“Hot” Topic: Interpreting and Applying the AAP Febrile Infant Clinical Practice Guidelines

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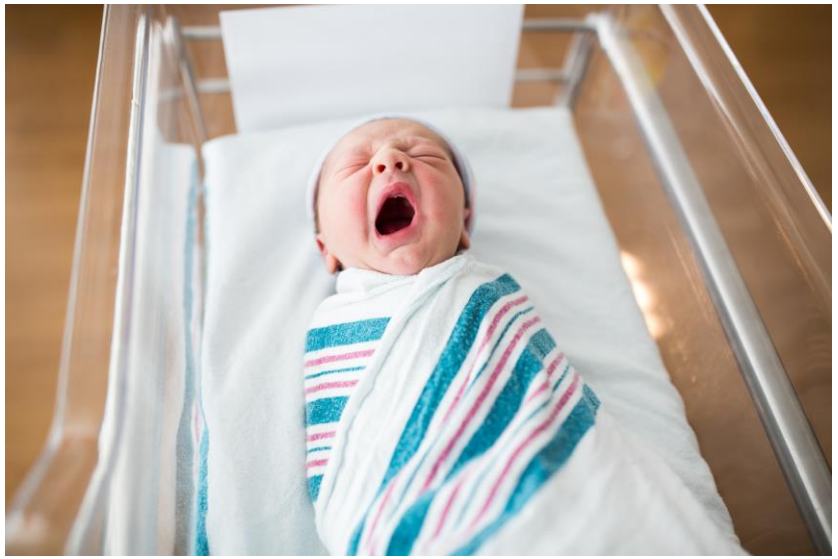


Disclosures

- I have no relevant financial relationships to disclose
- I do not intend to discuss an unapproved/investigative use of a commercial product/device
- I am leading a research project exploring parent experiences engaging in shared decision making in the care of febrile infants

Objectives

- Appraise the quality of evidence presented in American Academy of Pediatrics (AAP) clinical practice guidelines
- Distinguish key updates in the 2021 AAP Febrile Infant Clinical Practice Guidelines (CPG) and apply these recommendations to patient cases

What is your primary practice setting?

- Private practice
- Multi-specialty/health network practice
- Community hospital
- Academic or freestanding children's hospital
- Non-clinical setting

Guidelines → Clinical Practice

- Have the AAP febrile infant guidelines changed your clinical practice?
- What concerns, if any, do you have about the guidelines?
- What parts, if any, of the guidelines remain unclear?

2021 AAP clincal practice guideline (CPG) development: rationale

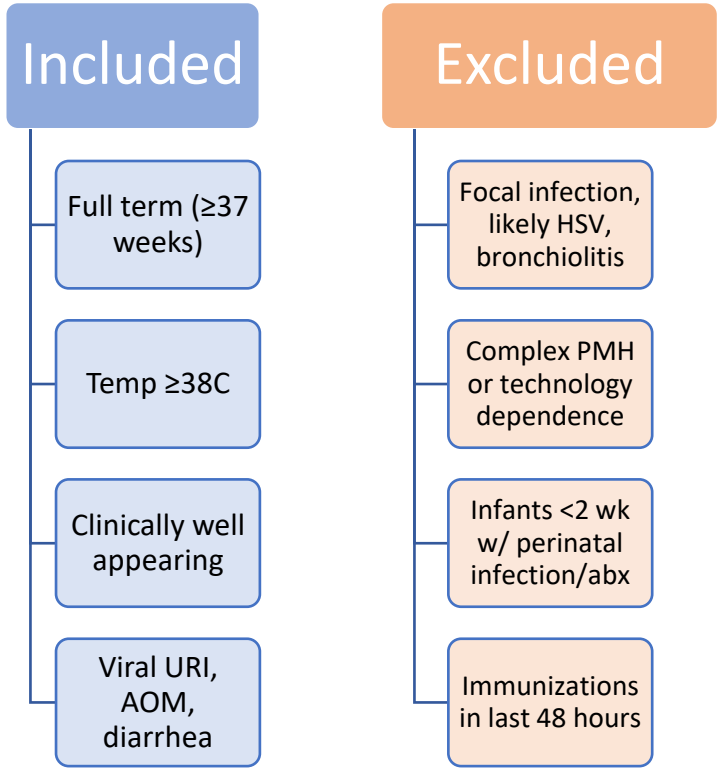
- 1980s clinical prediction rules for infants at low risk for invasive bacterial infections (IBI)
  - Low positive predictive values (20-40%)
  - Arbitrarily defined lab cut offs (ie. WBC <5000 or >15000)
  - Missed IBI are rare
- Changing bacteriology of infant infections (gram negative > gram positive infections)
- New inflammatory markers (CRP, procalcitonin), advanced bacterial/viral testing now available

