Colby College 44th Annual
“Problems in Pediatrics”

Top 10 - A Lit Review for You

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July 10th, 2018
Disclosure

• No financial relationships to disclose
• No conflicts of interest to resolve
• This presentation will not involve the discussion of unapproved, off-label, or experimental interventions or medications.
Objectives

• Review recent publications across broad topics in pediatrics

• Critically evaluate if recent literature should influence our medical decision making
The Power of Pulse Ox

Mandatory state screening for critical congenital heart disease saves lives
Association of US State Implementation of Newborn Screening Policies for Critical Congenital Heart Disease With Early Infant Cardiac Deaths

Rahi Abouk, PhD; Scott D. Grosse, PhD; Elizabeth C. Ailes, PhD, MPH; Matthew E. Oster, MD, MPH
Background

• 2011 screening recommendation for critical congenital heart disease (CCHD)
• Rate 200/100,000 live births, 6% fatality
• Variable implementation across states
• Hearing the only other non-dried blood spot recommendation
Methods

- CCHD is screened by pulse ox at 24hrs
- US Period Linked Birth/Infant Death Data
- 13 years; 2007-2013: over 25 million
- Compared states with mandates to others
- Evaluated death rates due to CCHD and other non-specified cardiac deaths
Results

• Mandatory states had 33.4% reduction in deaths attributed to CCHD
  –21.4% reduction in “other” cardiac category

• Largest effect in states with most recent mandate
## Results

Table 3. Characteristics of State-Month Periods With Critical Congenital Heart Disease Screening Policies or No Policies During the Period January 1, 2007, to June 1, 2013

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All States</th>
<th>States With No Policy Implemented</th>
<th>States With Mandatory Policy</th>
<th>States With Nonmandatory Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Before Enactment</td>
<td>After Implementation</td>
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<tr>
<td></td>
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<td>Between Enactment and</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Implementation</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>After Implementation</td>
<td></td>
</tr>
<tr>
<td>Births per mo, mean (95% CI)</td>
<td>6661.0</td>
<td>6610.9</td>
<td>4275.2 (4007.8-4542.6)</td>
<td>7946.3 (7271.9-8620.6)</td>
</tr>
<tr>
<td></td>
<td>(6417.3-6904.6)</td>
<td></td>
<td>(4810.4-6053.2)</td>
<td>(4825.3-6070.8)</td>
</tr>
<tr>
<td></td>
<td>9.8</td>
<td>10.0</td>
<td>8.3 (6.4-10.3)</td>
<td>10.6 (9.5-11.8)</td>
</tr>
<tr>
<td>Critical congenital heart disease deaths per 100 000 births (95% CI)</td>
<td>9.2-10.4</td>
<td>9.1-10.9</td>
<td>7.8 (3.9-11.8)</td>
<td>10.0 (6.1-13.9)</td>
</tr>
<tr>
<td>Other or unspecified congenital cardiac deaths per 100 000 births (95% CI)</td>
<td>13.5 (12.7-14.2)</td>
<td>13.4 (12.4-14.4)</td>
<td>12.0 (10.0-14.0)</td>
<td>14.8 (13.3-16.3)</td>
</tr>
<tr>
<td></td>
<td>11.5 (5.5-17.5)</td>
<td></td>
<td>8.5 (5.3-11.6)</td>
<td>13.8 (9.8-17.8)</td>
</tr>
<tr>
<td>Observations (state-months)</td>
<td>3978</td>
<td>2340</td>
<td>487 (4810.4-6053.2)</td>
<td>7946.3 (7271.9-8620.6)</td>
</tr>
<tr>
<td>No. of states</td>
<td>51</td>
<td>30</td>
<td>8</td>
<td>13d</td>
</tr>
</tbody>
</table>

\( ^{a} \)
Impact to practice

• Essentially costs nothing
• Very simple to do
  • You can make it your own practice
• Propensity to save 120 lives/year
• Opens avenue for point-of-care screening
Keto, neato

Ketone levels can predict severity of breastfeeding dehydration in newborns
Capillary Blood Ketone Levels as an Indicator of Inadequate Breast Milk Intake in the Early Neonatal Period

Takeshi Futatani, MD, Ayako Shimao, MD, Shihomi Ina, MD, Hiroyuki Higashiyama, MD, Shuhei Fujita, MD, Kazuyuki Ueno, MD, Noboru Igarashi, MD, and Kiyoshi Hatasaki, MD

J Pediatr 2017; 191:76-81
Background

- Tech for finger stick beta-hydroxybutyrate (βOHB) developed for DM already
- Large push for breastfeeding
- Recent large cohort of exclusive BF with 25% having >10% weight loss
- Need easy measurement for this as well as for hypernatremic dehydration
Methods

