Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world-wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Ashley Rose Date

Methods of Identifying *Staphylococcus aureus* Infections among Electronic Health Data to Inform Epidemiological Studies

By

Ashley Rose

Master of Public Health

Epidemiology

Scott Fridkin, MD
Committee Chair

Kelly Hatfield, MSPH
Committee Member

Methods of Identifying *Staphylococcus aureus* Infections among Electronic Health Data to Inform Epidemiological Studies

By

Ashley Rose

Bachelor of Arts
University of Virginia
2017

Faculty Thesis Advisor: Scott Fridkin, 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 for the degree of
Master of Public Health
in Epidemiology
2020

Abstract

Methods of Identifying *Staphylococcus aureus* Infections among Electronic Health Data to Inform Epidemiological Studies
By Ashley Rose

Background: Epidemiological studies utilize administrative discharge diagnosis codes to identify methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* (MRSA, MSSA) infections, trends, and clinical outcomes, despite debate regarding their accuracy for these purposes. We aimed to evaluate the impact that method of identification may have on epidemiological studies.

Methods: Clinical microbiology results and discharge data from U.S. hospitals participating in the Premier Healthcare Database from 2012 – 2017 were used in this analysis. Positive clinical cultures and/or a MRSA- or MSSA-specific *International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification* (ICD-9/10-CM) diagnosis codes from adult inpatients were included as *S. aureus* hospitalizations; positive blood cultures or septicemia codes denoted a septicemia hospitalization. To calculate sensitivity and PPV for codes true infection was considered a positive clinical culture. Negative binomial regression was used to measure trends in code and culture rates per 1,000 discharges. Logistic regression was used to examine the impact of method of identification on the adjusted risk of in-hospital mortality.

Results: Sensitivity of MRSA and MSSA codes was approximately 61% or less; results were similar when restricting to septicemia. MRSA trends in code and culture rates were not significantly different. However, MSSA code rates showed an increasing trend that was not observed among MSSA culture rates. Compared to hospitalizations with both a MRSA code and culture, code only hospitalizations had a decreased odds of in-hospital mortality (OR=0.90, 95% CI: (0.85, 0.94)); culture only hospitalizations had an increased odds of in-hospital mortality (OR=1.66, 95% CI: (1.59, 1.73)). MSSA culture only hospitalizations had an increased odds of in-hospital mortality compared with those identified by code and culture (OR=1.89, 95% CI: (1.81, 1.98)). However, there were no significant differences between code only and culture and code identified MSSA hospitalizations.

Conclusion: ICD diagnosis code sensitivity in identifying infections remain consistently poor in recent years, and differing methods of identification may identify conflicting trends, risk factors, and associations with outcomes. Using diagnosis codes to identify *S. aureus* infections may not be appropriate for assessing trends and clinical outcomes due to significant misclassification.

Methods of Identifying *Staphylococcus aureus* Infections among Electronic Health Data to Inform Epidemiological Studies

By

Ashley Rose

Bachelor of Arts
University of Virginia
2017

Faculty Thesis Advisor: Scott Fridkin, MD

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2020

Acknowledgement

Thank you to my thesis advisors, Kelly Hatfield, MSPH, and Scott Fridkin, MD, for their valuable guidance and mentorship. They shared their passion for healthcare epidemiology with me and challenged my thinking, for which I will always be grateful. I would like to express my gratitude to Isaac See, MD, Runa Gokhale, MD, MPH, James Baggs, PhD, and Rachel Slayton, PhD, MPH, for their expertise and contributions to this thesis, as well as others in the Epidemiology Research and Innovations Branch at CDC that made this work possible.

I also want to thank my family and close friends for their love and support throughout my graduate career.

Table of Contents

Introduction……1

Methods……15

Study Design, Population, Data Source……...15

Exposure, Outcomes, and Covariates……...16

Analytic Approach……...17

Objective One……...17

Objective Two……..20

Objective Three……20

Ethics Approval……....21

Results……..22

Characteristics of Hospitalizations……...22

Sensitivity and PPV of ICD Codes……..24

Trends in Culture and Code rates……25

Risk factors and In-hospital Mortality……25

Discussion……30

Sensitivity and PPV of ICD Codes……..30

Trends in Culture and Code rates……31

Risk factors and In-hospital Mortality……32

Limitations……...34

Strengths……...35

Future Directions……..35

Conclusion……37

References……38

Tables and Figures……...45

Appendix……..65

Introduction

Background

Staphylococcus aureus is one of the most common organisms causing infections in both healthcare and community settings. Infections caused by *S. aureus* account for significant morbidity in the United States and range in severity from skin and soft tissue infections (SSTI) to invasive infections, sepsis, and death (1). *S. aureus* is also a leading cause of surgical site infections (SSIs), infective endocarditis, osteomyelitis, indwelling medical device-related infections, and pneumonia (2, 3). Transmission of *S. aureus* occurs through person-to-person contact and contact with contaminated objects (4). Hand hygiene is an essential aspect of infection control practices aimed at preventing transmission of *S. aureus* (5).

Risk factors for acquiring a healthcare-associated *S. aureus* infection include prolonged hospitalization, intensive care unit (ICU) stay, outpatient visit, nursing home admission, surgical procedure, and presence of an indwelling medical device (4, 6). Prolonged antibiotic exposure is a specific risk factor for methicillin-resistant *Staphylococcus aureus* (MRSA) infection. Chronic illness (diabetes mellitus, end-stage renal disease, or malignancy), injection drug use, and proximity to an infected or colonized patient also increase risk of infection. Community-acquired *S. aureus* infections often occur in those who have at least one healthcare-associated risk factor for acquisition within the previous 12 months or had close contact with others who have these risk factors (6).

S. aureus infection is associated with increased morbidity and mortality, particularly among newborns, elderly, injection drug users, and those with an immunocompromising

comorbidity (4). Previous studies indicate an increased risk of outcomes such as mortality, readmission, prolonged hospitalization, and high cost among severe *S. aureus* infection types such as bacteremia or sepsis, pneumonia, endocarditis, and osteomyelitis (7, 8). Invasive MRSA infections are often associated with worse outcomes than invasive methicillin-susceptible *Staphylococcus aureus* (MSSA) infections (8).

S. aureus has the ability to evolve and quickly acquire antibiotic resistance through mutation and uptake of genetic elements, leading to the emergence of multidrug resistant strains (2). The majority of *S. aureus* clinical isolates among both hospital- and community-acquired infection are resistant to penicillin G (4). *S. aureus* strains resistant to cephalosporins, methicillin, and related antibiotics such as oxacillin and nafcillin limit treatment options and threaten public health (9). MRSA is a common antimicrobial resistant pathogen causing invasive infections in healthcare and community settings (10).

In the 1960s, the emergence and spread of healthcare-associated MRSA strains in U.S. hospitals presented the need for innovative treatment and prevention strategies (2). The first outbreak of MRSA in the United States occurred in a Boston hospital in 1968 (11). Incidence of MRSA continued to increase into the 1990s, leading to the view that resistant strains of *S. aureus* had become endemic in large, urban medical centers in the U.S. (12). Healthcare-associated MRSA strains increased exponentially during this time, however, due to concerted prevention efforts, those trends have greatly changed in recent years, as MRSA strains have decreased significantly, while MSSA has remained the same (13). The Centers for Disease Control and Prevention (CDC) estimates that due to this change in trends, MSSA currently causes about half of all healthcare-associated *S. aureus* infections (1).

Community MRSA strains, distinct from those circulating in healthcare settings, emerged in the 1980s, causing severe skin and respiratory infections (2). The epidemiology of *S. aureus* had two notable shifts, an increase in healthcare-associated infections, followed by the emergence of community-associated strains with resistance to β-lactam antibiotics (14). Prevalence of MRSA increased in the community at the same time MRSA became increasingly recognized as endemic in healthcare settings (12). By serving as a reservoir for MRSA, community-associated MRSA infections may contribute to the incidence of healthcare-associated MRSA infections and therefore support transmission in both healthcare and community settings (1). The ongoing opioid epidemic may contribute to community-associated *S. aureus* infections since those who inject drugs are estimated to be 16.3 times more likely to develop invasive MRSA infections than those who do not (1, 15). Recently reported national trend estimates from CDC show a slight increase in MSSA bloodstream infections in the community from 2012 – 2017, emphasizing the importance of surveillance to monitor changes in disease trends (1).

