

Disclosures. All Authors: No reported Disclosures.

1955. Novel Compound Reverses Vancomycin Resistance in Vancomycin-resistant Enterococci (VRE)

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Session: 227. Novel Antimicrobials and Approaches Against MDR Organisms
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Background. *Enterococcus* causes 14% of all hospital-associated infections (HAIs) according to Centers for Disease Control and Prevention (CDC) data. 35.5% of these HAIs are caused by Vancomycin-resistant *Enterococci* (VRE) including highly fatal bacteremia, surgical site infections, and urinary tract infections. We present a novel synthetic compound, HSD 03-21 that could make VRE completely susceptible to vancomycin in-vitro.

Methods. HSD 03-21 was synthesized de novo from a hydroxybenzylidene – indolinone backbone in our laboratory. The minimum inhibitory concentration (MIC) of HSD 03-21 and vancomycin against VRE were determined according to clinical laboratory standards institute (CLSI) guidelines. The standard checkerboard assay was used to determine vancomycin-HSD 03-21 interactions against VRE. Briefly, HSD 03-21 and vancomycin at 10 mg/mL were prepared and diluted serially along the ordinate and abscissa of 96-well microtiter plates, respectively. Bacteria was standardized using the 0.5 McFarland standard, diluted (1:100), aliquoted into respective wells and incubated at 37°C for 18–20 hours. All assays were run in triplicates. The fractional inhibitory concentration (FIC) index was calculated for each combination. The FIC of either agent was calculated as: FIC (vancomycin) = MIC of vancomycin in combination/MIC of vancomycin alone and FIC (HSD 03-21) = MIC of HSD 03-21 in combination/MIC of HSD 03-21 alone. The cumulative FIC index Σ FIC1 was then calculated as: Σ FIC = FIC(vancomycin) + FIC(HSD 03-21). The calculated Σ FIC indices were interpreted as synergistic if Σ FIC: ≤ 0.5 .

Results. The MIC of vancomycin for VRE faecalis was 256 $\mu\text{g mL}^{-1}$ while that of HSD 03-21 was 128 $\mu\text{g mL}^{-1}$. When vancomycin was combined with HSD 03-21 at 8 $\mu\text{g mL}^{-1}$ (1/16 MIC), there was a reduction in MIC of vancomycin to 0.5 $\mu\text{g mL}^{-1}$. The combination showed excellent synergy with Σ FIC of 0.06.

Conclusion. HSD 03-21 reduced the MIC of vancomycin from 256 to 0.5 $\mu\text{g mL}^{-1}$. This has an immense potential of changing the way we use vancomycin and in the treatment of VRE infections. Translation of this novel compound could save thousands of lives from VRE and the failures and inherent toxicities of current doses of vancomycin.

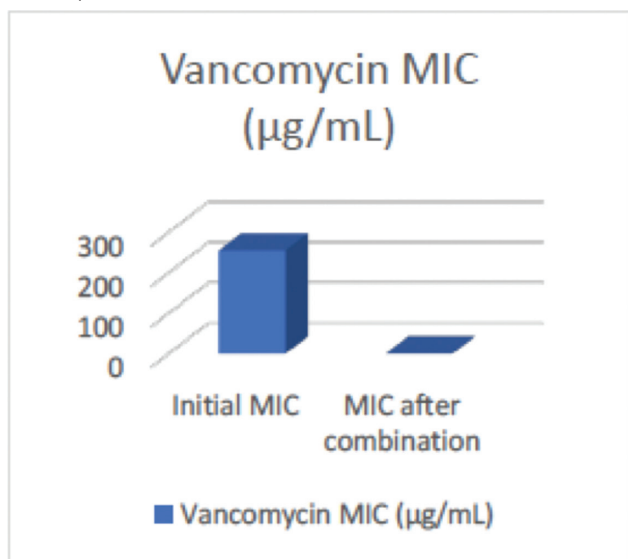


Figure 1. 500 fold reduction in vancomycin MIC

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1956. Reduction in Endotracheal Aspirate Cultures after Implementation of a Diagnostic Stewardship Intervention in a Pediatric Intensive Care Unit

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Background. Clinicians obtain endotracheal aspirate (ETA) cultures from mechanically ventilated patients in the pediatric intensive care unit (PICU) for the evaluation of ventilator-associated infection (i.e., tracheitis or pneumonia). Positive cultures prompt clinicians to treat with antibiotics even though ETA cultures cannot distinguish bacterial colonization from infection. We undertook a quality improvement initiative to standardize the use of endotracheal cultures in the evaluation of ventilator-associated infections among hospitalized children.

