For abstracts or full text of the evidence in the update please click on the hyperlinks within the update. If full text is not available please Click here to request a copy. You will need to be a member of the Library to access this service. You can join the library online via: http://www.porthosp.nhs.uk/Library/join-the-library.htm. You may be required to log in using your NHS Athens username and password. If you don’t have one, please log on to Openathens Registration and register for free. Back issues of the Evidence Updates are available on the PHT Library Website: http://www.porthosp.nhs.uk/Library/evidence-updates.htm

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To access app on iPhone visit iTunes App Store – (personal devices only) https://itunes.apple.com/gb/app/bnf-publications/id1045514038?mt=8
Developmental follow-up of children and young people born preterm – guidance (NG72)
This guideline covers the developmental follow-up of babies, children and young people <18yrs who were born preterm (<37 weeks of pregnancy). It explains the risk of different developmental problems and disorders, and specifies what extra assessments and support might be needed.

Asfotase alfa for treating paediatric-onset hypophosphatasia – guidance (HST6)
NICE recommends asfotase alfa as an option for paediatric-onset hypophosphatasia, restricted to use in people who meet the criteria of a set managed access arrangement.

BRIGHTON AND SUSSEX UNIVERSITY HOSPITALS NHS TRUST
Sepsis: 60 minutes to save a life
Summary: This guide outlines the 6 factors that have been shown to improve outcomes for patients and should be completed within the first hour following recognition of sepsis. Click to view

BRIGHTENED ASSOCIATION OF PERINATAL MEDICINE
Identification and Management of Neonatal Hypoglycaemia in the Full Term Infant – A Framework for Practice
The British Association of Perinatal Medicine (BAPM) has worked with stakeholders and in collaboration with UNICEF-Baby Friendly Initiative to develop this framework, as part of their programme to reduce admissions of full term babies to neonatal units. Click to view

PUBLIC HEALTH ENGLAND
Screening consultation on rare but serious condition in babies
Summary: The UK’s independent screening committee has launched a consultation to look at whether screening for Severe Combined Immune Deficiency (SCID) in babies should be tried within the NHS. SCID is a rare inherited condition which makes it difficult for babies to fight infection. Click to view

Baby at risk of having thalassaemia: description in brief
Summary: This updated patient information leaflet explains the risks for a foetus when both parents carry an unusual haemoglobin gene, at least one of which is for thalassaemia. Click to view

SPECIALIST PHARMACY SERVICE
Drug-induced hypersalivation – what treatment options are available?
Summary: This Medicines Q&A has recently been updated. It summarises published studies or case reports concerning the pharmacological treatment of drug-induced hypersalivation (drooling or sialorrhoea), particularly hypersalivation caused by clozapine. Click to view

Hypersalivation – what drug treatment options are available?
Summary: This updated document is one of a series of five Q&A documents to address the drug treatment of hypersalivation (drooling or sialorrhoea). It gives a general description of the pharmacological options that may be considered for the management of non drug-induced hypersalivation. Click to view

Hypersalivation – can hyoscine hydrobromide be used to treat it?
Summary: This Medicines Q&A has recently been updated. It evaluates the available evidence for the use of hyoscine hydrobromide for the management of non drug-induced hypersalivation. Click to view

Does randomized controlled trial evidence support early administration of inhaled corticosteroids for preventing chronic lung disease in ventilated very low birth weight preterm neonates? Click to view answer

What are the effects of nitric oxide in infants born at or near term with respiratory failure? Click to view answer

What are the benefits and harms of inhaled nitric oxide for preterm infants with respiratory failure? Click to view answer

Enteral lactoferrin supplementation for prevention of sepsis and necrotizing enterocolitis in preterm infants

Authors' conclusions: Evidence of low quality suggests that lactoferrin supplementation to enteral feeds with or without probiotics decreases late-onset sepsis and NEC stage II or III in preterm infants without adverse effects. Completed ongoing trials will provide data from more than 6000 preterm neonates, which may enhance the quality of the evidence. Clarification regarding optimal dosing regimens, types of lactoferrin (human or bovine), and long-term outcomes is needed.

Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes Online Publication Date: July 2017

Authors' conclusions: Sustained inflation was not better than intermittent ventilation for reducing mortality in the delivery room and during hospitalisation. The number of events across trials was limited, so differences cannot be excluded. When considering secondary outcomes, such as need for intubation, need for or duration of respiratory support, or bronchopulmonary dysplasia, we found no evidence of relevant benefit for sustained inflation over intermittent ventilation. The duration of mechanical ventilation was shortened in the SLI group. This result should be interpreted cautiously, as it can be influenced by study characteristics other than the intervention. Future RCTs should aim to enrol infants who are at higher risk of morbidity and mortality, should stratify participants by gestational age, and should provide more detailed monitoring of the procedure, including measurements of lung volume and presence of apnoea before or during the SLI.

Saline irrigation for the management of skin extravasation injury in neonates. Online Publication Date: July 2017

Authors' conclusions: To date, no RCTs have examined the effects of saline irrigation with or without prior hyaluronidase infiltration for management of extravasation injury in neonates. Saline irrigation is frequently reported in the literature as an intervention for management of extravasation injury in neonates. Research should focus first on evaluating the efficacy and safety of this intervention through RCTs. It will also be important for investigators to determine effect size by examining the timing of the intervention, the nature of the infusate, and severity of injury at the time of intervention.

Fluid supplementation for neonatal unconjugated hyperbilirubinaemia. Online Publication Date: August 2017
Authors' conclusions: There is no evidence that IV fluid supplementation affects important clinical outcomes such as bilirubin encephalopathy, kernicterus, or cerebral palsy in healthy, term newborn infants with unconjugated hyperbilirubinaemia requiring phototherapy. In this review, no infant developed these bilirubin-associated clinical complications. Low- to moderate-quality evidence shows that there are differences in total serum bilirubin levels between fluid-supplemented and control groups at some time points but not at others, the clinical significance of which is uncertain. There is no evidence of a difference between the effectiveness of IV and oral fluid supplementations in reducing serum bilirubin. Similarly, no infant developed adverse events or complications from fluid supplementation such as vomiting or abdominal distension. This suggests a need for future research to focus on different population groups with possibly higher baseline risks of bilirubin-related neurological complications, such as preterm or low birthweight infants, infants with haemolytic hyperbilirubinaemia, as well as infants with dehydration for comparison of different fluid supplementation regimen.

Late (≥ 7 days) inhalation corticosteroids to reduce bronchopulmonary dysplasia in preterm infants. Online Publication Date: August 2017

Authors' conclusions: Based on the results of the currently available evidence, inhalation corticosteroids initiated at ≥ 7 days of life for preterm infants at high risk of developing BPD cannot be recommended at this point in time. More and larger randomised, placebo-controlled trials are needed to establish the efficacy and safety of inhalation corticosteroids.

Slow advancement of enteral feed volumes to prevent necrotising enterocolitis in very low birth weight infants. Online Publication Date: August 2017

Authors' conclusions: Available trial data do not provide evidence that advancing enteral feed volumes at daily increments of 15 to 20 mL/kg (compared with 30 to 40 mL/kg) reduces the risk of NEC or death in very preterm or VLBW infants, extremely preterm or ELBW infants, SGA or growth-restricted infants, or infants with antenatal AREDFV. Advancing the volume of enteral feeds at a slow rate results in several days of delay in establishing full enteral feeds and may increase the risk of invasive infection.

