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Impact of Prior Hospitalization on Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections over Three Decades

BY

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M.P.H., Emory University, 2014
B.A., Emory University, 2004

Thesis Committee Chair: Jesse Jacob, MD

An abstract of
A Thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
In partial fulfillment of the requirements of the degree of
Master of Public Health in the Career MPH program 2014

Abstract

Impact of Prior Hospitalization on Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections over Three Decades

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The epidemiology of *Staphylococcus aureus* bloodstream infections has changed in recent decades, with an increase in the proportion due to methicillin-resistant *S. aureus* (MRSA) occurring outside of a hospital setting. This change is due in part to shifting of healthcare to the outpatient setting and the emergence of community-onset MRSA as a cause of skin and soft-tissue infections. Using all initial *S. aureus* positive blood cultures at one hospital during the first four years of 3 decades (1990-1993, 2000-2003, and 2010-2013), we hypothesized that prior hospital admission within one month would be associated with a greater risk for methicillin resistance among those with *S. aureus* bloodstream infection. The number of *S. aureus* bloodstream infections increased from 432 (1990-1993) to 637 (2000-2003), then decreased to 432 in the most recent study period (2010-2013). The decrease in the number of infections between the middle and last time periods was largely driven by a 50% decrease in infections occurring in the hospital. Similarly, the percent MRSA increased from 25% (1990-1993) to 52% (2000-2003) then declined to 47% in the most recent study period (2010-2013). The proportion with community-onset infections, end-stage renal disease, and HIV increased over time. Mortality was higher among those patients with MRSA in all study periods. The final model based on backward selection included patient age, whether the infection occurred in a community setting, HIV diagnosis, and the time period in which the culture was collected. Analysis showed no significant association between prior admission in the last month and methicillin resistance among these bloodstream infections (P= 0.35). While we could not demonstrate that prior hospitalization was a risk for developing MRSA bloodstream infections, the drop in hospital-onset *S. aureus* bloodstream infections in the last study period was striking. *S. aureus* bloodstream infections are still a problem, but prevention efforts may be decreasing the observed incidence. Future directions may include expanding hospital-based efforts to the outpatient setting.

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Introduction

Staphylococcus aureus is a common bacterium found on skin and is capable of causing serious infections among healthy individuals, though patients who are exposed to healthcare or have serious underlying medical conditions may be at higher risk. Serious staphylococcal infections often result in bloodstream infections, known as bacteremia, which can be both difficult to treat and result in significant morbidity and mortality.

The term bloodstream infection (BSI) commonly refers to the growth of any microorganism from a blood culture obtained from a patient with clinical signs of infection, after contamination has been ruled out. Of particular concern is the rise of BSIs involving drug-resistant organisms, such as methicillin-resistant *S. aureus* (MRSA), which can increase a patient's duration of hospital stay and carries an increased risk of mortality. The epidemiology of *S. aureus* BSIs has changed considerably over the past three decades, both in the emergence and increasing incidence of methicillin resistance and the importance of infections acquired outside of a hospital setting.

Background

S. aureus is one of the leading causes of both community-and hospital-acquired BSIs in population-based studies [1, 2]. With an incidence estimated between 20-50 per 100,000 persons per year[3] which lead to over 750,000 related hospitalizations from 1999-2005[4], *S. aureus* bacteremia is a serious concern when considering healthcare-associated infections, especially with given an estimated mortality rate between 10-30%[3].

First observed as an increasing risk to patients over two decades ago[5] but continuing to increase in incidence since[1, 4, 6, 7], the emergence of methicillin-resistant *S. aureus* (MRSA) has signaled an increased incidence of infection and worse outcome[8]. MRSA bacteremia has been associated with a significantly longer length of stay for hospitalized patients [9], as well as higher mortality rate than methicillin-susceptible *S. aureus* (MSSA) [10, 11].

Increasingly, patients are more likely to become infected with a MRSA bacteremia in the community setting rather than during an inpatient admission [12, 13]. This is in part due to the role of nasal colonization, in which an individual can carry *S. aureus* without clinical infection [14]. However, multiple studies have found that prior admission at a hospital can be the single-most important risk factor for the acquisition of community-acquired MRSA[13, 15, 16], with the risk even increasing in relation to a short duration between hospital stays[17].

As the nation's health care model has shifted more toward ambulatory care for chronic diseases[18], those individuals with repeated health care contacts are at increasing risk for *S. aureus* BSI. In addition to prior hospital admissions, conditions such as dialysis [11, 19], HIV infection [11, 19], residence in a nursing home [20] or long-term care facility [21], previous infections with MRSA bacteremia [21, 22], indwelling lines[6, 22], and other comorbidities [3, 9, 11, 20, 22] have been observed.

A previous study was performed in this downtown Atlanta hospital tracking the occurrence of *S. aureus* bacteremia over the four years of two decades (1990-93, and 2000-03)[7]. This study will expand upon the earlier work by collecting the data from 2010-13 *S. aureus* BSI, and analyzing all time periods for changing risk factors and trends. This study is unique because of both the time span (three decades) and completeness of the data (line

listings) available. Chart reviews were done on the earlier datasets, leading to a relatively comprehensive list of risk factors associated with each BSI. Finally, this specific hospital's unique position as an academic medical center with a large hemodialysis population makes it well-suited to studying infections that may be more susceptible to individuals with greater healthcare contact, including hemodialysis treatments, immunosuppression, and cancer diagnoses.

The objectives of this study are to determine if the proportion of methicillin-resistant *S. aureus* has significantly changed over time, and if there is any significant relationship between methicillin resistance among *S. aureus* BSI and prior admission in the past month. Additionally, the role of other risk factors that may have changed over time will be assessed.

Methods

This study is a retrospective cohort study involving all patients with a first-time positive *S. aureus* BSIs at Emory University Hospital Midtown. The study uses a previously collected dataset and adds data from patients between 2010 through 2013. In addition to the presence of a *S. aureus* BSI, data were also collected on methicillin resistance, clinical syndrome, and prior admissions, and patient demographics.

For the 1990 through 1993 and 2000 through 2003 time periods, data on *S. aureus* BSIs were prospectively collected for infection control surveillance from patients hospitalized at Emory University Hospital Midtown, Atlanta, GA, and selected information added by retrospective review of electronic medical records. Only the first isolate per patient was included in the analysis. For the most recent time period, data were collected using the

Infection Prevention department's clinical decision support system, TheraDoc™. Additional data were collected using the Emory Electronic Medical Record. Data were stored in a password-protected database and all identifiers were removed once the dataset was complete.

Age was categorized according to the quartile ranges of each variable. Age categories were 17-30 (reference), 31-50, 51-70, and 71-114. The time period of specimen collection was categorized by decade into the categories 1990-93, 2000-03, and 2010-13. Infections were considered community-acquired if they occurred within 48 hours of the patient being admitted to the hospital. Descriptive analysis was conducted using SAS version 9.3.

The proportions of each level of individual variables in relation to methicillin resistance or susceptibility were calculated, using the above categories for grouping when necessary. Significance was determined using either a Chi-Square or Fisher's Exact Test for frequency. Missing variables for each category were noted as either methicillin resistant or susceptible.

Stratified analysis was conducted showing first the crude odds ratios and 95% confidence intervals to test for any independent association with methicillin resistance and prior admission in the last six months, gender, community or nosocomial acquisition, end-stage renal disease diagnosis, diabetes mellitus diagnosis, HIV diagnosis, sickle-cell disease diagnosis, and date range of culture, then adjusted according to age categories. The Breslow-Day test for heterogeneity of odds ratios (OR) was calculated for each age-adjusted level of a variable, to test for interaction. Confounding was evaluated by monitoring whether the crude and adjusted odds ratios for a particular variable changed by more than 10%. The Mantel-Haenszel chi-square method was used to test for the presence of a monotonic trend among ordinal categorical variables. While odds ratios were calculated for the age variable, these odds ratios

are not interpretable because the study matched cases and controls on age. Each variable was tested as to its effect on the crude association between methicillin resistance and prior admission, as well as any presence of a dose-response effect, effect modification, and confounding.