Methods. A multidisciplinary team developed a clinical decision support algorithm to guide when to obtain ETA cultures from patients admitted to the PICU and ventilated for >1 day. We disseminated the algorithm to all bedside providers in the PICU in April 2018 and compared the rate of cultures one year before and after the intervention using Poisson regression and a quasi-experimental interrupted time-series models. Charge savings were estimated based on \$220 average charge for one ETA culture.

Results. In the pre-intervention period, there was an average of 46 ETA cultures per month, a total of 557 cultures over 5,092 ventilator-days; after introduction of the algorithm, there were 19 cultures obtained per month, a total of 231 cultures over 3,554 ventilator-days (incident rate 10.9 vs. 6.5 per 100 ventilator-days, Figure 1). There was a 43% decrease in the monthly rate of cultures (IRR 0.57, 95% CI 0.50–0.67, $P < 0.001$). The ITSA revealed a pre-existing 2% decline in the monthly culture rate (IRR 0.98, 95% CI 0.97–1.00, $P = 0.01$), an immediate 44% drop (IRR 0.56, 95% CI 0.45–0.69, $P = 0.02$) and a stable rate in the post-intervention period (IRR 1.03, 95% CI 0.99–1.07, $P = 0.09$). The intervention led to an estimated \$6000 in monthly charge savings.

Conclusion. Introduction of a clinical decision support algorithm to standardize the obtaining of ETA cultures from ventilated children was associated with a significant decline in the rate of ETA cultures. Additional investigation will assess the impact on balancing measures and secondary outcomes including mortality, duration of ventilation, duration of admission, readmissions, and antibiotic prescribing.

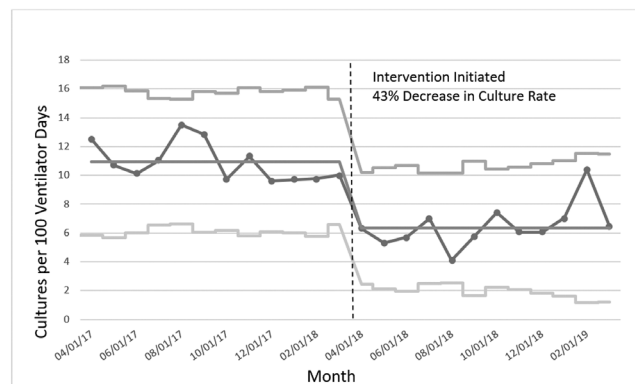


Figure 1. Monthly rate of endotracheal aspirate cultures per 100 ventilator-days in the pediatric intensive care unit. This control chart shows the monthly rate, upper and lower limits, and the overall rate before and after introduction of the intervention in April 2018.

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1957. Impact of β -Lactam Antibiotic Allergy on Antimicrobial Use, Clinical Outcomes, and Costs for Hospitalized Children

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Background. Most β -lactam antibiotic allergies (BLA) are incorrectly diagnosed and could be de-labeled. Adult patients with BLA are more likely to receive broader-spectrum antimicrobials and experience worse health outcomes than nonallergic patients. Similar studies on the impact of BLA on antimicrobial use and clinical outcomes are limited in pediatrics. Our objective was to compare antimicrobial use, and clinical and economic outcomes between hospitalized children with and without BLA.

Methods. This was a retrospective cohort of pediatric patients hospitalized at an Intermountain Healthcare (IH) hospital from 2007 to 2017. IH has 22 hospitals including one children's hospital. Patients aged 30 days-17 years who received ≥ 1 dose of an antimicrobial during hospitalization were included. The exposure variable was the presence of BLA (penicillins or cephalosporins) in the allergy field of the medical record. Patients with BLA were matched to nonallergic controls on age, sex, race, clinical service line, admission date, children's hospital or other hospital, and co-morbid conditions. We used multivariable log-transformed-linear and logistic regression models to compare patients with BLA to controls in terms of antibiotic selection and total antimicrobial days, antimicrobial cost, length-of-stay (LOS) and 30-day readmission. For antibiotic selection we examined the odds of receiving the following broader-spectrum agents individually and in composite: vancomycin, fluoroquinolones, clindamycin, carbapenems, and macrolides.