Active Detection of S. aureus

Active detection of *S. aureus* carriage informs development of effective prevention and treatment strategies by providing information about the epidemiology of the organism. In 2007, the U.S. Department of Veterans Affairs medical centers (VAMCs) implemented active detection for MRSA in acute care hospitals. This program includes screening of patients admitted to VAMC acute care facilities for MRSA nasal carriage at time of admission and testing of previously negative patients for MRSA carriage during unit-to-unit transfer and again at discharge (13, 16). When a patient tests

positive for nasal carriage of MRSA contact precautions are initiated, meaning that gowns and gloves must be used during all interactions with the patient or their environment, intending to target MRSA colonized patients to both interrupt transmission to healthcare workers and non-colonized patients, and prevent colonized patients from developing MRSA infection (16).

State health departments have shown an interest in monitoring MRSA in healthcare facilities. In 2007, the state of Illinois passed legislation mandating the use of *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) codes in administrative data to report MRSA infections and other healthcare-associated infections (HAIs). By 2009, 11 states passed legislation to require state-level reporting of MRSA infections (17). These surveillance efforts allow states to monitor trends, for example, data from the Illinois Department of Public Health show the incidence of MRSA decreased from 16.27 to 10.60 per 1,000 discharges during 2009 – 2016 (18).

In addition to increased awareness of MRSA in healthcare facilities at the state level, there are also ongoing national surveillance efforts. CDC partners with states and academia to receive data from the Emerging Infections Program (EIP) which conducts active population-based surveillance for high priority organisms, including MRSA (19). EIP surveillance for invasive *S. aureus* infections began in 2004 and focused on invasive MRSA infections until MSSA surveillance was added in 2016 (20). Data from 10 geographically distinct EIP sites are used to estimate the national burden of *S. aureus* infections (19, 21). CDC also uses Electronic Health Record (EHR) databases that include administrative and microbiology data to examine trends in infection and monitor

progress in disease prevention (21). CDC utilizes the National Healthcare Safety Network (NHSN) to conduct nationwide surveillance on HAIs. NHSN collects data from healthcare facilities on their infection prevention progress to identify and provide support to facilities with high infection rates (21). In August 2011, the Centers for Medicare and Medicaid Services (CMS) published final rules in the *Federal Register* that require facility-wide inpatient MRSA blood specimen (bacteremia) laboratory-identified (LabID) event reporting from acute care hospitals to NHSN in the CMS Hospital Inpatient Quality Reporting (IQR) Program requirements effective in January 2013 (22). This requirement in NHSN allows CDC to monitor severe hospital-onset (HO) MRSA bacteremia infections occurring within reporting facilities, that represent a vast majority of all U.S. hospitals. Tracking MRSA infections through multiple, distinct surveillance mechanisms allows CDC to describe nationwide trends and calculate burden estimates.

Recent national S. aureus trends and estimates

In 2011, EIP estimated that 80,461 invasive MRSA infections and 11,285 deaths occurred in the United States. Eighty percent of invasive MRSA infections had a positive blood culture and were considered bloodstream infections (BSIs) (10). From 2005 to 2011, overall rates of invasive MRSA declined 31% with the largest decline (54%) occurring among HO infections (9, 10). Healthcare-associated community-onset (HACO) infections decreased by almost 28% and community-associated infections decreased by 5% (10).

CDC also estimated the annual burden of *S. aureus* BSIs using administrative and microbiology data from large electronic health databases that were extrapolated to represent all hospital discharges in the United States from 2012 to 2017. In addition to

being able to produce national estimates, this analysis was able to describe the epidemiology of MSSA in addition to MRSA. This analysis estimated that 119,247 cases of *S. aureus* bloodstream infections and 19,832 associated deaths occurred in the U.S. in 2017. MRSA BSI data from both the EIP (2005 – 2012) and electronic health databases (2012 – 2017) show declines in HO rates. However, EIP data from 2013 – 2016 show no significant change in rates of HO MRSA BSIs. Electronic health databases show HO MRSA BSI rates declined 7.3% annually, while HO MSSA BSI infection rates remained stable. The electronic health data also show that community-onset (CO) MRSA BSI rates have not changed significantly since 2012, while CO MSSA BSI rates may be increasing slightly by about 3.9% annually (1).

The VAMC MRSA prevention program implemented in 2007 resulted in significant reductions in *S. aureus* infections. Clinical microbiology data from patients admitted to VAMCs from 2005 – 2017 show a decrease in *S. aureus* infections by 43% overall. HO MRSA infections declined by 66% over these 12 years, while HO MSSA declined by only 19%. Data show a 41% decline in CO MRSA infections, but no significant decline in CO MSSA infections (13).

The difference in trends between MRSA and MSSA seen in both the electronic health database and VA data may be due to differential detection bias as MRSA culturing has declined with time. Declines in the USA100 MRSA strain, most frequent in healthcare facilities, is responsible for almost all HO and CO MRSA reductions, compared with only modest reductions in the USA300 MRSA strain, which is more frequent in the community (13). This evidence may suggest that interrupting transmission in healthcare (i.e., reducing the spread of USA100 MRSA) is responsible for most of the

declines in MRSA trends. Currently, there is a need to study the epidemiology of MSSA infections to inform development of evidence-based prevention strategies, particularly for CO infections which may be increasing (1, 13).

Declining trends in the rate of HO MRSA BSIs seen in EIP, VA, and electronic health data are likely the result of successful interventions such as contact precautions, interruption of transmission and prevention of device- and procedure-associated infections in healthcare settings (1, 13). Since its emergence, there has been significant research focused on reducing HO MRSA infections, especially in critical care settings such as intensive care units (ICUs). The Randomized Evaluation of Decolonization versus Universal Clearance to Eliminate MRSA (REDUCE-MRSA) trial compared decolonization methods to reduce MRSA infection in ICUs. Participating hospitals were randomized into three groups: MRSA screening and isolation, targeted decolonization (screening, isolation, and decolonization of MRSA carriers) and universal decolonization. The REDUCE-MRSA trial contributed to HO MRSA prevention by finding that universal decolonization of patients in the ICU is the most effective way to reduce MRSA-positive cultures and bloodstream infection from any pathogen (23).

Clinical Microbiology Data

Describing the epidemiology of an organism requires researchers to identify true infections in data sources that also allow them to study risk factors and outcomes. Organism-specific characteristics and clinical evidence are the basis for definitions pertaining to specimen site and timing of culture for identifying infection among clinical microbiology data (16, 17, 24). Previous epidemiological studies use varying definitions to identify cultures indicative of true *S. aureus* infection. These definitions include

positive cultures taken from specimen sites such as blood, bone, sputum, wound, urine, or specimens from a device (1, 16, 17, 24). Classifying infections as hospital- and community-onset based on the timing of positive clinical cultures is widely applied in epidemiological surveillance and research. For example, several studies define a positive culture for which a specimen is taken on day four or later of a hospitalization as hospital-onset infection and specimens collected on days one through three or up to a week before hospital admission as community-onset infections (1, 17). Definitions used by these studies often include additional requirements for medical chart review, antimicrobial sensitivity results, prescription of a MRSA-specific antibiotic within 5 days of culture, and/or exclusion of surveillance cultures (1, 16, 17, 24). These additional requirements narrow definitions to ensure the cases they are ascertaining are representative of true infection. Some studies also use multiple infection definitions, ranging from broad to narrow, to observe results with varying sensitivity and specificity (16).

