(defined as non-susceptible to at least 1 of the following drugs: cefepime, ceftriaxone, cefotaxime, ceftolozane/tazobactam, ceftazidime/avibactam); CR = carbapenem resistance (defined as non-susceptible to at least 1 carbapenem); FR = fluoroquinolone resistance (defined as non-susceptible to at least 1 fluoroquinolone); AAPC = annual average percentage change; CI = confidence interval.

Conclusion. Overall, MDR, ESBL, CR, and FR in *Enterobacterales* and *P. aeruginosa* decreased from 2011 to 2020 in the VA. These results may be related to the robust infection control and antimicrobial stewardship programs instituted among VA Medical Centers nationally.

Disclosures. **Kerry LaPlante, PharmD**, **Merck** (Research Grant or Support)**Pfizer Pharmaceuticals** (Research Grant or Support)**Shionogi, Inc** (Research Grant or Support) **Aisling Caffrey, PhD**, **Merck** (Research Grant or Support)**Pfizer** (Research Grant or Support)**Shionogi, Inc** (Research Grant or Support)

176. Antibiotic Resistance Patterns, Seasonality, and Correlation with the Influenza Season in the United States: A Multicenter Evaluation Reveals Surprising Association Between Influenza Season and Gram Negative Pathogens

Amine Amiche, PhD[1]; Heidi Kabler, MD[1]; Janet Weeks, PhD[2]; Kalvin Yu, MD[2]; Vikas Gupta, PharmD, BCPS[2]; [1]Sanofi Pasteur, Dubai, Dubai, United Arab Emirates [2]Becton, Dickinson and Company, Franklin Lakes, New Jersey

Session: O-35. Trends in Gram-negative Resistance

Background. Influenza infection may affect bacterial transmission dynamics and seasonality of antimicrobial resistance (AMR). There is a paucity of data on the association of influenza season and AMR rates. We aimed to describe trends of AMR and their correlation with the influenza season in ambulatory and inpatient settings in the United States (US).

Methods. We used the *BD Insights Research Database* (Franklin Lakes, NJ USA) to identify 30 day non-duplicate isolates collected from patients >17 years old with susceptibility profile of Gram-negative (GN) (Enterobacterales (ENT), *P. aeruginosa* (PSA), *A. baumannii spp.* (ACB), and *S. maltophilia* (Sm)) and Gram-positive (GP) pathogens (*S. aureus* (SA), and *S. pneumoniae* (Sp)) in up to 257 US healthcare institutions from 2011-19. We defined the outcomes as rates per 100 admissions and % of non-susceptibility (NS), stratified by community and inpatient settings, resistance type (resistance to carbapenem (Carb-NS), quinolone (FQ-NS), macrolide (Macr NS), penicillin (PCN NS), and extended spectrum cephalosporin (ESC NS)) and isolate origin (respiratory and non-respiratory). Influenza data were presented as the % of positive laboratory tests. We used descriptive statistics and generalized estimating equations models to evaluate the monthly trends of AMR outcomes and correlation with the influenza season.

Results. We identified 16 576 274 confirmed non-duplicate pathogens, of which 154 841 were GN Carb-NS, 1 502 796 GN FQ-NS, 498 012 methicillin resistant SA (MRSA), and 44 131 Macr-NS, PCN-NS, and ESC-NS Sp. Among the Carb-NS pathogens, Influenza rate was correlated with % ACB-NS [β= 0.205, p< .001]. In the FQ-NS group, influenza was associated with overall % ENT-NS [β= 0.041 p< .001] and % PSA-NS [β= 0.039, p = .015]. For the GP pathogens, all Sp. rates were correlated with increased influenza positivity % (See Table). Only MRSA rates of respiratory source were associated with influenza [β= .066, p=.028].

