Infectious Diseases: Bacterial Infections and Antibiotic Stewardship

Friday, August 7  4:30-6:00 pm EDT

**Moderators**
Ishminder Kaur  
Saul Hymes

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<th>Abstract</th>
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<td>Introduction &amp; General Information</td>
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<td>4:35 pm</td>
<td>3375915</td>
<td>The Antibiotic Likelihood Index—A New Measure of Antimicrobial</td>
<td>Joshua Herigon</td>
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<td>Stewardship in Pediatric Primary Care</td>
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<td>Antibiotic Prescribing for Acute Respiratory Tract Infections in Children: Informing a New Benchmark</td>
<td>Alexander Fiks</td>
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<td>Association of Rurality and Incidence of Inappropriate Antibiotic Use among Young Children in Tennessee</td>
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Note: Schedule subject to change based on presenter availability.
BACKGROUND: Current pediatric antimicrobial stewardship measures focus on narrow aspects of antibiotic prescribing such as not prescribing antibiotics for upper respiratory infections (URI) and choosing narrow-spectrum antibiotics for acute otitis media. Such measures do not consider the overall antibiotic prescribing of individual clinicians and are prone to diagnosis bias (i.e., judiciousness in diagnosing conditions for which antibiotics are recommended) and diagnosis shifting (e.g., adding diagnoses to justify antibiotic prescribing for URI). A measure of clinicians’ overall antibiotic prescribing is needed that is independent of the diagnoses they assign. We hypothesized that we could create such a measure by utilizing Reason For Visit (RFV) to determine antimicrobial prescribing patterns.

OBJECTIVE: To define a new quality measure of antimicrobial stewardship in primary care pediatrics.

DESIGN/METHODS: Using electronic health record data from the Pediatric Physicians’ Organization at Children’s, a primary care network affiliated with Boston Children’s Hospital, we analyzed all office visits, excluding those with a RFV of well child visit or follow-up, for one year for children <18 years. The proportion of encounters with an antibiotic prescription for each RFV was calculated, and RFV were ranked by their accountable proportion of all antibiotic prescriptions. We defined the Antibiotic Likelihood Index (ALI) as the proportion of encounters with an antibiotic prescription out of all encounters with a RFV accounting for the top 80% of antibiotic prescriptions.

RESULTS: In 304,277 visits among 340 clinicians, 8 RFV (cough, fever, sore throat, ear problem, earache, rash, nasal congestion, and URI) accounted for 81.4% of all encounters with an antibiotic prescription. The network ALI was 30.7%. ALI for individual clinicians ranged from 7.3% to 58.3% (interquartile range: 24.5%-35.3%). ALI did not differ by patient sex (30.5% for females, 31.0% for males) and there was only modest variability by patient age (28.5% for infants, 35.1% for preschool aged children, 31.8% for school aged children, and 26.3% for adolescents).

CONCLUSION(S): The ALI, a measure of the proportion of visits with an antibiotic prescribed among 8 RFV that account for most antibiotic prescriptions in primary care pediatrics, can be used to assess variability in antimicrobial stewardship among clinicians independent of the diagnoses they assign. The ALI may serve as a useful quality measure for antimicrobial stewardship in primary care pediatrics.
Variability in the Antibiotic Likelihood Index among individual clinicians. Each gray dot represents one clinician.

**IMAGE CAPTION:**
Variability in the Antibiotic Likelihood Index among individual clinicians. Each gray dot represents one clinician.

**CONTROL ID:** 3378044

**TITLE:** Antibiotic Prescribing for Acute Respiratory Tract Infections in Children: Informing a New Benchmark

**PRESENTER:** Alexander Fiks

**AUTHORS (LAST NAME, FIRST NAME):** Gerber, Jeffrey S.¹; Hersh, Adam²; Grundmeier, Robert W.¹; Szymczak, Julia E.³; Mayne, Stephanie L.⁴; Frager, Nicole¹; Wright, Margaret⁵; Steffes, Jennifer⁶; Frantz, Jennifer⁵; Shone, Laura P.⁵; Fiks, Alexander⁷