Administrative Data

Administrative data describes test results, diagnosis, and healthcare services provided during hospitalization with diagnosis codes. It allows for the application of common administrative code definitions across similar datasets for easy comparison of study findings (25). However, the main purpose of assigning ICD diagnostic codes at patient discharge is for healthcare billing and not public health surveillance purposes (17, 24). CMS utilizes ICD diagnosis codes to determine the amount of reimbursement hospitals receive for services provided. The number of diagnostic codes submitted for payment and stored in hospital discharge databases may vary. In October 2008, CMS mandated the assignment of a present on admission (POA) indicator to discharge

diagnosis codes for providers to receive reimbursement (17). Prior to this requirement, researchers could not distinguish between HO and CO infections using administrative codes (25). At the same time, specific diagnosis codes for MRSA and MSSA were implemented. Before this, MRSA infections were identified in administrative discharge data with a combination of ICD-9-CM *S. aureus* infection codes and a resistance code (ICD-9-CM diagnosis codes: 041.12, 482.42, or 038.12 in addition to a resistance indication code: V09.0) (17, 24). Beginning in 2008, ICD-9-CM coding guidance discouraged the use of code combinations including a V09 code to indicate MRSA infections (26). In October 2015, ICD-10-CM codes replaced ICD-9-CM codes, introducing updated and more detailed codes that continued to differentiate between MRSA and MSSA (27).

Misclassification Bias

Epidemiological research studies relationships between exposures and health outcomes (28). Measurement of variables in an epidemiologic study is often imperfect and may result in bias (29). Information bias occurs when there are measurement errors in the information needed to examine the effect of an exposure on a health outcome of interest (30). Measurement error of a discrete variable is misclassification, a type of information bias. Misclassification of a variable commonly occurs in studies when an alternative measurement method replaces the "gold standard" method due to limited cost or available resources (28).

Misclassification occurs differentially or non-differentially by the exposure, outcome, or both. In differential misclassification, the probability of misclassifying subjects differs between groups in the analysis; however, the probability of

misclassifying subjects is the same across all groups in non-differential misclassification (31). Differential outcome misclassification occurs when misclassification of outcome status varies by the exposure status and differential exposure misclassification occurs when misclassification of exposure status varies by outcome status (28). In non-differential exposure misclassification, the proportion of study participants misclassified on exposure does not depend on their outcome status or other variables in the analysis (30). Similarly, non-differential outcome misclassification occurs when the proportion of study participants misclassified on disease or outcome does not depend on their exposure status or other variables in the analysis (30).

Sensitivity and positive predictive value (PPV) are measures of misclassification. The sensitivity of an exposure measurement method is the probability that a person who is truly exposed is correctly classified as exposed by the method. The probability that a person classified as exposed, is truly exposed is PPV (30). Misclassification can exaggerate or underestimate an observed association (31). In epidemiological studies, misclassification presents challenges in interpreting findings and drawing conclusions about an association between an exposure and disease or health outcome (30).

Common Misclassification in S. aureus research

Misclassification is a concern in studies using ICD codes from administrative data to detect infections. Previous studies describe limitations in the use of ICD codes as a measure of infection for MRSA and other multi-drug resistant organisms (MDROs), sepsis, *Clostridioides difficile* infection (CDI), and HAIs among administrative data (17, 24, 32–34). MRSA infections may not be accurately reflected in ICD diagnosis codes when laboratory culture results are not available at time of discharge, the number of

diagnosis codes for each hospitalization is limited, or there are coding errors (35). Previous studies using data collected prior to 2008, have shown that ICD-9-CM diagnosis code combinations have low sensitivity and PPV for identifying infections according to Schaefer et al. (i.e., 33% for HO MRSA and 62% for CO MRSA) and Schweizer et al. (sensitivity of 20% and a PPV of 34%) (17, 24). These studies indicate poor performance of ICD-9-CM codes in identifying MRSA infections during their study periods, prior to the implementation of organism-specific (i.e., MRSA and MSSA) codes and a POA indicator (17, 24). These coding elements may have been useful in these studies to better define hospital-onset and community-onset infections (epidemiology classification) and improve sensitivity and PPV of codes (17).

The potential for misclassifying infections also exists when using positive cultures among clinical microbiology data. Positive clinical cultures may not always represent true infection, and often a clinician relies on additional evidence to make this determination. Misclassification of disease may occur if one considers true infections as non-infections (e.g., excludes all non-sterile sites which may represent some true infections) or misidentifies not-true infections as infections (16). Some researchers may use additional criteria with a positive clinical culture as an indicator for infection (e.g., clinical signs and symptoms of an infection, or specific antibiotic use around the time of the positive culture) though this data is not always available (16). A clearly defined exposure and use of validated measures for the primary outcome reduce the potential for exposure and outcome misclassification (36).

Gaps in Research

Despite conclusions from studies published 10 years ago that ICD codes are poor indicators of MRSA infection, the debate surrounding administrative data is ongoing (17, 24). Changes in coding practices led some to question whether previously described concerns about using ICD-9-CM codes to identify infection still exist and how continued use of administrative coding in future epidemiological studies may affect findings. ICD-9-CM codes continue to be used in recently published epidemiological research to identify infections and determine clinical outcomes of *S. aureus* infection (8, 37-39).

Epidemiological studies that continue to use ICD codes to identify *S. aureus* infections result in different estimates compared to EIP studies using active population and laboratory-based surveillance (9-10, 35-38). EIP published data in 2013 showing a 31% decrease in invasive MRSA infections from 2005 to 2011 (9, 10). The majority (80%) of invasive MRSA infections identified in EIP were bloodstream infections. The 2014 HAI Progress report based on NHSN data reported a 13% decrease in HO MRSA bacteremia between 2011 and 2014 in acute care hospitals (40). These trend estimates seemed to show progress in prevention of invasive MRSA infections. However, in 2017, Klein et al. reported opposing estimates using National Inpatient Sample data from the Healthcare Cost and Utilization Project (HCUP) showing a slight increase in the rate of invasive MRSA-related septicemia, from 1.45 to 1.53 per 1,000 hospitalizations from 2010 – 2014 using MRSA-specific ICD-9-CM codes (37). Identification of infections using ICD codes among administrative discharge data is discouraged by previous literature, however, studies continue to report estimates based on this method, suggesting that MRSA-specific coding may have improved surveillance capability (17, 24, 37). A study published in 2019 cited Klein et al. as justification for using administrative data and

diagnosis codes to draw conclusions about outcomes of MRSA and MSSA bacteremia infections (8, 37).

A more recent study comparing infections captured by administrative codes in statewide hospital discharge data and those captured by EIP laboratory-based surveillance found that trends and case counts differed between identification methods within the same set of hospitals in Connecticut (38). It is unclear what the current sensitivity of MRSA- and MSSA-specific coding is or the impact of this on study results and interpretations. Validation of MRSA- and MSSA-specific coding for ICD-9-CM and ICD-10-CM eras since October 2008 has not been assessed in previous literature, providing the opportunity to assess these codes and the implications of their use in future epidemiological research (37, 38).

In the past decade, contrasting MRSA trend estimates between studies underscore the need and timeliness of this study (39). Previous studies cited lack of a POA indicator for codes and MRSA- and MSSA-specific coding as limitations and these elements have since been implemented (17, 26). Additionally, the introduction of ICD-10-CM codes in October 2015 brought about the opportunity for further study (27). At the time of this study, there are no studies published using ICD-10-CM coding to identify *S. aureus* infections among administrative data in the United States. Currently, there is a gap in the literature for comparing methods of case identification in research, given changes in coding practices, and there is an opportunity to assess whether outcomes and risk factors vary by methodology.

Thus, the objectives of this study are to:

1. Determine the sensitivity and positive predictive value of administrative codes in identifying MRSA and MSSA infections among hospitalized patients during both the ICD-9-CM and ICD-10-CM coding eras.
2. Assess trends in rates of positive MRSA and MSSA cultures and MRSA and MSSA diagnosis codes from 2012 through 2017.
3. Describe the impact of the method of identification on epidemiologic studies by examining whether in-hospital mortality and/or risk factors vary by method of identification.

Methods

Study design, Population and Data Source

This study is a retrospective cohort of adult patients (age ≥18) hospitalized in an acute care hospital participating in the Premier Healthcare Database (PHD) from January 1, 2012 to December 31, 2017. Hospitals included in the study were limited to those with available microbiology data and subsequent antimicrobial susceptibility testing. Premier microbiology tables were used to identify positive clinical cultures of *S. aureus*. Premier encounter tables provided information surrounding patients' hospitalizations and discharges, including *International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification* (ICD-9/10-CM) discharge diagnosis codes. There is no limit on the number of ICD diagnosis codes that are provided in Premier, therefore, all codes provided by the hospital are contained in the PHD (41).