Summary of Multivariate regressions of AMR and % Flu by Source and Setting (controlling for hospital level factors): 2011-2019

	Overall	Respiratory Source	Non-Respiratory Source	Outpatient	Inpatient
% Carb-NS ACB	.205 (< .001)***	.379 (<.001)***	.134 (.040)*	.123 (.077)+	.255 (<.001)***
% FQ-NS ENT	.041 (<.001)***	.130 (<.001)***	.031 (.030)*	.018 (.043)*	.048 (<.001)***
% FQ-NS PSA	.039 (.015)*	.022 (.036)*	.020 (.087)+	.032 (.172)	.044 (.015)*
MRSA Rate/ 100 Adm	.060 (.615)	.066 (.028)*	-.087 (.065)+		
Macr NS *S pneumo* Rate/ 100 Adm	.464 (<.001)***	.253 (<.001)***	.068 (.376)		
PCN NS *S pneumo* Rate/100 Adm	.062 (.011)*	.056 (.046)*	.044 (.103)		
ESC NS *S pneumo* Rate/100 Adm	.033 (.036)*	.032 (.012)*	.018 (.073)+		

Data in each cell is presented as the coefficient (β) and p-value is in parentheses. ^adjusted for region, teaching, urban, bed size, and season. + p<.10 *p<.05 **p<.01 ***p<.001

Data in each cell is presented as the coefficient and p-value is in parentheses. ^adjusted for region, teaching, urban, bed size, and season. + p<.10 *p <.05 **p <.01 ***p <.001

Conclusion. Our study revealed surprising association between influenza epidemics and GN resistance and corroborated the evidence of correlation between respiratory GP and influenza infections. These insights may help inform targeted antimicrobial stewardship initiatives during influenza season.

Disclosures. **Amine Amiche, PhD**, **Sanofi** (Employee, Shareholder) **Heidi Kabler, MD**, **Sanofi Pasteur** (Employee) **Janet Weeks, PhD**, **Becton, Dickinson and Company** (Employee) **Kalvin Yu, MD**, **BD** (Employee) **Vikas Gupta, PharmD, BCPS**, **Becton, Dickinson and Company** (Employee, Shareholder)

177. Distinctive Features of Ertapenem Mono-Resistant Carbapenem-Resistant Enterobacterales in the United States: A Cohort Study

Max W. Adelman, MD, MSc[1]; Chris W. Bower, MPH[2]; Julian E. Grass, MPH[3]; Uzma Ansari, MS[4]; Isaac See, MD[4]; Joseph D. Lutgring, MD[3]; Jesse T. Jacob, MD, MSc[5]; [1]Emory University School of Medicine, Atlanta, Georgia; [2]Georgia Emerging Infections Program, Decatur, GA; [3]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, GA; [4]Centers for Disease Control and Prevention, Atlanta, Georgia; [5]Emory University, Atlanta, GA

Session: O-35. Trends in Gram-negative Resistance

Background. Carbapenem-resistant Enterobacterales (CRE) are highly antibiotic-resistant bacteria. Whether CRE resistant only to ertapenem among carbapenems (ertapenem mono-resistant) represent a unique CRE subset with regards to risk factors, carbapenemase genes, and outcomes is unknown.

Methods. We analyzed laboratory- and population-based surveillance data from nine sites participating in CDC's Emerging Infections Program (EIP). We defined an incident case as the first isolation of *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *K. oxytoca*, *K. pneumoniae,* or *K. variicola* resistant to doripenem, ertapenem, imipenem, or meropenem (determined at clinical laboratory) from a normally sterile site or urine identified from a resident of the EIP catchment area in 2016-2017. We compared risk factors, carbapenemase genes (determined via polymerase chain reaction at CDC), and mortality of cases with ertapenem "mono-resistant" to "other" CRE (resistant to ≥ 1 carbapenem other than ertapenem). We additionally conducted survival analysis to determine the effect of ertapenem mono-resistant status and isolate source (sterile vs. urine) on survival.

Results. Of 2009 cases, 1249 (62.2%) were ertapenem mono-resistant and 760 (37.8%) were other CRE (**Figure 1**). Ertapenem mono-resistant CRE cases were more frequently ≥ 80 years old (29.1% vs. 19.5%, p< 0.0001), female (67.9% vs 59.0%, p< 0.0001), and white (62.6% vs. 45.1%, p< 0.0001). Ertapenem mono-resistant isolates were more likely than other CRE to be *Enterobacter cloacae* complex (48.4% vs. 15.4%, p< 0.0001) but less likely to be isolated from a normally sterile site (7.1% vs. 11.7%, p< 0.01) or have a carbapenemase gene (2.4% vs. 47.4%, p< 0.0001) (**Figure 2**). Ertapenem mono-resistance was not associated with difference in 90-day mortality (unadjusted odds ratio [OR] 0.82, 95% confidence interval [CI] 0.63-1.06) in logistic models or survival analysis (**Figure 3**).