CLINICAL PRACTICE GUIDELINE

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old

Robert H. Pantell, MD, FAAP,[a] Kenneth B. Roberts, MD, FAAP,[b] William G. Adams, MD, FAAP,[c] Benard P. Dreyer, MD, FAAP,[d] Nathan Kuppermann, MD, MPH, FAAP, FACEP,[e] Sean T. O'Leary, MD, MPH, FAAP,[f] Kymika Okechukwu, MPA,[g] Charles R. Woods Jr, MD, MS, FAAP[h] SUBCOMMITTEE ON FEBRILE INFANTS



CPG Development

Agency for Healthcare Research and Quality

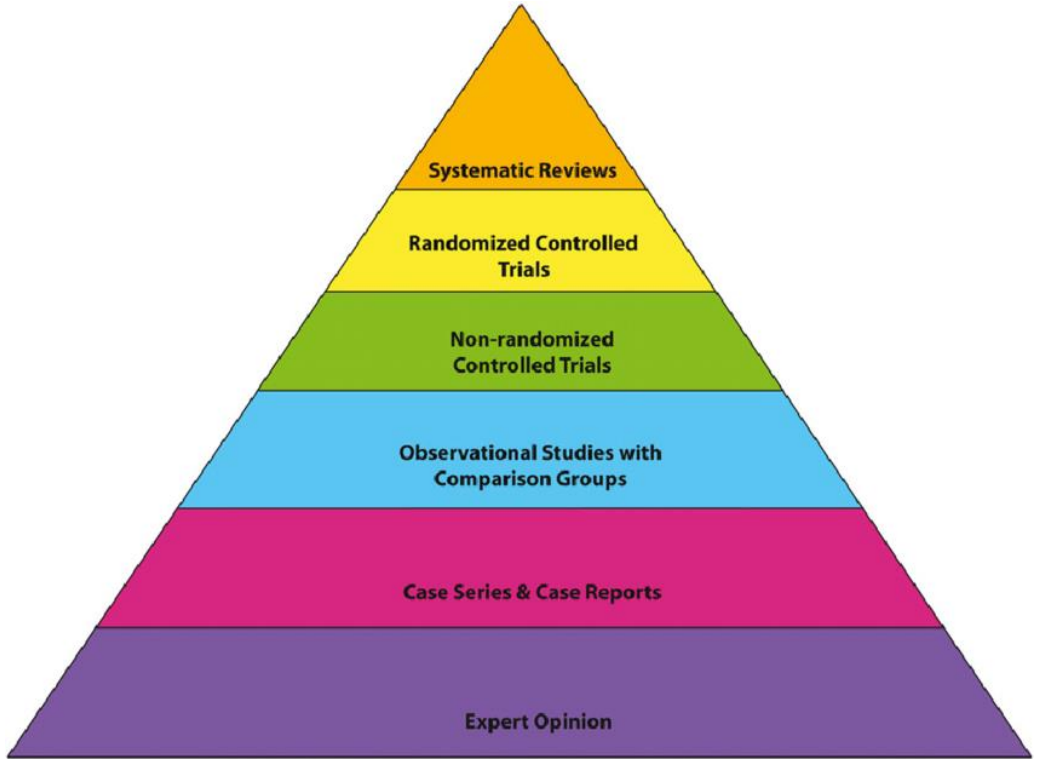
- Aim: “improve the diagnosis and treatment of UTIs, bacteremia, and bacterial meningitis”
- Committee: epidemiology, general pediatrics, emergency medicine, infectious disease, hospital medicine, family medicine
- Evidence review by AHRQ, committee members
- Further evidence solicited from researchers with prior publications if gaps in the literature existed
  - Kaiser Permanente Northern CA
  - AAP PROS network
  - Febrile Young Infant Research Collaborative (FYIRC)
  - PECARN
- Recommendations developed through strong consensus of committee
- Recommendations reviewed by additional focus groups including clinicians and parents