Hospitalizations included in this analysis were identified by positive clinical culture for *S. aureus* and/or presence of any *S. aureus* code (i.e., the MRSA- or MSSA-specific diagnosis codes shown in supplemental appendix Table A1). Because this study spanned the ICD-9-CM to ICD-10-CM switch, ICD-9-CM codes were used to identify eligible hospitalizations from January 1, 2012 – September 30, 2015 and ICD-10-CM codes identified hospitalizations from October 1, 2015 – December 31, 2017. Incident hospitalized positive clinical cultures for *S. aureus* with subsequent susceptibility testing for methicillin, oxacillin, and cefoxitin were categorized as MRSA if resistant to at least one of these medications and categorized as MSSA otherwise (42). For hospitalizations with more than one positive clinical culture, cultures from a blood specimen were chosen over those with other specimen sources within 14 days (42). Septicemia hospitalizations

had a positive *S. aureus* culture identified from a blood specimen source and/or MRSA or MSSA septicemia diagnosis code (i.e., ICD-9-CM code 038.11, 038.12, or ICD-10-CM code A41.01, A41.02). Hospitalizations were restricted to those with a length of stay (LOS) of 365 days or less, and cultures were limited to those collected at the same hospital between 3 days prior to admission and 3 days post discharge. Hospitalizations indicated as transfers from another acute care hospital were excluded from our analysis.

Exposure, Outcomes, and Covariates

The primary exposure in our study was method of identification. *S. aureus* hospitalizations were classified by method of identification as code and culture, code only, and culture only. The outcome of interest was in-hospital mortality (which we defined as a discharge status of death or transfer to hospice care). Covariates included in our analyses from the Premier data were age, gender, race, ethnicity, admission source, admission type, and payer status. We defined other covariates including comorbidities, infection type, and epidemiologic classification. To identify comorbidities, we used ICD-9/10-CM diagnosis codes for human immunodeficiency virus (HIV) infection, hematologic malignancy, hematopoietic stem cell transplant, solid organ malignant tumor, rheumatologic disorders, diabetes mellitus, congestive heart failure, chronic pulmonary disease, end stage renal disease (ESRD), and drug abuse, shown in supplemental appendix Table A3 (8). To categorize potential infection types, we used ICD-9/10-CM codes for urinary tract, pulmonary, skin and soft tissue, and intra-abdominal infections, shown in supplemental appendix Table A2 (43, 44). Cultures were categorized as HO or CO by date of specimen collection: positive cultures on day four of hospitalization or later were considered HO, and positive clinical cultures on or before day three of hospitalization considered CO (42).

Diagnosis codes were categorized using the code's specific presence on admission indicator (POA). Presence on admission is indicated when a diagnosis is present at the time of inpatient admission (45). Codes without a POA indicator were considered HO and codes with a POA indicator were considered CO.

Analytic Approach

All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). For statistical tests, $p < 0.05$ (two-tailed) were considered statistically significant.

Descriptive statistics for covariates and outcomes of interest were calculated for each exposure group (code and culture, code only, culture only). Categorical variables (e.g. gender, race, ethnicity, admission source, admission type, payer status) were described with frequencies and proportions. Differences between exposure groups for these categorical variables were assessed using a chi-square (χ^2) test. Continuous variables such as age and day of culture were described by the mean and standard deviation.; LOS was described by the median and interquartile range (IQR) for each exposure group. A One-Way Analysis of Variance (ANOVA) was used to assess differences in continuous variables between exposure groups.

Objective One

To address objective one, sensitivity and positive predictive value (PPV) of diagnosis codes in identifying *S. aureus* infections were calculated for all hospitalizations not indicated as a transfer. To calculate these statistics, the primary assumption made was that positive clinical cultures represent truth. True positives were considered as hospitalizations with a positive clinical culture and code. Hospitalizations with a code,

but not a positive clinical culture were considered false positives. Hospitalizations with a culture but not code were considered false negatives. Sensitivity and PPV calculations were performed overall (all *S. aureus*) and for *S. aureus* septicemia. Sensitivity was expressed as the proportion of true positives of the sum of true positives and false negatives. PPV was expressed as the proportion of true positives of the sum of true positives and false positives.

Overall

For MRSA-specific analyses, true positives were limited to all hospitalizations with a positive clinical culture for MRSA and MRSA-specific diagnosis code. False negatives were hospitalizations with a MRSA positive clinical culture, but no MRSA-specific diagnosis code, and false positives were hospitalizations with a MRSA diagnosis code, but no MRSA positive culture.

For MSSA-specific analyses, true positives were limited to all hospitalizations with a positive clinical culture for MSSA and MSSA-specific diagnosis code. False negatives were hospitalizations with a MSSA positive clinical culture, but no MSSA-specific diagnosis code, and false positives were hospitalizations with a MSSA diagnosis code, but no MSSA positive culture.

Septicemia

Among all septicemia hospitalizations, true positives were those with a positive blood culture for *S. aureus* and a MRSA- or MSSA-specific septicemia diagnosis code. For MRSA septicemia analyses, true positives were limited to all hospitalizations with a MRSA positive clinical culture from a blood specimen and MRSA-septicemia diagnosis

code. False negatives were hospitalizations with a MRSA positive clinical culture from a blood specimen, but no MRSA septicemia diagnosis code, and false positives were hospitalizations with a MRSA septicemia diagnosis code, but no MRSA positive blood culture. Likewise, true positives for MSSA septicemia analyses were limited to all hospitalizations with a MSSA positive clinical culture from a blood specimen and MSSA-septicemia diagnosis code. False negatives were hospitalizations with a MSSA positive clinical culture from a blood specimen, but no MSSA septicemia diagnosis code, and false positives were hospitalizations with a MSSA septicemia diagnosis code, but no MSSA positive blood culture.

Discordance between culture and code types (MRSA vs. MSSA, blood vs. non-blood culture site, and/or septicemia vs. non-septicemia code) resulted in the classification of some hospitalizations with both a code and culture as false negatives or false positives in subsequent analyses.

Epidemiology Classification

Sensitivity and PPV for *S. aureus* overall were also calculated by epidemiology classification. Epidemiology classification among all *S. aureus*, MRSA, and MSSA hospitalizations, both overall and septicemia were described with frequencies and proportions. True positives for all *S. aureus* HO infections were defined as positive HO *S. aureus* cultures with a HO MRSA or MSSA-specific code, and true positives for all *S. aureus* CO infections were positive CO *S. aureus* cultures with a CO *S. aureus* diagnosis code. True positive definitions were the same for *S. aureus* septicemia hospitalizations, however cultures were limited to those from blood specimen source only and codes were

limited to *S. aureus* septicemia diagnosis codes. MRSA and MSSA specific analyses were limited to HO and CO cultures and codes specific to the organism of interest as above.

Objective Two

Culture and code rates were calculated overall for all *S. aureus*, MRSA, and MSSA independently. Similar analyses were done for septicemia events. Hospitals with more than 75% of their discharges from patients aged 0 – 17 years old were excluded. Annual code and culture rates were calculated as the number of events per 1,000 discharges. Adjusted monthly trends in culture and code rates were assessed using negative binomial regression. The modeled outcome was the number of events, offset by the natural log of the number of discharges. Trends were measured using a continuous variable for time. We adjusted for age group, race, gender, discharge month, and hospital characteristics such as urban/rural status, teaching status, bed size, and region. Observed rates and adjusted trends were plotted annually from 2012 – 2017.

Objective Three

Multivariable models were used to assess the impact of method of identification on in-hospital mortality (death or discharge to hospice) while adjusting for several other covariates. First, we computed separate models for the outcome in-hospital mortality for the code only and culture only identified populations. Next, our full population was assessed in a logistic regression model where the main effect assessed was the method of identification (i.e., MRSA code only, MRSA culture only, or both MRSA code and MRSA culture). We adjusted for method of identification, epidemiology classification,

age, gender, race, ethnicity, admission source, payer, admission type, infection type, and comorbidities. In the multivariable models, "unknown" ethnicity was included in the "non-Hispanic" category and "unknown" race was included in the "other" race category. Hospitalizations with unknown gender were excluded from multivariable regression models.