Results. 39,785 patients were identified including 2897 (7%) with BLA. The prevalence of BLA increased with age (Figure 1). 2459 (85%) patients with BLA were matched to a control. Patients with BLA had higher odds of receiving broader-spectrum antibiotics (OR 2.35, 95% CI: 2.07–2.67) and had greater antimicrobial costs (1.21-fold increase, 95% CI: 1.08–1.35) than nonallergic patients (Figure 2). There were no differences in LOS, total antimicrobial days, or 30-day readmission (Figure 2).

Conclusion. Pediatric patients with BLA are more likely to receive broader-spectrum antibiotics and incur higher antimicrobial costs than matched controls. De-labeling interventions could reduce unnecessary exposure to these agents and lower costs.

Fig 1. Prevalence of Beta Lactam Allergy by Age

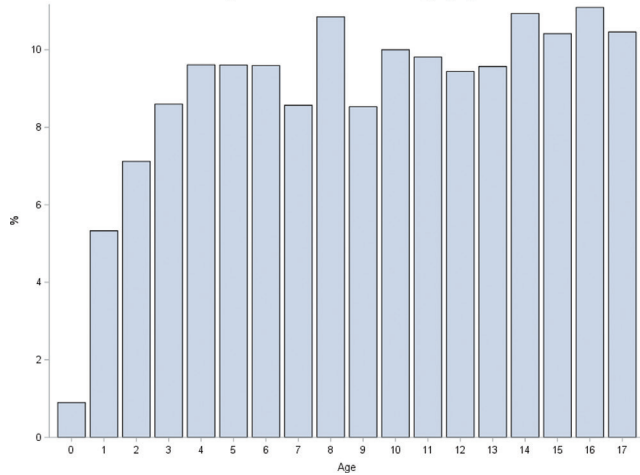
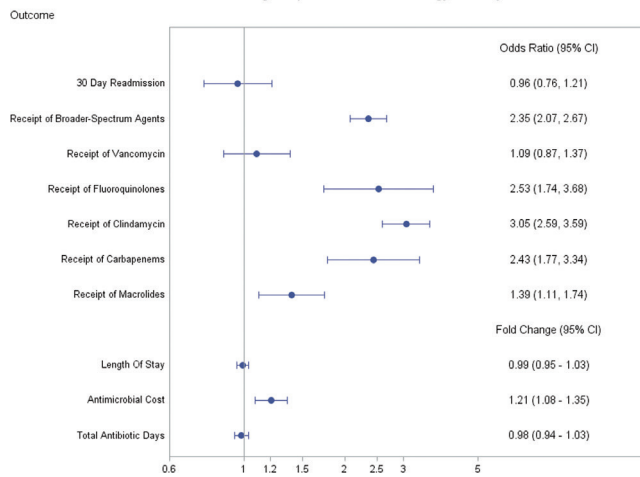


Fig 2. Impact of Beta Lactam Allergy on Study Outcomes



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1958. Assessment of Guideline-Concordant Antimicrobial Prescribing in Urgent Care Centers

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Background. In the United States in 2014, 266 million outpatient antibiotic prescriptions were dispensed. The Center for Disease Control and Prevention estimates that 30% of outpatient antibiotic prescriptions are inappropriate. These inappropriate prescriptions contribute to increased resistance, adverse events, and healthcare costs.

Methods. This was a retrospective study of patients presenting to 22 urgent care centers within a large healthcare system between September 1, 2018 and February 28, 2019. Data were collected from a dashboard designed to track antimicrobial prescribing data by indication, location, and provider. ICD-9 and -10 codes associated with otitis media, pharyngitis, sinusitis, cystitis, and upper respiratory infections (URI) were included. Guideline-concordant antimicrobial prescribing was determined based on compliance with national guideline recommendations, after taking patient allergies

into account. The URI category includes disease states in which antimicrobials are rarely appropriate (e.g., acute rhinitis, nasopharyngitis, and acute bronchitis).