• 585 FT, normal wt infants, from 2012-2015
• Exclusive breast feeding
• Single center in Japan
• Aged 48-95hrs
• Daily weight, serum electrolytes, blood gas
• ROC for βOHB to determine cut off for >10% wt loss, Na>150
Impact to practice

- Weight loss and βOHB only predictors of hypernatremic dehydration
- Also adds information to acid-base status
- Easy to use bedside tool
- Not widely available but near future
Judging Jaundice

Smartphones just got smarter: There’s an app for that!
Use of a Smartphone App to Assess Neonatal Jaundice

James A. Taylor, MD, a James W. Stout, MD, MPH, a Lilian de Greef, MS, a Mayank Goel, PhD, a,b Shwetak Patel, PhD, a Esther K. Chung, MD, MPH, c,d Aruna Koduri, MD, e Shawn McMahon, MD, f Jane Dickerson, PhD, g Elizabeth A. Simpson, MD, h Eric C. Larson, PhD i
Background

- 80% of newborns have visual jaundice
- 86% of nurseries with universal screening
  - Study of 60 nurseries in the US
- Blood testing is painful, disruptive, costly
- Jaundice peaks after discharge; 96hrs
- Visual inspection inaccurate
- Can we find low-cost, high-tech that works?
Methods

- Prospective, 530 newborns
- <7 days old, 7 sites, 2014-2016
- Paired image predictions with TSB levels
- Calibration card on child’s sternum
- Regression analysis and correlation
- Sensitivity and specificity calculated
  - For high risk
# Results

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Correlation Coefficient</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>530</td>
<td>0.91</td>
<td>0.89–0.92</td>
</tr>
<tr>
<td>White</td>
<td>293</td>
<td>0.92</td>
<td>0.90–0.93</td>
</tr>
<tr>
<td>African American</td>
<td>110</td>
<td>0.90</td>
<td>0.86–0.93</td>
</tr>
<tr>
<td>Asian American</td>
<td>112</td>
<td>0.88</td>
<td>0.81–0.91</td>
</tr>
<tr>
<td>Hispanic, Latino</td>
<td>139</td>
<td>0.91</td>
<td>0.88–0.94</td>
</tr>
</tbody>
</table>

CI, confidence interval.
Overall correlation: 0.91

**FIGURE 1**
The relationship between paired TSB and BCB values in 530 newborns. The linear regression line is shown, along with individual points.
Impact to Practice

• Best suited as a screening test
• Highest sensitivity in >17mg/dL
• Answers in just seconds
• Do need the calibration card
• Easy to use in the office
• Highest impact world wide
Besting Bronchiolitis

High Flow Oxygen vs Standard flow for Bronchiolitis, it works!
A Randomized Trial of High-Flow Oxygen Therapy in Infants with Bronchiolitis

Donna Franklin, B.N., M.B.A., Franz E. Babl, M.D., M.P.H.,
Luregn J. Schlapbach, M.D., Ed Oakley, M.B., B.S.,
Simon Craig, M.B., B.S., M.H.P.E., M.P.H., Jocelyn Neutze, M.B., Ch.B.,
Jeremy Furyk, M.B., B.S., M.P.H.&T.M., John F. Fraser, M.B., Ch.B., Ph.D.,
Stuart R. Dalziel, M.B., Ch.B., Ph.D., and Andreas Schibler, M.D.
Background

- Bronchiolitis most common admission
- 1.7B in US healthcare costs
- AAP recommends: oxygen, respiratory support, hydration
- HF emerged as mode of resp support, esp outside of ICUs
Methods

• Prospective, RCT, multicenter (17), Australia and New Zealand
• 1472 infants <12mos, 2013-2017
• Compared HF to standard oxygen therapy
• Primary outcome: escalation of care (3/4)
  • Tachycardia
  • Tachypnea
  • Hypoxemia
  • Medical review- early warning tool
Results

• Escalation in 12% in HF vs 23% standard.
• In standard arm – 61% of tx failures responded to HF therapy.
• No differences in secondary outcomes of hospital or oxygen duration.
• Number needed to treat: 9.
Figure 2. Kaplan–Meier Plot of the Proportion of Infants with Bronchiolitis Remaining Free from Treatment Failure.
Impact to practice

- Pragmatic trial, couldn’t be blinded
- Specific to hypoxic infants <12mos
- Use early in admission, on gen ward
- Avoid transfers and ICU admissions
UTI’m Not Sure

Development of a decision tool to aid in diagnosing and treating UTI in children
Development and Validation of a Calculator for Estimating the Probability of Urinary Tract Infection in Young Febrile Children

Nader Shaikh, MD, MPH; Alejandro Hoberman, MD; Stephanie W. Hum, BS; Anastasia Albery, BS; Gysella Muniz, MD; Marcia Kurs-Lasky, MS; Douglas Landsittel, PhD; Timothy Shope, MD, MPH
Background