This same modeling strategy was also used to assess differences in in-hospital mortality by method of identification for MSSA hospitalizations, both overall and septicemia.

Differences in risk factors were defined as (1) changes in significance (i.e., a parameter was significantly associated with in-hospital mortality in one model but not significantly associated with in-hospital mortality in the other) or (2) changes in directionality (i.e., a parameter was negatively associated with in-hospital mortality in one model and positively associated with in-hospital mortality in the other).

Ethics Approval

The use of the PHD for this study is deemed non-Human Subjects Research and was exempt from IRB review.

Results

Characteristics of Hospitalizations

A total of 306,991 *S. aureus* hospitalizations and a subset of 57,815 *S. aureus* septicemia hospitalizations were identified in a dynamic cohort of 256 Premier hospitals from 2012 – 2017. Hospitals reported a median of 51 months of data during the study period, and characteristics are shown in Table 1. Less than half of all *S. aureus* hospitalizations had both a positive culture and diagnosis code (140,468, 46%); 65,077 (21%) had a code, while 101,446 (33%) had only a positive culture (Figure 1). Among *S. aureus* septicemia hospitalizations 23,552 (41%) had both a positive blood culture and septicemia diagnosis code; 15,768 (27%) had a septicemia code only, while 18,495 (32%) had a positive blood culture only (Figure 1). For all *S. aureus* hospitalizations, demographics and characteristics of cases are shown in Table 2a. In-hospital mortality (death or discharge to hospice) was highest among those with a positive culture only (12.0%) compared to hospitalizations with both a code and culture (7.7%), and code only (6.8%). Unadjusted analyses show median LOS also differed by method of identification: code and culture (7 days), code only (6 days), and culture only (5 days). Demographics and characteristics among the subset of *S. aureus* septicemia hospitalizations are shown in Table 3a; in-hospital mortality was highest among those with a positive blood culture only (18.5%), compared with both a septicemia code and blood culture (16.6%), and septicemia code only (13.4%).

About half of all MRSA hospitalizations had both a positive culture and diagnosis code (82,194, 49%); 42,447 (25%) had a MRSA code only and 43,993 (26%) had only a

positive culture for MRSA (Figure 1). Among MRSA septicemia hospitalizations 10,551 (37%) had both a positive blood culture for MRSA and MRSA septicemia diagnosis code; 9,659 (34%) had a MRSA septicemia code only and 8,270 (29%) had only a positive blood culture for MRSA (Figure 1). For all MRSA hospitalizations, demographics and characteristics of cases are shown in Table 2b. In-hospital mortality was highest among those with a positive culture for MRSA only (13.1%) compared to hospitalizations with both a MRSA code and MRSA culture (8.5%), and MRSA code only (7.2%). Unadjusted analyses show median LOS also differed by method of identification similar to findings for all *S. aureus*: code and culture (7 days), code only (6 days), and culture only (5 days). Demographics and characteristics among the subset of MRSA septicemia hospitalizations are shown in Table 3b; in-hospital mortality was highest among those with a positive MRSA blood culture only (20.8%), compared with both a MRSA septicemia code and MRSA positive blood culture (19.3%), and MRSA septicemia code only (14.4%).

Approximately 46% (67,817) of all MSSA hospitalizations had both a positive culture and diagnosis code; 22,930 (15%) had a code only while, 58,029 (39%) had only a positive culture (Figure 1). Among MSSA septicemia hospitalizations 11,970 (38%) had both a positive blood culture for MSSA and MSSA septicemia diagnosis code; 7,768 (25%) had only a MSSA septicemia code and 11,373 (37%) had only a positive blood culture for MSSA (Figure 1). For all MSSA hospitalizations, demographics and characteristics of cases are shown in Table 2c. In-hospital mortality was highest among those with a positive culture for MSSA only (11.3%) compared to hospitalizations with both a MSSA code and MSSA culture (6.9%), and MSSA code only (6.0%). Unadjusted

analyses show median LOS also differed by method of identification similar to findings for both all *S. aureus* and MRSA: code and culture (7 days), code only (6 days), and culture only (5 days). Demographics and characteristics among the subset of MSSA septicemia hospitalizations are shown in Table 3c; in-hospital mortality was highest among those with a positive MSSA blood culture only (17.0%), compared with both a MSSA septicemia code and MSSA positive blood culture (13.8%), and MSSA septicemia code only (13.2%).

Sensitivity and PPV of ICD Codes

S. aureus diagnosis codes identified positive *S. aureus* clinical cultures with an overall sensitivity of 58% and 56% for septicemia, with a PPV of 69% and 61%, respectively. MRSA-specific diagnosis codes identified MRSA cultures with a sensitivity of 61% and 56% for MRSA septicemia, with respective PPVs of 62% and 53%. Sensitivity of MSSA-specific codes was 49% for all MSSA and 52% for MSSA septicemia with a PPV of 69% and 62%, respectively.

Among 130,451 true positives for all *S. aureus*, hospitalizations with both a positive *S. aureus* clinical culture and diagnosis code for *S. aureus*, 5.7% were HO and 79.3% were CO. The remaining 19,564 (15.0%) hospitalizations were discordant, 13.4% had a HO culture and CO code, 1.6% had a CO culture and HO code. Among 58,887 false positives, those with a *S. aureus* diagnosis code, but no *S. aureus* culture, 4.9% were HO and 95.1% were CO. Those with a positive *S. aureus* culture, but no *S. aureus* code of interest were considered false negatives. Of the 94,239 false negative hospitalizations, 20.8% of cultures were HO and 79.2% were CO. Septicemia hospitalizations considered

to be true positives had a positive *S. aureus* blood culture and a *S. aureus* septicemia code of interest. Of the 21,802 *S. aureus* septicemia true positives, 6.2% were HO and 76.0% were CO, with the remaining 3,883 hospitalizations being discordant (16.3% had a HO culture and CO code, 1.5% had a CO culture and HO code). Of the 14,024 *S. aureus* septicemia hospitalizations with a septicemia code and no blood culture (false positives), 43.7% had a positive *S. aureus* culture from a non-blood site. Among 17,076 septicemia hospitalizations with a positive *S. aureus* blood culture and no *S. aureus* septicemia code (false negatives), 55.1% had a non-septicemia *S. aureus* diagnosis code. Epidemiology results for true positives, false positives, and false negatives for all *S. aureus* and *S. aureus* septicemia hospitalizations are shown in Table 4a; results for MRSA and MRSA septicemia hospitalizations are shown in Table 4b and MSSA and MSSA septicemia specific hospitalizations are shown in Table 4c.

Trends in Culture and Code rates

Adjusted *S. aureus* culture rates decreased 3% annually ($p<.0001$) and adjusted *S. aureus* code rates decreased 1% annually ($p=0.0139$, Figure 2a). There was no significant trend in annual rates of *S. aureus* blood cultures, but *S. aureus* septicemia code rates increased 4% annually ($p<.0001$). Adjusted trends for MRSA and MSSA code and culture rates (overall and septicemia) are shown in Figures 2b and 2c. Negative binomial regression results are shown in the supplemental appendix (Tables A4a-c).

Risk factors and In-hospital mortality

For the separate models estimating in-hospital mortality for the code only and culture only populations, parameter estimates for risk factors and/or potential

confounders are shown in Tables 5a-5d, and differences in risk factors between the two methods of identification are highlighted. For MRSA overall, notable differences included associations between in-hospital mortality and human immunodeficiency virus (HIV), hematologic malignancy, diabetes mellitus, and chronic pulmonary disease which were not significantly associated among those identified by a code only but were significantly associated with in-hospital mortality among those identified by a positive culture only. However, gender, solid organ malignant tumor, and urinary tract infection (UTI) were significantly associated with in-hospital mortality among those identified by a code only but not significantly associated with the outcome among those identified by culture only (Table 5a).

