<6 months of age. We used these baseline estimates, an efficacy of 79% for both prod-
ucts, uptake of 60% for the maternal vaccine (based on uptake of maternal tetanus/ 
diphtheria/pertussis vaccine) or 70% for the monoclonal antibody (based on uptake of 
hepatitis B vaccine birth dose) and assumed a duration of protection of infants between 
3 and 5 months to assess immunization impact. With the immunization strategies ana-
lyzed, we estimated between 14,591 and 30,336 hospitalizations, 20,621 and 79,020 
ED visits, and 58,670 and 228,840 outpatient visits associated with RSVi could be pre-
vented each year.

Conclusion. Immunization products under development have the potential to substantially reduce MA-RSVi. This model will be used to assess the benefits of differ-
ent immunization strategies developed to protect infants against RSVi. The model is 
flexible and can be updated as more data become available.

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2558. Predicting β-Lactam Resistance Using Whole Genome Sequencing (WGS) in 
Klebsiella pneumoniae: The Challenge of β-Lactam Inhibitors
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Background. Antimicrobial susceptibility testing (AST) is the major driver in 
designing effective therapy. As multiple resistance determinants can demonstrate the same 
phenotype (e.g., inhibitor resistant [IR], extended spectrum [ES], and carbap-
enem hydrolyzing [CH] β-lactamasess), critical information provided from AST for 
therapy, stewardship, and infection control is currently lacking. WGS provides more 
comprehensive genetic data, explaining phenotype, and provides insight to clonality. 
Efforts are in development to apply novel statistical methods (e.g., PRIMERS I-IV 
and machine learning ) to interpret results accurately and anticipate AST. Using a collection of clinical strains that spanned a 3.5-year period, we tested how well the detection of problematic IR, ES, and CH β-lactamase genes predicted phenotype.

Methods. Forty-one isolates were chosen for AST from a collection of 1,777 
WGS K. pneumoniae. Isolates chosen possessed the following β-lactamases: (9 iso-
lates) NDM; (3) NDM and OXA-48; (5) KPC-8 or KPC-14: (24) with a very complex 
β-lactamase background (all possessed an inhibitor resistant TEM [IR] ESB-581, +/− CTX-M, and/or +/− KPC). AST was performed using CLSI methods for piper 
acillin/tazobactam (P/T/Z), cefazidime (CAZ/AVI), CAZ/AVI/ATM, and ceftolozane/tazobactam (TOL/TAZO) by disk diffusion assay.

Results. Presented below.

Prediction: β-lactamase detection in CAZ/AVI resistant. AST results. 

Conclusion. In all cases, blaqTEM and blaqOXA containing isolates were resis-
tant to CAZ/AVI; the addition of ATM fully restored susceptibility to CAZ/AVI. 
Surprisingly, ATM substantially reduced MA-RSVi. This model will be used to evaluate the benefits of different immunization strategies developed to protect infants against RSVi. The model is flexible and can be updated as more data become available.

Disclosures. All authors: No reported disclosures.

2559. Incidence and Clinical Impact of Discordant Genotypic and Phenotypic 
Categorization of Methicillin Susceptible in Staphylococcus aureus Bacteria 
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Background. Methicillin-susceptible/methicillin-resistant Staphylococcus aureus 
(MRSA/MSSA) can be directly identified from positive blood culture bottles using 
molecular methods. This provides faster results than traditional phenotypic testing, 
but discrepancies between the two tests are occasionally found. We sought to determine the incidence and clinical impact of such discrepancies.

Methods. Positive blood culture bottles are routinely tested in the hospital clinical 
laboratory for mecR by Xpert MRSA/SA BC (PCR), and antimicrobial susceptibility 
testing (AST) via MicroScan PNG is performed on recovered S. aureus isolates; dis-
crepancies between PCR and AST are resolved by repeat and supplemental (Kirby-
Bauer) testing. A retrospective review of medical and laboratory data from January 
2015 to December 2017 was performed on all patients that had discordant PCR and 
AST results.

Results. Approximately 1,200 PCR assays were performed from January 2015 to 
December 2017, and there were 5 (0.4%) cases with discordant AST Results. Four 
cases were classified as MSSA by PCR but MRSA by AST, and 1 case was classified as 
MRSA by PCR but MSSA by AST. For the former group, antimicrobial therapy was 
changed in 2 patients to cover MRSA and 1 patient was readmitted, while the remain-
ing 2 patients were already being treated for MRSA; for the latter case, this patient 
was treated for MRSA during the initial hospitalization, but was readmitted with dises-
minated MSSA and subsequently deceased. Based on genetic targets identified by PCR 
and MicroScan, oxacillin MICs were identical. In 2015 and 2016, 11 cases were discon-
tinued due to undetected CAZ/AVI resistance. In 2017, no cases were found.