**AUTHORS/INSTITUTIONS:** J.S. Gerber, R.W. Grundmeier, N. Frager, Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES;
A. Hersh, University of Utah, Salt Lake City, Utah, UNITED STATES;
J.E. Szymczak, Biostatistics, Epidemiology and Informatics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES;
M. Wright, J. Frantz, L.P. Shone, Research, American Academy of Pediatrics, Itasca, Illinois, UNITED STATES;
J. Steffes, Research, American Academy of Pediatrics, Itasca, Illinois, UNITED STATES;
A. Fiks, Pediatrics, Children's Hospital Philadelphia, Philadelphia, Pennsylvania, UNITED STATES;

**CURRENT CATEGORY:** Infectious Diseases

**CURRENT SUBCATEGORY:** None

**KEYWORDS:** antibiotic stewardship, acute respiratory tract infections, benchmark.

**SESSION TITLE:** Infectious Diseases: Bacterial Infections and Antibiotic Stewardship | Infectious Diseases: Bacterial Infections and Antibiotic Stewardship

**SESSION TYPE:** Platform|Webinar

**ABSTRACT BODY:**

**Background:** At least 30% of antibiotic prescriptions for pediatric acute respiratory tract infections (ARTIs) are unnecessary. Many outpatient stewardship interventions have focused on reducing prescribing for conditions coded as viral infections. However, diagnosis rates for bacterial ARTIs (e.g. acute otitis media, sinusitis) remain widely variable, reflecting the approach’s limitations in addressing overdiagnosis of bacterial infections.

**Objective:** Explore variability in diagnosis and antibiotic prescribing for ARTIs across pediatric primary care practices. Results will be used to inform a benchmark for total antibiotic prescribing rates for all ARTIs to inform outpatient antibiotic stewardship efforts.

**Design/Methods:** We examined diagnoses and antibiotic prescribing for common ARTIs in children 6 months-12 years who presented for acute care to pediatric primary care practices from Jan 1, 2014-Dec 31, 2016. EHR data from the AAP Comparative Effective Research through Collaborative Electronic Reporting (CER²) database were utilized. CER² includes a diverse population from urban, suburban, and rural settings across 27 US states. We included antibiotic
prescribing that occurred during an in-person encounter for an ARTI, defined by an ICD9/10 code for viral (acute nasopharyngitis, unspecified lower respiratory infections, unspecified upper respiratory infections, bronchiolitis, bronchitis, croup, influenza, laryngitis, tracheitis), and potentially bacterial (pharyngitis, acute otitis media (AOM), sinusitis, and pneumonia) infections. Antibiotic prescribing and ARTI diagnosis rates were standardized by patient age and sex using fixed-effect logistic regression models and marginal standardization.

**Results:** 51 sites and 2,583,053 patient encounters were included. Viral infections accounted for 36.6% (IQR 33.2-47.4%) of ARTI diagnoses across practices, followed by AOM (28.9%; 24.8-33.7%), pharyngitis (22.1%; 17.6-28.9%), sinusitis (5.6%; 3.1-5.9%), and pneumonia (3.1; 2.7-3.6%). By site, the proportion of ARTIs for which antibiotics were prescribed ranged from 26.8% to 63.1% (Fig 1). Rates of specific ARTI diagnosis varied widely by site (Fig 2).

**Conclusion(s):** Rates of antibiotic prescribing for ARTIs and the distribution of diagnoses for ARTIs varied widely by practice. The data illustrate the importance of tracking both diagnosis and prescribing patterns for effective antibiotic stewardship and provide ranges for each to inform future benchmarks.
SESSION TYPE: Platform/Webinar

ABSTRACT BODY:

Background: Acute respiratory infections (ARI) are the leading cause of antibiotic use among children, with much of this use not guideline-concordant and inappropriate. Rates of antibiotic use in Tennessee children are among the highest reported. Some studies suggest rurality of residence can influence antibiotic use.

Objective: To determine if rates of ARI-related inappropriate antibiotic use among young children in Tennessee vary by rurality of residence.

