Presentation Type:
Oral Presentation

Population-Level Burden of Delayed or In Vitro Discordant Empiric Antibiotics Among Bacteremic Patients at US Hospitals

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Background: Delayed or *in vitro* inactive empiric antibiotic therapy may be detrimental to survival in patients with bloodstream infections (BSIs). Understanding the landscape of delayed or discordant empiric antibiotic therapy (DDEAT) across different patient, pathogen, and hospital types, as well as by their baseline resistance milieu, may enable providers, antimicrobial stewardship programs, and policy makers to optimize empiric prescribing. **Methods:** Inpatients with clinically suspected serious infection (based on sampling of blood cultures and receiving systemic antibiotic therapy on the same or next day) found to have BSI were identified in the Cerner Healthfacts EHR database. Patients were considered to have received DDEAT when, on culture sampling day, they received either no antibiotic(s) or none that displayed in vitro activity against the pathogenic bloodstream isolate. Antibiotic-resistant phenotypes were defined by in vitro resistance to taxon-specific prototype antibiotics (eg, methicillin/oxacillin resistance in *S. aureus*) and were used to estimate baseline resistance prevalence encountered by the hospital. The probability of DDEAT was examined by bacterial taxon, by time of BSI onset, and by presence versus absence of antibiotic-resistance phenotypes, sepsis or septic shock, hospital type, and baseline resistance. **Results:** Of 26,036 assessable patients with a BSI at 131 US hospitals between 2005 and 2014, 14,658 (56%) had sepsis, 3,623 (14%) had septic shock, 5,084 (20%) had antibiotic-resistant phenotypes, and 8,593 (33%) received DDEAT. Also, 4,428 (52%) recipients of DDEAT received no antibiotics on culture sampling day, whereas the remaining 4,165 (48%) received in vitro discordant therapy. DDEAT occurred most often in *S. maltophilia* (87%) and *E. faecium* (80%) BSIs; however, 75% of DDEAT cases and 76% of deaths among recipients of DDEAT collectively occurred among patients with *S. aureus* and Enterobacteriales BSIs. For every 8 bacteremic patients presenting with septic shock, 1 patient did not receive any antibiotics on culture day (Fig. 1A). Patients with BSIs of hospital (vs community) onset were twice as likely to receive no antibiotics on culture day, whereas those with bloodstream pathogens displaying antibiotic-resistant (vs susceptible) phenotypes were 3 times as likely to receive in vitro discordant therapy (Fig. 1B). The median proportion of DDEAT ranged between 25% (14, 37%) in eight <300-bed teaching hospitals in the lowest baseline resistance quartile and 40% (31, 50%) at five ≥300-bed teaching hospitals in the third baseline resistance quartile (Fig. 2). **Conclusions:** Delayed or in vitro discordant empiric antibiotic therapy is common among patients with BSI in US hospitals regardless of hospital size, teaching status, or local resistance patterns. Prompt empiric antibiotic therapy in septic shock and hospital-onset BSI needs more support. Reliable detection of *S. aureus* and Enterobacteriales bloodstream pathogens and their resistance patterns earlier with rapid point-of-care diagnostics may mitigate the population-level impact of DDEAT in BSI.

