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Background. Fosfomycin is among the limited treatment options for carbapenem-resistant Enterobacteriaceae (CRE) infections. Despite its use, prevalence of fosfomycin resistance among CRE in the United States is largely unknown. In 2017, submission of Enterobacteriaceae isolates resistant to ≥1 carbapenem became mandated in Connecticut (CT), allowing further characterization at the state public health laboratory (SPHL). We analyzed fosfomycin resistance among CRE isolates in CT during 2017, and explored demographic and molecular factors potentially associated with resistance.

Methods. After confirming carbapenem resistance, SPHL tests fosfomycin susceptibility using disk diffusion. For each CRE patient, the isolate most resistant to fosfomycin was included in this analysis. We used the Clinical and Laboratory Standards Institute (CLSI) fosfomycin breakpoint for *Escherichia coli* (nonsusceptible <16 mm) to evaluate associations among fosfomycin resistance and demographic factors, carbapenemase activity (modified carbapenem inactivation method, mCIM) and carbapenemase genes tested at SPHL. We report fosfomycin resistance rate by European Committee on Antimicrobial Susceptibility Testing (EUCAST, resistance <24 mm for *E. coli*) criteria for comparison.

Results. Among 138 CRE isolates, 39 (28.3%) were fosfomycin nonsusceptible by CLSI criteria. Most nonsusceptible isolates were *Enterobacter cloacae* (18; 46.2%) or *Klebsiella pneumoniae* (17; 43.6%). Isolates from patients aged ≥65 years were more likely to be fosfomycin nonsusceptible than isolates from patients aged <65 years (χ^2 = 3.8; P = 0.050). No other demographic characteristics were statistically significant. Of fosfomycin nonsusceptible isolates, 12 (30.8%) produced a carbapenemase (mCIM-positive), and 9 (23.1%) had the bla_{KPC} gene. By EUCAST criteria, 96 (69.6%) CRE isolates were fosfomycin resistant.

Conclusion. A substantial proportion of CRE in CT during 2017 were fosfomycin nonsusceptible, and nonsusceptibility was associated with older patient age. Fosfomycin resistance risk factors and molecular mechanisms need further exploration. The substantial proportion of isolates with results falling between CLSI and EUCAST breakpoints warrants evaluation.

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2397. Comparing Predictive Performance of INCREMENT Scores on Mortality Among Patients With Carbapenem-Non-Susceptible (CNS) *Klebsiella pneumoniae* (*Kp*) and *Enterobacter cloacae* Complex (*Ecc*) Bloodstream Infections (BSI) in the Veterans Health Administration (VHA)

Nadim G. El Chakhtoura, MD, MPH[1]; Brigid Wilson, PhD[1]; Belen Gutíerrez-Gutíerrez, MD, PhD[2]; Federico Perez, MD, MS[3]; Elie Saade, MD, MPH[4]; Curtis J. Donskey, MD[1]; Jesus Rodriguez-Bano, MD[2] and Robert A. Bonomo, MD[1]; [1]Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Cleveland, Ohio, [2]Hospital Universitario Virgen Macarena, Seville, Spain, [3]Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio, [4]Division of Infectious Diseases and HIV Medicine, Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio

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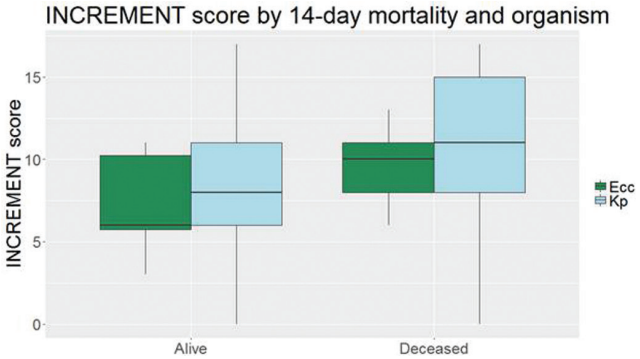
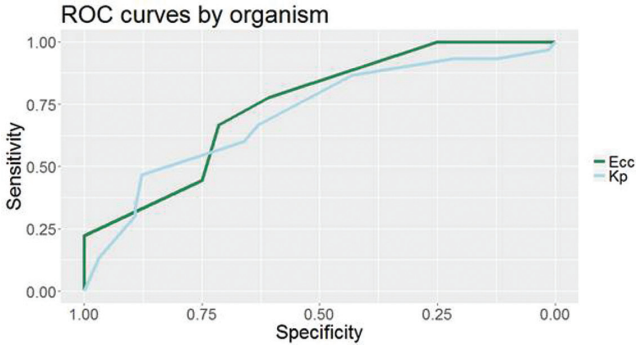
Background. INCREMENT is an international collaborative study of BSI caused by extended-spectrum β-lactamase (ESBL) or carbapenemase-producing *Enterobacteriaceae* (CPE) that has developed and validated predictive models for mortality. Most CNS *Enterobacteriaceae* BSI in the VHA are either *Klebsiella pneumoniae* (*Kp*) or *Enterobacter cloacae* complex (*Ecc*). We applied the INCREMENT score for CPE to predict mortality in patients with CNS-*Kp* and CNS-*Ecc* BSIs in the VHA and compared the distribution and predictive performance of the score across organisms.

Methods. Using nationwide VHA databases, unique patients in the continental United States with *Kp* or *Ecc* BSI post 48 hours of hospitalization from 2006 to 2015 were identified. Isolates with intermediate susceptibility or resistance to any tested carbapenem were considered non-susceptible. We used databases and medical records to obtain clinical characteristics, treatment, and outcomes, and applied INCREMENT criteria and definitions to calculate a prediction score. We compared the distribution of the scores by organism and used receiver operating curve methods to compare predictive performance between *Kp* and *Ecc* BSI.

Results. We identified 57 patients with CNS-*Ent* and 140 with CNS-*Kp* BSI. The demographics and infection characteristics were highly consistent across organisms, both afflicting patients who were predominantly male, older and chronically ill. Mortality at 14 days was 39% in CNS-*Ecc* and 38% in CNS-*Kp*. Similar proportions (65% of *Ecc* and 68% of *Kp*) met the criteria for an INCREMENT score: monomicrobial and alive over 48 hours after culture specimen. The distribution of scores was similar within mortality outcomes across organisms, with the highest scores observed in *Kp* patients who died (Figure 1). The ROC areas under the curve were 0.71 for CNS-*Ecc* and 0.75 for CNS-*Kp* (Figure 2). A multivariable logistic model predicting mortality detected neither an organism effect nor an interaction of organism and INCREMENT score.

Conclusion. The INCREMENT score, validated in a CPE cohort predominantly comprised of *Kp*, performed similarly well across CNS-*Ent* and CNS-*Kp* patients in our cohort. This suggests the model is robust to CNS organisms of undetermined resistance mechanism and that the association between INCREMENT and mortality is consistent across *Kp* and *Ecc*.





Disclosures. **All authors:** No reported disclosures.

