ARTICLES OF INTEREST – February 2023

Proportion of infant neurodevelopment trials reporting a null finding: a systematic review

This study screened 1283 records and included 21 studies; of 18 superiority studies, >70% reported a null finding. This review identifies several features that may contribute to the high proportion of null findings such as selection and timing of the primary outcome measure, anticipated effect size, sample size and power, and statistical analysis methodology and rigor. The authors conclude by making several recommendations for future trials, including more sophisticated approaches to trial design, outcome assessment, and analysis.

Considering antiviral treatment to preserve hearing in congenital CMV

The American Academy of Pediatrics currently recommends either intravenous ganciclovir or oral valganciclovir for infants with moderate to severe symptomatic congenital CMV disease who can start treatment within the first month of life. Despite the American Academy of Pediatrics’ recommendation, antiviral treatment in infants with asymptomatic congenital CMV without clinical findings has grown rapidly in the United States. This article reviews current evidence regarding whether improvements in hearing associated with antiviral treatment persist beyond early childhood, whether infants with symptomatic congenital CMV who have normal hearing and receive antiviral treatment are at lower risk of developing hearing loss, and whether antiviral medication results in hearing preservation in infants with asymptomatic congenital CMV

Umbilical cord milking in nonvigorous infants: a cluster-randomized crossover trial

This was a pragmatic cluster-randomized crossover trial of infants born at 35 to 42 weeks' gestation in 10 medical centers in 3 countries between January 2019 and May 2021. The centers were randomized to umbilical cord milking or early cord clamping for approximately 1 year and then crossed over for an additional year or until the required number of consented subjects was reached. Infants were eligible if nonvigorous at birth (poor tone, pale color, or lack of breathing in the first 15 seconds after birth) and were assigned to umbilical cord milking or early cord clamping according to their birth hospital randomization assignment. Umbilical cord milking did not reduce neonatal intensive care unit admission for predefined criteria. However, infants in the umbilical cord milking arm had higher hemoglobin, received less delivery room cardiorespiratory support, had a lower incidence of moderate-to-severe hypoxic-ischemic encephalopathy, and received less therapeutic hypothermia.
Neonatal hyperoxia induces activated pulmonary cellular states and sex-dependent transcriptomic changes in a model of experimental bronchopulmonary dysplasia

To investigate sex-dependent molecular and cellular programming involved in hyperoxia, these investigators surveyed the mouse lung using single cell RNA sequencing (scRNA-seq), and validated their findings in human neonatal lung cells in vitro. Hyperoxia-induced inflammation in alveolar type (AT) 2 cells gave rise to damage-associated transient progenitors (DATPs). It also induced a new subpopulation of AT1 cells with reduced expression of growth factors normally secreted by AT1 cells, but increased mitochondrial gene expression. Female alveolar epithelial cells had less EMT and pulmonary fibrosis signaling in hyperoxia. In the endothelium, expansion of Car4+ EC (Cap2) was seen in hyperoxia along with an emergent subpopulation of Cap2 with repressed VEGF signaling. This regenerative response was increased in females exposed to hyperoxia. These findings suggest that neonatal exposure to hyperoxia programs distinct sex-specific stem cell progenitor and cellular reparative responses that underpin lung remodeling in BPD.

Comparative efficacy and safety of restrictive versus liberal transfusion thresholds in anemic preterm infants: a meta-analysis of 12 randomized controlled trials

This meta-analysis aimed to compare the efficacy and safety of these restrictive vs. liberal thresholds for anemic preterm infants. Twelve RCTs with 4380 preterm infants were included. Liberal transfusion threshold significantly increased the level of hemoglobin after transfusion (mean difference (MD): -10.03; 95% confidence interval (CI): -15.98 to -4.08; p=0.001; I²=94%) and hematocrit (MD: -3.62; 95%CI: -6.78 to -0.46; p=0.02; I²=80%) compared with restrictive transfusion. Infants&93; age at first transfusion in restrictive transfusion group was higher than that of infants in liberal transfusion group (MD: 5.08; 95%CI: 2.27 to 7.89; p=0.004; I²=54%); however, restrictive transfusion was associated with more time on supplemental oxygen (MD: 3.56; 95%CI: 1.93 to 5.18; p&lt;0.001; I²=62%) and ventilator or CPAP (MD: 3.31; 95%CI: 1.42 to 5.20; p=0.006; I²=75%). Evidence with substantial heterogeneity indicates that liberal and restrictive transfusion thresholds are effective and safe blood cell transfusion strategies in anemic preterm infants, but the liberal strategy may be more effective in shortening the length of necessary respiratory support.