SYSTEMATIC REVIEWS FROM OTHER SOURCES

Click on titles to view

Role of oral zinc supplementation for reduction of neonatal hyperbilirubinemia: a systematic review of current evidence.
Conclusions: Role of zinc in the prevention of neonatal hyperbilirubinemia is not supported by the current evidence. Only one study was able to show reduction in the mean TSB level and requirement of phototherapy with zinc, and the remaining studies did not report any positive effect. None of the studies showed any effect on the duration of phototherapy, incidence of phototherapy, age of starting of phototherapy and any serious adverse effect

Role of lactoferrin in neonatal care: a systematic review.
Conclusions: LF has shown to be promising agent for reduction of LOS and NEC. The role of LF in prevention of neonatal mortality, BPD, and ROP needs further studies. The trials that are going on around the world may be able to give reply of this question in future.

Role of amino acid supplementation in the prevention of necrotizing enterocolitis in preterm neonates - a review of current evidences.
Conclusions: Role of amino acid in the prevention of neonatal NEC is not exclusively supported by the current evidence. Only three studies were able to show reduction in the incidence of NEC with amino acid supplementation (arginine, glutamine), and the remaining studies did not report any positive effect. Amino acid supplementation was not associated with significant reduction in mortality due to any causes. However, arginine supplementation was associated with significant reduction in mortality due to NEC. Two studies on glutamine were reported significant reduction in the incidence of invasive infection. Only one study reported significant positive effects on growth parameters and less time to reach full enteral feeds. None of the studies showed any effect on the duration of hospital stay.

Prenatal, perinatal and neonatal risk factors for perinatal arterial ischaemic stroke: a systematic review and meta-analysis.
Summary: This systemic review and meta-analysis provides a preliminary evidence-based assessment of the risk factors for PAIS. Patients with any of the risk factors identified in this analysis should be given careful consideration to ensure the
prevention of PAIS. Future studies focusing on the combined effects of multiple prenatal, perinatal and neonatal risk factors for PAIS are warranted.

**Parental perceptions of hypothermia treatment for neonatal hypoxic-ischaemic encephalopathy.**

**Conclusions:** Parents were worried about pain and distress, bonding and about outcomes after HT. Consistency in communication, regular updates, involvement of parents in decision making, strong support mechanisms and balanced discussions about long term outcomes at an early stage are of high importance to families whose babies undergo HT.

**Systematic Review and Meta-analysis: Gene Association Studies in Neonatal Sepsis.**

**Authors’ conclusions:** We uncovered an association between IL-10 1082 gene variation and sepsis in VLBW infants but did not identify associations between neonatal sepsis and TNF-α 308 or IL-6 gene variation. Larger cohort replication studies are required to validate these findings.

**American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock.**

**Conclusions:** The major new recommendation in the 2014 update is consideration of institution-specific use of 1) a “recognition bundle” containing a trigger tool for rapid identification of patients with septic shock, 2) a “resuscitation and stabilization bundle” to help adherence to best practice principles, and 3) a “performance bundle” to identify and overcome perceived barriers to the pursuit of best practice principles.

**Antimicrobial-resistant Gram-negative infections in neonates: burden of disease and challenges in treatment.**

**Summary:** Improved global neonatal AMR surveillance programmes including both epidemiology and clinical outcomes are critical for defining the burden and designing interventions. The optimal empiric treatment for neonatal sepsis in settings of high rates of AMR is currently unknown. Both strategic trials of older antibiotics and regulatory trials of new antibiotics are required to improve clinical outcomes in MDR-Gram-negative neonatal sepsis.

**Physiological effects of prebiotics and its role in prevention of necrotising enterocolitis in preterm neonates.**

**Summary:** Prebiotics may be potential alternatives or adjunctive therapies to probiotics, despite a lack of evidence supporting its clinical efficacy in prevention of NEC. In this article, the authors discuss evidence-based physiological effects of prebiotics and its therapeutic role in prevention of NEC.