Logistic regression was conducted to calculate crude odds ratios of each variable's relationship with methicillin resistance; then adjusted odds ratios were calculated to include prior admission and age category. Two-way interaction was tested between prior admission and gender, community acquisition, end-stage renal disease diagnosis, diabetes mellitus diagnosis, HIV diagnosis, sickle-cell disease diagnosis, and date range of culture using the Wald chi-square test for the significance of the combined cross-product terms. Confounding was assessed by comparing crude and adjusted odds ratios for each variable, using a 10% difference as the threshold. Model selection was conducted using backwards selection with an alpha level of 0.05, beginning with the exposure variable, all independent variables, and all two-way interaction terms between the exposure and interaction variables. Interaction terms were removed first, one at a time, if they did not meet the significance level, then the independent variables. The most parsimonious model was then determined by removing from the model any independent variable that did not confound the relationship between methicillin resistance and prior admission, using a 10% change as the threshold. A final model was then selected by retaining any independent variables which were effect modifiers, confounders, or significant at the 0.05 alpha level. To test whether the observed distribution of cases and controls was similar to the expected distribution based on the model, the Hosmer-Lemeshow goodness of fit test was conducted for each model.

To account for any difference contributed by grouping age in the categories 17-30, 31-50, 51-70, and 71-114, conditional logistic regression was then conducted using both above and 10-year groupings among the age categories to determine the best model. A sensitivity analysis was also conducted, censoring all patients with a diagnosis of HIV, to test for the effect of this population on the relationship. Odds ratios, 95% confidence intervals, overall significance of individual variables, and test for monotonic trends were calculated similarly to those performed in unconditional logistic regression.

Results

During the study period 1491 patients had a *S. aureus* BSI. Of these, 634 (42.5%) were MRSA, 378 (25.4%) had a prior admission in the last month, and 793 (53.4%) were male. The plurality of infections occurred in the 2000-2003 time period, with 627 (42.0%), while there were 432 (29.0%) each in the 1990-1993 and 2010-2013 time period, 905 (60.7%) infections were community-onset, and 200 (13.4%) resulted in the death of the patient.

The most common co-morbid conditions in patients were 85 (5.7%) with sickle-cell disease, 162 (10.9%) with HIV, 184 (12.3%) with cancer, 482 (32.3%) with diabetes mellitus, and 526 (35.3%) with end-stage renal disease. Antibiotic susceptibility was low overall, with 625 (41.9%) to trimethoprim/sulfamethoxazole, 505 (33.9%) to clindamycin, 486 (32.6%) to levofloxacin, and 214 (14.4%) to erythromycin, though data was missing for 46-49% for each of these antibiotics.

Age was skewed slightly to the right with a minimum of 17, Q1 of 41, median of 55, Q3 of 69, and maximum of 114. After age was transformed to a categorical variable, 130 (8.7%)

were between 17 and 30 years of age, 466 (31.3%) between 31 and 50, 495 (33.2%) between 51 and 70, and 333 (22.3%) between 71 and 114. 67 individuals were missing data on age.

Table 1a depicts the characteristics of patients comparing MRSA and MSSA, a majority of whom were male (MSSA: 52%, MRSA: 55%). The proportions with prior admission (25%) and community-onset (50%) were similar in those with MSSA and MRSA. There was no significant difference between the groups among those who had a prior admission ($P = 0.53$), community-onset ($P = 0.42$), sex ($P = 0.26$), end-stage renal disease ($P = 0.86$), diabetes mellitus ($P = 0.07$), HIV ($P = 0.06$), or cancer ($P = 0.66$). There was a significant difference in mortality ($P = 0.0013$), with MRSA infections having a higher rate (16.7%) compared to MSSA infections (11.0%). There was a significant difference in the distribution of MSSA and MRSA by time period ($P <0.001$), with MSSA occurring more frequently in the earlier time periods. Patients with sickle-cell disease were more likely to have MSSA (7.2%) than MRSA (3.6%, $P = 0.003$). Increasing age was significantly associated with MRSA ($P <0.001$). MRSA and MSSA had differing susceptibilities to other antibiotics ($P <0.001$) though many data points were missing.

Table 1b depicts the characteristics of patients separated by time period. The proportion with MRSA increased from 25.0% in the 1990-1993 time period to 51.7% in the 2000-2003 time period then dropped to 46.8% in the 2010-2013 time period, a significant difference ($P <0.001$). This change was more evident hospital-onset infections, which dropped from 41.4% of all MRSA BSIs in the second time period to 25.3% in the latest. Amongst the time periods there were significant differences, with prior admission ($P <0.001$) decreasing, then slightly increasing over time, age group ($P <0.001$) shifting more toward the third quartile over time, community-onset ($P <0.001$) increasing over time, the percentage of males ($P = 0.0387$)

increasing in the 2000-2003 time period, end-stage renal disease (*P* <0.001) increasing over time, diabetes mellitus (*P* <0.001) cancer (*P* = 0.0188), and HIV (*P* = 0.0169) increasing in the 2000-2003 time period then dropping for the 2010-2013 time period, and sickle-cell disease (*P* <0.001) decreasing over time. Patient mortality (*P* <0.001) more than doubled from 8.8% to 19.1% in the 2000-2003 time period, then returned to 9.5% for the 2010-2013 time period. All antibiotic susceptibilities were significant (*P* <0.001), but many data points were missing, mainly among the earliest time period.

In bivariate analysis, crude associations between MRSA and prior admission in the last month were not significant (Table 2), nor between MRSA and community onset, sex, end-stage renal disease, diabetes mellitus, HIV, or cancer. The association between sickle-cell disease and MRSA is significant, with those individuals with sickle-cell disease 0.48 times as likely to have a MRSA BSI (95% CI 0.30-0.79). Age was also significantly associated with MRSA among the 71 or greater age group, with those individuals 2.12 times more likely to have MRSA when compared to the youngest age group (95% CI 1.40-3.23), and an overall significant trend of increasing risk with age (*P* <0.001). There was also a significant association between MRSA and time period, with those in 2000-2003 3.21 times more likely to have MRSA than those in 1990-1993 (95% CI 2.45-4.19), those in 2010-2013 2.63 times more likely (95% 1.97-3.52), with an overall significant trend (*P* <0.001).

When adjusted for age, the significance of MRSA and prior admission, community-onset, sex, end-stage renal disease, diabetes mellitus, HIV, and cancer do not change. There is evidence of effect modification of age category on sickle-cell disease (*P* = 0.02), and the association is confounded (OR 0.61 95% CI 0.35-1.05). There is no other evidence of

confounding among the variables. The trend evident between time periods remains significant when adjusted for age category (P <0.001).

Simple stratified analysis was used to examine the relationship between MRSA BSIs and prior admission in the last month and adjusted for other characteristics (Table 3), and found no evidence of association. There is no evidence of effect modification by any of the adjusting variables. There is evidence of confounding among the association when controlling for time period, with an odds ratio of 0.88 (95% CI 0.69-1.12) compared to the unadjusted odds ratio of 1.08 (95% CI 0.85-1.37).

Using logistic regression analysis, when all variables are included significant associations are seen with age group (P <0.001), onset location (P = 0.037), HIV diagnosis (P = 0.014), and time period (P <0.001) (Table 4). Those with a community-onset infection are significantly less likely to have MRSA (OR 0.87 95% CI 0.61-0.99), while those with HIV were more likely (OR 1.59 95% CI 1.10-2.31). The individuals in the oldest age group, when compared to the youngest age group, were 2.32 times more likely to have MRSA (95% CI 1.47-3.64). Both later time periods were significantly more likely to develop MRSA compared to the 1990-1993 time period, with the 2000-2003 time period 3.24 times more likely (95% CI 2.41-4.35) and the 2010-2013 time period 2.61 times more likely (95% CI 1/90-3.60). There is evidence of confounding comparing the crude and adjusted odds ratios of sickle-cell disease (OR 0.88 95% CI 0.50-1.53) and community-onset (OR 0.78 95% CI 0.61-0.99). None of the variables showed significant modification of the effect of prior admission on the risk of developing a MRSA BSI (Table 5).

The initial model at the start of backward selection included all main effects terms plus all two-way interaction terms. Since all interaction terms were removed due to a lack of

significant effect modification, the fully-adjusted model contained all main effects terms but no interaction terms (Table 6). As the age at time of infection and time period of infection confounded the relationship between prior admission and methicillin-resistance, the most parsimonious model included these variables. For the final model, community-onset (P = 0.02) and HIV diagnosis (P = 0.009) were added due to significance in earlier logistic regression models (Table 7). The Hosmer-Lemeshow goodness of fit test for the fully-adjusted model (P = 0.63), and the fully-adjusted model (P = 0.63) were above the threshold, indicating agreement between the observed and expected distributions. This test was below the threshold for the most parsimonious model (P = 0.01), indicating a poor fit. In the final model, there was no significant association between a prior admission in the last month and MRSA infections (P = 0.35) when controlled for age category, community-onset of infection, HIV diagnosis, and time period. There was evidence of a trend among both age category (P <0.001) and time period (P <0.001).

