Results. A total of 6,055 resistant and 50,302 susceptible infections were identified; 2,800 and 16,585, respectively, received DAT. In multivariate analyses, DAT was associated with worse outcomes, including a 20% increased risk of composite mortality and an approximate 70% increase in LOS and total costs, respectively. The relative impact of DAT was nearly identical by antibiotic-resistant status (**Figure**).

Conclusion. Our study indicates that DAT is independently associated with poorer outcomes in serious infections due to GNB, irrespective of resistance status.

Figure. Association between Delayed Appropriate Therapy and Clinical and Economic Outcomes Stratified by Antibiotic Susceptibility Status

Outcome	Adjusted* Estimate (95% CI)	
	Antibiotic-resistant	Antibiotic-susceptible
Composite mortality endpoint (in-hospital death or discharge to hospice) (OR)	1.2 (1.1, 1.3)	1.2 (1.2, 1.3)
Discharge to home (OR)	0.7 (0.6, 0.8)	0.7 (0.6, 0.7)
Post-index duration of antibiotic therapy (RD)	1.5 (1.5, 1.6)	1.7 (1.7, 1.8)
Post-index LOS (RD)	1.6 (1.5, 1.6)	1.8 (1.8, 1.9)
Post-index total hospital cost (RD)	1.5 (1.5, 1.6)	1.8 (1.7, 1.8)

*Each outcome was adjusted for variables that were included in the inverse probability weight.
OR: Ocds ratio; CI: Confidence ratio; RD: Relative difference

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784. Effectiveness of Daptomycin in Patients with Persistent Methicillin-Resistant *Staphylococcus aureus* Bacteremia Despite Vancomycin

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Background. Clinicians often switch therapy in patients with persistent methicillin-resistant *Staphylococcus aureus*(MRSA) bacteremia despite prolonged vancomycin therapy. We evaluated the utilization of daptomycin in MRSA bacteremic patients who failed vancomycin therapy.

Methods. This single center, retrospective evaluation of adult patients who received daptomycin after receiving vancomycin for MRSA bacteremia from January 2011 to September 2016. Persistent bacteremia was defined as continued positive blood culture(s) despite receiving more than 72 hours of vancomycin. Patients with bacteremia from presumed pneumonia or MRSA bacteremia within 30 days of admission were excluded. Daptomycin dose was evaluated for appropriateness based upon patient weight and renal function. Duration of bacteremia was evaluated, including whether source control was achieved. Creatinine phosphokinase (CPK) levels drawn during daptomycin therapy were assessed to evaluate safety. Hospital length of stay and patient disposition were collected for each patient. Data were presented with descriptive statistics.

Results. 700 patient received daptomycin during this study period; 66 were duplicates, 596 did not meet inclusion criteria and 38 patients were included. Minimum inhibitory concentrations (MICs) of isolates were 1mcg/mL (31.6%), 1.5mcg/mL (42.1%) and 2mcg/mL (26.3%). Daptomycin dose was 4mg/kg (10.5%), 6mg/kg (63%), 8mg/kg (16%) and 10mg/kg (10.5%). Twenty-eight (73.7%) of 38 patients cleared bacteremia with daptomycin. Ten patients were switched back to vancomycin for the following reasons: persistent bacteremia (6), increase in daptomycin MIC (3), and blood culture was negative on the date daptomycin was initiated (1). Duration of bacteremia while receiving vancomycin vs. daptomycin was 8.5 ± 6.6 days and 4.9 ± 5.4 days, respectively. Only one patient experienced elevated CPK > 5 times upper normal limit. Daptomycin was utilized appropriately in 97.4 % of the patients who failed vancomycin according to our current protocol.

Conclusion. Daptomycin was effective in a majority of the patients in clearing bacteremia but MICs increased in some patients. Prospective studies should be performed to confirm these findings.

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785. Assessment of risk factors for inappropriate empiric antibiotic therapy in patients with Gram-negative sterile site infection complicated by sepsis or septic shock

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Background. The association between the administration of inappropriate empiric antibiotic treatment (IEA) and an increased risk of hospital mortality has been consistently reported. This study explores pre-infection risk factors for IEA in patients with Gram-negative (GN) sterile site infections complicated by sepsis or septic shock.

Methods. Retrospective cohort study at Barnes-Jewish Hospital (2010–2015). Risk factors including history of hospitalization, receipt of intravenous antipseudomonal antibiotics, and isolation of GN organisms 90 days prior to admission were collected. Process of care variables assessed included ICU admission, durations of mechanical ventilation, central venous catheter, and urinary catheter insertion, and antibiotic days prior to isolation of a GN pathogen(s). IEA was defined as receipt of antibiotic therapy that lacked in vitro activity against the identified pathogen(s) within the 24 hours of the culture being obtained. Multivariable logistic regression analysis (MVLRA) risk factor modeling that included IEA as the dependent outcome variable was conducted.