Moving from evidence to CPG recommendations

- 2004 Steering Committee developed standards to classify AAP guideline recommendations

Key considerations:

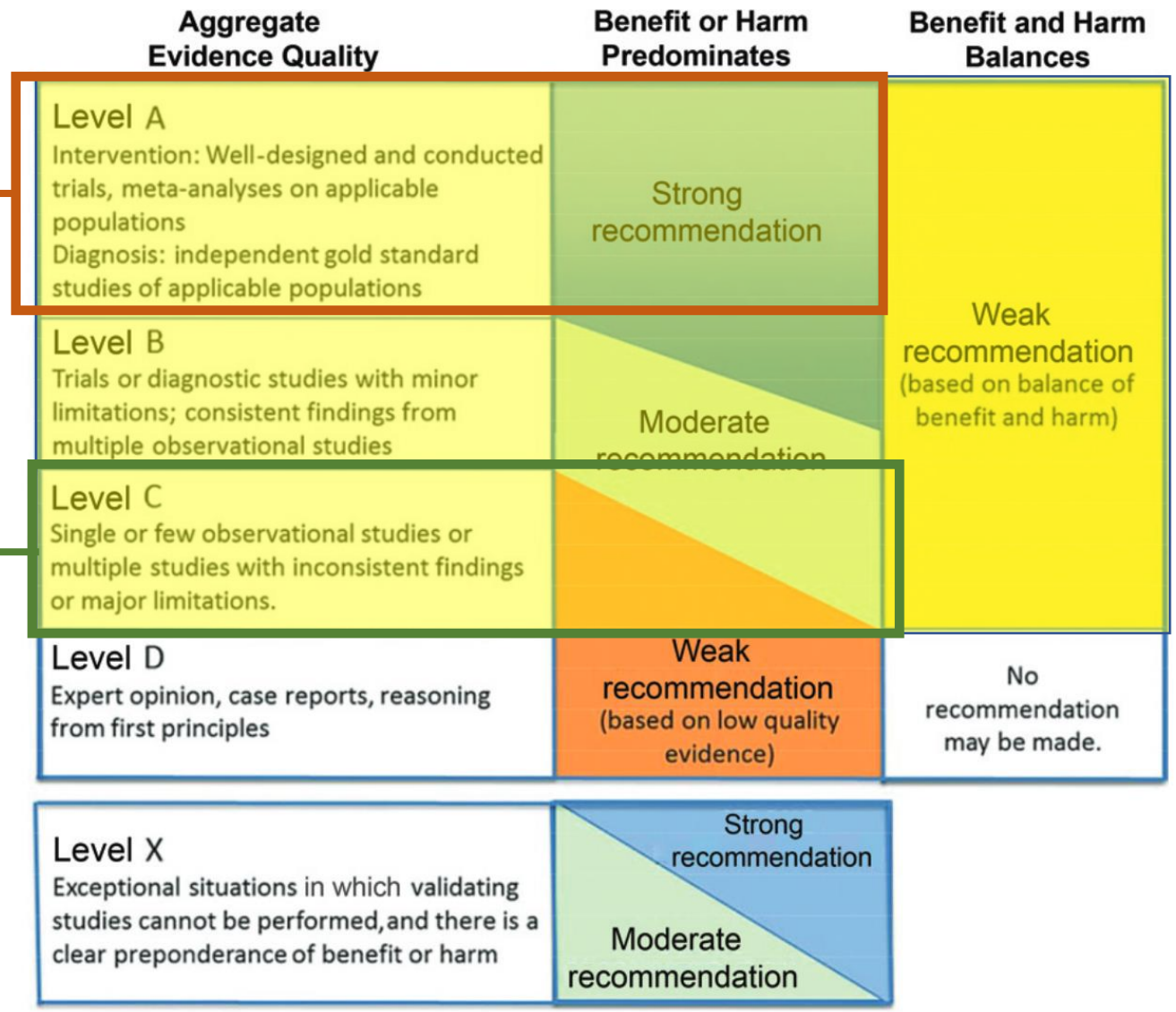
1. Aggregate evidence quality
    1. Types of studies
    2. Applicability to target population
    3. Sample size
    4. Bias, major errors
2. Balance of benefits, harms
    1. Magnitude
    2. Likelihood