Using age category as a conditional variable, no significant changes in individual odds ratios and 95% confidence intervals were evident (Table 8). Wald p-values and tests for trend are also unchanged. There are also no significant changes conditioning on age as a dichotomous variable (categories 17-64, 65-114). A sensitivity analysis excluding patients with HIV showed that there were no significant changes or confounding when compared to the final model (Table 9).

Discussion

Among *S. aureus* BSIs in this study population, there was no significant association between prior admission in the last month and methicillin resistance, when accounting for age, time period, community-onset of infection, and HIV diagnosis. Additionally, sex and the presence of a diagnosis of end-stage renal disease, diabetes mellitus, sickle-cell disease, or cancer did not either significantly affect the association or confound it.

The characteristics of those patients acquiring *S. aureus* BSIs have changed over time. Diagnoses of comorbidities such as cancer and sickle-cell disease have decreased, while those of end-stage renal disease and diabetes have increased. Furthermore, new antibiotics have entered the market or become more cost-effective for treatment as patents expire, making treatment more accessible and wider-ranging. Not fully explained by the normal fluctuations of rate of these diseases in the population, there must be another explanation.

Many conditions which would have necessitated a hospital stay in past decades are now treated in part or entirely in an outpatient or non-hospital setting. This change in healthcare delivery impacts *S. aureus* BSIs occurring outside the hospital. Many of these outpatient treatments, such as dialysis or chemotherapy, put a patient especially at risk to a BSI due to the presence of an indwelling intravenous catheter and/or the immunosuppressive effects of therapy.

The lack of significant association between prior admission and methicillin resistance may reflect the penetration of MRSA in non-hospital settings in this study population, particularly in recent years. This would explain why previous studies conducted over a decade ago [13, 15, 16] showed an association between prior admission, but this one did not. Patients may

become colonized with *S. aureus* (have bacteria on the body without symptoms of infection) and develop and an infection at a later date leading to infection after hospital discharge. However, the definition of what constitutes a prior admission as a risk factor for MRSA in the literature is variable, ranging from one year [13] to one month [15] to vaguely described 'previous contact' [16]. The one-month interval for prior admission was chosen for this analysis because the risk of MRSA bacteremia has been shown decrease with longer interval after hospital discharge [17].

Prevention efforts have focused largely on the hospital setting, and reducing transmission between patients and from healthcare workers to patients [23-25]. The fact that there was a small reduction in MRSA BSIs over time in the community setting, but a much larger reduction among those BSI in the hospital setting point to the efficacy of these hospital-based efforts. Given the number of MRSA BSIs in the community, an increased focus on prevention of these infections is warranted.

The study findings are consistent with the results of previously published studies in certain ways. The decline in MRSA BSI in recent years mirrors previous findings [6]. Additionally, increased patient age across age groups was a risk for MRSA, not merely when age was dichotomized into elderly and non-elderly, demonstrating that overall health was of more concern than a single line of demarcation. Finally, the mortality of MRSA infections was higher, mirroring previous studies [3].

Of interesting note is the change in HIV prevalence over time, with an expected increase in the middle time period decreasing slightly for the latter years. Fewer of these types of BSI

with among patients with this disease may indicate better treatment options with the development of novel antiretroviral therapies.

The strengths of this study include the large number of *S. aureus* BSIs. Additionally, the study encompassed a long time period (portions of three decades) at a single institution with a large at-risk patient population. Finally, chart review and electronic medical records allowed for a comprehensive detection of comorbidities and potential risk factors.

Limitations of the study include the lack of data on the presence of a central line. However, comorbidities such as diabetes mellitus, end-stage renal disease, and others were included. Those patients whose BSIs were considered community-onset included those with previous healthcare contact and those transferred to the hospital from other healthcare facilities (such as nursing homes). These patient populations likely differ in their risk for *S. aureus* BSI The difference in collection of data over time periods, moving from chart review to electronic records, may also have accounted for some variation among patients in the latest time period.

Finally, patient-level prior antibiotic use was not available for this study and could not be assessed as a risk factor for MRSA. The high number of missing results of antibiotic susceptibilities from the *S. aureus* BSIs from earlier time periods made looking for associations between other l antibiotic susceptibilities and MRSA difficult and led to them being dropped from all models.

Future studies could benefit from conducting a chart review or using more sophisticated electronic medical records to capture whether a patient had a central line at the time of infection, and whether it contributed to the infection. Efforts should also be made to translate

successful prevention efforts of *S. aureus* BSI from a hospital to a community setting, in the hopes of further reducing the burden of these infections on the population. Additionally, effective antibiotic stewardship can be used to combat antibiotic-resistant organisms such as MRSA as they become more prevalent.

Table 1a. Characteristics of Patients with Staphylococcus aureus Bloodstream Infections, Methicillin Susceptible or Resistant, Emory University Hospital Midtown

Characteristic	MSSA		MRSA			
	n=857	*%*	n=634	*%*	X^2 (d.f.)*	*p-value*
Previous Admission						
Yes	212	*24.7%*	166	*26.2%*		
No	645	*75.3%*	468	*73.8%*	0.40 (1)	*0.5259*
Age Group						
17-30	84	*10.5%*	46	*7.4%*		
31-50	289	*36.1%*	177	*28.4%*		
51-70	273	*34.1%*	222	*35.5%*		
71+	154	*19.3%*	179	*28.7%*	23.77 (3)	***<0.001***
Missing	*57*		*10*			
Community-Onset Infection						
Yes	429	*50.0%*	304	*47.9%*		
No	428	*50.0%*	330	*52.1%*	0.65 (1)	*0.4207*
Sex						
Male	444	*52.2%*	349	*55.1%*		
Female	407	*47.8%*	284	*44.8%*	1.28 (1)	*0.2582*
Missing	*6*		*1*			
End-Stage Renal Disease Diagnosis						
Present	304	*35.5%*	222	*35.0%*		
Not Present	553	*64.5%*	412	*65.0%*	0.03 (1)	*0.8552*
Diabetes Mellitus Diagnosis						
Present	261	*30.5%*	221	*34.9%*		
Not Present	596	*69.5%*	413	*65.1%*	3.23 (1)	*0.0723*
HIV Diagnosis						
Present	82	*9.6%*	80	*12.6%*		
Not Present	775	*90.4%*	554	*87.4%*	3.50 (1)	*0.0614*
Sickle-Cell Disease Diagnosis						
Present	62	*7.2%*	23	*3.6%*		
Not Present	795	*92.8%*	611	*96.4%*	8.82 (1)	***0.003***

Cancer Diagnosis						
Present	103	*12.0%*	81	*12.8%*		
Not Present	754	*88.0%*	553	*87.2%*	0.19 (1)	*0.6602*
Patient Died						
Yes	94	*11.0%*	106	*16.7%*		
No	763	*89.0%*	528	*83.3%*	10.38 (1)	***0.0013***
TMP/Sulfa Susceptibility†						
Yes	214	*91.1%*	411	*72.6%*		
No	21	*8.9%*	155	*27.4%*	32.97 (1)	***<0.001***
Missing	*622*		*68*			
Clindamycin Susceptibility†						
Yes	201	*86.3%*	304	*57.0%*		
No	32	*13.7%*	229	*43.0%*	61.67 (1)	***<0.001***
Missing	*624*		*101*			
Erythromycin Susceptibility†						
Yes	134	*56.5%*	80	*15.4%*		
No	103	*43.5%*	441	*84.6%*	136.37 (1)	***<0.001***
Missing	*620*		*113*			
Levofloxacin Susceptibility†						
Yes	232	*96.7%*	254	*48.7%*		
No	8	*3.3%*	267	*51.3%*	163.45 (1)	***<0.001***
Missing	*617*		*113*			
Time Period						
1990-93	324	*37.8%*	108	*17.0%*		
2000-03	303	*35.4%*	324	*51.1%*		
2010-13	230	*26.8%*	202	*31.9%*	78.9 (2)	***<0.001***

* Chi-square test, d.f. = degrees of freedom

† Intermediate or Resistant Susceptibility Outcomes were Considered Non-Susceptible. Those not tested were excluded

Table 1b. Characteristics of Patients with Staphylococcus aureus Bloodstream Infections, by Time Period of Collection, Emory University Hospital Midtown