Results. 855 consecutive patients with first episode sepsis or septic shock were included. Compared with patients receiving appropriate empiric therapy (n = 715), variables significantly associated with IEA (n = 140) within 90 days prior to admission included recent hospitalization (23.1% v. 34.3%, P = 0.005), mean days of meropenem (0 v. 2.1, P = 0.010) and piperacillin-tazobactam (0 v. 1.6, P <0.001) therapy, and isolation of a GN organism(s) (8.4% v. 20.0%, P <0.001). Prior to isolation of the GN pathogen(s), median hospital (0 v. 6 days, P < 0.001) and ICU (0 v. 0 days, P < 0.001) length of stay, as well as the median duration of CVC dwell time (10 v. 17 days, P = 0.050) was associated with IEA. MVLRA identified isolation of a GN pathogen (AOR 3.432 95% CI 2.024-5.820, P <0.001) and days of piperacillin-tazobactam therapy (AOR 1.149 95% CI 1.061–1.245, P <0.001) in the 90 days prior to admission, as well as Charlson score (AOR 1.097 95% CI 1.023-1.177, p + 0.010) as independent risk factors for IEA.

Conclusion. Consideration of risk factors prior to admission and prior to collection of a sterile site specimen appear to be critical when making empiric antibiotic decisions targeting GN pathogens in patients with sepsis or septic shock.

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786. Effect of Generic vs. Brand-Name Meropenem on Mortality in a Colombian Hospital's Intensive Care Unit

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Background. The quality of antibiotics is a crucial element in successful treatment of infections. Recently, the use of generic antibiotics has caused controversy because of studies reporting clinical failure and the emergence of antibacterial resistance associated with the sustained use of generic antibiotics. The present study was designed to determine the mortality associated with the use of generic meropenem (GM) and brand-name meropenem (BNM) used to treat Gram-negative infections.

Methods. We conducted an ambispective cohort study comparing adult patients who received GM and BNM while in the intensive care unit of a tertiary care hospital in Colombia. Patients treated between January 2011 and May 2014 received GM while patients treated between June 2014 and March 2017 received BNM. Patients were included in the study only if the infecting organism was susceptible to meropenem. The GM and BNM cohorts were paired by age, infection type, and infection severity as measured by Sequential Organ Failure Assessment score. Mortality was compared between groups. Data were analyzed using descriptive and inferential statistics.

Results. A total of 168 patients were included; 68 patients (40%) were treated with GM and 100 (60%) were treated with BNM. The mean age was 57 years old; 72 (43%) women and 96 (57%) men. The most common infecting organism was E. coli (35%) followed by K. pneumoniae (19%). Bacteremia (49%) was the most common infection type, followed by intraabdominal infection (24%). Multivariate analysis demonstrated that patients treated with GM had a risk of death 18 times higher (OR: 18.45 95% CI 1.47-232, *P* = 0.024) than patients treated with BNM. Patients with a history of cardiovascular disease had an independent risk of death compared with those without cardiovascular disease. Other comorbidities and time between bacterial culture and initiation of treatment with meropenem did not have a statistically significant effect on mortality.

Conclusion. The present study suggests that patients treated with GM have worse clinical outcomes compared with those treated with BNM. More studies are needed to confirm the clinical superiority of brand-name vs. generic antibiotics, not only for meropenem but also for other commonly-used molecules.

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787. Echinocandin-resistant *Candida tropicalis* Bloodstream Infections

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Background. The aim of this study is to describe the clinical manifestations, molecular mechanisms, and treatment outcomes of patients with echinocandin-resistant *Candida tropicalis* (*C. tropicalis*) bloodstream infections (BSI).

Methods. A PubMed search was conducted using the search terms related to *C. tropicalis* BSI and echinocandin resistance. Two previously unreported cases from our institution diagnosed with *C. tropicalis*BSI that developed resistance to echinocandins were also included. Demographics, comorbidities, treatment, clinical outcomes, and molecular mechanisms were analyzed.

Results. Seven patients with echinocandin-resistant *C. tropicalis* BSI were identified, including 5 previously reported cases and two from our institution. Median age was 58.7 ± 20.4 years; 3 (43%) patients were males. Three (43%) had acute myelogenous leukemia, 3 (43%) had acute lymphoblastic leukemia, and 1 (14%) had urothelial cancer. All patients were immunocompromised having received chemotherapy in the last six months and 3 (43%) were hematopoietic stem cell transplant recipients. Five (71%) had breakthrough of echinocandin resistance while receiving an echinocandin; one (14%) received caspofungin in the past 3 months and only one (14%) had no reported echinocandin exposure in the past 3 months.

DNA sequencing of the *FKS1* gene for mutations known to confer echinocandin resistance was performed in 4 cases, including our two index cases. Homozygous T-to-C mutations in two alleles of *FKS1*gene was detected in 2 cases, and a heterozygous mutation was detected in the other 2 cases, which resulted in a deduced serine-to-proline amino acid change at position 654 (S654P).

Six patients (86%) survived after being treated with an antifungal agent other than an echinocandin. Treatment was changed to liposomal amphotericin B in two cases, and one each to voriconazole, fluconazole, voriconazole plus liposomal amphotericin B, and caspofungin plus voriconazole. The one patient who died received intravenous voriconazole.