Conclusion. Rapid identification of MRSA bacteria via PCR provides action-
able information to direct empiric treatment. While highly accurate, PCR results are 
infrequently corroborated by AST. This rare possibility should be considered when 
modifying therapy based on initial PCR results, and there should be close communica-
tion between the clinical team and laboratory for these challenging cases.

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2560. Multispecies Outbreak of KPC-2 Producing Enterobacteriaceae in a Chilean 
Pediatric Hospital
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Background. Carbapenem-resistant Enterobacteriaceae (CRE) are a critical 
local health problem. We detected a surge of CRE cases in a pediatric hospital in 
Chile, a country with a low endemicity of KPC-producing organisms. Herein, we 
describe the molecular epidemiology of this outbreak.

Methods. CRE isolates from clinical specimens and surveillance rectal swabs (obtained using chromID CARBA SMART agar. BioMerieux) of pediatric patients 
were collected from July 2015 to January 2017. Species identity was confirmed by 
MALDI-TOF. Carbapenemase genes (blaKPC, blaNDM, and blaNMC1), and KPC-14 
detected by multiplex PCR, followed by amplification and sequencing of the blaqKPC 
allele. Conjugation experiments were conducted with representative species as donors and 
sodium azide-resistant E. coli J53 as recipient. PCR-based plasmid typing (PBBT 
Plasmid kit) was then performed on donors and recipients. For K. pneumoniae, genetic 
relatedness was investigated by PFGE, multilocus sequence typing and wzt typing.

Results. Sixty-one CRE clinical and surveillance isolates were obtained from 
groups aged 17 days to 16 years. blaqKPC was present in 57/62 isolates; no other 
carbapenemases were found. For 11 patients, multiple cultures were obtained; 4/11

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had more than one KPC-harboring species. KPC-harboring isolates displayed ertapenem MICs ranging from 1 to >8 mg/L. Preliminary analyses suggest that $\text{bla}_{\text{KPC}}$ is contained within a nonclassical $\text{IncN}$ plasmid structure (lacking the upstream promoter). Mating experiments indicate that $\text{bla}_{\text{KPC}}$ is carried by a conjugative $\text{IncN}$ backbone plasmid. Interestingly, \textit{E. pneumoniae} isolates were nonclonal by PFGE and belonged to multiple STs unrelated to $\text{CCG28}$ (ST34, ST36, among others) and different \textit{w}t strains (37, 154, among others).

### Conclusion.

We report a multispecies outbreak of KPC-2 producing CRE in children mainly driven by horizontal dissemination of a promiscuous $\text{IncN}$ plasmid. The nonclonal, multispecies nature of this outbreak provides insights into the complex dynamics of KPC dissemination in countries like Chile, where the clonal spread of highly successful clones like $\text{CCG28}$ is not the predominant dissemination vehicle, and instead HGT-related spread could be playing a more important role.

### Disclosures.

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### 2561. Using Whole Genome Sequencing to Assess the Emergence of Antibiotic Resistance During Treatment of Enterococcus faecium and Enterococcus faecalis Bacteremia at Mount Sinai Hospital

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### Background.

Multidrug-resistant Enterococci are a major cause of nosocomial infections, yet our understanding of how resistance emerges during antibiotic treatment remains incomplete. We performed whole- and complete-genome sequencing of all paired isolates from 11 \textit{Enterococcus faecium} and 10 \textit{Enterococcus faecalis} cases that acquired resistance during hospitalization at Mount Sinai Hospital. Comparative and phylogenomic analyses identified novel mechanisms of resistance and heteroresistance.

### Methods.

2.5 years of electronic health records were analyzed to identify cases of bacteremia that acquired resistance to at least 1 of the 8 antibiotics. Core genome phylogenetic analyses of paired susceptible and resistant isolates was performed to confirm persistent single clone infections. Long read sequencing data, with Illumina error correction, were used to assemble and align complete genomes. Population analysis profile (PAP) assays were performed to assess the prevalence of heteroresistance.

### Results.

Among the 102 persistent enterococcal bacteremia cases, 57 isolates from 24 cases (20.6%) cases experienced a gain in resistance. Phylogenetic analyses confirmed that 80% of cases had single clone blood infections, with maximum of 138 days separating paired isolates. Known genetic determinants were responsible for emerging linezolid (LIN), vancomycin (VAN), and gentamicin synergy resistance in almost all cases. 2 instances, emerging daptomycin (DAP) resistance was not accounted for by known resistance determinants. Notably, PAP assays revealed that LIN-, VAN-, and DAP-resistant subclones were present in only a subset of bacteria in clinical isolates. Longitudinal pairwise analyses of complete genomes revealed novel candidate SNPs for DAP resistance, both located in genes involving cell wall metabolism and maintenance, as well as multiplex recombination events that led to VAN heteroresistance.