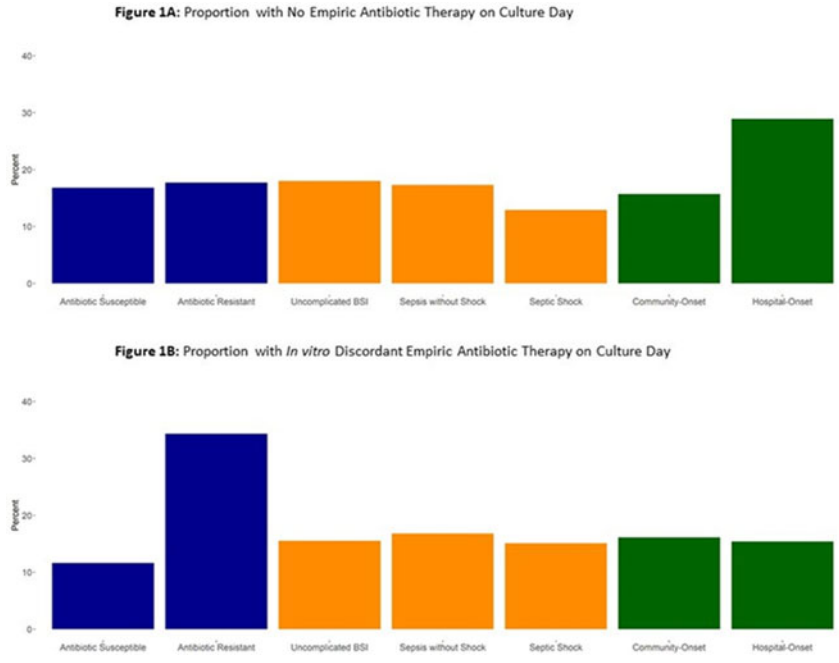

Figure 1: Probability of delayed or discordant empiric antibiotic therapy in BSI by time of onset and evidence of *in vitro* antibiotic-resistant phenotypes and sepsis respectively: Bars in subfigure A represent the proportion of patients who received no therapy on culture sampling day. Bars in subfigure B represent the proportion of patients who received empiric antibiotic(s) on culture sampling day but none of which displayed *in vitro* activity against the pathogenic bloodstream isolate. Note: Antibiotic-resistant phenotypes include intermediate *in vitro* susceptibility or resistance reported to methicillin/oxacillin in *S. aureus*, vancomycin in enterococci, penicillin in pneumococci, clindamycin in beta-hemolytic streptococci, trimethoprim-sulfamethoxazole, fluoroquinolones or ceftazidime in *S. maltophilia*, extended-spectrum cephalosporin or carbapenems in Enterobacteriales and other non-glucose fermenters respectively. Sepsis and septic shock defined by Sepsis III Criteria. Community-onset was defined as BSI detected on blood cultures obtained in the first two days of hospitalization. Test for significance not applied due to large sample size.

Fig. 1.

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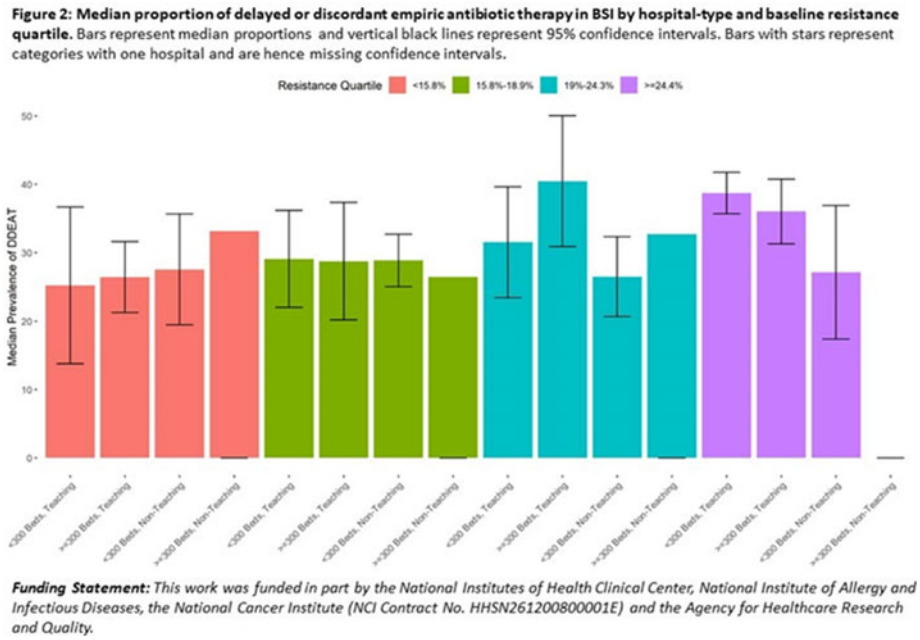

Fig. 2.

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Predicting Vancomycin-Resistant Enterococci (VRE) and Carbapenem-Resistant Organism (CRO) Colonization in the Intensive Care Unit

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Background: Rapidly identifying patients colonized with multidrug-resistant organisms (MDROs) upon ICU admission is critical to control and prevent the spread of these pathogens in healthcare facilities. Electronic health records (EHR) provide a rich source of data to predict the likelihood of MDRO colonization at admission, whereas surveillance methods are resource intensive and results are not immediately available. Our objectives were (1) to predict VRE and CRO colonization at ICU admission and (2) to identify patient subpopulations at higher risk for colonization with these MDROs. **Methods:** We conducted a retrospective analysis of patients aged ≥16 years admitted to any of 6 medical or surgical intensive care units (ICU) in the Johns Hopkins Hospital from July 1, 2016, through June 30, 2018. Perirectal swabs were collected at ICU unit admission and were tested for VRE and CRO. Patient demographic data, prior hospitalizations, and preadmission clinical data, including prior medication administration, prior diagnoses, and prior procedures, were extracted to develop prediction models. We employed the machine-learning algorithms logistic regression (LR), random forest (RF), and XGBoost (XG). The sum of sensitivity and specificity (ie, Youden's index) was selected as the performance metric. **Results:** In total, 5,033 separate ICU visits from 3,385 patients were included, where 555 (11%) and 373 (7%) admissions tested positive for VRE and CRO, respectively. The sensitivity and specificity of our models for VRE were 78% and 80% with LR, 80% and 82% with RF, and 77% and 87% with XG. Predictions for CRO were not as precise, with LR at 73% and 53%, RF at 81% and 48%, and XG at 69% and 61%. The XG algorithm was the best-performing algorithm for both VRE and CRO. Prior VRE colonization, recent (<180 days) long-term care facility stay, and prior hospitalization >60 days were the key predictors for VRE, whereas the primary predictor for CRO colonization was prior carbapenem use. **Conclusions:** We demonstrated that EHR data can be used to predict >75% of VRE positive cases with a <15% false-positive rate and ~70% of CRO cases with a <40% false-positive rate. Future studies using larger sample sizes may improve the prediction accuracy and inform model generalizability across sites and thus reduce the risk of transmission of MDROs by rapidly identifying MDRO-colonized patients.

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Prevalence and Epidemiology of Healthcare-Associated Infections (HAI) in US Nursing Homes (NH), 2017

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