NASEM Pediatric Disaster Science Symposium: Trials and Mechanistic Science to Increase Rigor

Experience from the Pediatric Emergency Care Applied Research Network (PECARN)

Nathan Kuppermann, MD, MPH
Departments of Emergency Medicine and Pediatrics
UC Davis School of Medicine and UC Davis Health
August 1st, 2022







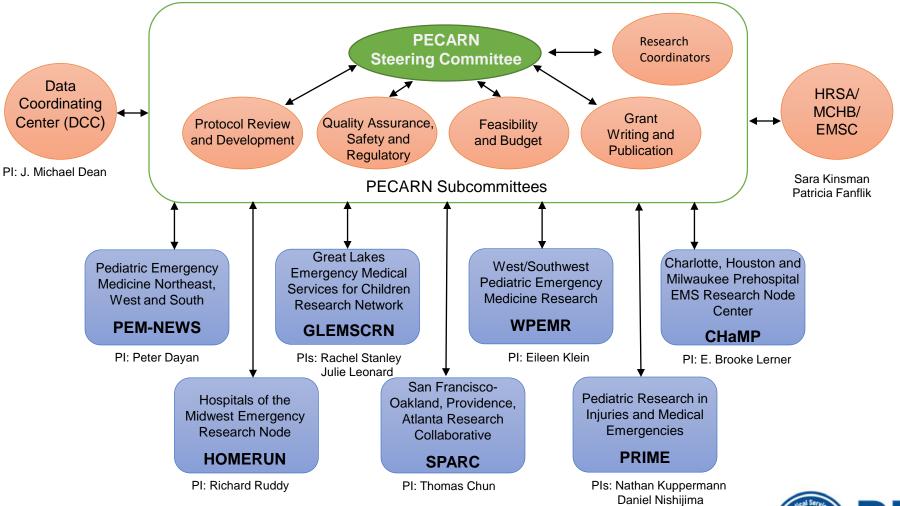
Disclosures

- Research funded by NICHD, NHLBI, PCORI, HRSA, EMSC
- No financial conflicts of interest to report

PECARN

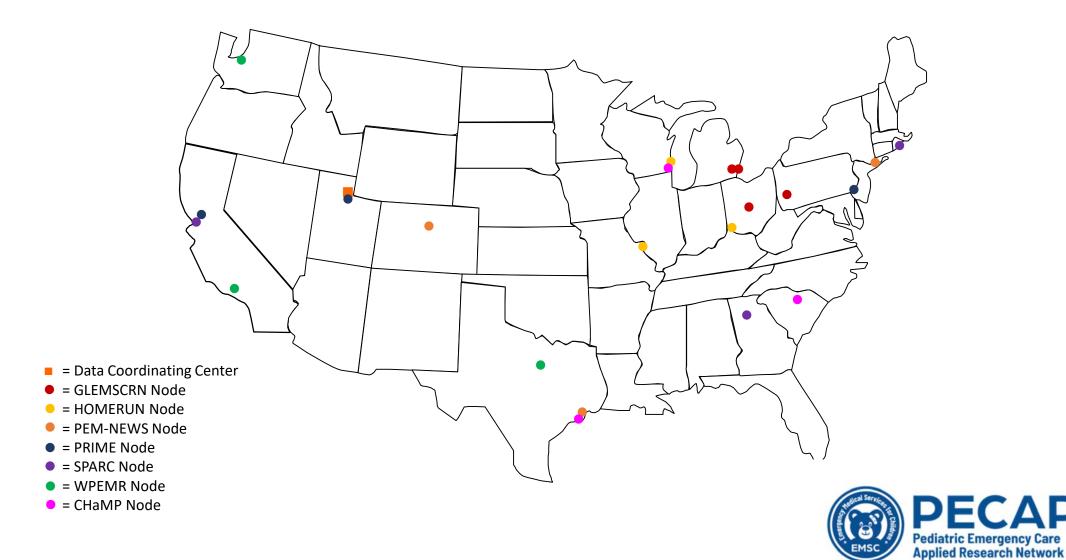
- The first federally-funded pediatric emergency medicine research network in the United States started 2002
- 6 research "nodes" with 18 Hospital Emergency Department Affiliates and a separate data center
 - One other node of 3 pre-hospital agencies
- > 1.3 million acutely ill and injured children yearly
- HRSA/EMSC funds the infrastructure; Studies funded by external funding from NIH and other sources