Design/Methods: This was a retrospective cohort study of children aged 2 months – 5 years enrolled in Tennessee Medicaid (TennCare) from July 1, 2007 – June 30, 2017. We used healthcare claims data to identify outpatient ARI visits and ARI-related antibiotic use. ARI visits were identified using International Classification of Diseases (ICD)-coded diagnoses, and ARI-related antibiotic use was defined as an antibiotic prescription filled within 72 hours of an ARI-associated encounter. ARI-related antibiotic use was classified as potentially appropriate or inappropriate using a previously published classification system based on ICD-9 and ICD-10 codes. Rurality of children’s county of residence was defined as mostly urban, mostly rural, or completely rural according to US Census Bureau definitions. We calculated incidence rates for ARI outpatient visits, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use. To assess the association of rurality of residence with these outcomes, we used multivariable Poisson regression, accounting for other factors including age, gender, race, comorbidities, calendar year and month, and history of antibiotic exposure.

Results: total of 813,432 children met cohort selection criteria and contributed 2,057,272 person-years of follow-up. Children residing in completely rural counties contributed 80,989 (4%) person-years of observation, children residing in mostly rural counties contributed 549,357 (27%) person-years, and children residing in mostly urban counties contributed 1,426,926 person-years (69%). Overall, the rates of ARI outpatient visits, ARI-related antibiotic use, and ARI-related inappropriate antibiotic use were higher among children who lived in mostly or completely rural counties compared to urban counties (Figure 1, Table 1).

Conclusion(s): Children who live in rural Tennessee counties are disproportionately affected by higher rates of inappropriate antibiotic use compared to those who live in urban counties. These findings can inform stewardship interventions to reduce inappropriate antibiotic use.

IMAGE CAPTION:
ABSTRACT BODY:
Background: Antibiotic exposure in newborns is associated with adverse outcomes, including increased risk for obesity, asthma, and antimicrobial resistance. Antibiotic stewardship programs (ASP) can reduce unnecessary antibiotic exposure in neonatal intensive care unit settings. However, many well-baby nurseries – particularly those in rural or medically underserved areas – do not have ASP or specialist support.

Objective: To determine the efficacy of a telehealth ASP for medically-underserved nurseries in South Texas

Design/Methods: We performed a 30-month (7/17-12/19) randomized, stepped-wedge trial of telehealth ASP in 8 medically-underserved nurseries. Baseline data were collected pre-rollout (7/17-8/18). Beginning 9/18, nurseries were stepped into telehealth ASP participation approximately monthly. The ASP consisted of prospective audit and feedback, continuing medical/nursing education, and teleconsultation available 24/7 with a neonatal infectious diseases specialist (JBC). Demographic and clinical information, including use of antimicrobials, was collected on every infant. Antibiotic use among infants born post-ASP participation was compared with antibiotic use among infants born pre-ASP participation. Primary outcome was the proportion of newborns exposed to antibiotics.

Results: 6,512 infants were born during the study period (4586 pre-ASP, 1926 post-ASP). The median gestational age and birth weight were 39 weeks and 3332 g, respectively. The prevalence of prolonged rupture of membranes (7.4%), chorioamnionitis (2.4%), and maternal group B streptococcal (GBS) colonization (14.5%) did not differ between pre- and post-telehealth ASP implementation. Two infants had early-onset sepsis, both GBS in the pre-ASP period, and no infants died. The proportion of infants exposed to antibiotics declined from 6.2% pre-ASP to 4.3% post-ASP (RR 0.69 [95% CI 0.62-0.76]), and total antibiotic use declined from 117 to 85.2 days of therapy per 1000 patient-days. Mean length of stay did not differ between pre- and post-ASP periods (1.84 vs. 1.82 days).

There were 236 teleconsultations during the study period (3.3 calls/participating center/month). Congenital syphilis and sepsis were the most common reasons for teleconsultation, but consults covered 31 distinct topics.

Conclusion(s): A nursery-specific telehealth ASP reduced antibiotic exposure 31% among infants born in medically underserved nurseries. Further research is needed to determine the scalability of telehealth ASP to other medically underserved areas.
Background: Meningitis is more common in infants than any other age group and is associated with significant mortality. The epidemiology of meningitis is changing due to use of intrapartum antibiotics and changing bacterial resistance patterns.

