined as 150 ml/kg enterally and/or caloric intake over 110 kcal/kg per day); and the feeding status at hospital discharge. The incidence of necrotizing enterocolitis (NEC) grades II–III and separately of surgical NEC was also examined.

Results
Enteral feeding was initiated at an average age of 5.7 hours (median 4 hours). Feeding was started within the first six hours of life in 82% (286/344) of infants, exceeding the target value of 80%. On the first day of life (DOL), enteral feeding at a volume of 10 ml/kg/day was initiated in 69% of infants, which fell significantly short of the set target of 100%. Feeding was initiated with the mother's own breast milk (BM) in 15%, donor BM in 55%, and formula in 20% of cases, in 10% data were missing. Among the subgroup born before 28 GW (ELGAN): donor BM in 61% (74/122), the mother's own BM in 11%; formula in 14% (14% data missing) - only 72% of ELGAN received any BM that was significantly below the target value of 100%. Transition to full enteral feeding was achieved in ELGAN on average on the 17th DOL (median 12 d), and on the 11th DOL (median 9 d) in those born between 28–31 GW - both later than the targets (14 and 7 days, respectively). NEC grades II and III were recorded in 6.1% (21/344) of infants, including surgical NEC in 4%, which was better than the target values (10% and 5%, respectively). Of the 308 infants discharged from the hospital by 44 PMW, 73.4% received only their mother's BM, whereas ELGAN - 62% (58/94). The target value - set as proportion of infants receiving their mother's breast milk > 50% - was well met.

Conclusion
Initiation of enteral feeding in VLGAN was delayed, and nearly one-third of ELGAN were started on formula feeding. Greater attention must be paid to early optimal enteral nutrition, and in the absence of the mother's own BM, access to donor BM should be ensured for all VLGAN in Estonia at the start of feeding.

Mehmet Vural: Iodine status of Turkish pregnant women and their offspring: A national cross-sectional survey

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Background
This national cross-sectional survey aimed to assess the iodine status in pregnant women and their offspring, and also to demonstrate regional differences by measuring urinary iodine concentration (UIC). For each woman and her newborn a questionnaire was prepared with basic facts as age, parity number or birth weight and additional information regarding thyroid diseases, use of iodized salt in the household, extra iodine supplementation during pregnancy, education level and wage income.

Methods
The target population represented 1444 pregnant women who gave birth between January 1 st, 2018 and 2019, and their offspring. Iodine deficiency for pregnant women and their offspring were defined as urine iodine level <150 µg/L and <100 µg/L, respectively. Results are given as median (25th–75th percentile).

Results
The median UIC in the group of pregnant woman was 94 (52–153) µg/L. Within the sample of 1444 pregnant women, UIC indicative of mild iodine deficiency (100– 149 µg/L) was present in 21 % (n = 306), moderate deficiency (50– 99 µg/L) in 30 % (n = 430), and severe deficiency (<50 µg/L) in 23 % (n = 337). This study showed a prevalence of 74 % of iodine deficiency in Turkish pregnant woman. The median UIC in the group of offspring was 96 (41– 191) µg/L. Within the new-borns, UIC indicative of mild iodine deficiency (50– 99 µg/L) was present in 22 % (n = 323), moderate deficiency (20– 49 µg/L) in 15 % (n = 222), and severe deficiency (<20 µg/L) in 13 % (n = 192). This survey showed a prevalence of 51 % of iodine deficiency in Turkish new-borns. Pregnant women with lower socioeconomic and education level, lower access to household iodized salt, lower rates of exposure to povidone-iodine containing skin disinfectant, higher parity and higher iodine deficiency had higher rates of iodine deficiency in their offspring. Regional differences were observed both in mothers and their offspring concerning their iodine status.

Conclusions
Our findings suggest that iodine deficiency is still an important public health problem in Turkey. More drastic measures should be taken to decrease these important iodine deficiencies, both in pregnant women and in their offspring.

Martin Wald: Recruitment manoeuvre on CPAP, is this new and is it actually possible?

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Background

There is consensus that small premature infants should receive surfactant while breathing spontaneously on CPAP. Despite this less invasive surfactant administration (LISA), the smallest premature infants in particular are often intubated and mechanically ventilated in the first days of life. Such CPAP failure is associated with higher morbidity and mortality. The literature recommends high-frequency CPAP or conventional noninvasive ventilation (nIPPV/nSIPPV) to prevent possible CPAP failure. Our own experience shows that premature infants tolerate shaking CPAP only to a very limited extent and that neither nIPPV nor nSIPPV ventilation sufficiently prevent CPAP failure in our setting. An alternative has been found in the use of a non-invasive open-lung strategy. This involves adequate recruitment of the lungs under CPAP in order to be able to perform CPAP ventilation on the descending arm of the lung hysteresis curve, which describes lung de-recruitment.
The aim of the study was to present initial data on the short-term effects on oxygenation and intubation.

