Top Articles in Pediatric Hospital Medicine:
July 2019 to June 2020

Corrie E. McDaniel, DO, and Christopher J. Russell, MD, MS

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Top Articles in Pediatric Hospital Medicine:
July 2019 to June 2020

Corrie E. McDaniel, DO¹, and Christopher J. Russell, MD, MS²

Affiliations:
¹Division of Hospital Medicine, Seattle Children’s Hospital, Seattle WA and Department of Pediatrics, University of Washington, Seattle WA
²Division of Hospital Medicine, Children’s Hospital of Los Angeles, CA and Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA

Address correspondence to: Corrie McDaniel, Seattle Children’s Hospital, 4800 Sandpoint Way NE, M/S FA.2.115, P.O. Box 5371, Seattle WA, 98105; telephone: 206-987-5888; email: corrie.mcdaniel@seattlechildrens.org

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The last academic year has been filled with discussions of inequality, overuse, and a chance to reflect upon our own biases within medicine. As a field, we took a momentous step forward with the first set of physicians qualifying and sitting for the Pediatric Hospital Medicine Subspecialty Boards. This event, however, was embroiled with concerns around gender disparities and inequity, sparking petitions signed by thousands of physicians and calls for accountability and transparency within our systems. Fast forward four months and the world was turned upside-down in the face of the SARS-CoV-2 pandemic. Pediatric hospitalists in locations like New York City converted pediatric units to adult units, precepted internal medicine residents, and within a period of weeks organized the Pediatric Overflow Planning Contingency Response Network. Finally, police violence, killings, and protests have brought systemic racism to the forefront as a public health crisis. We care for children regardless of their cultural backgrounds, gender orientation, and socioeconomic statuses, and as such, we as a community have the chance to play a critical role in instigating change for addressing and uprooting systemic racism.

In this context, we have reviewed with a critical lens articles published from July 2019 through June 2020 to winnow down the expanse of literature over the past 12 months into the Top Articles for Pediatric Hospital Medicine (PHM), an annual presentation at the PHM conference. In undertaking this endeavor, we reviewed 11,925 articles from 19 journals (Table). We conducted this review in three steps, detailed in Figure 1. In the first step, we reviewed manuscript titles and eliminated articles based on a series of questions to broadly assess relevance. In the second step, we conducted an abstract review of 918 articles. Given that hospitalists practice in many different settings, we considered the scope of PHM when eliminating articles within the second step. In the third step, we conducted an in-depth full text
review of 163 articles. Each article was categorized, summarized, and then evaluated for strengths and weaknesses. Although the ultimate decisions were subjective, from these articles we chose the final list of Top Articles.

Below we discuss each of the Top Articles and its implication to practice.

**Glucose Profiles in Healthy Term Infants in the First 5 Days: The Glucose in Well Babies (GLOW) Study¹ and Lower Versus Traditional Treatment Threshold for Neonatal Hypoglycemia²**

The GLOW study by Harris et al. is a prospective, observational study of continuous glucose levels for 67 term infants without risk factors for hypoglycemia. Continuous glucose monitors were placed within 1 hour of birth and remained in place until 120 hours. This study found that 39% of infants had at least 1 serum glucose measurement below 47 mg/dL, a commonly accepted threshold for treatment of hypoglycemia in at-risk infants, and 10% had levels less than 36 mg/dL. No infant required intervention or had an adverse outcome, although infants without risk factors for hypoglycemia have the physiologic ability to respond to a low glucose level when they experience one.

The second study, by van Kempen et al. is a multicenter, non-inferiority, randomized control trial (RCT) of 689 neonates born at >35 weeks gestational age, who had an indication for routine hypoglycemia screening (e.g. infant of a diabetic mother, late-preterm delivery, small or large for gestational age), and a birth weight > 2000g. Infants were randomized 1:1 to either receive treatment at glucose thresholds < 36 mg/dL or <47 mg/dL. Outcome measures were 1) psychomotor development at 18 months by the Bayley Scales of Infant and Toddler
Development and 2) measures of burden, efficacy, and healthcare utilization. Infants in the lower treatment threshold group were found to have no difference in cognitive or motor development compared to the higher threshold group. In addition, infants in the lower threshold group received fewer glucose measurements and less therapeutic interventions such as NG placement or intravenous glucose. No infant in either group experienced clinical signs or symptoms of hypoglycemia and both groups had similar durations of breastfeeding and length of stay (LOS).

