

epidemiology of adult patients hospitalized with iGAS in California and risk factors for in-hospital death.

**Methods.** Using 2000–2016 California hospital discharge data, we extracted records for adults (≥18 years) with ≥1 group A *Streptococcus* (GAS)-associated *International Classification of Diseases, Ninth or Tenth Revision* discharge diagnosis code (e.g., unspecified GAS; GAS-specific pharyngitis, pneumonia, and sepsis) or known GAS-associated syndromes (e.g., acute rheumatic fever, erysipelas, scarlet fever). To identify patients hospitalized with iGAS, we selected extracted records that also had codes consistent with invasive disease (e.g., sepsis, pneumonia, intubation, or central line placement). We calculated iGAS-associated hospitalization incidence rates per 100,000 population and described patient demographics and comorbidities. We calculated the odds of in-hospital death using multivariable logistic regression ( $P < 0.05$ ).

**Results.** During 2000–2016 in California, 37,532 adults were hospitalized with iGAS; 1,045 (3%) died in-hospital. Mean annual hospitalization incidence was 9.4/100,000 population, and was highest (16.3/100,000) in 2016 (Figure 1). Most patients were male (56%), aged 40–65 (45%) or ≥65 (28%) years, and white (60%); 18% were immunocompromised. The percent of patients who died in-hospital increased with age and was highest among those with comorbidities such as malnutrition, cardiovascular disease (CVD), and chronic kidney disease (CKD) (Figure 2). In a multivariable model including age as a continuous variable, sex, and race-ethnicity, the odds of in-hospital death was significantly increased for patients with diagnosis codes for malnutrition, liver disease, CVD, immunosuppression, and CKD (Figure 2); within the race/ethnicity variable Asian/Pacific Islander patients had a higher odds of death compared with white patients.

**Conclusion.** Hospitalization and subsequent in-hospital death due to iGAS is substantial in California. Adults with iGAS who have specific comorbidities are at greater risk for death when hospitalized with iGAS.

Figure 1: Annual number of patients hospitalized with invasive group A *Streptococcus* and hospitalization rate (per 100,000 population), California, 2000–2016.

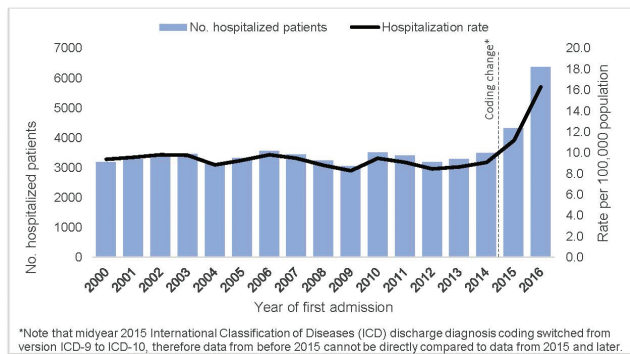
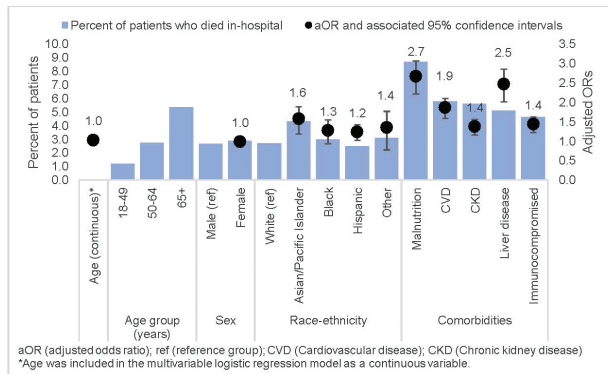


Figure 2: Percent of patients hospitalized with invasive group A *Streptococcus* infection who died in-hospital, and the adjusted odds of in-hospital death calculated using multivariable logistic regression, California, 2000–2016.