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**PRIMARY RESEARCH**

**Title: Homecare and Healthcare Utilization Errors Post–Neonatal Intensive Care Unit Discharge**

**Citation:** Advances in Neonatal Care: August 2017 - Volume 17 - Issue 4 - p 258–264

**Implications of Practice:** High-risk infants have complex care needs and can benefit from regular follow-up services. Home visits provide an opportunity to identify, intervene, and resolve homecare and healthcare utilization errors. [Click to view](#)

**Title: Risk of neonatal drug withdrawal after intrauterine co-exposure to opioids and psychotropic medications: cohort study.**

**Citation:** BMJ. 2017 Aug 2;358:j3326. doi: 10.1136/bmj.j3326.

**Conclusions:** During pregnancy, the use of psychotropic medications in addition to prescription opioids is common, despite a lack of safety data. The current findings suggest that these drugs could further increase the risk and severity of neonatal drug withdrawal. [Click to view](#)

**Title: The effects of enteral feeding improvement massage on premature infants: A randomised controlled trial.**

**Citation:** J Clin Nurs. 2017 Apr 17. doi: 10.1111/jocn.13850

**Conclusions:** This study demonstrates that enteral feeding improvement massage can be helpful for achieving earlier full enteral feeding, more increased superior mesentery artery, and faster growing. In particular, it can be a therapeutic, independent and evidence-based nursing intervention for feeding-intolerant premature infants.

**RELEVANCE TO CLINICAL PRACTICE:** Neonatal nurses in neonatal intensive care unit can apply enteral feeding improvement massage for feeding-intolerant infants. [Click to view](#)

**Title: Effect of Depth and Duration of Cooling on Death or Disability at Age 18 Months Among Neonates With Hypoxic-Ischemic Encephalopathy: A Randomized Clinical Trial**

**Citation:** JAMA. 2017 Jul 4;318(1):57-67. doi: 10.1001/jama.2017.7218
Conclusions: Among term neonates with moderate or severe hypoxic-ischemic encephalopathy, cooling for longer than 72 hours, cooling to lower than 33.5°C, or both did not reduce death or moderate or severe disability at 18 months of age. However, the trial may be underpowered, and an interaction was found between longer and deeper cooling. These results support the current regimen of cooling for 72 hours at 33.5°C. Click to view

Title: Towards evidence-based resuscitation of the newborn infant
Citation: The Lancet
Summary: This is the first in a Series of 3 papers about neonatal intensive care. This paper highlights some important advances in the understanding of how best to resuscitate newborn infants, which include monitoring techniques and increasing awareness of the adverse effects of hyperoxia. Click to view

Title: The evolution of modern respiratory care for preterm infants
Citation: The Lancet
Summary: This is the second in a Series of 3 papers about neonatal intensive care. This paper reviews the history of neonatal respiratory care and its effect on long-term outcomes, and outlines the future direction of research in this area. Click to view

Title: Advances in nutrition of the newborn
Citation: Lancet
Summary: This is the third in a Series of 3 papers about neonatal intensive care. This paper focusses on advances and controversies in nutrition of preterm infants but also briefly mentions some aspects of nutrition of infants born at term that pose challenges to clinicians and families. Click to view

Title: Neurodevelopmental Follow-Up After Early Low-Dose Hydrocortisone in Extremely Preterm Infants.
Citation: Robin Steinhorn, MD reviewing Baud O et al. JAMA 2017 Apr 4. Marlow N. JAMA 2017 Apr 4.
Summary: Low-dose hydrocortisone improves bronchopulmonary dysplasia-free survival in extremely preterm babies, without neurodevelopmental sequelae.
Comment: These findings provide important reassurance that prophylactic low-dose hydrocortisone during the first 10 days of life improves outcomes for extremely preterm infants without increasing risk for neurodevelopmental impairment. Given the risks reported in prior studies of steroids administered in alternate forms, in higher doses, or in combination with nonsteroidal anti-inflammatory drugs, the PREMILOC results should be interpreted with caution until they are replicated. Click to view