Implications to practice:

Nearly half of term infants without risk factors for hypoglycemia in the GLOW study experienced glucose levels below standard treatment thresholds for hypoglycemia (47 mg/dL). In addition, at-risk infants within the second study when treated at lower thresholds (37mg/dL) had fewer interventions without adverse events. Current treatment protocols should be evaluated to reduce unnecessary testing and treatment for infants at-risk for hypoglycemia.

Reducing Variability in the Infant Sepsis Evaluation (REVISE): A National Quality Initiative and Pathways for Improving Inpatient Pediatric Asthma Care (PIPA): A Multicenter, National Study

Biondi et al. led a quality improvement (QI) initiative across 124 university and community hospitals to standardize and improve appropriate hospitalization and LOS for febrile infants 7-60 days. Through participation in a national QI collaborative, data were collected on 20,570 infants who were evaluated for fever without a source. The Value in Inpatient Pediatrics (VIP) Network and study team provided hospitalists and emergency room physicians with tools for change management, including data support, mobile applications, webinars, coaching, and a Listserv.
Overall, the proportion of patients meeting appropriate hospitalization criteria increased from 75% to 82% during the study period. The proportion of patients meeting appropriate LOS criteria also increased by 15%, without any increases in missed infections. However, even after the intervention, more than 50% of patients did not meet appropriate LOS criteria.

Also through the VIP Network, Kaiser et al. led a diverse group of 68 hospitals to improve evidence-based care for 12,013 children hospitalized with asthma exacerbations. Through a learning collaborative model, pathway implementation was associated with higher odds of early metered dose inhaler bronchodilator administration (adjusted OR=1.18) and caregiver referral to smoking cessation (adjusted OR=1.93), but was not associated with improvements in LOS.

**Implications to practice:**

Translating evidence into bedside practice is challenging and requires context-specific implementation and multidisciplinary collaboration. Participating in national QI collaboratives, however, improves the quality of care for children hospitalized across the spectrum of hospital settings.

**Performance of the Modified Boston and Philadelphia Criteria for Invasive Bacterial Infections**

In this study, Lyons et al. evaluated the diagnostic accuracy of the modified Boston and Philadelphia criteria for well-appearing febrile infants. They conducted a retrospective, cross-sectional study of 10,928 infants, 29-60 days of life who were evaluated for meningitis across 23
hospitals. Primary outcomes included growth of a pathogenic bacteria in a blood or cerebrospinal fluid culture. Within the cohort, 264 infants (2.4%) had an invasive bacterial infection (IBI) with 71 (0.6%) infants with bacterial meningitis and 198 (1.8%) with bacteremia. When applied retrospectively, the modified Boston criteria misclassified 79 infants with bacteremia or meningitis as low risk, giving a 62.7% sensitivity and 59.2% specificity. Similarly, the Philadelphia criteria misclassified 62 infants with an IBI as low risk, giving a 72.7% sensitivity and 46.1% specificity. Only 4% of infants classified as high risk actually had an IBI.

**Implications to practice:**

One-third of infants with an IBI were misclassified using the modified Boston and Philadelphia criteria in this study. The high negative predictive value is driven by low prevalence rather than a high performing test and strong consideration should be given to discontinue the use of these two criteria. Risk-stratifying well-appearing febrile infants is more complicated than a binary determination and although there have been other criteria published since the Boston and Philadelphia Criteria that include more modern diagnostics, including procalcitonin, further research using modern biomarkers should be developed to re-conceptualize risk-stratification in well-appearing, febrile infants.