Results. A total of 57,799 encounters were included in this analysis (19,242 pediatric and 38,557 adult) and 60% of patients received an antibiotic prescription. Overall antimicrobial guideline concordance was higher in pediatrics (84%) than adults (62%). Rates of guideline-concordant antimicrobial selection are shown in Table 1. The most common guideline-discordant prescriptions were tetracyclines (39%), amoxicillin/clavulanate (26%), and macrolides (17%) in adult patients with sinusitis, pharyngitis, or otitis media. In pediatric patients, the most common discordant prescriptions were macrolides (32%), third-generation cephalosporins (30%), and amoxicillin/clavulanate (19%). Unnecessary antimicrobial prescribing for URI occurred in 23% of pediatric patients and 36% of adult patients.

Conclusion. Guideline-discordant antimicrobial prescribing is common in urgent care centers, particularly in adult patients. In addition to encouraging utilization of order sets, emphasis on education and feedback may be important to improve and sustain guideline-concordant prescribing rates and reduce prescribing for URI.

Table 1: Guideline-Concordant Antimicrobial Selection

Diagnosis	Pediatric	Adult
Otitis Media	4045/4727 (86%)	1674/3040 (55%)
Pharyngitis	3553/4151 (86%)	2182/3828 (57%)
Sinusitis	969/1166 (83%)	8778/11715 (75%)
Cystitis	223/281 (79%)	1954/3012 (65%)
Upper Respiratory Infection	1067/4600 (23%)	4705/13162 (36%)

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1959. Parent Satisfaction and Antibiotic Prescribing for Pediatric Respiratory Infections by Telemedicine

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Background. Respiratory tract infections (RTIs) are a common reason for direct-to-consumer (DTC) telemedicine consultation. Antibiotic prescribing during video-only DTC telemedicine consults was explored for pediatric RTIs, focusing on correlates with visit duration and patient satisfaction.

Methods. Data on pediatric (age less than 19 years) RTI consults were obtained from a large DTC nationwide telemedicine platform and included patient, physician, and encounter characteristics. Mixed-effects regression was used to assess variation in antibiotic receipt by patient and physician factors, as well as the association between antibiotic receipt and visit length or patient satisfaction.

Results. Of 12,842 RTI visits with 560 physicians, 55% of patients received an antibiotic prescription. Antibiotic prescribing rates among telemedicine providers were high: sinusitis (92.1%), otitis media (96.0%), pharyngitis (76.7%), and bronchitis/bronchiolitis (62.0%). A provider was more likely to receive a 5-star satisfaction rating from the parent when the child was provided a prescription for an antibiotic (OR 3.38; 95% CI 2.84–4.02), an antiviral (OR 2.56; 95% CI 1.81–3.64) or a nonantibiotic (OR 1.93; 95% CI 1.58–2.36). Visit length (mean 6.4 minute) was associated with higher satisfaction only when no antibiotic was prescribed (OR 1.03 per 6 seconds; 95% CI 1.01–1.06). Compared with nonpediatricians, pediatric providers were less likely to prescribe antibiotics (OR 0.44; 95% CI 0.29–0.68); however, patients of pediatricians were more likely to be highly satisfied (OR 1.50; 95% CI 1.11–2.03).

Conclusion. During DTC telemedicine video consultations for RTIs, pediatric patients were frequently prescribed antibiotics, which correlated with visit satisfaction. Although pediatricians prescribed antibiotics at a lower rate than other physicians, their satisfaction scores were higher. Especially problematic, adherence to guideline-concordant criteria for diagnosing acute otitis media and streptococcal pharyngitis, which, respectively, require otoscopy and throat culture, is not possible during a video-only telemedicine consult. High rates of antibiotic prescribing to children with RTIs suggest a need for antimicrobial stewardship efforts during video-only telemedicine consultation.

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1960. Lost in Translation: Comparing Rates of Outpatient Antibiotic Use in Three Metrics

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Background. The Centers for Disease Control and Prevention (CDC) tracks US outpatient antibiotic use in prescriptions per 1000 persons (Rx/1000), while the World Health Organization uses defined daily doses per 1000 persons (DDD/1000), which are based on average adult dose, for global surveillance. A third metric, days of therapy (DOT)/1,000 persons, has not been previously evaluated at the national level. We aim to compare time trends in outpatient oral antibiotic use as Rx/1000, DDD/1000, and DOT/1,000 in the same data to inform ongoing CDC surveillance and facilitate international comparison.