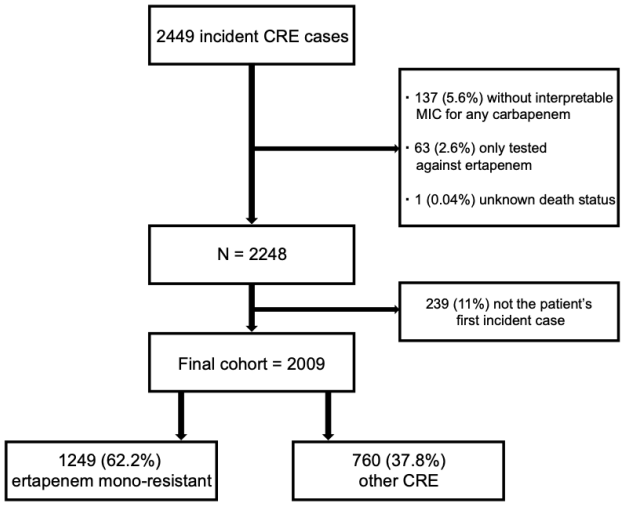


Figure 1. Flow diagram of carbapenem-resistant Enterobacterales cases included in analysis, 2017-2018. CRE, carbapenem-resistant Enterobacterales; MIC, minimum inhibitory concentration. Ertapenem mono-resistant CRE are only resistant to ertapenem (among carbapenems). Other CRE are resistant to ≥1 carbapenem other than ertapenem. We excluded isolates that (1) had no interpretable MICs for any carbapenem, (2) were only tested against ertapenem, (3) had unknown death status, or (4) were not associated with patient's first incident case.

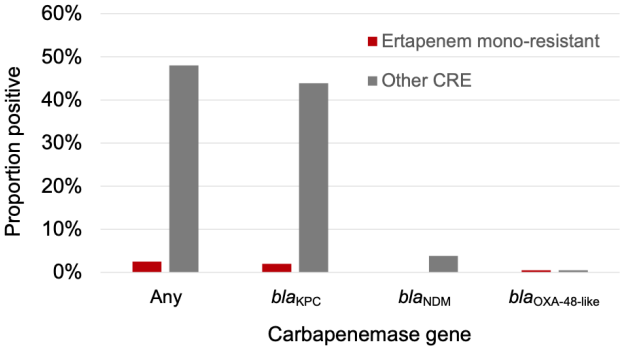
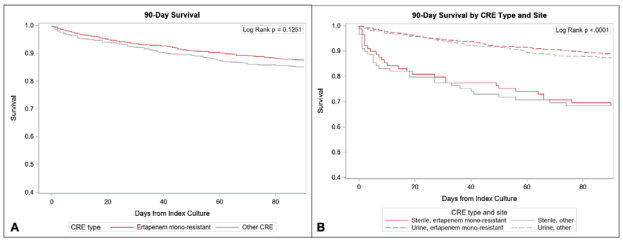


Figure 2. Proportion of ertapenem mono-resistant carbapenem-resistant Enterobacterales (CRE) vs. other CRE isolates with specific carbapenemase genes. KPC, Klebsiella pneumoniae carbapenemase; NDM, New Delhi metallo-ß-lactamase; OXA, oxacillinase. Ertapenem mono-resistant carbapenem-resistant Enterobacterales (CRE) are only resistant to ertapenem (among carbapenems). Other CRE are resistant to ≥1 carbapenem other than ertapenem. Testing via reverse transcriptase polymerase chain reaction.

Figure 3. Survival analysis comparing patients with carbapenem-resistant Enterobacterales (CRE) that are ertapenem mono-resistant to other CRE (i.e., resistant to ≥1 carbapenem other than ertapenem), either total (A) or stratified by isolate site (B).



Ertapenem mono-resistant) isolates were not associated with decreased mortality, and sterile isolate source (i.e., non-urinary isolates) was associated with increased mortality regardless of ertapenem mono-resistance.

Conclusion. Ertapenem mono-resistant CRE rarely have carbapenemase genes and have distinct clinical and microbiologic characteristics compared to other CRE. These findings may inform antibiotic choice particularly when testing for carbapenemases is not readily available.