**Prevalence of Continuous Pulse Oximetry Monitoring in Hospitalized Children with Bronchiolitis Not Requiring Supplemental Oxygen.**

Leading a group of 56 hospitals in the Pediatric Research in Inpatient Settings network, Bonafide et al. conducted a cross-sectional study of pulse oximetry overuse in 3612 patient observations of non-hypoxemic children admitted during the 2018-19 viral bronchiolitis season. Results
demonstrated that 48% of all children hospitalized with viral bronchiolitis remained on continuous pulse oximetry despite being off oxygen. They demonstrate wide variations in pulse oximetry overuse (adjusted overuse rate: 6-82%) with a substantial proportion of variation at the hospital level.

Implications to Practice:

Given that mild, transient hypoxemia has been demonstrated to have no long-term negative outcomes, and that continuous pulse oximetry prolongs LOS in viral bronchiolitis, future research should examine ways to systematically deimplement this overused technology.

Cost-Effectiveness of Screening Ultrasound after a First Febrile Urinary Tract Infection in Children Ages 2-24 months

In this study, Gaither et al. created a decision analytic model to simulate a population of children presenting with a first febrile UTI. Building the model based from patients enrolled in the Randomized Intervention for Children with Vesicoureteral Reflux and the Careful Urinary Tract Infection Evaluation trials, they compared the cost-effectiveness of obtaining a renal bladder ultrasound (RBUS) after the first, febrile UTI (intervention group) versus waiting until a second UTI (control group) in children ages 2-24 months. The recurrent UTI rate was 19.9% within the intervention group and 21.0% in the control group. 91 patients with their first febrile UTI would have to undergo a RBUS to identify one patient who has an underlying anomaly that would lead to a recurrent UTI. In addition, 21% of children in the intervention group were subjected to unnecessary voiding cystourethrograms (VCUG) due to false positives on the screening ultrasound. This unnecessary and invasive testing is reduced by 60% in the control group.
Analysis found that the ratio of cost to improvement in quality of life was such that even if a RBUS was free it would still not be cost-effective.

*Implications to practice:*

Increasingly, major genitourinary (GU) anomalies are diagnosed prenatally and when scaled to a population level, a screening RBUS after the first UTI is not cost effective. In children older than 2 months of age presenting with a first febrile UTI consider deferring a RBUS unless the child experiences a recurrent UTI.

**A Quality Improvement Initiative to Reduce Gastrostomy Tube Placement in Aspirating Patients**

Using QI methodology, McSweeney et al. aimed to reduce the rates of gastrostomy tube placement in children with oropharyngeal aspiration on videofluoroscopic swallow study (VFSS). Through creation of an evidence-based guideline, the multidisciplinary team decreased placement by over 50% (10.9% to 5.2%) that was sustained for over three years after implementation. This large decrease was also associated with lower rates of hospital reutilization (emergency room visits, hospitalizations) and costs.

*Implications to practice:*

Gastrostomy tube placement is associated with higher hospitalization rates, costs, and post-operative complications. Many children with oropharyngeal dysphagia and aspiration on VFSS may be able to safely avoid gastrostomy tube placement with a standardized criteria and
Impact of Socioeconomic Outcomes on Patients with Kawasaki Disease

Retrospectively examining 915 patients hospitalized with Kawasaki disease at one freestanding children’s hospital, Dionne et al. studied the association between neighborhood socioeconomic status and quality of care for Kawasaki disease. Those in the lowest SES quartile were more likely to present for treatment later, to have IVIG treatment delayed beyond 10 days, and to have longer length of stay. In a subgroup of white children (for whom there was sufficient power), those in the lowest SES quartile were associated with future development of large or giant coronary artery aneurysms.

Implications to practice:

Addressing disparities in socioeconomic status, including improving access to healthcare, and removing structural racism barriers, may mitigate the lifelong consequences caused by common pediatric diseases, such as Kawasaki disease.