Title: Procalcitonin-guided decision making for duration of antibiotic therapy in neonates with suspected early-onset sepsis: a multicentre, randomised controlled trial (NeoPIns)
Citation: The Lancet
Summary: RCT (n=1710) found procalcitonin-guided decision making was superior to standard care in reducing duration of antibiotic therapy in neonates with suspected early-onset sepsis (55.1 vs 65 hours, p<0.0001). Non-inferiority for re-infection/death could not be established.
UKMi comment: A commentary notes that although far from being a perfect marker, procalcitonin is the most reliable of the currently known circulating markers of systemic bacterial infections (sepsis). It highlights that procalcitonin-guided antibiotic de-escalation therapy is evidence-based and state-of-the-art for antibiotic therapy for suspected and proven bacterial infection in different clinical settings and different acuity of infections; It adds now there is an evidence base for all age groups, from neonates to centennials. Click to view

Title: Infant's Severe Bacterial Infection Is Traced to Contaminated Breast Pump
Citation: By Cara Adler Edited by - Andre Sofair, MD, MPH, and- William E. Chavez, MD, MS
Summary: The authors recommend, "Clinicians should provide detailed recommendations about hygienic expression and handling of human milk to parents who plan to feed [expressed maternal milk] to their infants." Click to view

Title: Neonatal Tremors Caused by Vitamin D Deficiency
Citation: Louis M. Bell, MD reviewing Collins M and Young M. Pediatrics 2017 Jul 26.
Summary: In a case report of two patients, neonatal shivers or tremors were most likely due to vitamin D deficiency.
Comment: I usually avoid reviewing case reports but decided to do so after reading the details of the first case and the thorough work-up that was completed. The second case was a bit less compelling. However, given the right context (e.g., exclusive breast-feeding and/or lack of prenatal care) and persistent or worsening tremors or shuddering lasting beyond the first few days of life, I will now consider vitamin D deficiency in my differential diagnosis. Click to view

Title: Rethinking the Value of Noninvasive Ventilation
**Summary:** Higher rates of noninvasive ventilation in extremely preterm infants did not translate into improved lung function at age 8.

**Comment:** One would have expected to see long-term improvements in lung function with the adoption of noninvasive ventilation techniques, but this did not occur. The rate of bronchopulmonary dysplasia (oxygen use at 36 weeks postmenstrual age) was higher in the 2005 cohort, which may indicate that this short-term marker of lung function has longer-term predictive value. It is important to note that while the forced expiratory volumes in the 8-year-olds did not improve between periods 1991 to 1992 and 2005, all three groups had volumes in the low normal range for their age and height. However, these data also indicate that the shift to noninvasive ventilation techniques was not associated with improved long-term respiratory function. Long-term studies are challenging to do in these populations, yet these results should encourage.

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**Title:** Incorporating Relationship-Based Care Into a Nurse Education Program for Managing Disruptive Patient Behaviors.

**Author(s):** Lee, Betty; Del Rosario, Kristian; Byron-Iyamah, Cecily

**Conclusion:** Effectively managing disruptive behaviors creates a safe, healthy environment for patients and nurses. Role-play and reflective practice are useful educational methods to teach skills to manage these encounters. Clinical nurse specialists can play a key role in developing innovative education programs through interprofessional collaboration.

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**NEONATOLOGY POINT OF CARE INFORMATION SUMMARIES UPDATES**

**Topic:** Neonatal hypoxic-ischemic encephalopathy (HIE)
Embrace Neonatal MRI System magnetic resonance imaging device FDA approved for neonatal brain and head imaging in neonatal intensive care units (FDA Press Release 2017 Jul 20)

**Topic:** Necrotizing enterocolitis
Arginine supplementation reduces risk of necrotizing enterocolitis in preterm neonates (Cochrane Database Syst Rev 2017 Apr 11)

**Topic:** Hemolytic disease of the fetus and newborn (HDFN)
Delayed cord clamping may reduce need for transfusions and anemia in neonates born after fetal anemia requiring in utero transfusion (Pediatrics 2016 Mar)