- 7% of febrile children <2yo presenting to ED have a UTI
- Catheterization is onerous, challenging
- Current algorithms underutilized
- Pre-test probability – who to test
- Post-test probability – who to treat
Methods

- Nested case-control study, 2013-2018
- UTI = pyuria (5WBC/HPF or 10WBC/microliter) AND >50,000 CFU of bacteria
- Created and tested several models
  - Calculated Area Under the Curve
- 2% deemed high risk for pre-test
- 5% deemed high risk for post-test
- Compared model to AAP clinical practice guideline algorithm
UTIcalc
Results

- Hypothetical 1,000 patients
- UTIcalc missed 0 vs 3 (AAP algorithm)
- Number needed to test was 9.8 vs 11.4
- 8.1% reduction in testing
- 10.6% reduction in treatment delay
Impact to practice

- Novel application of tech
- Clinicians rarely use algorithms
  - We need simple pragmatic tools
- This is ready to use when you want!
- Decrease overtesting and overdiagnosis
Bath, Boob, Book, Bed

Infants respond quickly to nightly bedtime routines
Implementation of a nightly bedtime routine: How quickly do things improve?

Jodi A. Mindell\textsuperscript{a,b,*}, Erin S. Leichman\textsuperscript{a}, Christina Lee\textsuperscript{c}, Ariel A. Williamson\textsuperscript{b,d}, Russel M. Walters\textsuperscript{c}
Bedtime routine is considered a key component of healthy sleep. Studies show that routines improve sleep in infants and children within two weeks. However, there is no data on the velocity at which this happens or when to expect results.
Methods

- Randomized prospective study
- Bath, massage, quiet activity, 30min max
- 134 Mothers and infants (8-18mos)
- Outcomes:
  - Sleep latency
  - Frequency of night time awakenings
  - Sleep consolidation
  - Maternal perceptions of sleep
    - Bedtime ease, sleep quality, infant mood
Fig. 1. (a) – Sleep onset latency. (b) – Night waking frequency. (c) – Night waking duration. (d) – Longest stretch asleep. (e) – Maternal perception of bedtime ease. (f) – Maternal perception of how well child slept. (g) – Maternal perception of child morning mood.
Impact to practice

- We have to be CONSISTENT!
- Easier pitch if parents know its quick
- Routines are associated with lifetime improvements in sleep and language
Endpoints Matter

Increasing ICS to prevent asthma exacerbations not all its cracked up to be
Quintupling Inhaled Glucocorticoids to Prevent Childhood Asthma Exacerbations

Background

- ICS help to control daily symptoms but unclear role in prevention of attacks
- Recent cochrane review that doubling ICS in “yellow” zone not effective
- So how about 4 or 5 times dosing?
  - Recent retrospective study in adults shows benefit
Methods

- Randomized, double-blind, parallel groups
- 17 sites in US, 192 mild-moderate asthma
- 75% adherence, 4 wk run-in, 3 yr study
- Fluticasone ICS, asthma control diary, PF
- Yellow zone = 5x ICS for 7 days
- 52 wk trial – high vs low ICS
- Primary outcome: # of exacerbations
- Secondary: time to attack, albuterol use, ED visits, hospitalization, total steroid use, and linear growth
Results

- In children 5-11yrs quintupling the ICS did not lead to less exacerbations.
- Did not prolong time to exacerbations.
- Did not reduce asthma symptoms scores.
- Lead to great total steroid exposure.
- 0.23cm of linear growth was observed (p=0.06).
Impact to practice

• Doesn’t answer the PRN question
  • Data may support this
• Loss of linear growth as downside
• Increased ICS does not reduce exacerbations
• Why did it work in adults??
Pesky penicillin allergy!

Can we risk stratify those with documented PCN allergy to be non-allergic?
Allergy Testing in Children With Low-Risk Penicillin Allergy Symptoms

David Vyles, DO, Juan Adams, MD, Asriani Chiu, MD, Pippa Simpson, PhD, Mark Nimmer, BA, David C. Brousseau, MD, MS
Background

- True PCN allergy is rare (0.004-0.015%)
- First line therapy often denied due to “allergic” designation
- Designation with low-risk symptoms
- Gold standard testing is three tiered:
  - Percutaneous
  - Intracutaneous
  - Oral challenge
- Adult study found 91.3% were not allergic
Methods

- 3.5-18yo children presenting to ED, 2yrs
- 17 point questionnaire developed
- Low risk – rash, itching, vomiting, diarrhea, runny nose, nausea, cough, FHx
- High risk – cardioresp symptoms: wheezing, difficulty breathing, airway swelling, syncope, drop in BP, etc.
Results