Characteristic		1990-93		2000-03		2010-13		X^2 (d.f.)*	*p-value*
		n=432	*%*	n=627	*%*	n=432	*%*		
Prior Admission (last 1 month)									
	Yes	59	*13.7%*	212	*33.8%*	107	*24.8%*		
	No	373	*86.3%*	415	*66.2%*	325	*75.2%*	55.0 (2)	***<0.001***
Age Group									
	17-30	32	*8.6%*	45	*7.3%*	53	*12.3%*		
	31-50	130	*34.8%*	217	*35.0%*	119	*27.6%*		
	51-70	112	*29.9%*	206	*33.3%*	177	*41.1%*		
	71+	100	*26.7%*	151	*24.4%*	82	*19.0%*	25.5 (6)	***<0.001***
	Missing	58		8		1			
Community-Onset Infection									
	Yes	204	*47.2%*	392	*62.5%*	309	*71.5%*		
	No	228	*52.8%*	235	*37.5%*	123	*28.5%*	55.0 (2)	***<0.001***
Sex									
	Male	214	*50.1%*	358	*57.3%*	221	*51.2%*		
	Female	213	*49.9%*	267	*42.7%*	211	*48.8%*	6.50 (2)	***0.0387***
	Missing	5		2		0			
End-Stage Renal Disease Diagnosis									
	Present	86	*19.9%*	241	*38.4%*	199	*46.1%*		
	Not Present	346	*80.1%*	386	*61.6%*	233	*53.9%*	69.5 (2)	***<0.001***
Diabetes Mellitus Diagnosis									
	Present	102	*23.6%*	160	*74.5%*	220	*50.9%*		
	Not Present	330	*76.4%*	467	*25.5%*	212	*49.1%*	96.6 (2)	***<0.001***
HIV Diagnosis									
	Present	32	*7.4%*	81	*12.9%*	49	*11.3%*		
	Not Present	400	*92.6%*	546	*87.1%*	383	*88.7%*	8.16 (2)	***0.0169***
Sickle-Cell Disease Diagnosis									
	Present	50	*11.6%*	22	*3.5%*	13	*3.0%*		
	Not Present	382	*88.4%*	605	*96.5%*	419	*97.0%*	39.1 (2)	***<0.001***
Cancer Diagnosis									
	Present	68	*15.7%*	75	*12.0%*	41	*9.5%*		

	Not Present	364	*84.3%*	552	*88.0%*	391	*90.5%*	7.94 (2)	***0.0188***
Patient Died									
	Yes	38	*8.8%*	120	*19.1%*	42	*9.7%*		
	No	394	*91.2%*	507	*80.9%*	390	*90.3%*	30.7 (2)	***<0.001***
TMP/Sulfa Susceptibility†									
	Yes	0	*0.0%*	266	*80.4%*	359	*85.1%*		
	No	48	*100.0%*	65	*19.6%*	63	*14.9%*	183.7 (2)	***<0.001***
	Missing	384		296		10			
Clindamycin Susceptibility†									
	Yes	0	*0.0%*	184	*55.9%*	321	*76.1%*		
	No	15	*100.0%*	145	*44.1%*	101	*23.9%*	63.0 (2)	***<0.001***
	Missing	417		298		10			
Erythromycin Susceptibility†									
	Yes	0	*0.0%*	48	*14.5%*	166	*39.3%*		
	No	5	*100.0%*	283	*85.5%*	256	*60.7%*	58.4 (2)	***<0.001***
	Missing	427		296		10			
Levofloxacin Susceptibility†									
	Yes	0	*0.0%*	54	*16.4%*	432	*100.0%*		
	No	0	*0.0%*	275	*83.6%*	0	*0.0%*	565.4 (2)	***<0.001***
	Missing	432		298		0			
Methicillin Resistance									
	Yes	108	*25.0%*	324	*51.7%*	202	*46.8%*		
	No	324	*75.0%*	303	*48.3%*	230	*53.2%*	78.9 (2)	***<0.001***
Methicillin Resistant									
Community-Onset		38	*35.2%*	190	*58.6%*	151	*74.7%*	46.2 (2)	***<0.001***
Hospital-Onset		70	*64.8%*	134	*41.4%*	51	*25.3%*		

* Chi-square test, d.f. = degrees of freedom

† Intermediate or Resistant Susceptibility Outcomes were Considered Non-Susceptible. Those not tested were excluded

Table 2. Unadjusted and age-adjusted of those with a Staphylococcus aureus bloodstream infection, methicillin-resistant or susceptible, Emory University Hospital Midtown

Characteristic	Crude			Age-Adjusted*			
	Odds Ratio	95% C.I.†	trend ¥ p-value	Odds Ratio	95% C.I.†	heterog. p-value ^	trend ¥ p-value
Age at Time of Infection							
17-30	1	---	<0.001	---			
31-50	1.12	0.75-1.68)		---			
51-70	1.48	(0.99-2.22)		---			
71+	2.12	(1.40-3.23)		---			
Previous Admission (1 month)							
Yes	1.08	(0.85-1.37)		1.05	(0.83-1.34)	0.36	
No	1	---		1	---		
Community-Onset Infection							
Yes	0.92	(0.75-1.13)		0.95	(0.77-1.17)	0.11	
No	1	---		1	---		
Sex							
Male	1.13	(0.92-1.38)		1.15	(0.93-1.43)	0.87	
Female	1	---		1	---		
End-Stage Renal Disease Diagnosis							
Present	0.98	(0.79-1.22)		0.99	(0.79-1.23)	0.47	
Not Present	1	---		1	---		
Diabetes Mellitus Diagnosis							
Present	1.22	(0.98-1.52)		1.12	(0.90-1.40)	0.07	
Not Present	1	---		1	---		
HIV Diagnosis							
Present	1.36	(0.98-1.89)		1.75	(1.23-2.49)	0.31	
Not Present	1	---		1	---		
Sickle-Cell Disease Diagnosis							
Present	0.48	(0.30-0.79)		0.61	(0.35-1.05)	0.02	
Not Present	1	---		1	---		

Cancer Diagnosis							
Present	1.07	(0.79-1.46)		1.01	(0.73-1.40)	0.85	
Not Present	1	---		1	---		
TMP/Sulfa Susceptibility‡							
Yes	0.26	(0.16-0.42)		0.26	(0.16-0.43)	0.96	
No	1	---		1	---		
Clindamycin Susceptibility‡							
Yes	0.21	(0.14-0.32)		0.24	(0.15-0.36)	0.12	
No	1	---		1	---		
Erythromycin Susceptibility‡							
Yes	0.14	(0.10-0.20)		0.14	(0.10-0.20)	0.35	
No	1	---		1	---		
Levofloxacin Susceptibility‡							
Yes	0.33	(0.02-0.07)		0.04	(0.02-0.08)	0.49	
No	1	---		1	---		
Time Period							
1990-93	1	---	<0.001	1	---		<0.001
2000-03	3.21	(2.45-4.19)		3.03	(2.27-4.06)	0.01	
2010-13	2.63	(1.97-3.52)		2.40	(1.76-3.27)	0.01	

* Age-adjusted by categories: 17-30, 31-50, 51-70, 71+

† C.I. Confidence interval

‡ Intermediate or resistant susceptibility outcomes were considered non-susceptible

^ Breslow-Day test for heterogeneity of odds ratios

¥ Mantel-Haenszel chi-square

Table 3. Association of previous hospital admission in the prior month with methicillin-resistance among those with a Staphylococcus aureus bloodstream infection, adjusted for other characteristics, Emory University Hospital Midtown

Adjusted For *	Prior Hospital Admission	Odds Ratio	*95% C.I.†*	*heterog. p-value ^*
Unadjusted (crude)	Yes	1.08	(0.85-1.37)	
	No	1	---	
Community-Onset Infection	Yes	1.09	(0.86-1.38)	*0.7157*
	No	1	---	
Sex	Yes	1.07	(0.84-1.35)	*0.1750*
	No	1	---	
End-Stage Renal Disease Diagnosis	Yes	1.08	(0.85-1.37)	*0.7932*
	No	1	---	
Diabetes Mellitus Diagnosis	Yes	1.09	(0.86-1.37)	*0.5169*
	No	1	---	
HIV Diagnosis	Yes	1.06	(0.84-1.35)	*0.0887*
	No	1	---	
Sickle-Cell Disease Diagnosis	Yes	1.09	(0.86-1.38)	*0.2903*
	No	1	---	
Cancer Diagnosis	Yes	1.08	(0.85-1.36)	*0.9114*
	No	1	---	
TMP/Sulfa Susceptibility‡	Yes	0.96	(0.68-1.37)	*0.1922*
	No	1	---	
Clindamycin Susceptibility‡	Yes	0.98	(0.68-1.41)	*0.4451*
	No	1	---	
Erythromycin Susceptibility‡	Yes	0.99	(0.68-1.45)	*0.9190*
	No	1	---	
Levofloxacin Susceptibility‡	Yes	0.84	(0.57-1.25)	*0.9294*
	No	1	---	

Time Period	Yes	0.88	(0.69-1.12)	*0.4643*
	No	1	---	

* For categories of adjustment variables, see Table 2

† C.I. Confidence interval

^ Breslow-Day test for heterogeneity of odds ratios

‡ Intermediate or resistant susceptibility outcomes were considered non-susceptible