2398. Utilization Practices of Ceftazidime–Avibactam at Academic Medical Centers in the United States

Jeffrey R. Strich, MD[1,2]; Emily Ricotta, PhD, ScM[3]; Yi Ling Lai, MPH[3]; Samuel Hohmann, PhD[4,5]; Sadia Hussain, MD[1]; Chanu Rhee, MD, MPH[6,7]; Michael Klompas, MD, MPH, FRCPC, FIDSA[6,7]; Tara N. Palmore, MD[8]; John H. Powers III, MD[9]; John P. Dekker, MD, PhD[10]; Jennifer Adjemian, PhD[2,3]; Robert L. Danner, MD[1]; Sameer S. Kadri, MD, MS[1] and NIH Antimicrobial Resistance Outcomes Research Initiative (ARORI); [1]Critical Care Medicine Department, National Institutes of Health Clinical Center, Bethesda, Maryland, [2]United States Public Health Service, Commissioned Corps, Rockville, Maryland, [3]Epidemiology Unit, Division of Intramural Research, NIAID, NIH, Bethesda, Maryland, [4]Center for Advanced Analytics, Vizient, Chicago, Illinois, [5]Department of Health Systems Management, Rush University, Chicago, Illinois, [6]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts, [7]Division of Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts, [8]Hospital Epidemiology Service, National Institutes of Health Clinical Center, Bethesda, Maryland, [9]Clinical Research Directorate/Clinical Monitoring Research Program, Leidos Biomedical Research, Inc., Frederick, Maryland, [10]Department of Laboratory Medicine, National Institutes of Health Clinical Center, Bethesda, Maryland

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Background. Ceftazidime–avibactam (CAV) was US FDA-approved for complicated intra-abdominal/urinary tract infections in 2015, and for hospital-acquired/ventilator-associated pneumonia in 2018. However, little is known about its real-world use.

Methods. Encounters of inpatients receiving CAV at academic hospitals in the Vizient™ Clinical Resource Manager were identified (CAV encounters). CAV administered for ≤2 consecutive days during an encounter or any duration of CAV within 2 days of admission (excluding acute care hospital transfers) was considered empiric therapy. Targeted therapy was defined as ≥4 consecutive days or death within 2 days of therapy; empiric and targeted therapy cohorts were mutually inclusive. CAV-encounter characteristics, use patterns and Infectious Disease (ID) consultation were examined. Quarterly hospital uptake of CAV and % change in CAV encounter prevalence (using Poisson regression) were calculated.

Results. From January 2015 to December 2017, 20,590 CAV doses occurred in 2,128 encounters among 1,652 patients. Mean duration of therapy was 8 ± 7.9 days (range 1–86); overall mortality was 24%. The number of hospitals prescribing CAV increased from 5 to 92/168 and quarterly prevalence of CAV encounters increased from 5/10,000 hospitalizations in 2015q1 to 9.8 in 2017q4 (% change=2.1[0.7–3.6] %/quarter; (P = 0.004). Therapy was empiric in 904 (42%) encounters and targeted in 1,472 (69%); 63% of empiric CAV was initiated within 2 days of admission. CAV was initiated in the ICU in 862 (40.5%) encounters. Infection site was coded as respiratory in 34%, urinary in 26% and abdominal in 16% of encounters. Within 31 hospitals reporting consultant specialty, 29% of targeted therapy occurred without ID consultation. For targeted therapy encounters, CAV monotherapy occurred in 841 (57%) and

combination therapy in 631 (43%) encounters, which most often included aminoglycosides, colistin or tigecycline. Mortality was 22% in the monotherapy and 25% in the combination therapy group ($P = 0.08$).

Conclusion. CAV use across US academic medical centers has increased modestly over 3 years. More than 40% of CAV prescriptions appear to be empiric and targeted therapy often occurs without ID consultation at academic centers.

Table 1: Demographics for Encounters Receiving Ceftazidime-avibactam

Variable	Encounters receiving ceftazidime-avibactam N = 2128 (%)
Age (median and IQR)	56 (27)
Sex	
Male	1254 (59)
Female	874 (41)
Race	
White	1358 (64)
African American	462 (22)
Other	240 (11)
Unknown	68 (3)
Comorbid condition	
Congestive heart failure	501 (24)
Diabetes mellitus	810 (38)
Transplant	141 (7)
Malignancy	86 (4)
Dialysis	202 (9)
Tracheostomy	423 (20)
Chronic kidney disease	667 (31)
Presumed site of infection#	
Abdominal	330 (16)
Bacteremia	100 (5)
Central nervous system	8 (0.4)
Central venous catheter	136 (6)
Respiratory	720 (34)
Skin/soft tissue	167 (8)
Urinary	557 (26)
Unknown/other	656 (31)
Admission APR DRG Severity of Illness assignment*	
Minor	12 (1)
Moderate	153 (8)
Major	669 (33)
Extreme	1204 (59)
Hospital Region	
Midwest	30 (33)
Northeast	27 (29)
South	21 (23)
West	14 (15)
Length of stay (median days and IQR)	19 (31)
ICU stay	862 (41)