Among MRSA septicemia hospitalizations notable differences included associations of in-hospital mortality with gender, HIV, hematologic malignancy, diabetes mellitus, and drug abuse which were not significantly associated among those identified by a MRSA septicemia code only but were significantly associated with in-hospital mortality among those identified by a MRSA positive blood culture only. Congestive heart failure and end stage renal disease (ESRD) were significantly associated with in-hospital mortality among those identified by a MRSA septicemia code only but were not significantly associated with the outcome among those identified by a positive MRSA blood culture only. Interestingly, endocarditis was positively associated with in-hospital mortality among those identified by a MRSA septicemia code only and negatively associated with in-hospital mortality among those identified by a MRSA positive blood culture only (Table 5b).

For MSSA overall, we found notable differences in estimates for gender, race (both black and other races), admission source (clinic), rheumatologic disorders, diabetes mellitus, and chronic pulmonary disease, all of which were only significantly associated with in-hospital mortality among those identified by a MSSA positive culture only. HIV was significantly associated with in-hospital mortality among those identified by a MSSA code only but was not significantly associated with the outcome among those identified with a MSSA positive culture only (Table 5c).

Among MSSA septicemia hospitalizations, notable differences in significance between code only and culture only models included solid organ malignant tumor, diabetes mellitus, and UTI which were only significantly associated with in-hospital mortality among those identified by a positive MSSA blood culture only. In contrast, HIV, solid organ transplant, and endocarditis were significantly associated with in-hospital mortality among those identified by a MSSA septicemia code only but not significantly associated with the outcome among those identified by a positive MSSA blood culture only (Table 5d). Interestingly, age, intra-abdominal, pulmonary, and hospital-onset infection were consistently associated with increased odds of in-hospital mortality for all models. The infection types osteomyelitis and skin and soft tissue infection (SSTI) were consistently associated with decreased odds of in-hospital mortality for all models (Tables 5a-d, Figures 3a-d).

In multivariable models for our entire population, in-hospital mortality was significantly associated with method of identification. Adjusting for epidemiology classification, age, gender, race, ethnicity, admission source, payer, admission type, comorbidities, and infection type, there was a decreased odds of in-hospital mortality

among MRSA hospitalizations identified by a code only compared to the odds of in-hospital mortality among MRSA hospitalizations identified by both a code and culture (OR=0.90, 95% CI: (0.85, 0.94)). The adjusted odds of in-hospital mortality among MRSA hospitalizations identified by a culture only was 66% higher than the odds of in-hospital mortality among MRSA hospitalizations identified by both a code and culture (OR=1.66, 95% CI: (1.59, 1.73)). The odds of in-hospital mortality was significantly higher among MRSA hospitalizations classified as HO than the odds of in-hospital mortality among CO MRSA hospitalizations (OR = 1.62, 95% CI: (1.55, 1.69)) (Figure 3a).

Among MRSA septicemia hospitalizations, the adjusted odds of in-hospital mortality among those identified with a MRSA septicemia code only was 0.92 times the corresponding odds among those identified by both a MRSA septicemia code and positive blood culture (95% CI: (0.86, 1.00), p=0.0432). The adjusted odds of in-hospital mortality among MRSA septicemia hospitalizations identified by a MRSA positive blood culture only was 2.79 times the odds of the outcome among those identified by both a MRSA septicemia code and positive blood culture (95% CI: (2.56, 3.05)). In-hospital mortality was significantly higher among MRSA septicemia hospitalizations classified as HO compared to those classified as CO (OR=1.81, 95% CI: (1.65, 1.99)) (Figure 3b).

The adjusted odds of in-hospital mortality among MSSA hospitalizations identified by a code only was not significantly different from those identified by both a code and culture (OR=1.05, 95% CI: (0.99, 1.12)). The adjusted odds of in-hospital mortality among MSSA hospitalizations identified by a culture only was 89% higher than the corresponding odds among MSSA hospitalizations identified by code and culture

(OR=1.89, 95% CI: (1.81, 1.98)). In-hospital mortality was significantly higher among MSSA hospitalizations classified as HO compared to those classified as CO (OR = 1.69, 95% CI: (1.61, 1.76)) (Figure 3c).

Among MSSA septicemia hospitalizations, the adjusted odds of in-hospital mortality among those identified with a MSSA septicemia code only was 1.32 times that of those identified by both a code and culture (95% CI: (1.21, 1.44)). The adjusted odds of in-hospital mortality among MSSA septicemia hospitalizations identified by a MSSA positive blood culture only is 2.83 times the odds among those identified by both a MSSA septicemia code and positive blood culture (95% CI: (2.61, 3.07)). In-hospital mortality was significantly higher among MRSA septicemia hospitalizations classified as HO compared to those classified as CO (OR=1.51, 95% CI: (1.39, 1.63)) (Figure 3d).

Discussion

When conducting epidemiologic research on MRSA and MSSA infections, meaningfully different populations are identified by ICD diagnosis codes than those identified using clinical culture surveillance. Among those hospitalizations with a code or culture for MRSA and MSSA, we found that fewer than half had both consistent codes and cultures. Because of these inconsistencies, we also found that the method of identification significantly impacts conclusions in epidemiologic risk studies and when measuring trends over time. Studies using only ICD diagnosis codes to identify infections should use caution when interpreting findings.

Sensitivity and PPV of diagnosis codes

Our findings show that ICD diagnosis codes included in this analysis were consistently poor in recent years at identifying positive clinical cultures, both overall and specifically for septicemia. Sensitivity was approximately 61% or less for all hospitalizations. Our findings update those previously presented in Schaefer et al. (for ICD-9-CM codes only, pre-2008 coding changes) and show almost no improvement in sensitivity (previous estimates had a cumulative sensitivity of 59% compared to 61% shown in our study) (17). Our study also corroborated the earlier ICD-9-CM finding presented by Schaefer et al. that code combinations were almost twice as sensitive for CO MRSA infections as for cases of HO MRSA (62% and 29%, respectively) in this updated time period. Schaefer et al. authors speculated that the use of a POA indicator and implementation of new MRSA-specific diagnosis codes may have improved sensitivity and enabled better distinction between HO and CO MRSA infections, however, our

findings are similar and suggest that the addition of these elements to coding practices did not improve sensitivity.

It is possible that some of the positive cultures included in our study were not interpreted to be clinically relevant infections and therefore we would not expect them to be coded in the discharge diagnosis codes. However, we assessed sensitivity and PPV of ICD diagnosis codes among septicemia hospitalizations and among all hospitalizations, speculating a positive culture taken from a normally sterile site such as blood may be more indicative of true infection (and therefore more likely to be coded amongst discharge diagnosis codes). However, we found that sensitivity and PPV did not improve, and in some cases was worse, for *S. aureus* and MRSA septicemia. However, MSSA septicemia codes were more sensitive than all MSSA-specific codes. It is important to note, though, that MSSA codes were less sensitive than MRSA codes both overall and septicemia. MRSA may be coded more frequently than MSSA due to increased clinical awareness or other unstudied reimbursement practices.

Trends in code and culture rates

We examined trends in code and culture rates for each group of hospitalizations (*S. aureus*, MRSA, and MSSA, both overall and septicemia). Despite low sensitivity of codes, we found similar decreasing trends in annual code and culture rates among all *S. aureus* and all MRSA hospitalizations. While these trends decreased significantly during the study period, the magnitude at which code and cultures rates were decreasing differed, with cultures decreasing faster. There were increasing trends in code rates for

both *S. aureus* septicemia and MSSA septicemia, however MRSA septicemia code rates did not change significantly over time.

Trends in MSSA and MSSA blood culture rates did not change significantly, however trends in annual MSSA and MSSA septicemia code rates increased significantly, indicating that codes identify potential trends that are not observed when evaluating culture rates. Using MSSA-specific diagnosis codes to identify infections may be inappropriate for assessing trends due to significant misclassification. It may result in differing trends between studies using positive clinical cultures to identify MSSA infections and those using diagnosis codes alone (i.e., one method concluding no change in trend and another concluding there is a significant increasing trend).

Risk factors and In-hospital mortality

Our findings show that in-hospital mortality and risk factors do appear to differ by method of identification and could impact findings of studies that rely on one method over another which may lead to incorrect interpretations of the effect of certain risk factors on outcomes from *S. aureus* (i.e., identifying infections using administrative codes alone).