A prospective, longitudinal, case–control study to evaluate the neurodevelopment of children from birth to adolescence exposed to COVID-19 in utero

This paper outlines the designs and methodology for a prospective, case-controlled study aimed to investigate the long-term impacts of SARS-CoV2 exposure on children exposed in utero. Women infected with SARS-CoV-2 during pregnancy are being recruited from two centers in Melbourne, Australia and Londrina, Brazil. Cases are matched 2:1 with women who gave birth in the same month of delivery, are of similar age but did not contract SARS-CoV-2 during their pregnancy. The study aims to collect developmental data at various time-points from birth to 15 years of life as well as biospecimens.

Cerebral regional tissue Oxygen Saturation to Guide Oxygen Delivery in preterm neonates during immediate transition after birth (COSGOD III): multicentre randomised phase 3 clinical trial.
Gerhard Pichler, Katharina Goeral, Marlene Hammerl, et al. BMJ.

This multicenter randomized controlled phase 3 trial assessed whether monitoring of cerebral tissue oxygen saturation using near infrared spectroscopy in addition to routine monitoring combined with defined treatment guidelines during immediate transition and resuscitation increases survival without
Neonates were randomly assigned to either standard care or standard care plus monitoring of cerebral oxygen saturation with a dedicated treatment guideline during immediate transition (first 15 minutes after birth) and resuscitation. The primary outcome was a composite of survival without cerebral injury. In the near infrared spectroscopy, delivery room Fio2 was titrated based on cerebral regional tissue oxygen saturation (crSO2) in addition to SpO2. 607 infants (304 and 303, respectively) were included in the final analysis. The incidence of delivery room interventions within the first 15 minutes after birth did not differ between the groups except for a significantly higher number of neonates receiving intravenous fluids in the near infrared spectroscopy group (12 (4.0%) v 2 (0.7%), P=0.007; table 2). CrSO2 values at each minute during the first 15 minutes after birth did not differ between the groups. FiO2 was slightly higher in the near infrared spectroscopy group than control group in the first minutes after birth, and SpO2 values during the first 15 minutes after birth were similar in both groups. Overall, 252 (82.9%) out of 304 neonates in the near infrared spectroscopy group survived without cerebral injury compared with 238 (78.5%) out of 303 in the control group (relative risk 1.06, 95% confidence interval 0.98 to 1.14). Monitoring of cerebral tissue oxygen saturation in combination with dedicated interventions in preterm neonates (<32 weeks’ gestation) during immediate transition and resuscitation after birth did not result in substantially higher survival without cerebral injury compared with standard care alone.

The utility of serial echocardiography parameters in management of newborns with congenital diaphragmatic hernia (CDH) and predictors of mortality

Ventricular dysfunction may be found in 40% of newborns with CDH, and is not only a predictor of disease severity, but also mortality and need for ECMO. In this retrospective study the authors sought to assess the utility of serial echocardiography in the management of 42 newborns with CDH and their survival outcomes. Markers of elevated pulmonary pressures and cardiac function were useful in guiding therapy. Serial timed functional echocardiography (f-Echo) monitoring allows targeted therapy of patients with CDH. Birth weight, initial severity of pulmonary hypertension and postoperative RSS and VIS may be useful in predicting mortality.

Development of a bedside tool to predict the diagnosis of cerebral palsy in term-born neonates

Cerebral palsy (CP) is the most common abnormality of motor development and causes lifelong impairment. Early diagnosis and therapy can improve outcomes, but early identification of infants at risk remains challenging. In this case-controlled study using data from the Canadian Cerebral Palsy Registry, the authors sought to develop a CP prognostic tool that can be applied to all term neonates to identify those at increased risk of developing CP. They found that a prognostic model using 12 clinical variables improved the prediction of CP compared with clinical presentation with encephalopathy. This tool can be applied to all term newborns to help select infants for closer surveillance or further diagnostic tests, which could improve outcomes through early intervention.