#Not mutually exclusive
*1 Encounter missing APR DRG SOI data
APR DRG= All patients refined diagnosis related groups (provided by 3M™)

Figure 1A: Cumulative Increase in the Number of Hospital Prescribing Ceftazidime-avibactam within the Vizient Database (168 hospitals) by Quarter, 2015q1–2017q4

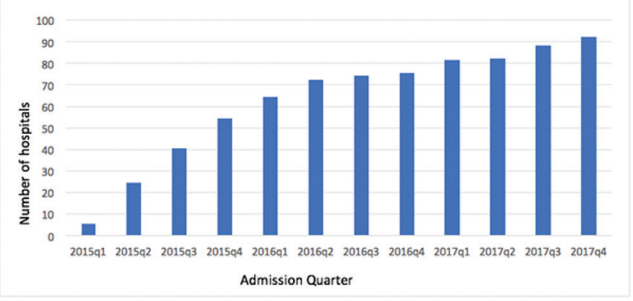
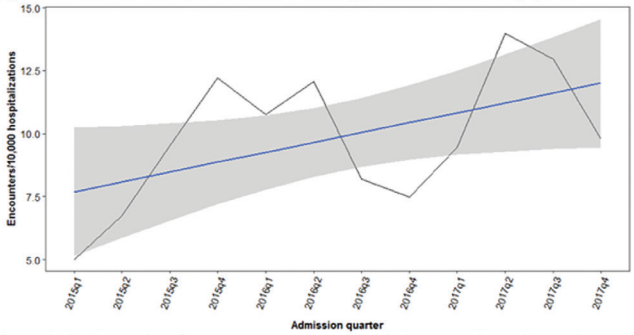
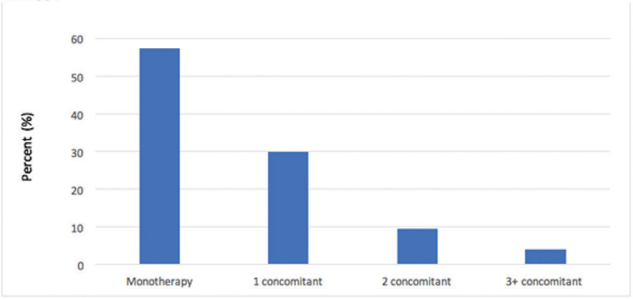


Figure 1B Trends in the Number of Encounters Prescribing Ceftazidime-Avibactam by Quarter



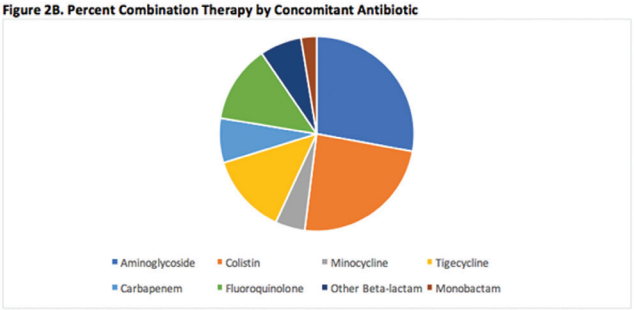
*Rate calculated as number of encounters receiving CA per total admissions in hospitals prescribing ceftazidime-avibactam by quarter.
**Quarterly Percent Change: 2.1 [0.7-3.6], (p=0.004)

Figure 2A. Percent of Targeted Therapy Encounters that Received Monotherapy versus Combination Therapy.