PECARN – Network Structure





PECARN – Large and diverse sites

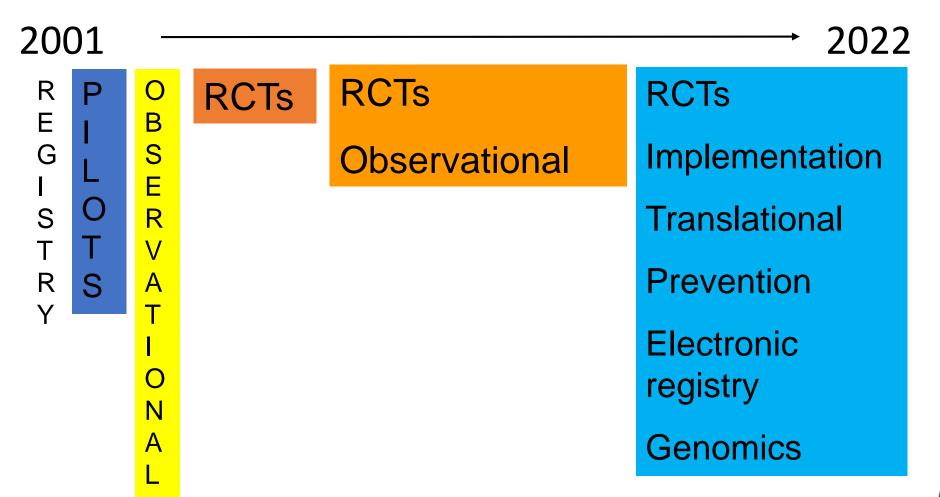


Past and Current PECARN Research

- Patient safety and error reduction
- Quality of PEM care
- Evaluation of head trauma
- C-Spine trauma/immobilization
- Steroids in acute bronchiolitis
- Mental illness/psychiatric emergencies
- RCT of fluids for DKA
- Magnesium for sickle cell pain

- Therapeutic hypothermia in pediatric cardiopulmonary arrest
- Management of status epilepticus
- Evaluation of abdominal trauma
- Screening for alcohol abuse
- Probiotics for gastroenteritis
- Knowledge translation of TBI rules
- RNA transcription biosignatures to diagnose febrile infants
- TXA for hemorrhagic trauma

PECARN Progress





Clinical Trial of Fluid Infusion Rates for Pediatric Diabetic Ketoacidosis

Nathan Kuppermann, M.D., M.P.H., Simona Ghetti, Ph.D., Jeff E. Schunk, M.D., Michael J. Stoner, M.D., Arleta Rewers, M.D., Ph.D., Julie K. McManemy, M.D., M.P.H., Sage R. Myers, M.D., M.S.C.E., Lise E. Nigrovic, M.D., M.P.H., Aris Garro, M.D., M.P.H., Kathleen M. Brown, M.D., Kimberly S. Quayle, M.D., Jennifer L. Trainor, M.D., Leah Tzimenatos, M.D., Jonathan E. Bennett, M.D., Andrew D. DePiero, M.D., Maria Y. Kwok, M.D., M.P.H., Clinton S. Perry III, Ph.D., Cody S. Olsen, M.S., T. Charles Casper, Ph.D., I. Michael Dean, M.D., and Nicole S. Glaser, M.D., for the PECARN DKA FLUID Study Group*

ABSTRACT

BACKGROUND

Diabetic ketoacidosis in children may cause brain injuries ranging from mild to severe. The authors' affiliations are listed in the Whether intravenous fluids contribute to these injuries has been debated for decades.

We conducted a 13-center, randomized, controlled trial that examined the effects of the rate of administration and the sodium chloride content of intravenous fluids on neurologic outcomes in children with diabetic ketoacidosis. Children were randomly assigned to one of four treatment groups in a 2-by-2 factorial design (0.9% or 0.45% sodium chloride content and rapid or slow rate of administration). The primary outcome was a decline in mental status (two consecutive Glasgow Coma Scale scores of <14, on a scale ranging from N Engl J Med 2018;378:2275-87. 3 to 15, with lower scores indicating worse mental status) during treatment for diabetic DOI: 10.1056/NEJMoa1716816 ketoacidosis. Secondary outcomes included clinically apparent brain injury during treatment for diabetic ketoacidosis, short-term memory during treatment for diabetic ketoacidosis, and memory and IQ 2 to 6 months after recovery from diabetic ketoacidosis.