Table 4. Unadjusted and adjusted odds ratios of various characteristics with methicillin resistance among those with Staphylococcus aureus bloodstream infections, Emory University Hospital Midtown

Characteristic	Stratified Analysis Crude		Logistic regression analysis Crude			Logistic regression analysis Adjusted*		
	Odds Ratio	*95% C.I.†*	Odds Ratio	95% C.I.†	p-value‡	Odds Ratio	95% C.I.†	p-value‡
Previous Admission (1 month)					*0.5248*			*0.354*
Yes	1.08	(0.85-1.37)	1.08	(0.85-1.37)		0.89	(0.69-1.14)	
No	1	---	1	---		1	---	
CRUDE MODEL: logit (P(D=1 | Prev1Mo)) = b_0 + b_1*Prev1Mo								
ADJUSTED MODEL: logit (P(D=1 | Prev1Mo, AGEGP, COMM, MALE, ESRD, DM, HIV, SCD, CA, COHORT)) = b_0 + (b_1*Prev1mo) + (b2*AgeGP1 + b3*AgeGP2 + b4*AgeGP3) + (b5*COMM)+ (b6*MALE) +(b7*ESRD) +(b8*DM) + (b9*HIV) + (b10*SCD) + (b11*CA)+ (b12*COHORTGP1 + b13*COHORTGP2)								
Age at Time of Infection					*<0.001*			*<0.001*
17-30	1	---	1	---		1	---	
31-50 AGEGP1	1.12	0.75-1.68)	1.12	*(0.75-1.68)*		1.10	*(0.72-1.68)*	
51-70 AGEGP2	1.48	(0.99-2.22)	1.49	*(0.99-2.22)*		1.51	*(0.99-2.31)*	
71+ AGEGP3	2.12	(1.40-3.23)	2.12	*(1.40-3.23)*		2.32	*(1.47-3.64)*	
Community-Onset Infection					*0.421*			*0.037*
Yes	0.92	(0.75-1.13)	0.92	(0.75-1.13)		0.78	(0.61-0.99)	
No	1	---	1	---		1	---	
Sex					*0.258*			*0.454*
Male	1.13	(0.92-1.38)	1.13	(0.92-1.39)		1.09	(0.87-1.36)	

Female	1	---	1	---		1	---	
End-Stage Renal Disease Diagnosis					*0.855*			*0.259*
Present	0.98	(0.79-1.22)	0.98	(0.79-1.22)		0.87	(0.68-1.11)	
Not Present	1	---	1	---		1	---	
Diabetes Mellitus Diagnosis					*0.073*			*0.301*
Present	1.22	(0.98-1.52)	1.22	(0.98-1.52)		1.14	(0.89-1.45)	
Not Present	1	---	1	---		1	---	
HIV Diagnosis					*0.062*			*0.014*
Present	1.36	(0.98-1.89)	1.37	(0.98-1.89)		1.59	(1.10-2.31)	
Not Present	1	---	1	---		1	---	
Sickle-Cell Disease Diagnosis					*0.004*			*0.643*
Present	0.48	(0.30-0.79)	0.48	(0.30-0.79)		0.88	(0.50-1.53)	
Not Present	1	---	1	---		1	---	
Cancer Diagnosis					*0.659*			*0.790*
Present	1.07	(0.79-1.46)	1.07	(0.79-1.46)		1.05	(0.75-1.47)	
Not Present	1	---	1	---		1	---	
Time Period					<0.001			<.001
1990-93	1	---	1	---		1	---	
2000-03 COHORTGP1	3.21	(2.45-4.19)	3.21	(2.45-4.20)		3.24	(2.41-4.35)	
2010-13 COHORTGP2	2.63	(1.97-3.52)	2.64	(1.98-3.52)		2.61	(1.90-3.60)	

* Adjusted simultaneously for all other factors

† C.I. Confidence interval

‡ Wald Chi-square Test

Table 5. Adjusted* odds ratios for Previous Admission within the Last Month and Methicillin-Resistance among Staphylococcus aureus bloodstream infections, with various effect modifiers, among patients at Emory University Hospital Midtown, 1990-93, 2000-03, 2010-13.

Interaction with		Previous Admission (Last 1 Month) Odds Ratios	
		Yes	
		Odds Ratio	95% C.I.†
No Interaction		0.89	(0.69-1.14)
Age at Time of Infection			
	17-30	1.66	*(0.73-3.77)*
	31-50 AGEGP1	0.96	*(0.64-1.46)*
	51-70 AGEGP2	0.74	*(0.48-1.15)*
	71+ AGEGP3	0.78	*(0.46-1.32)*
	homogeneity p-value = 0.35 ‡		
Community-Onset Infection			
	Yes	1.05	*(0.78-1.43)*
	No	0.62	*(0.40-0.96)*
	homogeneity p-value = 0.05 ‡		
Sex			
	Male	1.03	*(0.74-1.44)*
	Female	0.74	*(0.51-1.07)*
	homogeneity p-value = 0.18 ‡		
End-Stage Renal Disease Diagnosis			
	Present	1.00	*(0.68-1.48)*
	Not Present	0.82	*(0.59-1.13)*
	homogeneity p-value = 0.43 ‡		

Diabetes Mellitus Diagnosis			
	Present	0.86	*(0.55-1.33)*
	Not Present	0.90	*(0.66-1.22)*
	homogeneity p-value = 0.86 ‡		
HIV Diagnosis			
	Present	1.63	*(0.83-3.23)*
	Not Present	0.81	*(0.62-1.06)*
	homogeneity p-value = 0.06 ‡		
Sickle-Cell Disease Diagnosis			
	Present	1.18	*(0.68-1.13)*
	Not Present	0.87	*(0.40-3.45)*
	homogeneity p-value = 0.60 ‡		
Cancer Diagnosis			
	Present	0.98	*(0.49-1.97)*
	Not Present	0.87	*(0.67-1.14)*
	homogeneity p-value = 0.75 ‡		
Time Period			
	1990-93	1.30	*(0.69-2.46)*
	2000-03 COHORTGP1	0.82	*(0.58-1.15)*
	2010-13 COHORTGP2	0.86	*(0.55-1.34)*
	homogeneity p-value = 0.14 ‡		

* Models include Previous admission, Age group, Time Period, Gender, Acquisition Type, and Diagnoses for End-Stage Renal Disease, Diabetes Mellitus, HIV, Sickle-Cell Disease, and Cancer.

† C.I. Confidence interval

‡ Homogeneity p-value is from the Wald chi-square test for the significance of the combined cross-product terms

Table 6: Backwards Elimination of Crossproduct and Main Effects Terms

Backwards Elimination of Crossproduct Terms

Initial Model: Logit (P(D=1|Prev6Mo, AGEGP, COMM, MALE, ESRD, DM, HIV, SCD, CA, COHORT) = b0 + (b1*Prev1Mo) + (b2*AgeGP1 + b3*AgeGP2 + b4*AgeGP3) + (b5*COMM)+ (b6*MALE) +(b7*ESRD) +(b8*DM) + (b9*HIV) + (b10*SCD) + (b11*CA) + (b12*COHORTGP1 + b13*COHORTGP2) + (b14-15)*(Prev1Mo1-2)*(AgeGrp1-3) + [(b16-17)*Prev1Mo*COMM] + [(b18-19)*Prev1Mo*MALE] + [(b20-21)*Prev1Mo*ESRD] + [(b22-23)*Prev1Mo*DM] + [(b24-25)*Prev1Mo*HIV] + [(b26-27)*Prev1Mo*SCD] + [(b28-29)*Prev1Mo*CA] + [(b30-32)*Prev1Mo*(COHORT1-2)

	Cross-Product Term	Removed or retained p-value
Step 1:	Prev6Mo*DM	0.9882 (removed)
Step 2:	Prev6Mo*Agegrp	0.6663 (removed)
Step 3:	Prev6Mo*CA	0.5654 (removed)
Step 4:	Prev6Mo*ESRD	0.5767 (removed)
Step 5:	Prev6Mo*SCD	0.4220 (removed)
Step 6:	Prev6Mo*Cohort	0.3778 (removed)
Step 7:	Prev6Mo*Male	0.2872 (removed)
Step 8:	Prev6Mo*HIV	0.0799 (removed)
Step 9:	Prev6Mo*Community	0.0512 (removed)