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

178. Endemic Carbapenem Resistance Driven By Clonal and Horizontal Spread of *bla*$_{IMP-4}$ Across Diverse Enterobacterales: Jumping Genes, Promiscuous Plasmids and Killer Clones

Nenad Macesic, MBBS MA PhD[1]; Luke Blakeway, PhD[2]; Adam W. Jenney, MBBS, FRACP, FRCPA, PhD[3]; Anton Peleg, MBBS MPH PhD[1]; [1]Monash University / Alfred Hospital, Melbourne, Victoria, Australia; [2]Alfred Hospital / Monash University, Melbourne, Victoria, Australia; [3]Alfred Health, Melbourne, Victoria, Australia

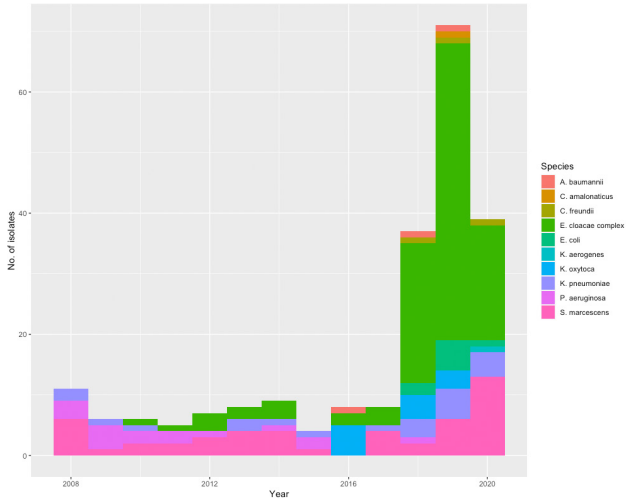
Session: O-35. Trends in Gram-negative Resistance

Background. Carbapenem-resistant Enterobacterales (CRE) have become endemic and cause significant morbidity and mortality globally. The metallo-beta-lactamase gene *bla*$_{IMP-4}$ is a key CRE resistance determinant in Australia and Asia but its genomic context remains unknown. We aimed to determine the genomic epidemiology of *bla*$_{IMP-4}$ in clinical and environmental isolates from 2008 – 2020 at our institution.

Methods. We performed whole genome sequencing on 219 *bla*$_{IMP-4}$-carrying isolates from 134 patients (219 short-read and 75 long-read). Multi-locus sequence types (MLSTs), resistance determinants and plasmid replicons were assessed. High-quality *de novo* hybrid assemblies were used to identify location of *bla*$_{IMP-4}$ gene. We conducted phylogenetic analysis for key MLSTs and plasmids.

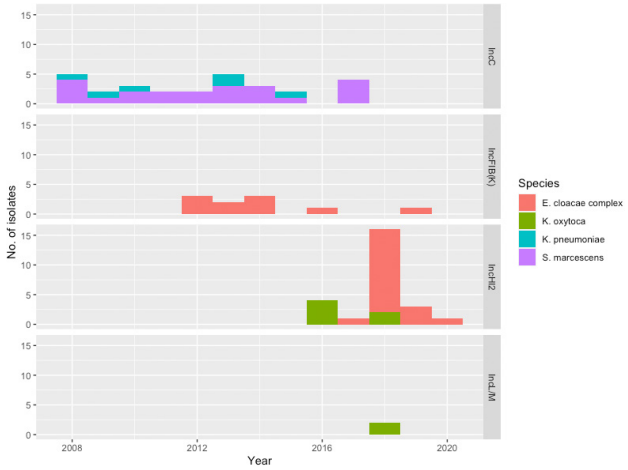
Results. *Bla*$_{IMP-4}$ was noted on a class I integron also harboring aminoglycoside, sulfamethoxazole, chloramphenicol and quaternary ammonium compound resistance genes. This integron was able to migrate over time to 10 bacterial species (42 STs) and 6 different plasmid types (Figure 1 and Figure 2). From 2008-2020, *bla*$_{IMP-4}$ was present on IncC plasmids in *Serratia marcescens* and *Klebsiella pneumoniae*. We noted small outbreaks of *Pseudomonas aeruginosa* ST111 with chromosomal integration of *bla*$_{IMP-4}$ from 2008-2018 (16 isolates) and *Enterobacter cloacae* complex ST114 with *bla*$_{IMP-4}$ on IncFIB(K)/IncFIA(HI1) plasmids from 2011-2020 (19 isolates). From 2016-2020, there was an explosion of diverse IncHI2 plasmids carrying *bla*$_{IMP-4}$. This was driven by clonal expansion of *E. cloacae* complex ST93/ST190 (79 isolates), with spillover of IncHI2 plasmids to *Klebsiella* spp (13 isolates), *Citrobacter* spp (2 isolates), *S. marcescens* (1 isolate), *Escherichia coli* (4 isolates). In addition to *bla*$_{IMP-4}$, these plasmids carried *mcr-9.1*, a colistin resistance gene, and resistance determinants to nearly all key classes of Gram-negative antimicrobials.

