



## Journal Review

# Journal watch

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**Source:** von Drygalski A, Chowdary P, Kulkarni R, Susen S, Konkle BA, Oldenburg J, Matino D, Klamroth R, Weyand AC, Jimenez-Yuste V, Nogami K, Poloskey S, Winding B, Willemze A, Knobe K, & XTEND-1 Trial Group (2023). Efanesoctocog Alfa Prophylaxis for Patients with Severe Hemophilia A. *The New England Journal of Medicine*, 388(4), 310–318. <https://doi.org/10.1056/NEJMoa2209226>

This study evaluated the efficacy, safety, and pharmacokinetics of efanesoctocog alfa (it provides high sustained factor VIII activity by overcoming the von Willebrand factor-imposed half-life ceiling) when used for prophylaxis and treatment of bleeding episodes in previously treated patients with severe hemophilia A. Results showed that weekly prophylaxis with efanesoctocog alfa provided superior bleeding prevention when compared to pre-study prophylaxis, with the majority of bleeding episodes resolving with one injection. In addition, factor VIII activity levels were normal to near-normal and physical health, pain and joint health all improved. Overall, efanesoctocog alfa had an acceptable side-effect profile and no development of inhibitors to factor VIII was detected.

**Source:** Neligan A, Adan G, Nevitt SJ, Pullen A, Sander JW, Bonnett L, & Marson AG. (2023). Prognosis of adults and children following a first unprovoked seizure. *The Cochrane Database of Systematic Reviews*, 1(1), CD013847. <https://doi.org/10.1002/14651858.CD013847.pub2>

The study aimed to provide estimates of the proportion of people who have further seizures after a single unprovoked seizure and to evaluate the mortality rate following a first unprovoked seizure. The study included 58 studies with a total of 12,160 participants and found that the estimated risk of seizure recurrence was 27% at 6 months, 36% at 1 year, and 43% at 2 years. The risk was slightly lower for adults and slightly higher for children. However, there were not enough data to provide estimates for longer than 2 years. The evidence presented was found to be of moderate certainty. The study's limitations include clinical and methodological heterogeneity and the lack of long-term recurrence data beyond 10 years. Despite these limitations, the study provides useful information for clinicians and patients to counsel them on the probable risk of further seizures in the short term.

**Source:** Ratnjeet K, Pallavi P, Jhamb U, & Saxena R. (2022). 0.45% Versus 0.9% Saline in 5% Dextrose as Maintenance Fluids in Children Admitted With Acute Illness: A Randomised Control Trial. *Pediatric Emergency Care*, 38(9), 436–441. <https://doi.org/10.1097/PEC.0000000000002621>

The safety of using IV maintenance fluids for hospitalised children based on Holliday and Segar's recommendations from 1957 has been called into question due to reports of complications caused by hyponatremia. The preferred type of IV maintenance fluid varies worldwide. This study aimed to compare the effects of administering 0.45% and 0.9% saline in 5% dextrose at standard

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maintenance rates in hospitalised children aged 3 months to 12 years. The primary objective was to measure the change in serum sodium levels at 24 h, while the secondary objectives were to observe the changes from baseline to 48 or 72 h and to determine the incidence of hyponatremia and hypernatremia. It was found that the fall in mean serum sodium from baseline was greater with increasing duration of IV fluids until 24 h in the 0.45% saline group, and the risk of hyponatremia was significantly higher in the hypotonic group at 12 and 24 h.

Thus, this study reinforces that isotonic fluids are more suitable for use among hospitalised children.

**Source:** Babl FE, Herd D, Borland M, Kochar A, Lawton B, Hort J, West A, George S, Zhang M, Velusamy K, Sullivan F, Oakley E, Davidson A, Hopper SM, Cheek JA, Berkowitz R, Hearps S, Wilson CL, Williams A, Elborough H,... Paediatric Research in Emergency Departments International Collaborative (PREDICT) (2022). Efficacy of Prednisolone for Bell Palsy in Children: A Randomised, Double-Blind, Placebo-Controlled, and Multicenter Trial. *Neurology*, 10.1212/WNL.0000000000201164. Advanced online publication. <https://doi.org/10.1212/WNL.0000000000201164>

This study aimed to investigate whether prednisolone is effective in improving facial function recovery in children with Bell's palsy. The study was conducted using a double-blind and randomised control trial with placebo control. Children aged 6 months to <18 years with Bell's palsy were given either prednisolone or a placebo and their facial function was measured at 1, 3, and 6 months. The study recruited 187 children, with 94 receiving prednisolone and 93 receiving a placebo. At the 1-month mark, there was no significant difference in the proportion of patients with complete recovery between the prednisolone and placebo groups. At 3 and 6 months, the proportions of patients with complete recovery were similar in both groups. The study suggests that early treatment with prednisolone does not significantly improve complete recovery in children with Bell's palsy.