Postnatal CMV infection and antiviral treatment in extremely premature infants: a 12-year retrospective analysis

This is a single center retrospective study to assess the treatment outcomes of postnatal CMV infection. Infants <29 weeks gestational age were included. CMV infected infants were compared to uninfected infants (control). Within the CMV infected infants, the two subgroups were those treated with ganciclovir and/or valganciclovir (CMVPT group) or no treatment (CMVPNT group). The primary outcomes assessed were length of stay, death before discharge and hearing impairment, cognitive and motor development as assessed by the Denver Developmental Screening Test II, and neurologic
impairment at the corrected age of 1.5-2 years. The study found that the associations between antiviral treatment of postnatal CMV infection and better treatment outcomes were nonsignificant.

**Association between perivable delivery and new onset of or exacerbation of existing mental health disorders**

This is a retrospective cohort study to evaluate whether there is an association between perivable delivery and new onset of or exacerbation of existing mental health disorders within 12 months postpartum. The study included individuals with liveborn singleton neonates delivered at perivable period of 22 0/7 to 25 6/7 weeks gestation. The primary outcome was a mental health morbidity composite of one or more of the following: ED encounter a/w depression, anxiety, psychosis, posttraumatic stress disorder, adjustment disorder, self-harm, or suicide; new psychotropic medication prescription; new behavioral therapy; and inpatient psychiatry admission in the 12 months postdelivery. The study found that individuals with perivable delivery were more likely to have a chronic health condition, to have undergone cesarean delivery, and to have experienced severe maternal morbidity. The highest-risk period was the first 90 days. Overall, perivable delivery was associated with a modestly increased risk of mental health morbidity in the 12 months postpartum.

**OTHER NOTEWORTHY ARTICLES – February, 2023**

**COVID-19**
Undetected fetal growth restriction during the coronavirus disease 2019 (COVID-19) pandemic

Maternal mRNA COVID-19 vaccination during pregnancy and delta or omicron infection or hospital admission in infants: test negative design study

Protecting breastfeeding during the COVID-19 pandemic

Maternal and newborn hospital outcomes of perinatal SARS-CoV-2 infection: a national registry
[https://publications.aap.org/pediatrics/article/151/2/e2022059595/190431/](https://publications.aap.org/pediatrics/article/151/2/e2022059595/190431/)

Reducing MRSA infection in a new NICU during the COVID-19 pandemic

**Pediatrics**
Maternal-and-newborn-hospital-outcomes-of racial inequity in high-risk infant follow-up among extremely low birth weight infants

Fever, absolute neutrophil count, procalcitonin, and the AAP febrile infant guidelines

Considering antiviral treatment to preserve hearing in congenital CMV

Prevalence and predictors of breastfeeding duration of 24 or more months

Proportion of infant neurodevelopment trials reporting a null finding: a systematic review
2022 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations: summary from the basic life support; advanced life support; pediatric life support; neonatal life support; education, implementation, and teams; and first aid task forces

Recommended guideline for uniform reporting of neonatal resuscitation: the neonatal utstein style

Propranolol therapy for congenital chylothorax
Archives of Disease in Childhood - Fetal & Neonatal Edition
Caffeine to prevent intermittent hypoxaemia in late preterm infants: randomised controlled dosage trial
Early-onset neonatal sepsis in the Paris area: a population-based surveillance study from 2019 to 2021
Outcome at 4.5 years after dextrose gel treatment of hypoglycaemia: follow-up of the Sugar Babies randomised trial
Low dose paracetamol for management of patent ductus arteriosus in very preterm infants: a randomised non-inferiority trial
Automatic oxygen control for reducing extremes of oxygen saturation: a randomised controlled trial
Bronchopulmonary dysplasia and neurobehavioural outcomes at birth and 2 years in infants born before 30 weeks
Growth trajectory during the first 1000 days and later overweight in very preterm infants
Laryngeal mask airway versus face mask ventilation or intubation for neonatal resuscitation in low- and-middle-income countries: a systematic review and meta-analysis
Sociodemographic risk factors, parental stress and social support in the neonatal intensive care unit
Lung volume changes during apnoeas in preterm infants
Immunoreactive trypsinogen in healthy newborns and infants with cystic fibrosis
Management of pneumothorax in neonatal retrieval: a retrospective cohort study
Use of ventilation/perfusion mismatch to guide individualised CPAP level selection in preterm infants: a feasibility trial
Views of parents, adults born preterm and professionals on linkage of real-world data of preterm babies

Journal of Perinatology
Chorionicity and neurodevelopmental outcomes in twin pregnancy: a systematic review and meta-analysis
Perinatal and neonatal outcomes for fetoscopic laser ablation for the treatment of twin twin transfusion syndrome at a single center
Association of placental histology and neonatal hematologic outcomes
Arterial pressure is not reflective of right ventricular function in neonates with hypoxic ischemic encephalopathy treated with therapeutic hypothermia