A total of 1389 episodes of diabetic ketoacidosis were reported in 1255 children. The Glasgow Coma Scale score declined to less than 14 in 48 episodes (3.5%), and clinically apparent brain injury occurred in 12 episodes (0.9%). No significant differences among the treatment groups were observed with respect to the percentage of episodes in which the Glasgow Coma Scale score declined to below 14, the magnitude of decline in the Glasgow Coma Scale score, or the duration of time in which the Glasgow Coma Scale score was less than 14; with respect to the results of the tests of short-term memory; or with respect to the incidence of clinically apparent brain injury during treatment for diabetic ketoacidosis. Memory and IQ scores obtained after the children's recovery from diabetic ketoacidosis also did not differ significantly among the groups. Serious adverse events other than altered mental status were rare and occurred with similar frequency in all treatment groups.

Neither the rate significantly in (Funded by the Development as FLUID Clinical'

Downloade

Lorazepam vs Diazepam for Pediatric Status Epilep A Randomized Clinical Trial

James M. Chamberlain, MD: Pamela Okada, MD: Maiia Holsti, MD: Prashant Mahaian, MD, MBA: athleen M. Brown, MD; Cheryl Vance, MD; Victor Gonzalez, MD; Richard Lichenstein, MD Rachel Stanley, MD, MPH; David C. Brousseau, MD, MPH; Joseph Grubenhoff, MD; Roger Zemek, MD; lavid W. Johnson, MD; Traci E. Clemons, PhD; Jill Baren, MD, MPH; for the Pediatric Emergency Care Applied

IMPORTANCE Benzodiazepines are considered first-line therapy for pediatric status epilepticus. Some studies suggest that lorazepam may be more effective or safer than diazepam, but lorazepam is not Food and Drug Administration approved for this indication.

OBJECTIVE To test the hypothesis that lorazepam has better efficacy and safety than diazenam for treating pediatric status epilepticus.

DESIGN, SETTING, AND PARTICIPANTS This double-blind, randomized clinical trial was conducted from March 1, 2008, to March 14, 2012, Patients aged 3 months to younger than 18 years with convulsive status epilepticus presenting to 1 of 11 US academic pediatric emergency departments were eligible. There were 273 patients: 140 rand diazenam and 133 to lorazenam.

INTERVENTIONS Patients received either 0.2 mg/kg of diazepam or 0.1 mg/kg of lorazepam intravenously, with half this dose repeated at 5 minutes if necessary. If status epilepticus continued at 12 minutes, fosphenytoin was administered

MAIN OUTCOMES AND MEASURES The primary efficacy outcome was cessation of status epilepticus by 10 minutes without recurrence within 30 minutes. The primary safety outcome was the performance of assisted ventilation. Secondary outcomes included rates of seizure recurrence and sedation and times to cessation of status epilepticus and return to baseline mental status. Outcomes were measured 4 hours after study medication administration.

→ (Identification of children at very low risk of clinicallyimportant brain injuries after head trauma: a prospective cohort study

Nathan Kuppermann, James F Holmes, Peter S Dayan, John D Hoyle, Jr., Shireen M Atabaki, Richard Holubkov, Frances M Nadel, David Monroe Rachel M Stanley, Dominic A Borgialli, Mohamed K Badawy, Jeff E Schunk, Kimberly S Quayle, Prashant Mahajan, Richard Lichen Kathleen A Lillis, Michael G Tunik, Elizabeth S Jacobs, James M Callahan, Marc H Gorelick, Todd F Glass, Lois K Lee, Michael C Bachmar Arthur Cooper, Elizabeth C Powell, Michael J Gerardi, Kraig A Melville, J Paul Muizelaar, David H Wisner, Sally Jo Zuspan, J Michael Dea Sandra L Wootton-Gorges, for the Pediatric Emergency Care Applied Research Network (PECARN):

Lancet 2009; 374: 1160-70 Background CT imaging of head-injured children has risks of radiation induced malignancy. Our aim was to identify Published Online children at very low risk of clinically-important traumatic brain injuries (ciTBI) for whom CT might be unnecessar