Method

This retrospective data collection included all premature infants with a gestational age of up to 28+0 weeks who were treated in Salzburg between 2019 and 2024. Since 2023, recruitment maneuvers have been performed on these children from day 7 of life if the oxygen requirement under CPAP rises continuously. During the 60-minute recruitment maneuver, the PEEP is rapidly increased by 5 cmH2O, maintained at this level for 30 minutes, and then reduced back to the initial PEEP in three steps. The oxygen saturation index (OSI=CPAPxFiO2x100/SpO2) was measured before, during, and after the first 10 recruitment maneuvers in children who underwent such maneuvers during the study period. In addition, the study investigated whether and how often CPAP failure occurred between the 7th and 21st day of life in children who underwent recruitment maneuvers compared to preterm infants who did not undergo recruitment maneuvers.

Results

During the study period, 115 premature infants with a mean gestational age of 25.6 weeks (±1.4) and a birth weight of 758 g (±215) were treated in Salzburg. Before 2023, 17 of 47 premature infants (36.2%) were intubated between the 7th and 21st day of life; from 2023 onwards, 1 of 15 premature infants were intubated during this period (6.7%) (p=0.103). During the study period, recruitment maneuvers were performed in 11 premature infants (birth weight 561 g (±180.9), gestational age 24,9 weeks (±1.08)) due to a steadily increasing oxygen requirement. A total of 98 recruitment maneuvers were evaluated. The OSI averaged 4.20 (±1.91) before recruitment and 3.69 (±1.69) after recruitment (p<0.001) (FIGURE 1). The data show that the higher the OSI was before recruitment, the greater the reduction in OSI achieved by recruitment (FIGURE 2; r: Pearson correlation coefficient).

Conclusion

Recruitment maneuvers in small preterm infants on CPAP lead to improved oxygenation. The poorer the oxygenation prior to the recruitment maneuver, the more effective the maneuvers were. Since the introduction of recruitment maneuvers, there has been a trend toward fewer CPAP failures. A prospective study is in preparation

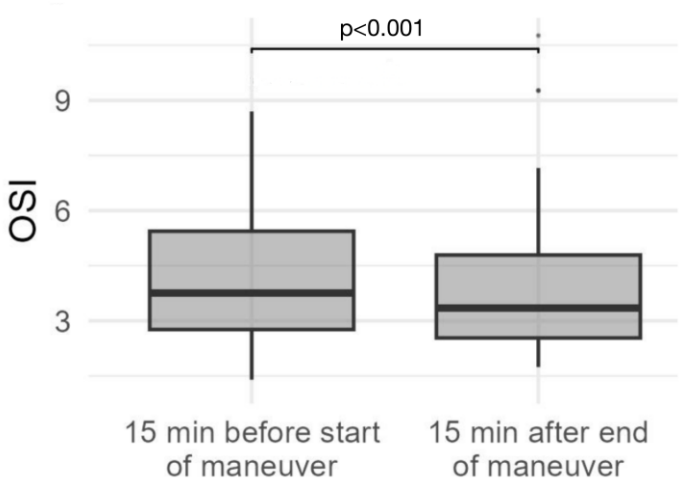

FIGURE 1. The OSI averaged 4.20 (±1.91) before recruitment and 3.69 (±1.69) after recruitment (p<0.001)

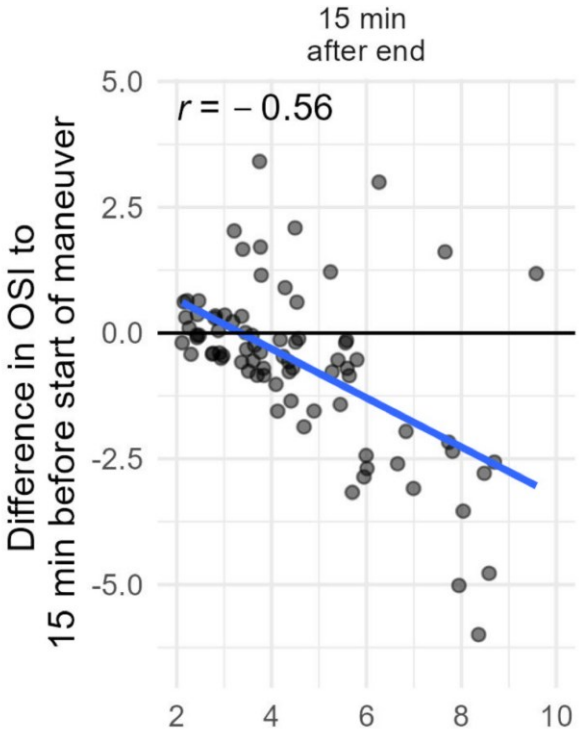

FIGURE 2. The data show that the higher the OSI was before recruitment, the greater the reduction in OSI achieved by recruitment, r: Pearson correlation coefficient

Sven Wellmann: Erythropoiesis-stimulating agents in very preterm infants for improved neurodevelopmental outcome, state-of-the-art of latest clinical research

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Background
Infants born very preterm are at high risk for long-term neurodevelopmental impairment, especially when intraventricular haemorrhage (IVH) occurred. Preclinical studies have gathered compelling evidence that erythropoiesis-stimulating agents such as erythropoietin or darbepoetin protect the developing brain and improve neurodevelopmental outcome.