Objective: Evaluate epidemiology and outcomes of bacterial meningitis, and antibiotic resistance patterns in NICUs.

Design/Methods: We identified all infants < 90 days of age, with a positive cerebrospinal fluid (CSF) culture for a bacterial pathogen, between 2013-2017 at Pediatrix Medical Group NICUs. We excluded infants with a viral CSF isolate. We divided infants into 3 groups: early onset (0-6 days of age), late onset (7-29 days of age) and extremely late onset (30-90 days of age). We assessed the epidemiology and hospital outcomes of meningitis, distribution of causative organisms, and their resistance patterns. Outcomes of interest were a failed hearing screen, and death before discharge.

Results: 325/452,258 infants from 332 NICUs were diagnosed with meningitis; nearly half of the infants were in the late onset group (n=151; Table 1). The median (25th-75th percentile) gestational age of the cohort was 35 (26 – 39) weeks. 32% (n=97) of infants with meningitis had a positive blood culture within 7 days of positive CSF culture. Group B Streptococcus (GBS) (n=38) and Escherichia coli (E. coli) (n=38) were the most common infecting organisms overall. For the 38 infants with E. coli, 18 (47%) were ampicillin-resistant (Table 2). Infants in the very late onset group had the highest prevalence of adverse outcomes (Table 3).

Conclusion(s): In this cohort of infants diagnosed with meningitis in the first 90 days of age, GBS and E. coli were the most prevalent causative organisms, with substantial proportion of ampicillin resistant E. coli. Infants with very late onset meningitis were more likely to have an adverse outcome prior to discharge.

Table 1: Demographics and clinical characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Early onset meningitis (n=27)</th>
<th>Late onset meningitis (n=71)</th>
<th>Very late onset meningitis (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, weeks (SD)</td>
<td>28.2 (2.9)</td>
<td>29.5 (2.8)</td>
<td>29.4 (2.6)</td>
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<td>Birthweight, g (SD)</td>
<td>1160 (310)</td>
<td>1250 (350)</td>
<td>1290 (380)</td>
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<td>Antimicrobial therapy (n=68)</td>
<td>42 (61%)</td>
<td>45 (63%)</td>
<td>43 (79%)</td>
</tr>
<tr>
<td>Prior maternal GBS status (n=57)</td>
<td>18 (32%)</td>
<td>18 (25%)</td>
<td>18 (33%)</td>
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<tr>
<td>Prior ampicillin resistance (n=75)</td>
<td>21 (28%)</td>
<td>21 (28%)</td>
<td>21 (28%)</td>
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<tr>
<td>Prior E. coli resistance (n=38)</td>
<td>18 (47%)</td>
<td>18 (47%)</td>
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GBS = Group B streptococcus

Table 2: Antibiotic resistance patterns of causative organisms

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<thead>
<tr>
<th>Organism</th>
<th>Ampicillin</th>
<th>Ceftriaxone</th>
<th>EBL</th>
<th>Vancomycin</th>
<th>Meropenem</th>
<th>Polymyxin</th>
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<tr>
<td>GBS (n=38)</td>
<td>18 (47%)</td>
<td>18 (47%)</td>
<td>18 (47%)</td>
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<tr>
<td>E. coli (n=38)</td>
<td>18 (47%)</td>
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Table 3: Hospital outcomes and clinical characteristics of infants with bacterial meningitis

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<thead>
<tr>
<th>Outcome</th>
<th>n</th>
<th>Early onset meningitis (n=27)</th>
<th>Late onset meningitis (n=71)</th>
<th>Very late onset meningitis (n=54)</th>
</tr>
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<tr>
<td>Hearing</td>
<td>53</td>
<td>15 (56%)</td>
<td>31 (44%)</td>
<td>27 (50%)</td>
</tr>
<tr>
<td>Death</td>
<td>53</td>
<td>4 (15%)</td>
<td>11 (15%)</td>
<td>18 (33%)</td>
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</table>
Background: Little is known about the composition of the upper respiratory tract microbiome in newborns and its changes over the first year of life. This early period of bacterial colonization is highly variable and has been suggested to induce critical events in immune development. The predominant potentially pathogenic bacteria (PPB) found in the nasopharynx are *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, and *S. aureus*.