Fully Adjusted Model: Logit (P(D=1|Prev6Mo, AGEGP, COMM, MALE, ESRD, DM, HIV, SCD, CA, COHORT) = b0 + (b1*Prev6Mo) + (b2*AgeGP1 + b3*AgeGP2 + b4*AgeGP3) + (b5*COMM)+ (b6*MALE) +(b7*ESRD) +(b8*DM) + (b9*HIV) + (b10*SCD) + (b11*CA) + (b12*DEATH) + (b15*COHORTGP1 + b16*COHORTGP2) + [(b17-18)*Prev6Mo*MALE]

Backwards Elimination of Main Effects Terms

		Fully Adjusted Model
Prior Admission (Last 1 month)		
	Yes	**0.89**

	No	**1**
Step1:		
	Main Effects Term	Removed or retained p-value
	CA	**.7896 (removed)**
		Step 1 Model
Prior Admission (Last 1 month)		
	Yes	**0.88**
	No	**1**
Step 2:		
	Main Effects Term	Removed or retained p-value
	SCD	**.6193 (removed)**
		Step 2 Model
Prior Admission (Last 1 month)		
	Yes	**0.88**
	No	**1**
Step 3:		
	Main Effects Term	Removed or retained p-value
	MALE	**.4414 (removed)**
		Step 3 Model
Prior Admission (Last 1 month)		
	Yes	**0.89**
	No	**1**
Step 4:		

	Main Effects Term	Removed or retained p-value
	ESRD	**.2752 (removed)**
		Step 3 Model
Prior Admission (Last 1 month)		
	Yes	**0.89**
	No	**1**
Step 5:		
	Main Effects Term	Removed or retained p-value
	DM	**.3146 (removed)**
		Step 3 Model
Prior Admission (Last 1 month)		
	Yes	**0.89**
	No	**1**
Step 7:		
	Main Effects Term	Removed or retained p-value
	Community	0.0244 (retained)
	HIV	0.0086 (retained)
	AgeGrp	<.0001 (retained)
	Cohort	<.0001 (retained)

Table 7: Logistic regression summary: fully adjusted, most parsimonious and final models. Methicillin-resistance among Staphylococcus aureus bloodstream infections, Emory University Hospital Midtown, 1990-93, 2000-03, 2010-13.

	Fully Adjusted Model			Most Parsimonious Model			Final Model		
	OR*	95% C.I.†	*Wald p-value* ^	OR	95% C.I.†	*Wald p-value* ^	OR	95% C.I.†	*Wald p-value* ^
Previous Admission (last 1 month):			0.3537			0.3353			0.3495
Yes	0.89	(0.69-1.14)		0.89	(0.69-1.14)		0.89	(0.69-1.14)	
No	1	--		1	--		1	--	
Sex:			0.4542						
Male	1.09	(0.87-1.36)							
Female	1	--							
Age at Time of Infection			<.0001			<.0001			<.0001
17-30	1	--		1	--		1	--	
31-50	1.10	(0.72-1.68)		1.13	(0.75-1.72)		1.12	(0.74-1.71)	
51-70	1.51	(0.99-2.31)		1.45	(0.97-2.19)		1.57	(1.03-2.37)	
71+	2.32	(1.47-3.64)		2.26	(1.47-3.47)		2.42	(1.56-3.75)	
	trend‡ p = <.0001			trend‡ p = <.0001			trend‡ p = <.0001		
Community-Onset			0.0374						0.0244
Yes	0.78	(0.61-0.99)					0.77	(0.61-0.97)	
No	1	--					1	--	
End-Stage Renal Disease Diagnosis			0.2593						
Present	0.87	(0.68-1.11)							
Not Present	1	--							
Diabetes Mellitus Diagnosis			0.3014						
Present	1.14	(0.89-1.45)							
Not Present	1	--							
HIV Diagnosis			0.0142						0.0086
Present	1.59	(1.10-2.31)					1.62	(1.13-2.33)	
Not Present	1	--					1	--	
Sickle-Cell Disease Diagnosis			0.6431						
Present	0.88	(0.50-1.53)							
Not Present	1	--							
Cancer Diagnosis			0.7896						
Present	1.05	(0.75-1.47)							
Not Present	1	--							
Time Period			<.0001			<.0001			<.0001
1990-93	1	--		1	--		1	--	
2000-03	3.24	(2.41-4.35)		3.22	(2.41-4.28)		3.26	(2.44-4.35)	
2010-13	2.61	(1.90-3.60)		2.58	(1.90-3.49)		2.68	(1.97-3.66)	
	trend‡ p = <.0001			trend‡ p = <.0001			trend‡ p = <.0001		
	HL GOF test$^{\$}$: 0.63			HL GOF test$^{\$}$: 0.01			HL GOF test$^{\$}$: 0.63		

*OR=Odds Ratio
†95% C.I. = 95% Confidence Interval
^Wald p-value = chunk test for overall significance of variable
‡test for trend: significance of beta for an ordinal variable
$^{\$}$: Hosmer-Lemeshow goodness of fit test (pvalue)

Table 8: Methicillin-resistance among Staphylococcus aureus bloodstream infections, Emory University Hospital Midtown, 1990-93, 2000-03, 2010-13. Logistic regression summary: Comparison of unconditional model, and models conditioned on age.

	Final Model Unconditional Logistic Adjusted for age (17-30, 31-50, 51-70, 71+)			Final Model Conditional Logistic Adjusted for age (17-30, 31-50, 51-70, 71+)			Final Model Conditional Logistic Adjusted for age (17-64, 65-114)		
Previous Admission	**OR***	**95% C.I.†**	***Wald p-value*** ^	**OR***	**95% C.I.†**	***Wald p-value*** ^	**OR***	**95% C.I.†**	***Wald p-value*** ^
(last 1 month):			0.3495			0.3504			0.2914
Yes	0.89	(0.69-1.14)		0.89	(0.69-1.14)		0.88	(0.68-1.12)	
No	1	--		1	--		1	--	
Age at Time of Infection			<.0001						
17-30	1	--							
31-50	1.12	(0.74-1.71)							
51-70	1.57	(1.03-2.37)							
71+	2.42	(1.56-3.75)							
	trend‡ p = <.0001								
Community-Onset			0.0244			0.0246			0.018
Yes	0.77	(0.61-0.97)		0.77	(0.61-0.97)		0.76	(0.60-0.95)	
No	1	--		1	--		1	--	
HIV Diagnosis			0.0086			0.0087			0.0322
Present	1.62	(1.13-2.33)		1.62	(1.13-2.32)		1.47	(1.03-2.08)	
Not Present	1	--		1	--		1	--	
Time Period			<.0001			<.0001			<.0001
1990-93	1	--		1	--		1	--	
2000-03	3.26	(2.44-4.35)		3.25	(2.43-4.34)		3.33	(2.50-4.45)	
2010-13	2.68	(1.97-3.66)		2.68	(1.96-3.65)		2.76	(2.03-3.76)	
	trend‡ p = <.0001			trend‡ p = <.0001			trend‡ p = <.0001		
	HL GOF test$: 0.63			(no HL GOF test)			(no HL GOF test)		

*OR=Odds Ratio

†95% C.I = 95% Confidence Interval

^Wald p-value = chunk test for overall significance of variable in the model

‡test for trend: significance of beta for an ordinal variable

$: Hosmer-Lemeshow goodness of fit test

Table 9: Methicillin-resistance among Staphylococcus aureus bloodstream infections, Emory University Hospital Midtown, 1990-93, 2000-03, 2010-13.
Sensitivity Analysis Comparing Final Model with and without HIV+ Patients

	Final Model All Patients Included			Final Model HIV+ Patients Removed		
Previous Admission	**OR***	**95% C.I.†**	***Wald p-value*** ^	**OR***	**95% C.I.†**	***Wald p-value*** ^
(last 1 month):			0.3495			0.1845
Yes	0.89	(0.69-1.14)		0.83	(0.64-1.09)	
No	1	--		1	--	
Age at Time of Infection			<.0001			<.0001
17-30	1	--		1	--	
31-50	1.12	(0.74-1.71)		1.13	(0.70-1.81)	
51-70	1.57	(1.03-2.37)		1.68	(1.06-2.65)	
71+	2.42	(1.56-3.75)		2.59	(1.61-4.17)	
	trend‡ p = <.0001			trend‡ p = <.0001		
Community-Onset			0.0244			0.0037
Yes	0.77	(0.61-0.97)		0.70	(0.55-0.89)	
No	1	--		1	--	
HIV Diagnosis			0.0086			
Present	1.62	(1.13-2.33)				
Not Present	1	--				
Time Period			<.0001			<.0001
1990-93	1	--		1	--	
2000-03	3.26	(2.44-4.35)		2.99	(2.21-4.04)	
2010-13	2.68	(1.97-3.66)		2.68	(1.93-3.70)	
	trend‡ p = <.0001			trend‡ p = <.0001		
	HL GOF testϕ: 0.63			HL GOF testϕ: 0.05		