Methods
Clinical observational studies have supported the positive preclinical findings and paved the way for eight randomized controlled trials (RCT) in very preterm infants to date, with data published from 2004 until 2025. Among them, the EpoRepair trial was the only one that included exclusively patients with confirmed moderate to severe IVH.

Results
In the EpoRepair randomized double-blind clinical trial 121 infants were treated with intravenous high-dose Epo or placebo between April 2014 and August 2018 and all survivors (n=101) were serially assessed for neurodevelopment until 5-6 years of age with final data not published yet. Results of all eight RCTs investigating erythropoiesis-stimulating agents in very preterm infants for improved neurodevelopmental outcome will be presented collectively, including the final EpoRepair data.

Conclusions
The findings of all eight RCTs to date will be discussed and possible conclusions will be drawn.

Cornelia Wiechers: Preterm Infants with Bronchopulmonary Dysplasia: Neurocognitive Development at 2 Years and Body Composition at School Age

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Background
Bronchopulmonary dysplasia (BPD) in preterm infants is associated with impaired growth and delayed neurocognitive development. The aim of this study was to compare former very preterm infants with and without BPD in terms of cognitive outcomes at two years and growth/body composition at school age.

Methods
Children born before 32 weeks of gestation who underwent testing using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) at 2 years of age, and who underwent body composition assessment using air displacement plethysmography at 6–10 years of age, were included in the study. Groups with and without BPD (defined as oxygen requirement at 36 weeks' postmenstrual age) were compared using the Mann–Whitney U test. Multiple linear regression with stepwise backward selection was used to examine the predictors of (i) the Bayley-III Cognitive Composite score and (ii) the fat mass index (FMI) or the fat-free mass index (FFMI). The candidate variables were BPD, sex, gestational age, birth weight z-score and change in weight z-score from birth to discharge. Results are reported as median (Q1–Q3).

Results
A total of 237 former preterm infants were included in the study (median gestational age: 29.4 weeks [27.0–30.9]; median birth weight: 1,130 g [800–1,415]). The median FFMI and FMI at school age were 12.9 (12.1–13.6) kg/m² and 1.95 (0.73–2.89) kg/m², respectively. The Bayley-III Cognitive score was available for 177 children, with a median score of 101.0 (92.0–110.0). BPD was present in 16 children. There were significant differences in anthropometrics at birth between the BPD and non-BPD groups. At school age (median 8.1 [7.0–9.3] years), only head circumference differed. Other anthropometrics and body composition did not differ univariately. In multivariable models, BPD and sex were associated with FFMI (lower FFMI with BPD), while FMI was associated with sex, birth weight z-score and change in weight z-score from birth to discharge. No examined factor, including BPD, was associated with the Bayley-III Cognitive score at two years.

Conclusions
In this cohort of infants born before 32 weeks, BPD was associated with altered anthropometrics at birth and a smaller head circumference at school age, but not with poorer cognitive performance at two years. However, BPD was independently associated with a lower FFMI at school age, highlighting the importance of follow-up informed by body composition and targeted nutritional and rehabilitative strategies.

Lyudmyla Zakharchenko: Delayed Cord Clamping for Preterm Deliveries <32 GA Using "LifeStart" Trolley

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Background
Delayed Cord Clamping (DCC) is an essential part of the stabilisation process for newborns on delivery. By facilitating a placental transfusion, the physiological transition from intrauterine to extrauterine life is supported. DCC has been shown to reduce mortality and morbidity in premature infants. Using the "LifeStart" trolley, a portable bed side resuscitative, the rate of DCC for premature infants will improve.

Objectives
To increase the rate and documentation of DCC in preterm newborns >26/40 and <32/40, by using the "LifeStart" trolley. To facilitate resuscitation and stabilisation of newborns with an intact umbilical cord at delivery. To facilitate a common approach between members of the multidisciplinary team in the management of DCC for preterm infants born at ≤32 weeks' gestational age. To provide education, guidance, and rationale for safe and effective use of the Lifestart Trolley delivering DCC, during initial stabilisation.

Methods
A quality improvement initiative between October 2022 to October 2023. A cohort of premature newborns born >26/40 and <32/40 gestation were eligible for using the "LifeStart" trolley to promote DCC provision.
Results: Demonstrated significant improvement in the documentation of DCC which rose to 97.9% from 51%. Remarkable rise in the number of infants receiving DCC from 49% to 73.1%.

Conclusion
Using the "LifeStart" trolley for DCC demonstrated a significant improvement in documentation practices and an increase in the rate who received DCC in this premature cohort. The Rotunda is the first hospital in Ireland to introduce the "LifeStart" trolley via a quality improvement initiative.
It's crucial to continue encourage for DCC to ensure that all babies received the benefits of DCC.

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