The use of milrinone in neonates with persistent pulmonary hypertension of the newborn - a randomised controlled trial pilot study (MINT 1)

The biventricular contribution to chronic pulmonary hypertension of the extremely premature infant

Hospital variation in neonatal echocardiography among very preterm infants at US children’s hospitals

Cardiac morphology in neonates with fetal growth restriction

Cannulation approach and mortality in neonatal ECMO

The dilemma of feeding during the treatment of patent ductus arteriosus with oral ibuprofen in preterm infants ≤30 weeks of gestation—a randomized controlled trial

Prediction of extubation failure among low birthweight neonates using machine learning

A tiny baby intubation team improves endotracheal intubation success rate but decreases residents’ training opportunities
https://www.ncbi.nlm.nih.gov/pubmed/36309565

Transcutaneous bilirubin levels in extremely preterm infants less than 30 weeks gestation

Fresh frozen plasma and cryoprecipitate: Can we safely reduce their use in the NICU?

Neonatology
No new articles

American Journal of Perinatology
General versus regional anesthesia and neonatal data: a propensity-score-matched study

Glucose testing in an index pregnancy and outcomes in a subsequent pregnancy: implications for screening and a novel risk calculator

Reading aloud with infants in the neonatal intensive care unit: a unit-based program to enhance language enrichment and support early foundational relationships

A randomized controlled trial on the effect of standardized video education on prenatal genetic testing choices: uptake of genetic testing

The association between the number of vacuum pop-offs and adverse neonatal outcomes

Unexpected term neonatal intensive care unit admissions and a potential role for centralized remote fetal monitoring

Comparison of maternal and neonatal subspecialty care provision by hospital

Journal of Neonatal-Perinatal Medicine
No new content
Maternal Health, Neonatology and Perinatology
Addressing ethical issues related to prenatal diagnostic procedures (PDF)

Neoreviews
History of neonatal resuscitation: from uncivilized to evidence-based practices
Minimally invasive fetal surgery and the next frontier
Surgical management of congenital lung malformations
Abdominal surgical emergencies in neonates
Respiratory failure in an infant with known congenital anomalies and novel genetic defect
Pneumoperitoneum in a small-for-gestational age preterm infant
A rare case of neonatal oral tumor
A fungating mass in pregnancy: maternal management and neonatal implications
Late preterm infant presenting with petechiae
Two severely edematous infants with local area of drainage

JAMA Pediatrics
New screening tool for term-born infants enables update to the clinical practice guideline for early diagnosis of cerebral palsy
Obstetric and perinatal outcomes of singleton births following single- vs double-embryo transfer in Sweden
Development of a bedside tool to predict the diagnosis of cerebral palsy in term-born neonates

BMC Pediatrics
The relationship between hematological indices as indicators of inflammation and 25-hydroxyvitamin D3 status in newborns
Awareness and diagnosis for intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) in neonatal (NICU) and pediatric intensive care units (PICU) – a follow-up multicenter survey
Survey on human milk feeding and enteral feeding practices for very-low-birth-weight infants in NICUs in China Neonatal Network
Development a prediction model for identifying bacterial meningitis in young infants aged 29–90 days: a retrospective analysis
A neonate with multiple hand flexor tendon ruptures due to methicillin-susceptible Staphylococcus aureus sepsis: a case report

**Pediatric Critical Care Medicine**
Timing of tracheostomy in critically ill infants and children with respiratory failure: a pediatric health information system study
The use and impact of diaries in PICUS and neonatal ICUS: a scoping review

**New England Journal of Medicine**
No relevant articles

**Lancet**
Marketing of commercial milk formula: a system to capture parents, communities, science, and policy
Breastfeeding: crucially important, but increasingly challenged in a market-driven world
Congenital adrenal hyperplasia

**JAMA**
No relevant articles

**BMJ**
Health and nutrition claims for infant formula: international cross sectional survey

**Pediatric Infectious Disease Journal**
Serratia infection epidemiology among very preterm infants in the neonatal intensive care unit
Postnatal CMV Infection and antiviral treatment in extremely premature infants: a 12-year retrospective analysis