Figure 1. Bacterial species harboring blaIMP-4 2008-2020



BlaIMP-4 was noted in diverse bacterial species over the study period. Serratia marcescens and Klebsiella pneumoniae were present throughout. Outbreaks of Enterobacter cloacae complex ST114, ST190 and ST93 and Pseudomonas aeruginosa ST111 were noted.

Figure 2. Diverse plasmids associated with blaIMP-4 carriage determined by de novo hybrid assembly



Presence of blaIMP-4 on diverse plasmids that varied through the study period was noted. Plasmids were charaterised by analysing de novo hybrid assembly data and co-location of blaIMP-4 and plasmid replicons on the same contigs.

Conclusion. *Bla*$_{IMP-4}$ spread on a class I integron was responsible for endemic carbapenem resistance at our institution. This mobile genetic element was able to persist due to both clonal spread and entry into diverse plasmids. Concerningly, we noted a large outbreak driven by IncHI2 plasmids harboring colistin resistance genes with spread to multiple bacterial species.

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

179. Identification and Whole Genome Sequencing Analysis of an Oxacillinase (OXA)-48-like-producing *Acinetobacter baumannii* Outbreak in California, January-May 2021

Diana Holden, MPH[1]; Matthew Sylvester, PhD[1]; John Crandall, n/a[1]; Fengfeng Xu, n/a[1]; Emily C. Schneider, MPH[2]; Hillary Berman Watson, PhD, MPH, PHM[1]; Peng Zhang, PhD[1]; Jaclyn Bacud, n/a[1]; Rafael Mejia, n/a[1]; Erin Epson, MD[1]; Zenda Berrada, PhD[1]; Tisha Mitsunaga, DrPH, ScM[1]; Rituparna Mukhopadhyay, PhD[1]; [1]California Department of Public Health, Richmond, CA; [2]Washington State Department of Health, Shoreline, Washington

Session: O-35. Trends in Gram-negative Resistance

Background. In January 2021, a California acute care hospital (ACH A), a sentinel site for *Acinetobacter baumannii* (AB) surveillance, identified OXA-48-like-carbapenemase producing (CP) AB in a patient admitted from a ventilator-equipped skilled nursing facility (vSNF A); OXA-48-like AB had not been previously reported in the United States.

Methods. Our investigation included onsite infection control (IC) assessments, contact tracing, and point prevalence surveys (PPS) at vSNF A. The Antibiotic Resistance (AR) Laboratory Network performed carbapenemase testing on AB isolates (including those from ACH A) and PPS swabs. A case was defined as a patient with an OXA-48-like AB isolate, or an epidemiologically-linked patient with an OXA-48-like gene detected via screening. We performed whole genome sequencing (WGS) of OXA-48-like AB and other CP organisms on the Illumina MiSeq and Oxford Nanopore MinION for short and long read sequencing, respectively.

Results. Since January 2021, we have identified five OXA-48-like AB cases (including the index), six OXA-48-like cases (no organism recovered), and six patients with other CP organisms at ACH A and vSNF A. Since August 2019, vSNF A has concurrently been experiencing an OXA-109 AB outbreak. A second vSNF A patient, Patient 2, who overlapped with the index patient, had OXA-48-like *Klebsiella pneumoniae* (KP) (November 2019) and OXA-109 AB (May 2020) isolates. WGS of the index patient's AB and Patient 2's KP isolates identified a rare OXA-48-like gene located on the AB chromosome and a KP plasmid. The OXA-48-like AB was also carrying an OXA-109 gene, and hqSNP analysis indicated it varied by 9-44 single-nucleotide polymorphisms (SNPs) from 14 OXA-109 AB isolates linked to that outbreak, and 0-3 SNPs from the other OXA-48-like AB case isolates.

Figure 1. Phylogenetic Tree Comparison of OXA-109 AB and OXA-48-like AB Isolates