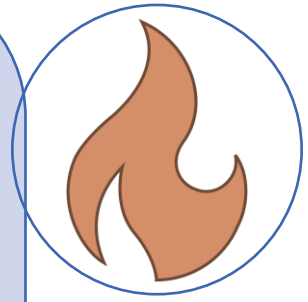
Grading AAP recommendations

Obtain UA for all infants

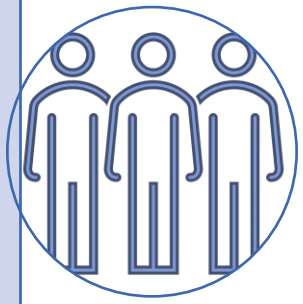
Dose of IV antibiotics for 22-28do infants discharging home



CPG Key Updates



Inflammatory markers



3 age-based algorithms

Shared decision making

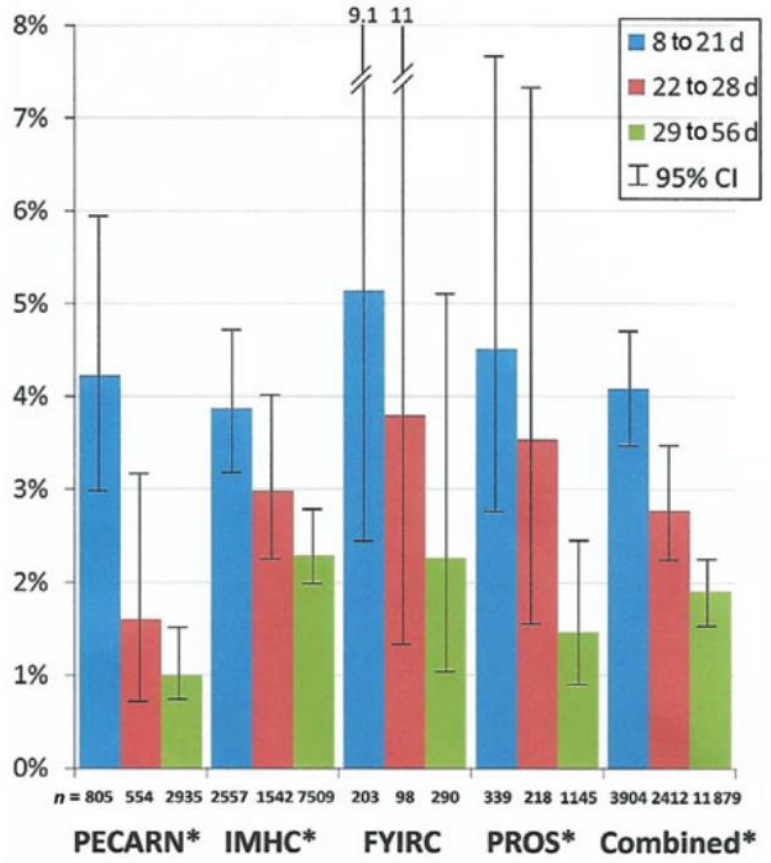
CPG Key Updates: inflammatory markers (IM's)

Abnormal/elevated IM's

- Best performance when interpreted together
  - Even procalcitonin has insufficient sensitivity when used alone to predict IBI
  - Lower sensitivity in infants <21 days

*based on separate study findings using ANC as part of clinical prediction tool for IBI

CPG Key Updates: 3 algorithms!