> Methods We enrolled patients younger than 18 years presenting within 24 h of head trauma with Glasgow Coma Scale scores of 14–15 in 25 North American emergency departments. We derived and validated age specific prediction rules for ciTBI (death from traumatic brain injury, neurosurgery, intubation >24 h, or hospital admission ≥2 nights).

with tapausstate the description of the property of the community of the c according to the parents) had a negative predictive value for ciTBI of 1175/1175 (100.0%, 95% CI 99.7-100.0) and sensitivity of 25/25 (100%, 86.3-100.0). 167 (24.1%) of 694 CT-imaged patients younger than 2 years were in this ur. suppermant at the Department of mentions are listed in the Englishment of the Department of the De fornia, Davis, School of pregrams, Annual Community, Stockton Blvd., Sacramento, CA 95817, orSurgery (Prof DH Wisner MD), and Radiology 2223 CT-imaged patients aged 2 years and older were in this low risk group. Neither rule missed neurosurgery in

*Additional members of the PECARN inventive of cliffonis, basis
DKA FLUID Study Group are listed School Medicine, Davis, CA, the acknowledgments.
Columbia University College of nterpretation These validated prediction rules identified children at very low risk of ciTBIs for whom CT can routinely

Physicians and Surgeons,
New York, NY, USA
Funding The Emergency Medical Services for Children Programme of the Maternal and Child Health Bureau, and the Maternal and Child Health Bureau Research Programme, Health Resources and Services Administration, US (P S Daysin MD)); Division of Diemergency Medicine, Michigan State University School of Medicine/Helen DeVos Children's Hoop, Grand Rapids, MI, USA (I D Hoyle MD); Traumatic heal Department of Health and Human Service

epartments of Polistrics and disability in children worldwide. In the USA, head CT findings as the outcome measure for identifying Washington/University School of Medicine, Washington, Washington, University School of Medicine, Washington, USAS (MAIDBAIN MOI)
Department of Pedatrics,
university of Usas
U REMARKAN PRO. injury (ciTBI) needing acute intervention, especially commonly undergo neuroimaging and account fo neurosurgery, should be identified rapidly. CT is the 60% of those with traumatic brain injuries seen on 5720span RN,
Prof J M Down MD, and PECARN reference standard for emergently diagnosing traumatic Less than 10% of CT scans in children with minor Central Data Management and brain injuries, although some brain injuries are not seen trauma, however, show traumatic brain injuries Coordinating Center on CT. About 50% of children assessed in North Furthermore, injuries needing neurosurgery are (RHORGHER, S.) Ziospan, American emergency departments for head trauma uncommon in children with GCS scores of 14–15.7° TIMUSIN, SHEAKEUK, UNDERGO CT^{1,6} (Faul M, Centers for Disease Control and Reduction of CT use is important because ion Prediatrics, University of Prevention, personal communication). Between 1995 radiation from CT scans can cause lethal m

need acute intervention, and some are false positives o Traumatic brain injury is a leading cause of death and non-traumatic findings. Clinical studies using abnormal

Efficacy of levetiracetam, fosphenytoin, and valproate for established status epilepticus by age group (ESETT): a double-blind, responsive-adaptive, randomised controlled trial

James M Chamberlain, Jaideep Kapur, Shlomo Shinnar, Jordan Elm, Maija Holsti, Lynn Babcock, Alex Rogers, William Barsan, James Cloyd Daniel Lowenstein, Thomas P Bleck, Robin Conwit, Caitlyn Meinzer, Hannah Cock, Nathan B Fountain, Ellen Underwood, Jason T Conna Robert Silbergleit, for the Neurological Emergencies Treatment Trials* and the Pediatric Emergency Care Applied Research Network investigators

at nkuppermann@ucdavis.edu.

Background Benzodiazepine-refractory, or established, status epilepticus is thought to be of similar pathophysiology Loncet 2020 in children and adults, but differences in underlying aetiology and pharmacodynamics might differentially affect Published On after extending enrolment in children to compare outcomes in three age groups.