**Source:** Quitadamo P, Battagliere I, Del Bene M, Caruso F, Gragnaniello P, Dolce P, Caldore M, Bucci C. Sharp-Pointed Foreign Body Ingestion in Pediatric Age. *J Pediatr Gastroenterol Nutr*. 2023 Feb 1;76(2):213-217. doi: 10.1097/MPG.0000000000003655

This study aimed to investigate the clinical complications arising from the ingestion of sharp and pointed objects in children, the incidence of these ingestions, and the characteristics of the affected children. The study included 580 children, mostly male, with a mean age of 50.5 months (aged 0–14 years) who had been admitted for the ingestion of sharp/pointed foreign bodies. They obtained clinical data until hospital discharge and recorded the clinical outcomes.

The most commonly ingested objects were fragments of metal (46.55%) and glass (31%). Endoscopy was used to remove the objects in 13.6% of cases, and the remaining objects exited the gastrointestinal tract with a mean time of 29 h. There were no cases of intestinal perforation or prolonged retention. In 4.6% of cases, the endoscopist found the shape and size of the object challenging to remove. The results of this very interesting study demonstrate that the ingestion of sharp/pointed foreign bodies is still a problem in paediatric age, especially in toddlers, and metal and glass objects are the most common culprits. Endoscopy can be difficult in around 5% of cases, but fortunately, no surgery was needed in our sample.

**Source:** Scheffer IE, Bennett CA, Gill D, de Silva MG, Boggs K, Marum J, Baker N; Australian Genomics DEE Flagship; Palmer EE, Howell KB. Exome sequencing for patients with developmental and epileptic encephalopathies in clinical practice. *Dev Med Child Neurol*. 2023 Jan;65(1):50-57. doi: 10.1111/dmnc.15308. Epub 2022 Jun 14. PMID: 35701389.

The purpose of this study was to investigate the usefulness of exome sequencing for patients with developmental and epileptic encephalopathies (DEEs). Over 2 years, patients with DEEs were recruited for exome sequencing, with parental segregation when appropriate. Out of 103 patients (54 males, 49 females; ages 2 weeks to 17 years), a genetic cause was identified in 36 (35%) cases, and the findings had implications for management in 13 of these cases. Exome sequencing led to the discovery of pathogenic or likely pathogenic variants in 30 patients (29%), variants of unknown significance in 39 (38%), and negative results in 34 (33%). *KCNQ2*, *CDKL5*, *SCN1A*, and *STXBP1* were the most frequently identified genes. Six additional patients were diagnosed after the description of new genetic diseases or through chromosomal microarray testing. A genetic aetiology was identified in 41% of children with seizure onset under 2 years, compared to 18% with older onset. The study confirms the value of exome sequencing in clinical care for children with DEEs, as it can inform management and provide accurate prognostic and reproductive counselling. The authors recommend the routine use of genomic testing in the care of these patients.

**Source:** Lebeaux RM, Madan JC, Nguyen QP, Coker MO, Dade EF, Moroishi Y, Palys TJ, Ross BD, Pettigrew MM, Morrison HG, Karagas MR, Hoen AG. Impact of antibiotics on off-target infant gut microbiota and resistance genes in cohort studies. *Pediatr Res*. 2022 Dec;92(6):1757-1766. doi: 10.1038/s41390-022-02104-w. Epub 2022 May 14. PMID: 35568730; PMCID: PMC9659678.

This study aimed to investigate the effects of antibiotic exposure on the gut microbiome, including off-target microbes and antibiotic resistance genes (ARGs). The researchers analysed metagenomic sequencing data from

paired stool samples collected from over 200 infants, taken before and after antibiotic treatment. The study used a difference-in-differences approach and adjusted for covariates to evaluate the impact of subsequent antibiotic exposure on microbial abundance and compositional diversity. The researchers found that antibiotic use led to changes in the abundance of multiple species and ARGs, including the class A beta-lactamase gene CfxA6 differed by antibiotic exposure after 1 year. For example, *Bacteroides vulgatus* relative abundance increased while *Bacteroides fragilis* decreased. *Bifidobacterium* species showed opposing trends. The study also found that antibiotic use in infants attending daycare was positively associated with *Escherichia coli* and ARG abundance. These novel findings suggest that the effects of antibiotic exposure on the gut microbiome should be considered when evaluating the unintended impacts of antibiotics, especially in young children.

**Source:** Sarid EB, Stoopler ML, Morency AM, Garfinkle J. Neurological implications of antenatal corticosteroids on late preterm and term infants: a scoping review. *Pediatr Res.* 2022 Nov;92(5):1225-1239. doi: 10.1038/s41390-022-02135-3. Epub 2022 Jun 9. PMID: 35681094.

It is hard to anticipate when a preterm birth will occur, so around 40% of babies who were exposed to antenatal corticosteroids (ACSs) are delivered at full term (37 weeks or more of gestation). This research aimed to analyse the existing literature on the connection between administering ACS to prevent preterm delivery and brain development in infants who were ultimately born late preterm and term. The researchers conducted a thorough search of three databases and eight conference proceedings from 1972 to 2021. The inclusion criteria were ACS used to prevent preterm delivery, a cohort of late preterm and term infants and an assessment of brain development. Data on the study characteristics, ACS administration and neurological outcomes were collected and analysed based on themes. The neurological outcomes of the 27 studies included in the review were categorised into four themes, including reduced neonatal head circumference, structural cortical differences on magnetic resonance imaging, increased prevalence of psychiatric problems and an elevated risk of neurodevelopmental delays in ACS-exposed late preterm and term infants. The review concluded that ACS exposure for preventing preterm delivery might have significant neurological effects in late preterm and term infants. However, the existing research could be vulnerable to bias, and more research that accounts for confounders is needed to better understand the long-term neurological effects of ACS on late preterm and term infants.