Rates of bacteremia by infant age

CPG Key Updates: 3 algorithms!

8-21 days old

- **Full court press** (blood, urine, CSF cultures, IV antibiotics, admission)
- No need for IM's
- Discharge when cultures negative at 24-36h or infection appropriately treated

22-28 days old

- Blood, urine, inflammatory markers
- **Normal** IM's → **MAY*** obtain CSF → **MAY** discharge home if CSF cell counts normal
- Give dose of IV antibiotics if discharging home

29-60 days old

- Blood, urine, inflammatory markers
- Normal IM's → no CSF studies, discharge
  - UA+ with normal IM's → PO antibiotics
  - UA- with normal IM's → no antibiotics
- **Abnormal** IM's → **MAY*** obtain CSF → **MAY** hospitalize/give antibiotics if CSF cell counts normal

***May=opportunity for shared decision making**

CPG Key Updates: shared decision making (SDM)

Broad definition: collaborative decision-making process between patient and provider, considering both available evidence and patient/family values

Consider **variation** in:
- Risk tolerance (of clinician and family)
- Comfort monitoring infant at home
- Access to follow up

Equitable SDM requires attention to:
- Primary language
- Communication preferences
- Preferences for level of involvement in decisions
- Varied healthcare experiences

AHRQ SHARE approach to SDM

CPG Key Updates: shared decision making (SDM)

KAS 12b: 22-28 day old infants with abnormal IM's should receive empiric antibiotics

KAS 12b

Benefits	An abnormal IM indicates a risk of bacteremia >5%, a threshold sufficiently high to recommend empirical treatment. Anticipated reduction in morbidity and mortality.
Risks, harm, cost	Adverse drug reactions including anaphylaxis (rare). Complications related to intravenous lines including infiltration, infection, nerve compression (in ankle). Potential disruption of evolving microbiome. Development of antimicrobial resistance.
Benefit–harm assessment	Preponderance of benefit.
Key references	18–20, 60

KAS 18a: 29-60 day old infants with abnormal IM's may receive a lumbar puncture

Benefits	The prevalence of meningitis in this age group is 0.12–0.32.[17,22,24,61,94] Early detection of meningitis. Early treatment may lead to decreased neurologic morbidity. Identification of pathogen from CSF to target type and duration of antimicrobial treatment. Avoids unnecessarily prolonged antimicrobial therapy if CSF was obtained after antimicrobial agents started and diagnosis of meningitis is uncertain.
Risks, harm, cost	Discomfort for infant. Potential for transient respiratory compromise during positioning for LP. Traumatic LPs have been documented to prolong length of stay for hospitalized infants. Unnecessary prolongation of hospitalization from false-positive bacterial culture result. Substantial cost if hospitalizing because of ambiguous CSF or prolonged hospitalization for bacterial contaminant. Parental anxiety.
Benefit–harm assessment	Preponderance of benefit if CSF obtained.
Shared decision-making	Because parents must consent for this procedure, shared decision-making is required and their risk tolerances a consideration. KAS 4 extensively discusses rates and consequences of unsuccessful LPs, uninterpretable CSF analysis, and false-positive bacterial culture rates. If, for whatever reason, a parent is resistant or unwilling to consent to an LP, risk of meningitis, the evidence quality, benefit/harm assessment, and value judgments should be communicated to the parent to foster informed decision-making. The potential need for a future LP, depending on further clinical information and progress, is an important part of the discussion. These discussions should be documented.
Key references	65–70, 94, 165–166

Case 1

A 14 day old full term infant with a normal prenatal and newborn course comes to the ED after parents measured a rectal temperature of 38.2 C at home. She is fussy but alert and non-toxic appearing without focal signs of infection.

A 14 day old full term infant with a normal prenatal and newborn course is febrile to 38.2C without focal signs of infection. What studies should you (routinely) obtain on initial evaluation?

Blood culture	Chest X-ray	CSF studies	Inflammatory markers	Liver function tests	Urinalysis +/- urine culture

Why are inflammatory markers not universally recommended in evaluation of 8-21 day old infants with fever?