• 597 filled questionnaire
• 434 (72.6% low risk) 163 (27.3% high risk)
• First 100 children tested
• All 100 children (100%, 95% CI 96.4-100%) had no PCN allergy on 3-tier
Impact to practice

• The questionnaire was validated with 3-tier testing
• Convenience sampling could be bias
• Safe alternative to costly (time and labor), PCN skin testing in ED setting
• Might not be ready for office based challenge – yet!
Broad Spectrum not Better for Bacterial URIs

Treatment failure in broad vs narrow antibiotics for acute resp infections
JAMA | Original Investigation

Association of Broad- vs Narrow-Spectrum Antibiotics With Treatment Failure, Adverse Events, and Quality of Life in Children With Acute Respiratory Tract Infections

Jeffrey S. Gerber, MD, PhD; Rachael K. Ross, MPH; Matthew Bryan, PhD; A. Russell Localio, PhD; Julia E. Szymczak, PhD; Richard Wasserman, MD; Darlene Barkman, MA; Folasade Odeniyi, MPH; Kathryn Conaboy, BA; Louis Bell, MD; Theoklis E. Zaoutis, MD, MSCE; Alexander G. Fiks, MD, MSCE
Background

- Acute bacterial respiratory infections account for majority of abx exposure
- Broad-spectrum Rx on the rise
- Unclear if broad-spectrum Tx = better outcomes
Methods

• Retrospective cohort for clinical outcomes
• Prospective cohort for patient-centered
  • Quality of life
• 6mos-12yo, 31 primary care sites, PA, 2yr
• 30,159 pts, 4307 Rx broad-spectrum
  – 19,179 AOM, 6,746 GAS, 4,234 sinusitis
• Stratified propensity matched analysis
Results

- Treatment failure:
  - 3.4% in broad
  - 3.1% for narrow

- Quality of life
  - 90.2 for broad
  - 91.5 for narrow

- Adverse events
  - 3.7% for broad (MD reported); 35.6% (Pt)
  - 2.7% for narrow (MD reported); 25.1% (Pt)
Impact to practice

• Critical time with rising use of broad-spectrum abx
• Resistance is growing due to increased exposure
• Data tells us stick with the Amocillins
  • Tried and true!
Misguided Macrolide Use

No benefit of adding macrolide to treatment of children hospitalized with pneumonia
Effectiveness of β-Lactam Monotherapy vs Macrolide Combination Therapy for Children Hospitalized With Pneumonia

Derek J. Williams, MD, MPH; Kathryn M. Edwards, MD; Wesley H. Self, MD, MPH; Yuwei Zhu, MD, MS; Sandra R. Arnold, MD; Jonathan A. McCullers, MD; Krow Ampofo, MD; Andrew T. Pavia, MD; Evan J. Anderson, MD; Lauri A. Hicks, DO; Anna M. Bramley, MPH; Seema Jain, MD; Carlos G. Grijalva, MD, MPH
Background

- PNM
Methods

- Analysis from prospective, multicenter, population-based study of CAP, 2yrs
- 1,418 patients, 1,019 with Beta-lactam vs 399 in BL+ macrolide group
- Primary outcome- Length of stay
- Secondary – ICU, readmission, recovery
Figure 2. Cumulative Incidence of Discharge According to Antibiotic Treatment and Propensity Score-Matched Cohort

No. at risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>0</th>
<th>24</th>
<th>48</th>
<th>72</th>
<th>96</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Lactam</td>
<td>280</td>
<td>254</td>
<td>162</td>
<td>96</td>
<td>59</td>
<td>33</td>
</tr>
<tr>
<td>β-Lactam plus macrolide</td>
<td>280</td>
<td>261</td>
<td>174</td>
<td>104</td>
<td>57</td>
<td>41</td>
</tr>
</tbody>
</table>
Impact to practice

- Adding a macrolide to beta-lactam therapy confers no benefit to treatment of kids hospitalized with community acquired pneumonia.
- Not a clear line to futility of macrolide therapy in outpatient setting but data suggest treatment of atypicals may not be necessary altogether.
Post Lecture Question 1

• Mother of 1 year old is having trouble with getting her son to sleep. You suggest a routine for bedtime. When should she expect results?

A. 2 weeks
B. 5 days
C. 1 week
D. 3 days
Post Lecture Question 2

• You have a 8 yo with mild persistent asthma who is controlled with an ICS. The child is having increased symptoms and enters the yellow zone, you suggest starting albuterol and:

A. Double the ICS
B. Quintuple the ICS
C. Neither has proven to decrease attacks
Post Lecture Question 3

• You have a 12 mo that is diagnosed with acute otitis media. He has had 3 days of fever, and mom perceives pain, as child is irritable and cyring. You decide to treat (vs watchful waiting). Which antibiotic?

A. Azithromycin
B. Cefdinir
C. Amoxicillin
D. Amoxicillin-clavulonate