Effect on Patient Safety of a Resident Physician Schedule without 24-Hour Shifts

In a multicenter, cluster-randomized, crossover trial, Landrigan et al. compared serious medical errors made by resident physicians when working shifts ≥24 hours to shifts ≤16 hours in 6 pediatric intensive care units. In an analysis of 38,821 patient-days, residents working shifts ≤16...
hours made 50% more serious medical errors than those working shifts ≥24 hours. However, the rates of serious errors made by residents increased proportionately to resident workload. The relative risk of serious medical errors made by a resident increased by almost 10% per additional patient (RR=1.09). Accordingly, sites with the highest resident-to-patient workloads also experienced the most errors when transitioning from longer to shorter shifts as these further increased the individual resident workload.

*Implications to practice:*

Transitioning to shorter shift lengths has serious implications upon patient safety if the necessary infrastructure and support is not in place to mitigate the increase in patient workload and volume.

**The Patient Experience Debrief Interview: How Conversations With Hospitalized Families Influence Medical Student Learning and Reflection**

In this mixed-methods, cluster randomized trial involving medical students from two institutions during their core pediatric clerkship, Chua et al. evaluated the effect of a patient debrief interview on a student’s depth of reflection and learning from a given experience. At the completion of their pediatric clerkships, students were asked to write a reflective essay about their experience. Students within the intervention arm during their clerkship used the debrief interview tool to facilitate a conversation between a primary caregiver of a hospitalized patient and themselves. Essays were scored for reflective capacity based off a standardized rubric and the content was analyzed inductively. Students who conducted the interviews with families to understand their experiences demonstrated higher levels of critical reflection when reflecting
upon their own clerkship experience and described experiences that were more patient rather than physician or professional development focused.

*Implications to practice:*

Patients are often our best educators. Incorporating an intentional opportunity for students to explore the experience of patients and families can facilitate building a patient-centered lens for students and can be integrated into student curriculums across diverse hospital settings.

**Gender Differences in Earnings of Early- and Midcareer Pediatricians**

In a survey of more than 1200 early and midcareer pediatricians across a variety of work settings, Fritner et al. explored pay disparities by gender. Unadjusted, women earned $51,000/year less than men. After adjusting for labor force characteristics (e.g., years in practice, race/ethnicity), specific job characteristics (e.g., setting, hours worked, primary specialty), and work-family characteristics (e.g., marital status, number of children, part-time status), women still earned $8,000/year less than what men earned. Using the fully adjusted pay disparity ($8,000/year) and assuming investment return ranges of 3-7%, the earnings disparity may lead to a pre-tax loss of $400,000-800,000 over a 30-year career.

*Implications to practice:*

Employers ought to provide (and physicians demand) transparency about physician pay. Employers should examine and mitigate any pay inequity.
Clinical Take-Aways

Beyond the selection of the Top Articles, in our full review of the 163 articles, we uncovered many other impactful studies, which have implications to practice when taken in context together. This next section highlights six areas where the literature in this past year provides opportunity for further improvement in the care for hospitalized children.

The discharge processes and follow-up for infants with prenatal substance exposure.

Through a holistic approach to discharging infants with NAS that included referrals to a primary care physician, early intervention, in-home nursing, developmental outpatient clinic, and referral to gastroenterology or infectious disease if exposed to hepatitis C, Crook et al. increased the percentage of infants receiving all the indicated discharge follow-up from 2.6% to 60.3%.13 This is particularly important in the light of work done by Bell et al. where only half of infants born to hepatitis C positive mothers received outpatient testing, leading to an estimated risk of 60% of hepatitis C-positive infants going undiagnosed.14

Antibiotic stewardship for common pediatric illnesses. Antibiotic overuse is seen in children hospitalized with asthma,15 pneumonia,16, 17 skin and soft tissue infections,16 and urinary tract infections.18, 19 Infants with suspected early onset sepsis (EOS) are a key population where studies this year help decrease antibiotic overuse. Integration and use of the EOS calculator is feasible, safe, and reduces antibiotic therapy.20, 21 Repeat physical exam assessments even in newborns with suspected EOS can safely reduce antibiotic utilization.22 If antibiotics must be
started, consider stopping after 24 hours if cultures remain negative, and if cultures are positive, consider switching to oral amoxicillin. Lastly, in the context of late-onset sepsis, including infants <32 weeks of age or <1500g, the sensitivity and specificity of the C-reactive protein is 62% and 74%, respectively. Given the poor test characteristics, we should stop using C-reactive protein to guide decision-making in late-onset neonatal sepsis.