Methods In this multicentre, double-blind, response-adaptive, randomised controlled trial, we recruited patients from 58 hospital emergency departments across the USA. Patients were eligible for inclusion if they were aged 2 years or older, had been treated for a generalised convulsive seizure of longer than 5 min duration with adequate doses of benzodiazepines, and continued to have persistent or recurrent convulsions in the emergency department for at least 5 min and no more than 30 min after the last dose of benzodiazepine. Patients were randomly assigned in a response (Prof.) M.Chz adaptive manner, using Bayesian methods and stratified by age group (<18 years, 18-65 years, and >65 years), to levetiracetam, fosphenytoin, or valproate. All patients, investigators, study staff, and pharmacists were masked to before treatment allocation. The primary outcome was absence of clinically apparent seizures with improved consciousness and without additional antiseizure medication at 1 h from start of drug infusion. The primary safety outcome was life-threatening hypotension or cardiac arrhythmia. The efficacy and safety outcomes were analysed by intention to Prof N B Fountain MD); treat. This study is registered in ClinicalTrials gov. NCT01960075.

Findings Between Nov 3, 2015, and Dec 29, 2018, we enrolled 478 patients and 462 unique patients were included: Center, Albert 225 children (aged <18 years), 186 adults (18-65 years), and 51 older adults (>65 years). 175 (38%) patients were of the control of the contr randomly assigned to levetiracetam. 142 (31%) to fosphenyltoin, and 145 (31%) were to valproate. Baseline re balanced across treatments within age groups. The primary efficacy outcome was met in those

(145 patients), fosphenytoin (118), or valproate (121). Reenrollment of patients with a National Institute of Neurological Disorders and Stroke

The NEW ENGLAND JOURNAL of MEDICINE ORIGINAL ARTICLE

Lactobacillus rhamnosus GG versus Placebo for Acute Gastroenteritis in Children

David Schnadower, M.D., M.P.H., Phillip I. Tarr, M.D., T. Charles Casper, Ph.D., Marc H. Gorelick, M.D., M.S.C.E., J. Michael Dean, M.D., Karen J. O'Connell, M.D., Prashant Mahajan, M.D., M.P.H., Adam C. Levine, M.D., M.P.H., Seema R. Bhatt, M.D., Cindy G. Roskind, M.D., Elizabeth C. Powell, M.D., Alexander J. Rogers, M.D., Cheryl Vance, M.D., Robert E. Sapien, M.D., Cody S. Olsen, M.S., Melissa Metheney, B.S., R.N., Viani P. Dickey, A.B., Carla Hall-Moore, B.S., and Stephen B. Freedman, M.D.C.M., for the PECARN Probiotics Study Group

ARSTRACT

The authors' affiliations are listed in the Acute gastroenteritis develops in millions of children in the United States every year and treatment with probiotics is common. However, data to support the use of probiot ics in this population are limited. Hospital Medical Center 3333 Burnet

Ave., MLC 2008, Cincinnati, OH 45229,

We conducted a prospective, randomized, double-blind trial involving children 3 months to 4 years of age with acute gastroenteritis who presented to one of 10 U.S. pediatric This article was updated on February 14, emergency departments. Participants received a 5-day course of Lactobacillus rhamnosu. GG at a dose of 1×1010 colony-forming units twice daily or matching placebo. Follow-ur surveys were conducted daily for 5 days and again 14 days after enrollment and 1 month after enrollment. The primary outcome was moderate-to-severe gastroenteritis, which

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus

Jaideep Kapur, M.B., B.S., Ph.D., Jordan Elm, Ph.D., James M. Chamberlain, M.D., William Barsan, M.D., James Cloyd, Pharm.D., Daniel Lowenstein, M.D., Shlomo Shinnar, M.D., Ph.D., Robin Conwit, M.D., Caitlyn Meinzer, Ph.D. Hannah Cock, M.D., Nathan Fountain, M.D., Jason T. Connor, Ph.D., and Robert Silbergleit, M.D., for the NETT and PECARN Investigators*

ABSTRACT

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N Engl J Med 2018;379:2002-14.

DOI: 10.1056/NEJMoa1802598

The choice of drugs for patients with status epilepticus that is refractory to treatment From the Department of Neurology, Uni with benzodiazepines has not been thoroughly studied.