*OR=Odds Ratio

†95% C.I = 95% Confidence Interval

^Wald p-value = chunk test for overall significance of variable in the model

‡test for trend: significance of beta for an ordinal variable

ϕ: Hosmer-Lemeshow goodness of fit test

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Appendix A: SAS Code

```
proc import datafile = 'H:\My Documents\Thesis\SABSIforSAS.xls' dbms = excel replace out =
thesisxls;
sheet = 'Main';
run;

proc sort data = thesisxls;
by ID;
run;

proc contents data = thesisxls;
run;

proc print data = thesisxls (obs = 20);
run;

/*Labels and categorizing age, recoding sex for easier interpretation*/
data thesis2;
set thesisxls;
label Numdays = 'Date from Admission to Culture';
label Cohort = 'Time Period';
if ( 1 <= Age <= 30) then Agegrp = 1;
if ( 31 <= Age <= 50) then Agegrp = 2;
if ( 51 <= Age <= 70) then Agegrp = 3;
if ( 71 <= Age <= 115) then Agegrp = 4;
if Sex = 'F' then Male = 0;
if Sex = 'M' then Male = 1;
drop Sex;
run;

/*Data Cleaning*/
proc freq data=thesis2;
tables MALE MRSA ESRD DM HIV SCD CA DEATH TMPSXT CLINDAMYCIN ERYTHROMYCIN
LEVOFLOXACIN Cohort Prev1MO;
run;

proc freq data=thesis2;
tables Class;
run;

/*Adding formats and recoding antibiotics / dichotomizing class*/
proc format;
value Cohortx 1 = '1990' 2 = '2000' 3 = '2010';
```

```
value AgeGrp 1 = '17-30' 2 = '31-50' 3 = '51-70' 4 = '71+';
run;
data thesis3; set thesis2;
format Cohort Cohortx.;
format agegrp Agegrp.;
if TMPSXT = 'R' then TMPSXTS = 0;
if TMPSXT = 'S' then TMPSXTS = 1;
if TMPSXT = 'U' then TMPSXTS = .;
if Clindamycin = 'I' then CLINDS = 0;
if Clindamycin = 'R' then CLINDS = 0;
if Clindamycin = 'S' then CLINDS = 1;
if Clindamycin = 'U' then CLINDS = .;
if Erythromycin = 'I' then ERYTHS = 0;
if Erythromycin = 'R' then ERYTHS = 0;
if Erythromycin = 'S' then ERYTHS = 1;
if Erythromycin = 'U' then ERYTHS = .;
if Levofloxacin = 'R' then LEVOS = 0;
if Levofloxacin = 'S' then LEVOS = 1;
if Levofloxacin = 'U' then LEVOS = .;
if Class = 'CA' then Community = 1;
if Class = 'Ca' then Community = 1;
if Class = 'HCA' then Community = 1;
if Class = 'NOSOCOMIAL' then Community = 0;
if Class = 'Nosocomial' then Community = 0;
run;

libname cjr 'H:\My Documents\Thesis';

data cjr.thesiscjr;
set thesis3;
run;

proc print data=thesis3 (obs = 20);
run;


/*----------------------UNIVARIATE ANALYSIS----------------------*/
proc freq data=thesis3;
tables COMMUNITY MALE MRSA ESRD DM HIV SCD CA DEATH TMPSXTS CLINDS ERYTHS LEVOS
Cohort Prev1MO agegrp;
run;

proc univariate data=thesis3;
var age;
```

```
histogram age;
run;

proc means data=thesis3 min q1 median q3 max;
var age numdays;
run;

proc freq data=thesis3;
tables PrevAdmit__1wk PrevAdmit__1mo PrevAdmit__6mos PrevAdmit__12mos
PrevAdmit__12mos0;
run;

proc print data=thesis3;
where age <18;
run;


/*----------------------TABLE 1a STARTS----------------------*/
proc freq data=thesis3 order = formatted;
tables (COMMUNITY Agegrp MALE ESRD DM HIV SCD CA DEATH TMPSXTS CLINDS ERYTHS
LEVOS Cohort Prev1Mo) * MRSA/norow nopercent chisq;
exact fisher;
run;

proc freq data=thesis3 order = formatted;
tables (COMMUNITY Agegrp MALE ESRD DM HIV SCD CA DEATH TMPSXTS CLINDS ERYTHS
LEVOS Cohort Prev1Mo agegrp) * MRSA/missing norow nopercent;
run;


/*----------------------TABLE 1b STARTS----------------------*/
proc freq data=thesis3 order = formatted;
tables agegrp * Cohort/norow nopercent chisq;
run;

proc freq data=thesis3 order = formatted;
tables (COMMUNITY MALE ESRD DM HIV SCD CA DEATH) * Cohort/norow nopercent chisq;
exact fisher;
run;

proc freq data=thesis3 order = formatted;
tables (TMPSXTS CLINDS ERYTHS LEVOS MRSA Prev1Mo) * Cohort/norow nopercent chisq;
exact fisher;
run;
```

```
proc freq data=thesis3 order = formatted;
tables (Agegrp MALE TMPSXTS CLINDS ERYTHS LEVOS) * Cohort/missing norow nopercent;
run;

proc freq data=thesis3 order=formatted;
tables MRSA*Community*Cohort/norow nopercent chisq;
exact fisher;
run;


/*----------------------TABLE 2 STARTS----------------------*/

/*Initial test of MRSA / Prev Admit*/
proc freq data=thesis3 order = formatted;
tables Prev1mo*MRSA / norow nocol nopercent cmh;
run;

/*2-level variable Crude Odds Ratios*/
proc freq data=thesis3 order = formatted;
tables Community*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables Male*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables ESRD*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables DM*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables HIV*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables SCD*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
```

```
tables CA*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables DEATH*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables TMPSXTS*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables CLINDS*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables ERYTHS*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables LEVOS*MRSA / norow nocol nopercent cmh;
run;

/*COHORT Trend*/
proc freq data=thesis3 order = formatted;
tables COHORT*MRSA / norow nocol nopercent cmh;
run;

/*Cohort Crude Odds ratio - 3 levels*/
proc freq data=thesis3 order = formatted;
tables COHORT*MRSA / norow nocol nopercent cmh;
where cohort = 1 or cohort = 2;
run;

proc freq data=thesis3 order = formatted;
tables COHORT*MRSA / norow nocol nopercent cmh;
where cohort = 1 or cohort = 3;
run;

/*Age Group Trend*/
proc freq data=thesis3 order = formatted;
tables agegrp*MRSA / norow nocol nopercent cmh;
run;
```

```
/*Age Group Crude Odds ratio - 4 levels*/
proc freq data=thesis3 order = formatted;
tables agegrp*MRSA / norow nocol nopercent cmh;
where agegrp = 1 or agegrp = 2;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*MRSA / norow nocol nopercent cmh;
where agegrp = 1 or agegrp = 3;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*MRSA / norow nocol nopercent cmh;
where agegrp = 1 or agegrp = 4;
run;

/*Age-Adjustting Prev Admit / MRSA*/
proc freq data=thesis3 order = formatted;
tables agegrp*Prev1mo*MRSA / norow nocol nopercent cmh;
run;

/*Age-Adjusting 2-level Variables*/
proc freq data=thesis3 order = formatted;
tables agegrp*Community*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*Male*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*ESRD*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*DM*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*HIV*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*SCD*MRSA / norow nocol nopercent cmh;
```

```
run;

proc freq data=thesis3 order = formatted;
tables agegrp*CA*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*DEATH*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*TMPSXTS*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*CLINDS*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*ERYTHS*MRSA / norow nocol nopercent cmh;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*LEVOS*MRSA / norow nocol nopercent cmh;
run;

/*Age-Adjusted COHORT Trend*/
proc freq data=thesis3 order = formatted;
tables agegrp*COHORT*MRSA / norow nocol nopercent cmh;
run;

/*Age-Adjusted Cohort Odds ratio - 3 levels*/
proc freq data=thesis3 order = formatted;
tables agegrp*COHORT*MRSA / norow nocol nopercent cmh;
where cohort = 1 or cohort = 2;
run;

proc freq data=thesis3 order = formatted;
tables agegrp*COHORT*MRSA / norow nocol nopercent cmh;
where cohort = 1 or cohort = 3;
run;

/*----------------------TABLE 3 STARTS----------------------*/
proc freq data=thesis3 order = formatted;
```

```
tables community*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables Male*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables ESRD*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables DM*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables HIV*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables SCD*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables CA*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables DEATH*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables TMPSXTS*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables CLINDS*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables ERYTHS*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
```

```
tables LEVOS*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;

proc freq data=thesis3 order = formatted;
tables COHORT*prev1mo*MRSA / norow nocol nopercent relrisk cmh;
run;


/*----------------------TABLE 4 STARTS----------------------*/

proc freq data=thesis3 order = formatted;
tables (COMMUNITY Agegrp MALE ESRD DM HIV SCD CA DEATH TMPSXTS CLINDS ERYTHS
LEVOS Cohort Prev1Mo) * MRSA/norow nopercent chisq;
exact fisher;
run;

proc logistic data=thesis3;
class Agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo agegrp cohort MALE COMMUNITY ESRD DM HIV SCD CA
DEATH TMPSXTS CLINDS ERYTHS LEVOS;
run;

/*CRUDE LOGISTIC REGRESSION MODELS*/
proc logistic data=thesis3;
model MRSA (Event = '1') = Prev1mo;
run;

proc logistic data=thesis3;
Class Agegrp (param=ref ref='17-30');
model MRSA (Event = '1') = agegrp;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = agegrp;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = COMMUNITY;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = MALE;
run;
```

```
proc logistic data=thesis3;