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

## 216. Association Between Days to Initiate Appropriate Therapy and Hospital Length of Stay Among Adult Hospitalized Patients With Gram-negative Bloodstream Infections (GN-BSI)

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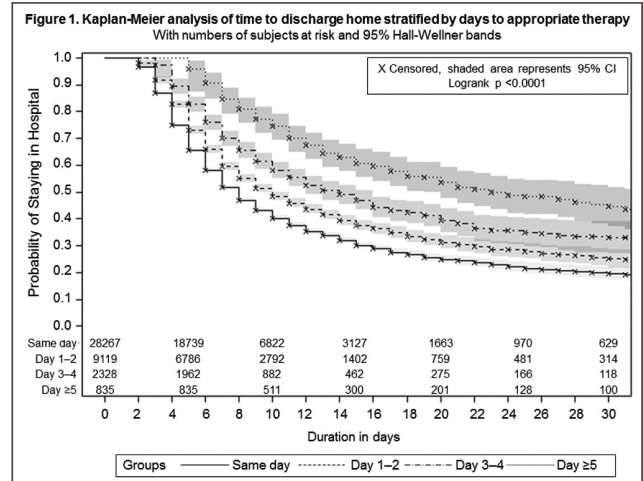
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**Background.** The deleterious outcomes associated with delay receipt of appropriate therapy are well documented. However, scant data exists on the consequences of each day delay of appropriate therapy and subsequent outcomes among adult hospitalized patients with GN-BSIs.

**Methods.** Study design: a retrospective cohort analysis. Study population: consecutive adult, hospitalized patients with a GN-BSI (11 most prevalent pathogens) in 1 of 181 institutions contributing microbiology data to the Premier Healthcare Database (October 2010–Sep 2015). Exclusion criteria: age < 18 years; diagnosis of pregnancy or cystic fibrosis, died or discharged within 2 days of index GN-BSI culture, lack of sufficient antibiotic susceptibility or treatment data to determine appropriateness. Day of initiating appropriate therapy was defined as the first day when the patient received an antibiotic with *in vitro* activity against the GN-BSI post index culture. Results were summarized by Kaplan–Meier estimates, and Cox Proportional-Hazards (CPH) analyses modeling discharge to home were conducted. Time to initiate appropriate therapy (0, 1–2 days, 3–4 days, ≥5 days) was included in the CPH model as an ordinal variable.

**Results.** A total of 40,549 patients met selection criteria. Mean (SD) age was 67.5 (16.1) years and 54% were female. *E. coli* and *K. pneumoniae* were the most common GN-BSI (58.0% and 18.3%, respectively). Approximately 30% of patients were in the ICU at index GN-BSI and in-hospital mortality was 6.8%. The mean (SD) time to receive appropriate therapy post index GN-BSI culture was 0.6 (2.7) days, and 69.7%, 22.5%, 5.7% and 2.1% received appropriate therapy in 0, 1–2, 3–4, and ≥5 days of index GN-BSI, respectively. The mean/median LOS post index GN-BSI by 0, 1–2, 3–4, and ≥5 days delays in appropriate treatment were 8.3/6, 9.8/7, 11.5/8, and 19.2/11 days respectively. Kaplan–Meier plots are shown in Figure 1. In the CPH model, each interval delay in appropriate therapy was associated with a 21% decrease in the likelihood of being discharged home for patients with GB-BSIs.

**Conclusion.** Hospital length of stay was found to increase when appropriate therapy was delayed. These findings highlight the critical need for early appropriate therapy among patients with GN-BSIs.



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## 217. Combination Salvage Therapy with Cefazolin Plus Ertapenem for Refractory Methicillin-Susceptible *Staphylococcus aureus* Bacteremia

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**Background.** Suboptimal therapy against methicillin-sensitive *Staphylococcus aureus* (MSSA) may have catastrophic consequences in severe infections such as endocarditis or epidural abscess. High MSSA inocula have been associated with clinical failure in patients receiving cefazolin (CZ), particularly when used at low doses, associated with a CZ inoculum effect. We previously described that adding ertapenem (ETP) to CZ led to synergism against MSSA and sensitized the pathogen to host innate immune factors. Here we expand our experience with CZ plus ETP as salvage therapy for 11 cases of refractory MSSA bacteremia (lacking source control problems) and explore CZ+ETP combination *in vitro* and *in vivo*.

**Methods.** Six available MSSA strains from patients treated with CZ+ETP for refractory bacteremia were tested in Mueller–Hinton Broth or RPMI media at standard ( $10^5$  CFU/mL) or high ( $10^7$  CFU/mL) inocula by MIC, checkerboard, and time-kill assays using ETP, CZ or nafcillin (NAF) alone vs. ETP+NAF or ETP+CZ. Disk diffusion synergy assays between CZ and ETP were also performed. CZ, ETP and CZ+ETP were tested in a rat endocarditis model using well described MSSA, TX0117 and TX0117c.