The proportion of those who died or were discharged to hospice care (in-hospital mortality) and LOS differed by method of identification in unadjusted analyses for all *S. aureus* and *S. aureus* septicemia. Among all groups of hospitalizations, culture only identified hospitalizations had the highest proportion of in-hospital mortality and the shortest median LOS. The proportion of in-hospital mortality was highest among the culture only group, followed by those identified by a code and culture, and then those

identified by a code only in descriptive analyses. Median LOS was usually highest among the code and culture group, followed by code only, and culture only. It is unclear if the shorter LOS does not allow clinicians to collect clinical cultures, so they code based on presumption, instead of waiting for positive cultures. Positive cultures may not be coded if results are pending at the time of discharge. Alternatively, one could speculate that if there only was a culture or code, the clinician interpreted this as not being the main reason for hospitalization and therefore did not treat for this infection.

In our multivariable analyses, three of the assessed covariates showed differing associations with in-hospital mortality depending on which method of identification was used. First, endocarditis was positively associated with in-hospital mortality among those identified by a MRSA code only but was negatively associated with the outcome among those identified by a MRSA culture only. For MRSA (overall and septicemia), HIV was positively associated with in-hospital mortality among culture only but not code only identified hospitalizations. For MSSA (all and septicemia), HIV was positively associated with the outcome among those identified by code only but not culture only. Also, of note, diabetes mellitus was a risk factor associated with a decreased odds of in-hospital mortality among those identified by a culture only in all models, but was non-significant among those identified by a code only in all models.

However, there were also many notable similarities in risk factors across all models, regardless of method of identification. Age, intra-abdominal infection, pulmonary infection, and hospital-onset infections were associated with an increased odds of in-hospital mortality. Osteomyelitis and SSTI were consistently associated with decreased odds of the outcome across all models.

Adjusted analyses show that the outcome in-hospital mortality differed by method of identification. For all models, the culture only group had the highest odds of in-hospital mortality; this was significantly higher than those identified by both a code and culture, consistently higher than the corresponding odds ratio among the code only group.

For all MRSA and MRSA septicemia, the code only identified hospitalizations had a decreased odds of in-hospital mortality compared to those identified by both a code and culture. For all MSSA and MSSA septicemia, the code only identified hospitalizations had an increased odds of in-hospital mortality compared to those identified by both a code and culture, however the odds ratio for code only among all MSSA was not statistically significant.

Limitations

Our study has several limitations. We used positive clinical cultures as the "gold standard" in our sensitivity and PPV calculations to observe how well ICD diagnosis codes identified positive clinical cultures, however positive clinical cultures may not always indicate true infection. Clinicians often rely on additional evidence, usually clinical symptoms and medical history, to determine whether an infection is present or not. To address this limitation, we excluded surveillance cultures and only included cultures with susceptibility results. We also performed our analysis among septicemia hospitalizations to improve the likelihood that a positive culture was indicative of true infection since blood is a normally sterile site. Administrative coding practices vary across hospitals and codes may not always be applied in a standardized way (17). Some hospitalizations may have been accurately coded with MRSA and MSSA diagnosis codes

without a clinical culture, potentially due to clinician knowledge of clinical history. Also, the hospitals in this study did not all contribute data during the entirety of the study period (median number of months reported by facilities was 51), so fluctuation could have impacted trend analyses. However, we performed statistically rigorous methods that allowed for missingness in our data.

Strengths

The PHD contains data from geographically distinct hospitals nationwide (40). Our study included data from 256 hospitals compared to previous studies which were focused in one or a small number of hospitals, improving the external validity of our findings (17, 24). The number of diagnosis codes maintained in the PHD is not limited, therefore all codes reported by the facility were included in our analysis (40). Other studies have described the number of available diagnosis codes as a limitation. In previous studies, validation of codes only focused on MRSA infections. Our study examined the impact of method of identification across multiple populations: *S. aureus*, MRSA, and MSSA, both overall and septicemia to observe differences and similarities in findings.

Future Directions

Our analysis is timely, as more data from recent years become available, we expect to see studies using the newer ICD-10-CM codes to identify infections among administrative data. Previous studies using ICD-9-CM MRSA- and MSSA-specific codes emphasized that caution is required when using these codes as their validity has not been studied (38, 39). The findings from this study address this gap and inform future

research by studying the validity of these coding changes and addressing the assumption that ICD coding changes have improved the ability of diagnosis codes to more accurately identify *S. aureus* infections for epidemiological research purposes. This study shows that evaluation of the impact of using administrative codes to identify infections may be needed prior to using diagnosis codes to study trends and clinical outcomes as this may be problematic for epidemiological research of other organisms as well.

Conclusion

This study sought to expand on findings from Schaefer et al. and Schweizer et al. on the use of administrative codes to identify MRSA infections among data collected prior to 2008. The implementation of MRSA- and MSSA-specific codes, introduction of a POA indicator, and the newer ICD-10-CM coding version provided the opportunity for further study. Continued use of ICD-9-CM diagnosis codes to describe trends and clinical outcomes in epidemiologic studies as well as conflicting trends between studies using active population and laboratory-based surveillance and ICD diagnosis codes further emphasized the need for validation of diagnosis codes and evaluation of the impact of method of identification on trends and clinical outcomes (8, 38-39).

Our findings on the sensitivity and PPV of codes for identifying positive clinical cultures are similar to previous studies in which diagnosis codes were found to be poor indicators of infection. Recent changes to coding practices, thought to improve the ability of codes to more accurately detect infections, have been shown by this study to have little impact. Caution should be used when interpreting findings from studies identifying infections with the use of ICD diagnosis codes alone as our study has shown that method of identification significantly impacts findings of trends, risk factors and outcomes.

References

1. Kourtis AP, Hatfield K, Baggs J, et al. Vital Signs: Epidemiology and Recent Trends in Methicillin-Resistant and in Methicillin-Susceptible Staphylococcus aureus Bloodstream Infections – United States. *MMWR Morb Mortal Wkly Rep* 2019;68(9):214-9.
2. Rappuoli R, Grandi G, Bagnoli F. Staphylococcus aureus: Microbiology, Pathology, Immunology, Therapy and Prophylaxis. Springer, 2017.
3. Jernigan JA. Is the burden of Staphylococcus aureus among patients with surgical-site infections growing? *Infect Control Hosp Epidemiol* 2004;25(6):457-60.
4. Heymann D. Control of communicable diseases manual: An official report of the American Public Health Association 20 ed. Washington, DC: American Public Health Association; 2015.
5. Bharadwaj S, Ho SK, Khong KC, et al. Eliminating MRSA transmission in a tertiary neonatal unit-A quality improvement initiative. Am J Infect Control 2019;47(11):1329-35.
6. Salgado CD, Farr BM, Calfee DP. Community-acquired methicillin-resistant Staphylococcus aureus: a meta-analysis of prevalence and risk factors. Clin Infect Dis 2003;36(2):131-9.
7. Centers for Disease Control and Prevention (CDC). Staphylococcus aureus in Healthcare Settings. 2011. (https://www.cdc.gov/hai/organisms/staph.html). (Accessed).
8. Inagaki K, Lucar J, Blackshear C, et al. Methicillin-susceptible and Methicillin-resistant Staphylococcus aureus Bacteremia: Nationwide

Estimates of 30-Day Readmission, In-hospital Mortality, Length of Stay, and Cost in the United States. Clin Infect Dis 2019;69(12):2112-8.

9. Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2013. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2013.

10. Dantes R, Mu Y, Belflower R, et al. National burden of invasive methicillin-resistant Staphylococcus aureus infections, United States, 2011. JAMA Intern Med 2013;173(21):1970-8.

11. Barrett FF, McGehee RF, Jr., Finland M. Methicillin-resistant Staphylococcus aureus at Boston City Hospital. Bacteriologic and epidemiologic observations. N Engl J Med 1968;279(9):441-8.

12. Sievert DM, Wilson ML, Wilkins MJ, et al. Public health surveillance for methicillin-resistant Staphylococcus aureus: comparison of methods for classifying health care- and community-associated infections. Am J Public Health 2010;100(9):1777-83.

13. Jones M, Jernigan JA, Evans ME, et al. Vital Signs: Trends in Staphylococcus aureus Infections in Veterans Affairs Medical Centers – United States, 2005-2017. MMWR Morb Mortal Wkly Rep 2019;68(9):220-4.