### Conclusion.

Our study demonstrates the high prevalence of emerging antibiotic resistance during treatment. We find previously unreported single and structural genomic events that contribute rapid adaptation to antibiotic treatment.

### Disclosures.

All authors: No reported disclosures.

### 2562. Re-Appraisal of Aminoglycoside (AG) Susceptibility Testing Breakpoints Based on the Application of Pharmacokinetics–Pharmacodynamics (PK-PD) and Contemporary Microbiology Surveillance Data

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### Background.

Resistance to AGs and numerous other classes continues to emerge. To ensure that susceptibility is accurately characterized and that clinicians have reliable data to select effective agents, appropriate in vitro susceptibility testing interpretive criteria (susceptible breakpoints [BKPTs]) are crucial to ensure optimal patient care. Recently, USCAST, the USA voice to EUCAST/EMA, evaluated the BKPTs for the 3 most commonly used AGs, gentamicin, tobramycin, and amikacin [Bhavnani et al., IDWeek 2016; P-1977]. As a result of consultation from interested parties, which included evaluating AG dosing regimens provided in the US-FDA product package inserts and simulated patients with varying creatinine clearance, these BKPTs were reassessed.

### Methods.

Data sources considered included longitudinal US reference MIC distributions using in vitro surveillance data collected over 18 years, QC performance (MIC, disk diffusion), population pharmacokinetics (PK), and in vivo PK-PD models. Using population PK models, PK-PD targets for efficacy and Monte Carlo simulation, percent probabilities of PK-PD target attainment by MIC after administration of traditional and extended interval AG dosing regimens were evaluated among simulated patients. Epidemiological cut-off and PK-PD BKPTs were considered when recommending BKPTs for AG-pathogen pairs.

### Results.

An example of PK-PD target attainment analysis output is provided in Table 1 and a subset of recommended AG BKPTs for 3 pathogens is shown in Table 1. Updated USCAST BKPTs, which were based on the application of population PK and PK-PD models, simulation techniques, and contemporary MIC distribution statistics, are generally lower than those of EUCAST/EMA, USA-FDA, and CLSI. Adequate PK-PD target attainment was not achieved for some AG-pathogen pairs, even when high-dose AG dosing regimens and PK-PD targets for stasis were evaluated (e.g., gentamicin vs. \textit{P. aeruginosa}; amikacin vs. \textit{S. aureus}).

### Conclusion.

These revised AG BKPT recommendations, which will be made freely available to EUCAST, USA-FDA, and CLSI, will be finalized after considering comments from additional interested stakeholders. This process will be followed in an effort to bring harmonization to global BKPTs for AGs.

### Figure 1. Percent probabilities of PK-PD target attainment by MIC value for tobramycin dosing regimens using total drug plasma PK-PD targets for Enterobacteriaceae based on pooled data from a murine thigh-infection model among simulated patients with normal renal function

### Table 1. Summary of candidate USCAST aminoglycosides in vitro test interpretive BKPT criteria and those of other BKPT organizations

| Pathogen/aminoglycoside | MIC breakpoints in mg/L, by criteria organization | Susceptible/Resistant* |
|-------------------------|-----------------------------------------------|------------------------|
| **Enterobacteriaceae**   |                                               |                        |
| Amikacin                | $\leq 16$ / $\geq 64^4$                     | $\geq 16$ / $\leq 16$  |
| Gentamicin              | $\leq 4$ / $\leq 16^4$                      | $\geq 2$ / $\leq 4$   |
| Gentamicin - pneumonia  | $\leq 4$ / $\leq 16^4$                      | $\geq 2$ / $\leq 4$   |
| Tobramycin              | $\leq 4$ / $\leq 16^4$                      | $\geq 2$ / $\leq 4$   |
| Tobramycin - pneumonia  | $\leq 4$ / $\leq 16^4$                      | $\geq 2$ / $\leq 4$   |
| **Pseudomonas spp.**    |                                               |                        |
| Amikacin                | $\leq 16$ / $\geq 64^4$                     | $\geq 16$ / $\leq 16$  |
| Tobramycin              | $\leq 4$ / $\leq 16^4$                      | $\leq 4$ / $\leq 4$   |
| Staphylococci           | $\leq 4$ / $\leq 16^4$                      | $\geq 1$ / $\leq 2$   |

- **CLSI M100-S28** (2018) interpretive criteria.
- Amikacin package insert (Teva Parenteral Medicines, Inc.).
- Gentamicin package insert (Preserior Kabi USA, LLC.).
- Tobramycin package insert (Akor, Inc.).
- Based primarily on the assessment of high dose, extended interval regimens and the assumption of combination therapy.

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