**Lumbar punctures in febrile infants <60 days of life.** Compared to the first week of life, the incidence of invasive bacterial infection (IBI) drops by 89% at 4 weeks of life. In a sub-analysis from REVISE, Wang et al. demonstrate that well-appearing infants >30 days old with a positive UA had zero cases of bacterial meningitis and may not need a LP. In a single center study of infants <30 days with a UTI, Cano et al. showed in that if the procalcitonin was 0.35ng/mL, then the infant was low risk for bacterial meningitis and proposed the LP could be avoided. In addition, afebrile infants with only a history of fever have a lower odds of serious bacterial infections and a prediction model involving the highest temperature, age, urinalysis, and absolute neutrophil count may help to stratify infants <60 days at low risk of an IBI.

**Overuse of high flow nasal cannula (HFNC) in viral bronchiolitis.** HFNC for bronchiolitis is associated with increased intensive care utilization, is costly when used early in therapy rather than as a rescue, and does not demonstrate a lower rate of treatment failure compared to low-flow nasal cannula. These studies should prompt a consideration of the efficacy of HFNC for the treatment of bronchiolitis, particularly with ongoing overutilization without clear evidence of effectiveness.
Health disparities in hospitalized children and families. Families with limited English proficiency (LEP) experience barriers in utilizing interpreter services. Families with low health literacy have decreased comprehension of discharge instructions with higher rates of adherence errors. Black, Asian, and Hispanic infants are less likely to receive human donor milk than white, non-Hispanic infants. In addition, we can continue to improve screening for social risk factors for children when hospitalized and asking about firearms and firearm safety in the household.

SARS-CoV-2 and Multisystem Inflammatory Syndrome in Children (MIS-C). While this is a rapidly evolving field of literature, Jones et al. published one of the first case reports of a six-month-old with SARS-CoV-2/Kawasaki Disease in Hospital Pediatrics on April 7, 2020. Since this initial case report, larger case series out of Italy demonstrated a 30-fold increase in Kawasaki and Kawasaki-like illness between February and April 2020, when compared to the previous five years. Nearly 80% patients in the SARS-CoV-2 cohort demonstrating SARS-CoV-2 IgM or IgG antibodies. These patients were older (mean age 7.5 years), demonstrated more severe illness (e.g., cardiac involvement, Kawasaki disease shock syndrome), and required corticosteroid therapy. This new disease, initially called pediatric inflammatory multisystem (PIMS), was renamed MIS-C in May 2020 by the World Health Organization and the Centers for Disease Control and Prevention. In late June, Feldstein et al. published a report of 186 patients in the United States diagnosed with MIS-C; of those patients, half received vasoactive support, 20% received mechanical ventilation, and 2% died. Given the evolution of the SARS-CoV-2 pandemic, the true morbidity and mortality for children may not be known for some time. The
risk of misdiagnosis of Kawasaki disease in the setting of SARS-CoV-2 and over-diagnosis of MIS-C may subject children to over-treatment and harms.

Conclusion

As we continue to reflect critically upon the literature, we look forward to this next year and the incredible research that will continue to advance our field.

References


Table: Journals Reviewed from July 2019 through June 2020

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1. Is the article low impact or too narrow in scope? These are articles that are potentially relevant to a narrow subset of PHM providers, but that we did not feel would be generalizable to practice for enough of the general community of PHM (e.g. Acinetobacter baumannii Is a Risk Factor for Lower Respiratory Tract Infections in Children and Adolescents with a Tracheostomy).

2. Does the article have weak or flawed methodology? These are articles where the stated methods had flaws that we felt were unable to be overcome.

3. Is the article not original research? Articles such as editorials or perspective pieces were excluded here.

4. Does the article focus on the wrong scope? These articles may be of great interest or of excellent quality but are primarily targeting populations not routinely cared for by pediatric hospitalists (e.g. Six-Year Follow-up of a Trial of Antenatal Vitamin D for Asthma Reduction).

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