Objective: To analyze the detection and dynamics over time of PPB in healthy infants and to identify potential factors that influence the evolution of the nasal microbiome.

Design/Methods: Healthy children from <1 to 15 months of age were enrolled and sampled. 66 were sampled once and 81 were sampled multiple times at 2, 6, and 12 months. None received antimicrobial therapy within 2 weeks before sample collection. Nasopharyngeal (NP) swabs were analyzed by quantitative PCR for the presence of four PPB: *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, and *S. aureus*. The frequency of bacterial detection in the nasopharynx was assessed and compared according to age and mode of delivery.

Results: A total of 420 NP bacterial swabs were collected from 147 children (56% male, 63% breastfed, 32% born by cesarean section). Identification of more than one bacterial species per sample significantly increased (P < 0.0001) throughout the first year of life. Detection of ≥1 PPB was 4.7% at 0-1 months of age and 56.7% at 12-13 months. In particular, one-year old infants were more frequently colonized with *S. pneumoniae* (7.0% vs. 58.2%), *M. catarrhalis* (18.6% vs. 59.7%), and *H. influenzae* (0.0% vs. 26.9%) than newborns. Infants delivered vaginally were more frequently colonized with *M. catarrhalis* from 6-12 months of age (25.0% vs. 48.6%; P = 0.01).

Conclusion(s): Upper respiratory tract microbiota diversity rose over time during the first year of life as *S. pneumoniae*, *M. catarrhalis*, and *H. influenzae* colonization rates increased. Colonization patterns differed between vaginally delivered and cesarean section born infants in early life.
Background: Azithromycin is the second most commonly prescribed antibiotic to children, even though it only has three FDA-approved pediatric indications. No national study has assessed the appropriateness of azithromycin prescribing across all conditions or the prevalence of off-label azithromycin prescribing among children.

Design/Methods: We conducted a cross-sectional analysis of the 2017 IBM MarketScan Commercial Database. The sample included privately insured children aged 0-17 years continuously enrolled in 2017. We compiled ICD-10-CM diagnosis codes on claims occurring during a look-back period that began three days prior to antibiotic prescription claims and ended on the claim date. For these codes, we applied a scheme that classifies whether each of the 94,000+ ICD-10-CM diagnosis codes “always”, “sometimes”, or “never” justifies antibiotics. We assigned claims to one of four
categories: 1) “Appropriate” if associated with ≥1 “always” diagnosis code; 2) “Potentially appropriate” if associated with ≥1 “sometimes” code but no “always” codes; 3) “Inappropriate” if associated only with “never” codes; and 4) “Not associated with a recent diagnosis code” if there were no claims during the look-back period. We determined the proportion of azithromycin claims in each category and the proportion of all inappropriate claims accounted for by azithromycin and by 38 other antibiotics. We calculated the proportion of azithromycin claims that were off-label, or associated only with codes that were not FDA-approved pediatric indications (acute otitis media, pneumonia, pharyngitis/tonsillitis).

Results: The 4.1 million children accounted for 3.3 million antibiotic claims. The most common antibiotics were amoxicillin (38%), azithromycin (16%), and cefdinir (12%). Overall, 18% of claims were appropriate, 50% were potentially appropriate, 16% were inappropriate, and 16% were not associated with a recent diagnosis code. In contrast, 31% of azithromycin claims were inappropriate. Azithromycin accounted for 30% of all inappropriate antibiotic claims, the highest proportion among 39 antibiotics (Figure). 46% of azithromycin claims were off-label.

Conclusion(s): Among privately insured U.S. children in 2017, azithromycin accounted for the second highest proportion of antibiotic claims and the highest proportion of inappropriate claims. 31% of azithromycin claims were inappropriate and 46% were off-label. Pediatric antibiotic stewardship initiatives focused on azithromycin may be warranted given its high rate of use and overuse.

Image Caption: Percentage of all antibiotic claims and inappropriate antibiotic claims accounted for by the second most frequently prescribed antibiotics in children.