In a randomized, blinded, adaptive trial, we compared the efficacy and safety of three In a randomized, blinded, adaptive trial, we compared the efficacy and safety of three intravenous anticonvulsive agents — levetiracetam, fosphenytoin, and valproate — in Medicine, Children's National Medica children and adults with convulsive status epilepticus that was unresponsive to treat- Center, Washington, DC (J.M.C.); the Dement with benzodiazepines. The primary outcome was absence of clinically evident partners seizures and improvement in the level of consciousness by 60 minutes after the start the College of Pharmacy, Department of of drug infusion, without additional anticonvulsant medication. The posterior probabilities that each drug was the most or least effective were calculated. Safety outcomes included life-threatening hypotension or cardiac arrhythmia, endotracheal intubation, seizure recurrence, and death,

A total of 384 patients were enrolled and randomly assigned to receive levetiracetam ter-

ent of Public Health Sciences, Medical University of South Carolina, Charlesto partment of Emergency Medicine, Univer-sity of Michigan, Ann Arbor (W.B., R.S.); University of Minnesota, Minneapol (J.C.); the Department of Neurology, University of California, San Francisco, Sa Francisco (D.L.): the Departments of Neulege of Medicine, Montefiore Medical Cer New York (S.S.); the National Institut

versity of Virginia, Charlottesville (J.K.

JAMA Pediatrics | Original Investigation

A Clinical Prediction Rule to Identify Febrile Infants 60 Days and Younger at Low Risk for Serious Bacterial Infections

ermann, MD, MPH: Peter S, Davan, MD, MSc; Deborah A, Levine, MD; Welssa VItale, MD; Leah Tzimenatos, MD; Michael G, Tunik, MD; Habita Hugoperman, Mo, Merry et al. 5 dayst, Mo, Mor. Coloroda N. Ceverie, Mo. Needa Victae, Mr. Cara Extrementa, Mr. Monario I. 1411 My Sunders, Mr. Michard M. Rody, Mol. Ceri Robovsek, U. Mortaned & Roger, Mr. Michard C. Needa M. White Lie N. Rogero, Mr. Laed Monario H. Rody, J. Michard C. Severber, M. S. Hallender Germ, M.D. Andrea T. Cruz, Mr. M. Hift, Effer, Caris, Mr. Phol. Deviel M. Cohen, M.D. Arned Breyer, M.D. Charlet Green Expert. Mr. Charlet G. Michard Green Control, Mr. Michard Green Company, Mr. Mortaned Cara Mr. M. Andrea M. Charlet G. Michard Green Control, Mr. M. Michard Green Cara Mr. Michael M. M. Michard Green Cara Mr. Michael Mr. M lizabeth R. Albern, MD, VISCE: Benamin Miller MS: T. Charles Calper PhD: J. Michael Dean, MD, NBA: Dotavio Ramio, MC: nt Mahajan, MD, MPH, MBA; for the Febrile Infant Working Group of the Pediatric Emergency Care Applied Research N

infections, tracteremia, and meningitis, may lead to dangerous complications. However, lumbar punctures and hospitalizations involve risks and costs. Clinical prediction rules using biomarken beyond the white blood cell count (WBO) may accurately identify febrile infants at low risk for SBI

OBJECTIVE To derive and validate a prediction rule to identify febrile infants 60 days and younger at low risk for Sills.

DESIGN, SETTING, AND PARTICIPANTS. Prospective, observational study between March 20T and May 2013 at 26 emergency departments. Convenience sample of previously healthy between April 2014 and April 2018.

SURES. Clinical and laboratory data (blood and urine) including patient demographics fever height and duration, clinical appearance, WBC, absolute neutrophil count (ANC), serun procalcitonin, and urinalysis. We derived and validated a prediction rule based on these

MAIN OUTCOMES AND MEASURES. Serious bacterial infection, defined as urinary tract. infection, bacteremia, or bacterial meningitis.

OUTS. We derived the prediction rule on a random sample of 908 infants and validated it on 913 infarts (mean age was 36 days, 765 were girls [42%], 783 were white and non-Hispanic [43%], 366 were black [20%], and 535 were Hispanic [29%]). Serious bacterial infections were present in 170 of 1821 infants (9.3%), including 26 (1.4%) with bacteremia, ISI (8.3%) with urinary tract infections, and IO (0.5%) with bacterial meningitis; 16 (0.9%) had concurrent SBI The prediction rule identified infants at lownisk of SBI using a negative urinallysis result, an ANC of 409/0/µL or less (to convert to ×10° per liter, multiply by 0.00°), and serum procalcitonin of 17l ng/mL or less. In the validation cohort, the rule sensitivity was 97.7% (95% CL 91.3-99.6). licity was 60.0% (96% Ct, 56.6-63.3), negative predictive value was 99.6% (95% Ct. 98.4-99.9), and negative likelihood ratio was 0.04 (95% CI, 0.01-0.15). One infant with cteremia and 2 infants with urinary tract infections were misclassified. No patients with bacterial meningitis were missed by the rule. The rule performance was nearly identical when the outcome was restricted to bacteremia and/or bacterial meningitis, missing the same infant with bacteremia.