**Pediatric Cardiology**
What is known about critical congenital heart disease diagnosis and management experiences from the perspectives of family and healthcare providers? A systematic integrative literature review
Octreotide for acquired chylothorax in pediatric patients post-cardiothoracic surgery for congenital heart disease: a systematic review
Pulmonary venous gradients in healthy controls and following the repair of total anomalous pulmonary venous return
The utility of serial echocardiography parameters in management of newborns with congenital diaphragmatic hernia (CDH) and predictors of mortality
Ectopic atrial tachycardia in infants following congenital heart disease surgery
Gabapentin can improve irritability and feeding tolerance in single ventricle interstage patients: a case series

**Pediatric Neurology**
Paroxysmal tonic upgaze in a patient with congenital ataxia due to a de novo missense variant of CACNA1G
Neonatal arterial ischemic stroke secondary to carotid artery dissection: a case report and systematic literature review
The utility of simulation-based training in teaching frontline providers modified sarnat encephalopathy examination: a randomized controlled pilot trial

**Obstetrics and Gynecology**
Association between periviable delivery and new onset of or exacerbation of existing mental health disorders

**American Journal of Obstetrics & Gynecology**
Updating the balance between benefits and harms of antenatal corticosteroids
Prenatal exome and genome sequencing for fetal structural abnormalities
Umbilical cord milking in nonvigorous infants: a cluster-randomized crossover trial
The cardiac-fetal-placental unit: fetal umbilical vein flow rate is linked to the maternal cardiac profile in fetal growth restriction
Associations between provider-assigned Apgar score and neonatal race
Placental delayed villous maturation is associated with fetal congenital heart disease

**Hospital Pediatrics**
Variation in NICU head CT utilization among U.S. children’s hospitals

**BASIC SCIENCE SELECTIONS**
Screening inflammatory protein biomarkers on premature infants with necrotizing enterocolitis
Preterm rabbit-derived Precision Cut Lung Slices as alternative model of bronchopulmonary dysplasia in preclinical study: a morphological fine-tuning approach
Sexual dimorphic vulnerability of respiratory control in a neonatal rodent model of fetal alcohol spectrum disorder
Therapeutic hypothermia demonstrates sex-dependent improvements in motor function in a rat model of neonatal hypoxic ischemic encephalopathy
Downregulation of TRIM27 alleviates hypoxic-ischemic encephalopathy through inhibiting inflammation and microglia cell activation by regulating STAT3/HMGB1 axis
Neonatal overnutrition, but not neonatal undernutrition, disrupts CCK-induced hypophagia and neuron activation of the nucleus of the solitary tract and paraventricular nucleus of hypothalamus of male Wistar rats

Neonatal hyperoxia induces activated pulmonary cellular states and sex-dependent transcriptomic changes in a model of experimental bronchopulmonary dysplasia

**ADDITIONAL JOURNAL SELECTIONS**

Comparative efficacy and safety of restrictive versus liberal transfusion thresholds in anemic preterm infants: a meta-analysis of 12 randomized controlled trials

Capnometry during neonatal transport - mini review

Glucose-to-lactate ratio and neurodevelopment in infants with hypoxic-ischemic encephalopathy: an observational study

The dilemma of feeding during the treatment of patent ductus arteriosus with oral ibuprofen in preterm infants <=30 weeks of gestation-a randomized controlled trial

Considerations for practice in supporting parental bereavement in the neonatal intensive care unit-a systematic review

Safety of performing classical versus low transverse caesarean sections in extremely preterm and very preterm births: Maternal and neonatal complications

Comparison of lung ultrasound scores with clinical models for predicting bronchopulmonary dysplasia

Effects of erythropoietin in neonates with hypoxic-ischemic encephalopathy receiving therapeutic hypothermia

Identification of genetic susceptibility in preterm newborns with bronchopulmonary dysplasia by whole-exome sequencing: BIVM gene may play a role

Late-onset sepsis mortality among preterm infants: beyond time to first antibiotics

Accuracy of lung and diaphragm ultrasound in predicting successful extubation in extremely preterm infants: A prospective observational study

Two-year outcomes following a randomised platelet transfusion trial in preterm infants

Association between gastrointestinal perforation and patent ductus arteriosus in extremely-low-birth-weight infants: a retrospective study of our decade-long experience

Characteristics of babies with unstable clinical course screened for retinopathy of prematurity

Physical activity levels, pulmonary function, and MRI in children born extremely preterm: A comparison between children with and without bronchopulmonary dysplasia

Probiotics to prevent necrotizing enterocolitis and reduce mortality in neonates: A meta-analysis
A review of the genomics of neonatal abstinence syndrome