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**NEONATOLOGY**

**Procalcitonin monitoring to reduce antibiotic exposure in neonatal sepsis (August 2017)**
In a multicenter randomized controlled trial in neonates with suspected early-onset sepsis, a risk assessment protocol that included serial procalcitonin (PCT) measurements reduced the duration of antibiotic therapy [20]. Rates of reinfection were low in both groups, and there was only one death (in the control group). Important limitations of the study include its fairly liberal suggested antibiotic duration for infants with negative cultures and high rates of noncompliance with the treatment protocols by the treating clinicians. Despite these limitations, the results suggest that PCT may have some utility in guiding the duration of antibiotic therapy in neonates with suspected sepsis. If PCT levels are obtained, they should be used in conjunction with other clinical indicators of sepsis and should not be the sole basis of decision-making. (See "Clinical features, evaluation, and diagnosis of sepsis in term and late preterm infants", section on ‘Other inflammatory markers’.)
Neonatal nCPAP and long-term adverse outcome (July 2017)
Nasal continuous positive airway pressure (nCPAP) is the preferred initial intervention to manage neonatal respiratory distress syndrome (RDS) versus a more invasive regimen (e.g., endotracheal intubation and surfactant administration). However, an observational study of extremely preterm survivors (gestational age <28 weeks) has shown that the use of nCPAP is associated with long-term morbidity [21]. Data comparing use of respiratory support over three historical time periods showed that patients managed in the most recent period (2005) had the longest median duration of nCPAP use, the highest degree of airflow obstruction at eight years of age, and the greatest risk of bronchopulmonary dysplasia. Interpretation of these results must account for factors other than duration of nCPAP that also changed over time (decreasing use of postnatal steroids, decreasing neonatal mortality, and increasing use of nCPAP for other conditions). While these findings emphasize that clinicians need to follow the criteria for initiation and discontinuation of CPAP to avoid overuse and minimize long-term sequelae, CPAP remains the preferred intervention for the management of neonatal RDS based on evidence from clinical trials. (See "Prevention and treatment of respiratory distress syndrome in preterm infants", section on 'Long-term outcome'.)

First Neonatal MRI Device Cleared for Marketing
The FDA has cleared the first magnetic resonance imaging device designed for use in neonatal ICUs. The Embrace Neonatal MRI System may be used for newborns with a head circumference up to 38 centimeters (15 inches) and weighing 1.0–4.5 kilograms (roughly 2–10 pounds). "Although we can use traditional MRI scanners to image neonates, taking babies outside of the neonatal intensive care unit to MRI suites presents great challenges," said an FDA official. "Having a system in the neonatal intensive care enables safer imaging for this vulnerable patient population." Click to view

Experts Issue Specific Definition for Neonatal ARDS. Reuters
NEW YORK (Reuters Health) - Experts have issued the first specific definition for neonatal acute respiratory distress syndrome (ARDS), the Montreux definition, with the endorsement of the European Society of Neonatal Intensive care and the European Society for Paediatric Research... Click to view

Parents often make follow-up care mistakes after kids leave hospital. Reuters
When sick kids leave the hospital, parents often don’t understand what follow-up care is needed or how to give children medicine at home, a research review suggests. Click to view

Shared Understanding With Patients JAMA Internal Medicine
This Viewpoint addresses the need for clinicians to refine and practice good communication skills to enable shared decision making with patients. Click to view

Family wins high court challenge against decision of NHS to refuse funding for sapropterin (Kuvan) for child with severe autism and phenylketonuria. BBC Health News
A judge has overturned decision and sent it for reconsideration, adding that if term "clinical effectiveness" was properly interpreted, the evidence that drug was clinically effective was "overwhelming." NHS England said it will reconsider but ruling will not affect other cases. Click to view

Online Journals
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- British Association of General Paediatrics - [www.bagp.org.uk](http://www.bagp.org.uk)
- Cochrane Child Health Evidence - [http://childhealth.cochrane.org/cochrane-reviews-child-health](http://childhealth.cochrane.org/cochrane-reviews-child-health)
- Royal College of Paediatrics and Child Health - [www.rcpch.ac.uk](http://www.rcpch.ac.uk)
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