ONS AND RELEVANCE. We derived and validated an accurate prediction rule to identify febrile infants 60 days and younger at low risk for 58 is using the urinalysis, ANC, and procalcitorin levels. Once further validated on an independent cohort, clinical application of the rule has the potential to decrease unnecessary lumbar punctures, antibiotic administration, and hospitalizations.

JAMA Pediatr. doi:10.30/01/jamapediatrics.2018.5501 Published online February 18, 2019.

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

IULY 26, 2007

A Multicenter, Randomized, Controlled Trial of Dexamethasone for Bronchiolitis

Howard M. Corneli, M.D., Joseph J. Zorc, M.D., Prashant Mahajan, M.D., M.P.H., Kathy N. Shaw, M.D., M.S.C.E., Richard Holubkov, Ph.D., Scott D. Reeves, M.D., Richard M. Ruddy, M.D., Baqir Malik, M.D., Kyle A. Nelson, M.D., M.P.H., Joan S. Bregstein, M.D., Kathleen M. Brown, M.D., Matthew N. Denenberg, M.D. Kathleen A. Lillis, M.D., Lynn Babcock Cimpello, M.D., James W. Tsung, M.D., Dominic A. Borgialli, D.O., M.P.H., Marc N. Baskin, M.D., Getachew Teshome, M.D., M.P.H., Mitchell A. Goldstein, M.D., David Monroe, M.D., J. Michael Dean, M.D., and Nathan Kuppermann, M.D., M.P.H., for the Bronchiolitis Study Group of the Pediatric Emergency Care Applied Research Network (PECARN)*

ABSTRACT

Bronchiolitis, the most common infection of the lower respiratory tract in infants. From the University of Utah (H.M.C.) and is a leading cause of hospitalization in childhood. Corticosteroids are commonly used to treat branchialitis, but evidence of their effectiveness is limited

We conducted a double-blind, randomized trial comparing a single dose of oral Gincinati Children's Hospital Medical dexamethasone (1 mg per kilogram of body weight) with placebo in 600 children (age range, 2 to 12 months) with a first episode of wheezing diagnosed in the emergency department as moderate-to-severe bronchiolitis (defined by a Respiratory Children's National Medical Center, Wash

ing Center (R.H., J.M.D.), Salt Lake City the Children's Hospital of Philadelphia Philadelphia (J.J.Z., K.N.S.); Children's Hospital of Michigan, Detroit (P.M., B.M.); Center, Cincinnati (S.D.R., R.M. R.): Wash umbia University, New York (I.S.B.)

PECARN RESEARCH PRIORITIES	
1. Respiratory Illnesses/Asthma	2. Prediction Rules for High Stakes/Low Likelihood Diseases
3. Medication Error Reduction	4. Injury Prevention
5. Urgency and Acuity Scaling	6. Race, Ethnic, Class Disparities in Health
7. Mental Health	8. Treatment of Infectious Diseases
Best practices in patient care	10. Pain & Anxiety Management
11. Education/Training Outcomes	12. Development of Treatment Algorithms
13. Improvement in Health Outcomes for Cardiac Arrest	14. Practice Protocols
15. Seizure Management	16. C-Spine Immobilization
Special Mention: Prehospital Research	



Any investigator can submit a 2 page concept

All concepts are routed through a node

Concept presented to steering committee (vote)

Concept developed into protocol/grant with help from data center and input from subcommittees and steering committee