**Results.** 11 consecutive patients with MSSA bacteremia (6 confirmed endocarditis) refractory to standard CZ or NAF rapidly cleared with CZ+ETP. 9 patients had daily positive blood cultures, and 8 cleared in  $\leq 24$  hr, including those with  $\geq 2$  cm vegetations. All 11 survived hospitalization. In MHB, 3/6 MSSA exhibited a CZ inoculum effect (CZ MIC  $>3 \log_{10}$  vs.  $10^3$  CFU/mL), but only 1 showed a significant CZ inoculum effect in RPMI. CZ+ETP was significantly more efficacious than CZ in a rat model of MSSA endocarditis utilizing a strain displaying a CZ inoculum effect, despite only modest benefit observed *in vitro* for 6 MSSA isolates.

**Conclusion.** CZ+ETP combination therapy yielded profound clinical success in severe MSSA infections with high bacterial densities, as demonstrated by rapid bacteremia clearance. Enhanced efficacy was also observed in a rat endocarditis model. The anti-staphylococcal activity of CZ+ETP *in vivo* exceeded that observed *in vitro*, consistent with our prior observations of host innate immune cooperativity with the regimen. CZ+ETP warrants further study for the treatment of refractory MSSA bacteremia and endocarditis.

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**218. Evaluation of Clinical Outcomes with Shorter Vs. Longer Duration of Treatment for Common Inpatient Bacterial Infections Associated with Bacteremia**

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**Background.** Pneumonia (PNA), urinary tract infection (UTI), and acute bacterial skin and skin structure infection (ABSSSI) are the most common infections treated in the inpatient setting and often are associated with bacteremia. Though short courses of treatment are advocated for these infections in general, no established guidelines exist for cases involving bacteremia. We evaluated the clinical outcomes of patients receiving short (5–9 days) vs. long (10–15 days) duration of antibiotic treatment.

**Methods.** A retrospective study was conducted at 3 area hospitals comprising a university-based tertiary center, a public safety net hospital, and a Veterans' Affairs hospital. We included hospitalized adult patients with transient bacteremia associated with uncomplicated cases of PNA, UTI, or ABSSSI. The primary outcome consisted of a composite of rehospitalization or resumption of antibiotic treatment attributed to the original infection or death due to any cause within 30 days of the antibiotic start date. Secondary outcomes included the individual composite components, Clostridioides difficile infection, and antibiotic-related adverse effects leading to change in antibiotic therapy. A propensity score weighted logistic regression model was used to mitigate factors which could bias a patient toward receiving a shorter or longer treatment duration.

**Results.** Of 411 patients included in the study, 123 (29.9%) received a short duration of therapy and 288 (70.1%) received a long duration of therapy. The median duration of treatment was 8 days in the short group and 13 days in the long group. In the propensity-weighted analysis, the probability of meeting the composite primary outcome was not statistically different between the short and long groups (Table 1). However, receiving a short course was associated with a higher probability of restarting antibiotics and Clostridioides difficile infection.

**Conclusion.** Shorter vs. longer courses of antibiotic treatment for bacteremia associated with PNA, UTI, and ABSSSI were not significantly different in a composite of readmission, restart of antibiotics, and mortality; however, further study is needed to evaluate the safety and effectiveness of short-course therapy.

Table 1

	Long course (n=288)		Short course (n=123)		Odds ratio	P-value
	Frequency, n (%)	Predicted probability	Frequency, n (%)	Predicted probability		
Composite primary outcome	35 (12.2)	11.1%	15 (12.2)	15.9%	1.51	0.2220
Secondary outcomes						
Rehospitalization attributable to original infection	13 (4.5)	3.9%	2 (1.6)	2.5%	0.64	0.7120
Restarted antibiotics for original infection	28 (9.7)	8.8%	15 (12.2)	15.9%	1.97	0.0030
All-cause mortality	6 (2.1)	2.1%	0	0.0%		
C. difficile infection	4 (1.4)	1.1%	5 (4.1)	4.5%	4.02	0.0000
Antibiotic change due to adverse effect	4 (1.4)	1.4%	0	0.0%		

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**219. Is the modified quick SOFA scale superior to quick SOFA in patients with diagnosed septic shock?**

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**Background.** In this study it was aimed to compare the effects of qSOFA (Quick Sequential Organ Failure Assessment) score with modified qSOFA score (PLoS One. 2018 Sep 26;13(9):e0204608) for predicting one month survival in patients with diagnosed septic shock (SS) in a tertiary-care educational university hospital in a developing country.