**Source:** Gentile Á, Areso MS, Degiuseppe JI, Orqueda A, Turco M, Sabbaj L, Rodrigo A, Juárez MD, Stupka JA. Role of Noroviruses in Sporadic Acute Gastroenteritis Cases from Children Attending a Large Referral Children's

Hospital in Buenos Aires City, Argentina. *Pediatr Infect Dis J.* 2023 Feb 1;42(2):94-98. doi: 10.1097/INF.0000000000003775. Epub 2022 Jan 11. PMID: 36638391.

This Argentinian study analysed the prevalence of noroviruses in children under the age of five. Stool samples were collected and tested for norovirus, and the results showed that 24.4% of the children tested positive. Vomiting, moderate/severe diarrhoea, watery diarrhoea and a history of rotavirus vaccination were all significantly associated with norovirus aetiology. GII and GII.4 were the most frequently detected genogroups and genotypes, respectively. The findings of the study suggest that noroviruses are highly prevalent in children under five, particularly in children between 6 months and 2 years old, and the presence of watery diarrhoea, complete rotavirus vaccination and vomiting should raise suspicion of norovirus gastroenteritis. NVs were detected with high frequency, suggesting a shift toward norovirus predominance over rotavirus. The study highlights the need for continuous and active norovirus surveillance in this age group, as children are a priority group for norovirus vaccine design and development.

**Source:** Boghi D, Kim KW, Kim JH, Lee SI, Kim JY, Kim KT, Ambrosoli A, Guarneri G, Landoni G, Cabrini L. Non-invasive Ventilation for Acute Respiratory Failure in Pediatric Patients: A Systematic Review and Meta-Analysis. *Pediatr Crit Care Med.* 2023 Feb 1;24(2):123-132. doi: 10.1097/PCC.0000000000003109. Epub 2022 Dec 13. PMID: 36521191.

This systematic review and meta-analysis aimed to assess the efficacy of non-invasive ventilation (NIV) for acute respiratory failure (ARF) in paediatric patients. A search of PubMed, EMBASE, the Cochrane Central Register of Clinical Trials, and Clinicaltrials.gov was conducted up to 31 July 2022. The authors included randomised controlled trials (RCTs) comparing NIV with any comparator (standard oxygen therapy and high-flow nasal cannula [HFNC]) in paediatric patients with ARF and excluded studies on neonates and chronic respiratory failure. 15 RCTs (2679 patients) were included in the final analysis. The intubation rate was lower in the NIV group than in the control group (11.5% vs. 14.5%; risk ratio: 0.791, 95% CI: 0.629–0.996,  $P = 0.046$ ). When studies with intervention duration shorter than an hour and those with cross-over as rescue treatment were excluded, the results were strengthened. These results suggest that NIV might be an effective treatment for paediatric patients with ARF as it reduces the risk of intubation compared with standard oxygen therapy or HFNC. However, it does not appear to have an effect on mortality or the length of hospital and intensive care unit stays.

**Source:** Gutiérrez Moreno M, Del Villar Guerra P, Medina A, Modesto I Alapont V, Castro Bournissen L, Mirás Veiga A, Ochoa-Sangrador C. High-Flow Oxygen and Other Non-

invasive Respiratory Support Therapies in Bronchiolitis: Systematic Review and Network Meta-Analyses. *Pediatr Crit Care Med.* 2023 Feb 1;24(2):133-142. doi: 10.1097/PCC.0000000000003139. Epub 2022 Dec 19. PMID: 36661419.

This systematic review explored the effectiveness of non-invasive respiratory support techniques in bronchiolitis in patients aged below 24 months. Randomised controlled trials (RCTs), non-RCTs, and cohort studies were analysed which compared high-flow nasal cannula (HFNC) with conventional low-flow oxygen therapy (LFOT) and/or non-invasive ventilation (NIV). Results indicated that HFNC was associated with a lower risk of invasive mechanical ventilation (MV) than NIV in non-experimental studies; however, no differences were observed in experimental studies. In addition, HFNC was more effective than LFOT in reducing oxygen days and treatment failure. Through network meta-analyses of clinical trials, it was found that NIV was the most effective intervention to avoid invasive MV and reduce oxygen therapy days. Methodological heterogeneity was observed and was statistically significant for the reduction

of oxygen therapy days and length of hospital stay. Overall, experimental evidence did not suggest that HFNC has any advantages over LFOT as an initial treatment or over NIV as a rescue treatment.

#### **Declaration of patient consent**

Patient's consent not required as there are no patients in this study.

#### **Financial support and sponsorship**

Nil.

#### **Conflicts of interest**

Dr. Vikram Sakleshpur Kumar is one of the State Advisory Members of the journal.

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