*Concomitant antibiotic was any of the select gram-negative active antibiotics (see below) prescribed for 3 consecutive days in addition to ceftazidime-avibactam, except for aminoglycosides which could be prescribed on day 1 and day 3 of the overlap period

Figure 2B. Percent Combination Therapy by Concomitant Antibiotic



*Aminoglycoside (amikacin, gentamicin, tobramycin), Carbapenem (ertapenem, doripenem, imipenem, meropenem), Fluoroquinolone (ciprofloxacin, levofloxacin), Other β-lactam (piperacillin-tazobactam, ampicillin-sulbactam, ceftazidime, cefepime), Monobactam (aztreonam)
#Reserve agents include: aminoglycosides, colistin, and tigecycline
** Funding Source: Division of Intramural Research, NIAID, NIH and NCI Contract No. HHSN261200800001E

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2399. β-Lactam Therapy for Potential AmpC-Producing Organisms: A Cohort Study and an Updated Systematic Review and Meta-Analysis

Matthew P. Cheng, MD[1]; Robyn Lee, PhD[2]; Alexandre P. Cheng, BSc[3]; Samuel De L'Étoile-Morel, MD[4]; Koray Demir, MDCM Candidate[5]; Cedric Yansouni, MD[6]; Patrick Harris, MBBS FRACP FRCPA[7]; Emily Mcdonald, MDCM, MSc[8] and Todd C. Lee, MD, MPH[8]; [1]Harvard Medical School, Boston, Massachusetts, [2]Harvard School of Public Health, Boston, Massachusetts, [3]École Polytechnique de Montréal, Montréal, QC, Canada, [4]McGill University, Montreal, QC, Canada, [5]McGill University Faculty of Medicine, Montreal, QC, Canada, [6]Infectious Diseases, McGill University, Montreal, QC, Canada, [7]Central Pathology, Pathology Queensland, Brisbane, Australia, [8]Clinical Practice Assessment Unit, McGill University, Montréal, QC, Canada

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Background. Certain organisms, including *Serratia, Providentia, Acinetobacter, Citrobacter, Enterobacter*, and *Morganella* species (SPACE-M) may possess an inducible broad-spectrum β-lactamase, AmpC, which is not inhibited by most β-lactamase inhibitors. Our objective was to determine whether treating SPACE-M bloodstream infections (BSI) with potentially hydrolyzable β-lactams was associated with increased risk of 30-day mortality.

Methods. A retrospective cohort study was performed including all adult cases of bacteremia attributed to SPACE-M species between April 2010 and June 2015 at the McGill University Health Centre (Montreal, Canada). We used multivariable logistic regression to estimate the odds ratio (OR) of death or recurrence within 30 days for potentially hydrolyzable β-lactams vs. other therapies. We then updated a systematic review and meta-analysis comparing carbapenems to β-lactam/β-lactamase inhibitors (BL/BLIs). We included studies published up to December 31, 2017 and calculated the unadjusted OR for mortality within 30 days comparing BL/BLI vs. carbapenems as definitive therapy.

Results. Over the 5-year period, there were 173 BSI involving SPACE-M organisms at our center. After adjusting for patient comorbidities and severity of the initial illness, the use of hydrolyzable β-lactams as definitive therapy was not associated with an increased risk of death or recurrence when compared with other antimicrobial agents (OR 1.20, 95% CI 0.40–3.62). The meta-analysis further suggested that patients treated with BL/BLI therapy have similar outcomes to those treated with carbapenems (30-day mortality OR 1.13, 95% CI 0.58–2.20).

Conclusion. The use of β-lactam/β-lactamase inhibitors may remain a viable carbapenem-sparing option for patients with potential AmpC-producing organisms.

Disclosures. **All authors:** No reported disclosures.