**Methods.** Modified qSOFA was created by adding age factor ( $>50$  years=1 point) to patients with qSOFA scale 1 or 2 or 3 who had SS (sepsis+hypotension+adrenergic agent) and consulted by Infectious Diseases consultants between December 2013–December 2018. Arterial lactate level of  $>2$  mmol/L criterion was added as an including criteria for SS according to 3<sup>rd</sup> International Sepsis and Septic Shock Consensus Statement after 23<sup>rd</sup> February 2016. Statistical analysis was performed via Chi-square test and a p-value  $<0.05$  was considered significant.

**Results.** The number of patients with qSOFA score of 1 or 2 or 3 from 527 patients are in Table1 [some of the cases were diagnosed as septic shock according to elder definition (without lactate criterion) and there was a subgroup with qSOFA score 1]. Among the  $>50$ -year aged group, the 30-day survival rate was lower in patients with qSOFA3 vs. qSOFA 2 vs. qSOFA 1 (Table1, 3x2 Chi Square test,  $P = 0.0057$ ). Among the  $<50$  years group, the qSOFA one month survival rate was lower in patients with qSOFA 3 vs. qSOFA 2 vs. qSOFA 1 (Table, 3x2 Chi Square Test,  $P = 0.0052$ ). According to modified qSOFA, there was a significant difference for one month survival among SS cases with scores of 1, 2, 3 and 4 (12/21 57% vs. 50/126 40% vs. 78/269 29% vs. 22/111 20%, 4x2 Chi-square test,  $P = 0.0003$ ). On the other hand, there was no significant difference in terms of one month survival when we performed subgroup analysis in qSOFA score 1, 2, or 3 subgroups, as  $\leq 50$  years vs.  $>50$  years (table, Chi-square test, 12/21 vs. 39/97  $P = 0.224$ , 11/29 vs. 75/244  $P = 0.526$ , 3/25 vs. 22/111  $P = 0.572$ ).

**Conclusion.** In terms of survival at one month, there was a significant difference between qSOFA score 1, 2, 3 and 4 subgroups. In patients with qSOFA score of 1 or 2 or 3, being under 50 years did not have a significant effect on one-month survival. Modified qSOFA may be beneficial to foresee the probable mortality but these findings need to be validated in larger cohorts

Table.1 Findings

	A (qSOFA 1+ $\leq 50$ years)	B (qSOFA 1+ $>50$ years)	C (qSOFA 2+ $\leq 50$ years)	D (qSOFA 2+ $>50$ years)	E (qSOFA 3+ c)	F (qSOFA 3+ $>50$ years)
Number of patients	21	97	29	244	25	111
Mean age (min-max)	36.7 (20-50)	67.7 (51-92)	40.1 (23-50)	70.7 (51-117)	40.1 (21-50)	71.6 (51-94)
One month survival	12 (57.1%)	39 (40.2%)	11 (37.9%)	75 (30.7%)	3 (12%)	22 (19.8%)

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**220. Characteristics and Outcomes of Veterans with Invasive Group B Streptococcal Infection Vary with the Type of Syndrome**

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**Background.** Surveillance from the US Center for Disease Control and Prevention (CDC) has detected an increase in the prevalence of invasive Group B streptococcus (GBS) infections between 2008 and 2016 among non-pregnant adults. Here, we use data from the US Veterans Health Administration (VHA) to assess the underlying clinical characteristics and outcomes associated with specific types of invasive GBS infection among veterans.

**Methods.** We used the VA Corporate Data Warehouse to identify patients with invasive GBS infection diagnosed between 2008–2017 using CDC's surveillance definitions. Data on the microbiological source of infection (e.g., GBS in cultures from blood, bone or sterile fluids) and associated International Classification of Disease (ICD) codes were used to classify the type of invasive infection. We determined associated co-morbid conditions and 30-day all-cause mortality for incident cases.

**Results.** Between 2008 and 2017, there were 4780 incident cases of invasive GBS infection in veterans with a mean age of 66.6 years ( $\pm 11.7$ ) and 30-day all-cause mortality of 8%. The most common syndrome was osteomyelitis (23%,  $N = 1078$ ) with 30-day mortality of 1%. Other common infections, such as bacteremia (20%;  $N = 972$ ), skin and soft-tissue infections (18%, 853), and pneumonia (14%,  $N = 664$ ), had higher mortality (13%, 4% and 17%, respectively; Figure). In patients with GBS peritonitis, present in 3% ( $N = 138$ ) incidence cases, 46% had chronic liver disease with a 30-day mortality of 28%. Diabetes mellitus (DM) occurred in 66% of patients with any invasive GBS infection and in 86% of patients with GBS osteomyelitis. Chronic heart, kidney, or lung disease affected  $>25\%$  of patients (table).