model MRSA (Event = '1') = ESRD;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = DM;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = HIV;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = SCD;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = CA;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = DEATH;
run;

proc logistic data=thesis3;
Class COHORT (param=ref ref=first);
model MRSA (Event = '1') = Cohort;
run;

proc logistic data=thesis3;
model MRSA (Event = '1') = Cohort;
run;

/*ADJUSTED MODEL*/
/*HAD TO LEAVE LEVOS OUT - MISSING ALL FROM 1990 Cohort*/
/*LEFT ALL Antibiotics OUT - TOO MISSING*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
```

```
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA;
run;

proc logistic data=thesis3;
class Cohort (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA;
run;


/*----------------------TABLE 5 STARTS----------------------*/
/*Logistic Regression - Categorical Variables with Interaction*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*Agegrp;
oddsratio Prev1mo / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*COMMUNITY;
oddsratio Prev1mo / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class MALE (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*MALE;
oddsratio Prev1mo / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class ESRD(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*ESRD;
oddsratio Prev1mo / diff = ref;
```

```
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class DM (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*DM;
oddsratio Prev1mo / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class HIV (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*HIV;
oddsratio Prev1mo / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class SCD (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*SCD;
oddsratio Prev1mo / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class CA (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*CA;
oddsratio Prev1mo / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*COHORT;
oddsratio Prev1mo / diff = ref;
```

```
run;


/*----------------------TABLE 6&7 START----------------------*/
/*Initial Model for Backward Elimination*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class MALE (param=ref ref=first);
class ESRD (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
class SCD(param=ref ref=first);
class CA(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
Prev1mo*Agegrp prev1mo*cohort prev1mo*community prev1mo*male prev1mo*ESRD
prev1mo*DM
prev1mo*HIV prev1mo*SCD prev1mo*CA /
        hierarchy = single selection = backward SLSTAY = 0.05 include =10
        Details lackfit;
run;

/*FULLY ADJUSTED MODEL*/
proc logistic data=thesis3;
class Prev1mo (param=ref ref=first);
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class MALE (param=ref ref=first);
class ESRD (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
class SCD(param=ref ref=first);
class CA(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
        / details lackfit;
run;

/*For all ORs*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
```

```
class MALE (param=ref ref=first);
class ESRD (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
class SCD(param=ref ref=first);
class CA(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
        / details lackfit;
run;

/*Tests for Trend in Fully Adjusted Model*/
/*Age Group*/
proc logistic data=thesis3;
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class MALE (param=ref ref=first);
class ESRD (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
class SCD(param=ref ref=first);
class CA(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
        / details lackfit;
run;

/*Time Cohort*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class COMMUNITY (param=ref ref=first);
class MALE (param=ref ref=first);
class ESRD (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
class SCD(param=ref ref=first);
class CA(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE COMMUNITY ESRD DM HIV SCD CA
        / details lackfit;
run;

/*Removing Main Effects Terms*/
/*CA*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
```

```
class MALE (param=ref ref=first);
class ESRD (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
class SCD(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE ESRD DM HIV SCD COMMUNITY
        / Details lackfit;
Oddsratio Prev1mo / diff = ref;
run;

/*SCD*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class MALE (param=ref ref=first);
class ESRD (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort MALE ESRD DM HIV COMMUNITY
        / Details lackfit;
Oddsratio Prev1mo / diff = ref;
run;

/*MALE*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class ESRD (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class DM (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort ESRD DM HIV COMMUNITY
        / Details lackfit;
Oddsratio Prev1mo / diff = ref;
run;

/*ESRD*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class DM (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
```

```
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort DM HIV COMMUNITY
        / Details lackfit;
Oddsratio Prev1mo / diff = ref;
run;

/*DM*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY
        / Details lackfit;
Oddsratio Prev1mo / diff = ref;
run;
/*ALL OTHERS RETAINED*/

/*MOST PARSIMONIOUS MODEL*/
/*Removing Community / HIV*/
/*ALL ORs*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort
        / Details lackfit;
run;

/*Test of Trend for Cohort*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
model MRSA (Event = '1') = Prev1mo Agegrp Cohort
        / Details lackfit;
Oddsratio Prev1mo / diff = ref;
run;

/*Test of Trend for AgeGrp*/
proc logistic data=thesis3;
class Cohort (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort
        / Details lackfit;
Oddsratio Prev1mo / diff = ref;
run;
```

```
/*FINAL MODEL*/
/*Final Model for all ORs*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY
        / Details lackfit;
run;

/*Final Model Tests for Trend*/
/*Age Group*/
proc logistic data=thesis3;
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY
        / Details lackfit;
run;

/*Time Period*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class COMMUNITY (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY
        / Details lackfit;
run;


/*----------------------TABLE 8 STARTS----------------------*/
/*Running final conditional regression model - age in previously-listed groups*/
proc logistic data=thesis3;
strata agegrp;
class Prev1mo (param=ref ref=first);
class Cohort (param=ref ref=first);
class Community (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort COMMUNITY HIV;
run;

/*New dataset to create new intervals for age groups for second conditional model*/
data thesis4;
```

```
set thesis3;
if ( 1 <= Age <= 64) then Agegrp2 = 1;
if ( 65 <= Age <= 114) then Agegrp2 = 2;
run;

proc freq data=thesis4;
tables agegrp2;
run;

/*Running final conditional regression model - age dichotomized 17-64 & 65+*/
proc logistic data=thesis4;
strata agegrp2;
class Prev1mo (param=ref ref=first);
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp2 Cohort COMMUNITY HIV;
run;

/*Final Model - UnConditional on binomial age groups */
proc logistic data=thesis4;
class agegrp2 (param=ref ref=first);
class Prev6mo (param=ref ref=first);
class Cohort (param=ref ref=first);
class MALE (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev6mo Agegrp2 Cohort MALE HIV
        prev6mo*male;
Oddsratio Prev6mo / diff = ref;
Oddsratio Male / diff = ref;
run;


/*----------------------TABLE 9 STARTS----------------------*/
/*Per Jesse Jacob's Request - testing for interaction between HIV/MALE and HIV/Cohort*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY HIV*MALE
         / Details lackfit;
run;
```

```
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class COMMUNITY (param=ref ref=first);
class Cohort (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY HIV*COHORT
        / Details lackfit;
run;

/*Odds ratios for HIV / Cohort*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class COMMUNITY (param=ref ref=first);
class Cohort (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY HIV*COHORT
        / Details lackfit;
oddsratio HIV / diff = ref;
run;

proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class COMMUNITY (param=ref ref=first);
class Cohort (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY HIV*COHORT
        / Details lackfit;
oddsratio COHORT / diff = ref;
run;

/*3-way interaction*/
proc logistic data=thesis3;
class agegrp (param=ref ref='17-30');
class COMMUNITY (param=ref ref=first);
class Cohort (param=ref ref=first);
class HIV(param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort HIV COMMUNITY prev1mo*COHORT*HIV
        / Details lackfit;
run;

/*Removing HIV patients from the dataset and re-running final model to check for sensitivity*/
data thesis5;
set thesis3;
where hiv = 0;
```

```
run;

/*Re-reunning Final Model to test for change in ORs after removing HIV+ pts*/
proc logistic data=thesis5;
class agegrp (param=ref ref='17-30');
class Cohort (param=ref ref=first);
class COMMUNITY (param=ref ref=first);
model MRSA (Event = '1') = Prev1mo Agegrp Cohort COMMUNITY
        / Details lackfit;
run;
```