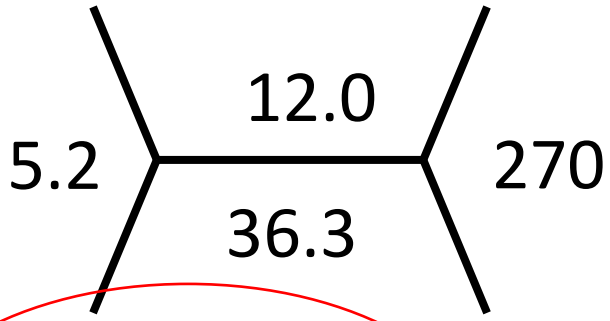
- Low specificity in young infants
- Low sensitivity in young infants
- Large blood volume required
- Not clinically useful
- High risk of lab error

Case 2

A 25 day old full term infant with a normal prenatal and newborn course presents to clinic for evaluation of 2 days of nasal congestion and diarrhea. He has a temperature of 38.4 C and otherwise normal vitals. He has clear lungs on exam. He is referred to the ED for further work up.

Case 2, cont.

In the ED, the following labs are obtained:



ANC 2600/mm^3
PCT 0.2 ng/mL
CRP 1.2 mg/dL
UA: normal
Blood culture: pending

Normal IMs

What do you consider as you discuss next steps in evaluation (ie. lumbar puncture, disposition) for this 25 day old infant?

Takeaways

The AAP uses a universal framework to grade recommendations in clinical practice guidelines based on quality of evidence and preponderance of risk/benefit

The 2021 AAP febrile infant CPG includes several key changes based on evidence we can safely do less for some infants

- Risk stratification with inflammatory markers
- 3 age-based algorithms
- Shared decision making (SDM) explicitly recommended in certain clinical scenarios

Inflammatory markers should be interpreted together for highest sensitivity/specificity

SDM is not a “one size fits all” process

- Variable values, risk tolerance, access to f/u are key considerations
- Equitable SDM requires patient-centered and individualized communication

Thank you!

References

1. American Academy of Pediatrics Steering Committee on Quality Improvement and Management. Classifying recommendations for clinical practice guidelines. *Pediatrics*. 2004 Sep;114(3):874-7. doi: 10.1542/peds.2004-1260. PMID: 15342869.
2. Aronson, Paul L., Paula Schaeffer, Linda M. Niccolai, Eugene D. Shapiro, and Liana Fraenkel. "Parents' Perspectives on Communication and Shared Decision Making for Febrile Infants ≤60 Days Old." *Pediatric Emergency Care* (January 21, 2020). https://doi.org/10.1097/PEC.0000000000001977.
3. Sarah M. Eaton, Jonna D. Clark, Christy L. Cummings, Alexander A. Kon, Wynne Morrison, Chris Feudtner, Jürg C. Streuli; Pediatric Shared Decision-Making for Simple and Complex Decisions: Findings From a Delphi Panel. *Pediatrics* November 2022; 150 (5): e2022057978. 10.1542/peds.2022-057978
4. Pantell, Robert H., Kenneth B. Roberts, William G. Adams, Benard P. Dreyer, Nathan Kuppermann, Sean T. O'Leary, Kymika Okechukwu, and Charles R. Woods. "Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old." *Pediatrics*, August 1, 2021. https://doi.org/10.1542/peds.2021-052228.
5. Sara Taub, Natalie Lanocha; Shared Decision-making in Pediatrics: Toward a More Participatory Model. *Pediatr Rev* January 2023; 44 (1): 50–52. https://doi-org.libproxy1.usc.edu/10.1542/pir.2021-004984
6. The SHARE Approach. Content last reviewed March 2023. Agency for Healthcare Research and Quality, Rockville, MD. https://www.ahrq.gov/health-literacy/professional-training/shared-decision/index.html
7. Wynne Morrison, Jonna D. Clark, Mithya Lewis-Newby, Alexander A. Kon; Titrating Clinician Directiveness in Serious Pediatric Illness. *Pediatrics* November 2018; 142 (Supplement_3): S178–S186. 10.1542/peds.2018-0516I