Protocol/grant vote by steering committee



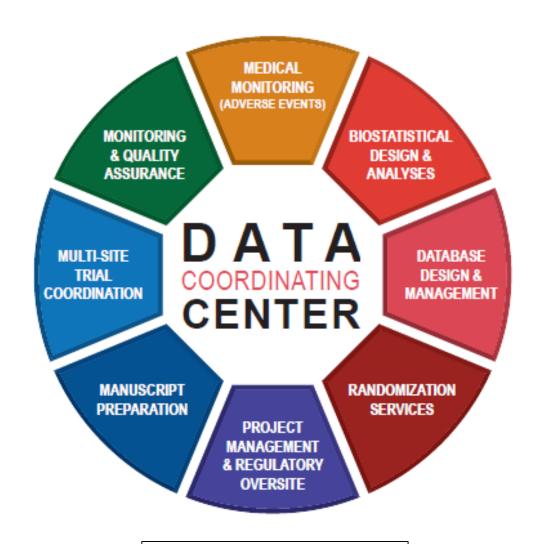
- Large samples sizes enhance reproducibility
 - Definitive research
- Diverse patient cohorts enhance generalizability
- Senior scientists working with clinicians and early investigators
 - Enhance sustainability
- Independent data center
 - Minimizes "analytic bias" from study PIs
 - Investigators have learned to live with loss of control



PECARN Data Coordinating Center



The Data Coordinating Center (DCC), in conjunction with the Clinical Trials Office (CTO), have extensive experience with coordinating single and multicenter observational studies, and randomized controlled trials in rare diseases, pediatrics, and in adult populations



Accelerate research to the bedside

"One stop shopping"

- Explicit protocol development
- Uniform standards for clinical research
- Site monitoring requirements
 - Improvement efforts for poorly performing sites
 - Willingness to terminate sites for persistent poor performance
- Strict data transmission and security requirements
- Central IRB, EFIC studies, above cap funding standard



Results of Rigor

- Widespread implementation
- Adoption by national and international guidelines

Often, CT scans aren't necessary.

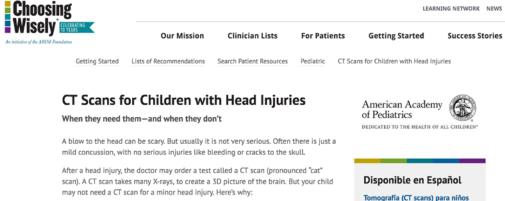
FROM THE AMERICAN ACADEMY OF PEDIATRICS | CLINICAL PRACTICE GUIDELINE NOVEMBER 01 2014

Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis 🔗

Shawn L. Ralston, MD; Allan S. Lieberthal, MD; H. Cody Meissner, MD; Brian K. Alverson, MD; Jill E. Baley, MD; Anne M. Gadomski, MD; David W. Johnson, MD; Michael J. Light, MD; Nizar F. Maraga, MD;

Eneida A. Mendonca, MD; Kieran J. Phelan, MD; Joseph J. Zorc, N Mark A. Brown, MD; Ian Nathanson, MD; Elizabeth Rosenblum, Sinsi Hernandez-Cancio, JD; Shawn L. Ralston, MD; Allan S. Liebe Brian K. Alverson, MD; Jill E. Baley, MD; Anne M. Gadomski, MD; Nizar F. Maraqa, MD; Eneida A. Mendonca, MD; Kieran J. Phelan Danette Stanko-Lopp, MA; Mark A. Brown, MD; Ian Nathanson, Stephen Sayles, III, MD; Sinsi Hernandez-Cancio, JD

Pediatrics (2014) 134 (5): e1474–e1502. https://doi.org/10.1542/peds.2014-2742



con lesiones en la cabeza

FROM THE AMERICAN ACADEMY OF PEDIATRICS | CLINICAL PRACTICE GUIDELINE AUGUST 01 2021

Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old *⊙*

Robert H. Pantell, MD, FAAP; Kenneth B. Roberts, MD, FAAP; William G. Adams, MD, FAAP;
Benard P. Dreyer, MD, FAAP; Nathan Kuppermann, MD, MPH, FAAP, FACEP; Sean T. O'Leary, MD, MPH, FAAP;
Kymika Okechukwu, MPA; Charles R. Woods, Jr, MD, MS, FAAP SUBCOMMITTEE ON FEBRILE INFANTS

3yington is affiliated with BioFire and IDbyDNA. Dr Woods is is affiliated with UpToDate, Moderna, and Pfizer; the other authors flicts of interest to disclose.

ve indicated they have no financial relationships relevant to this

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Questions?

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