Conclusion. Echinocandin resistance emerged in neutropenic patients with *C. tropicalis* fungemia through a characteristic mutational hot-spot amino acid change in the target *FKS1* gene. Although alternative antifungal agents may be successfully used as salvage therapy, the outcome may still be fatal.

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788. Factors Associated with Mortality in Carbapenem-Resistant *Enterobacteriaceae* Bacteremia: Focus on Antibiotic Therapy

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Background. Infections caused by carbapenem resistant *Enterobacteriaceae* (CRE) are associated with high mortality. Optimal treatment for CRE bacteremia remains unclear, including the role of combination therapy, carbapenem-containing regimens, or newer antimicrobials, such as ceftazidime-avibactam (CAZ-AVI). The objective of this study was to evaluate risk factors associated with mortality in patients with CRE bacteremia, with a focus on antimicrobial therapy.

Methods. This was a multicenter, retrospective cohort study of inpatients within Carolinas HealthCare System who had a positive blood culture with CRE (*Klebsiella* spp., *Enterobacter* spp., or *Escherichia coli)* between January 1, 2010 and September 30, 2016. CRE isolates were identified as pathogens with an ertapenem MIC ≥ 1 mcg/mL. The primary endpoint was death within 28 days after the first positive blood culture in patients with CRE bacteremia. Clinical variables, including the use of specific antimicrobials and combination therapy, were compared between 28-day survivors vs. non-survivors.

Results. A total of 73 patients were included with CRE bacteremia. The most common sources of infection identified were urine (42.5%) and intra-abdominal (38.4%). The overall 28-day mortality was 26%. Fifty-three (72.6%) patients received combination antibiotic therapy and 20 (27.4%) received monotherapy. Combination therapy with *in vitro* active agents (36.8% vs. 33.3%, $P = 0.87$) and the use of carbapenem-containing regimens (47.4% vs. 46.3%, $P = 0.74$) did not differ between those who died and survived, respectively. One patient treated with CAZ-AVI as monotherapy died, but only eight patients received this antibiotic. There was a trend towards higher use of tigecycline in the group that died compared with the group that survived (73.7% vs. 59.3%, $P = 0.26$).

Conclusion. There did not appear to be a difference in mortality at 28 days with the use of combination therapy or a carbapenem-containing regimen. While a statistically significant difference was not demonstrated, tigecycline-containing regimens may be associated with increased mortality in the treatment of CRE bacteremia. Larger prospective studies are necessary to further elucidate the role of combination therapy and newer agents, such as CAZ-AVI, in this patient population.

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789. Ceftolozane-tazobactam for the Treatment of Multi Drug-resistant *Pseudomonas aeruginosa* (MDRPA) Infections

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Background. Ceftolozane-tazobactam (TOL-TAZ) is a novel cephalosporin/β-lactamase inhibitor combination with potent activity against *Pseudomonas aeruginosa*, including MDRPA. TOL-TAZ use for MDRPA infections has not been well-studied.

Methods. We conducted a retrospective study to describe outcomes of patients treated with TOL-TAZ for MDR *Pseudomonas aeruginosa* infections at 3 academic medical centers. Patients were age ≥ 18 years who had MDRPA isolated in culture and received TOL-TAZ for at least 24 hours. The primary outcomes were 30-day and in-hospital mortality. Secondary outcomes were microbiological cure and clinical success. Microbiological cure was defined as negative culture at end of therapy; cure was presumed when clinical success occurred without follow-up cultures. Clinical success was defined as resolution of all signs and symptoms of infection. TOL-TAZ susceptibility results were collected when available.

Results.

Characteristics	Results (*N* = 34)
Male gender, n(%)	21 (61.8)
Age (median, IQR)	57 (42-66)
Charlson Comorbidity Index (median, IQR)	4 (2.25-5)
APACHE II score (median, IQR)	20 (13-26.8)
ICU, n(%)	23 (67.7)
Solid organ transplant recipient, n(%)	15 (44.1)
Primary infection, n(%)	
Pneumonia	22 (64.7)
Bacteremia	6 (17.6)
Urinary tract	4 (11.8)
Wound	4 (11.8)
Intra-abdominal	2 (5.8)
Hospital day index infection diagnosed (median, IQR)	8 (1-35)
Hospital day TOL-TAZ started (median, IQR)	18.5 (3-52)
Patients receiving concomitant therapy for index pathogen, n(%)	20 (58.8)
Isolates susceptible to TOL-TAZ, n/N (%)	16/17 (94)
30-day mortality, n (%)	7 (20.6)
In-hospital mortality, n(%)	8 (23.5)
Microbiologic cure, n(%)	21 (61.8)
Clinical success, n(%)	24 (70.6)

Conclusion. In this severely ill population with MDRPA infections, 79.4% and 76.5% of patients were alive at 30-days and at the end of their stay, respectively. Some patients had positive cultures despite clinical resolution. TOL-TAZ is a potential option for patients with MDRPA infections.