14. Tong SY, Davis JS, Eichenberger E, et al. Staphylococcus aureus infections: epidemiology, pathophysiology, clinical manifestations, and management. Clin Microbiol Rev 2015;28(3):603-61.

15. Jackson KA, Bohm MK, Brooks JT, et al. Invasive Methicillin-Resistant Staphylococcus aureus Infections Among Persons Who Inject Drugs – Six Sites, 2005-2016. MMWR Morb Mortal Wkly Rep 2018;67(22):625-8.

16. Nelson RE, Evans ME, Simbartl L, et al. Methicillin-resistant Staphylococcus aureus Colonization and Pre- and Post-hospital Discharge Infection Risk. Clin Infect Dis 2019;68(4):545-53.

17. Schaefer MK, Ellingson K, Conover C, et al. Evaluation of International Classification of Diseases, Ninth Revision, Clinical Modification Codes for reporting methicillin-resistant Staphylococcus aureus infections at a hospital in Illinois. Infect Control Hosp Epidemiol 2010;31(5):463-8.

18. Illinois Department of Public Health (IDPH). Methicillin-resistant Staphylococcus aureus trend report. Illinois Department of Public Health, 2018. (http://www.healthcarereportcard.illinois.gov/files/pdf/HDD_MRSA_2016_Trend_Report.pdf). (Accessed).

19. Centers for Disease Control and Prevention (CDC). About EIP. 2018. (https://www.cdc.gov/ncezid/dpei/eip/eip-about.html). (Accessed).

20. Centers for Disease Control and Prevention (CDC). Tracking Staph Infections. 2016. (https://www.cdc.gov/hai/eip/saureus.html). (Accessed).

21. Centers for Disease Control and Prevention (CDC). What CDC is Doing. 2019. (https://www.cdc.gov/mrsa/tracking/index.html). (Accessed).

22. Centers for Disease Control and Prevention (CDC). Updated Operational Guidance for Acute Care Hospitals for 2015. 2015.

(https://www.cdc.gov/nhsn/pdfs/cms/FINAL-ACH-MRSA-Bacteremia-Guidance.pdf). (Accessed).

23. Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection. N Engl J Med 2013;368(24):2255-65.

24. Schweizer ML, Eber MR, Laxminarayan R, et al. Validity of ICD-9-CM coding for identifying incident methicillin-resistant Staphylococcus aureus (MRSA) infections: is MRSA infection coded as a chronic disease? Infect Control Hosp Epidemiol 2011;32(2):148-54.

25. Sherman ER, Heydon KH, St John KH, et al. Administrative data fail to accurately identify cases of healthcare-associated infection. Infect Control Hosp Epidemiol 2006;27(4):332-7.

26. Centers for Medicare and Medicaid Services (CMS), National Center for Health Statistics (NCHS). ICD-9-CM Official Guidelines for Coding and Reporting 2011. (https://www.cdc.gov/nchs/data/icd/icd9cm_guidelines_2011.pdf). (Accessed).

27. Centers for Medicare and Medicaid Services (CMS), National Center for Health Statistics (NCHS). ICD-10-CM Official Guidelines for Coding and Reporting 2018. (https://www.cms.gov/Medicare/Coding/ICD10/Downloads/2018-ICD-10-CM-Coding-Guidelines.pdf). (Accessed).

28. Chen Q, Galfalvy H, Duan N. Effects of disease misclassification on exposure-disease association. Am J Public Health 2013;103(5):e67-73.

29. Hernán MA, Robins JM (2020). Causal Inference: What If. Boca Raton: Chapman & Hall/CRC.

30. Rothman K GS, Lash TL. *Modern Epidemiology*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008.

31. Nunan D, Heneghan C, Spencer EA. Catalogue of bias: allocation bias. BMJ Evid Based Med 2018;23(1):20-1.

32. Dubberke ER, Butler AM, Yokoe DS, et al. Multicenter study of surveillance for hospital-onset Clostridium difficile infection by the use of ICD-9-CM diagnosis codes. Infect Control Hosp Epidemiol 2010;31(3):262-8.

33. Burnham JP, Kwon JH, Babcock HM, et al. ICD-9-CM Coding for Multidrug Resistant Infection Correlates Poorly With Microbiologically Confirmed Multidrug Resistant Infection. Infect Control Hosp Epidemiol 2017;38(11):1381-3.

34. Rhee C, Kadri S, Huang SS, et al. Objective Sepsis Surveillance Using Electronic Clinical Data. Infect Control Hosp Epidemiol 2016;37(2):163-71.

35. David MZ, Medvedev S, Hohmann SF, et al. Increasing burden of methicillin-resistant Staphylococcus aureus hospitalizations at US academic medical centers, 2003-2008. Infect Control Hosp Epidemiol 2012;33(8):782-9.

36. Kallen AJ, Mu Y, Bulens S, et al. Health care-associated invasive MRSA infections, 2005-2008. JAMA 2010;304(6):641-8.

37. Klein EY, Mojica N, Jiang W, et al. Trends in Methicillin-Resistant Staphylococcus aureus Hospitalizations in the United States, 2010-2014. Clin Infect Dis 2017;65(11):1921-3.

38. Rose AN, Clogher P, Hatfield KM, Gokhale RH, See I, Petit S. Trends in methicillin-resistant Staphylococcus aureus bloodstream infections using statewide population-based surveillance and hospital discharge data, Connecticut, 2010–2018. Infection Control & Hospital Epidemiology. 2020:1-3. doi:10.1017/ice.2020.72

39. Kavanagh KT, Abusalem S, Calderon LE. The incidence of MRSA infections in the United States: is a more comprehensive tracking system needed? Antimicrob Resist Infect Control 2017;6:34.

40. Centers for Disease Control and Prevention (CDC). Healthcare-associated infections (HAI) progress report 2014. (https://www.cdc.gov/hai/data/archive/2014-progress-report.html). (Accessed).

41. Premier healthcare database white paper: data that informs and performs. 2018. (https://learn.premierinc.com/white-papers/premier-healthcare-database--whitepaper) (Accessed).

42. Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.

43. Hatfield KM, Dantes RB, Baggs J, et al. Assessing Variability in Hospital-Level Mortality Among U.S. Medicare Beneficiaries With Hospitalizations for Severe Sepsis and Septic Shock. Crit Care Med 2018;46(11):1753-60.

44. McCarthy NL, Baggs J, See I, et al. Bacterial Infections Associated with Substance Use Disorders, Large Cohort of United States Hospitals, 2012-2017. Clin Infect Dis 2020.

45. Centers for Medicare and Medicaid Services (CMS). Hospital-Acquired Conditions (Present on Admission Indicator) Coding. 2019. (https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalAcqCond). (Accessed).

Tables and Figures

Table 1. Description of participating hospitals, 2012 – 2017, N= 256		
Characteristic	**N**	**%**
Number of months reported (median (Q1 – Q3))	51.0	(24.0, 66.0)
Year		
2012	164	64.1
2013	192	75.0
2014	184	71.9
2015	162	63.3
2016	170	66.4
2017	194	75.8
Urban	186	72.7
Rural	70	27.3
Teaching	66	25.8
Non-Teaching	190	74.2
No. of beds, <300	168	65.6
No. of beds, ≥300	88	34.4
Region		
New England (CT, MA, ME, NH, RI, VT)	12	4.7
Mid-Atlantic (NJ, NY, PA)	31	12.1
South Atlantic (DC, DE, FL, GA, MD, NC, SC, VA, WV)	14	5.5
Northeast Central (IL, IN, MI, OH, WI)	56	21.9
Southeast Central (AL, KY, MS, TN)	12	4.7
Northwest Central (IA, KS, MN, MO, ND, NE, SD)	70	27.3
Southwest Central (AR, LA, OK, TX)	33	12.9
Mountain (AZ, CO, ID, MT, NM, NV, UT, WY)	3	1.2
Pacific (AK, CA, HI, OR, WA)	25	9.8
Total Discharges	11,581,385	---
Total Patient Days	51,328,546	---

Figure 1. Proportion of *S. aureus*, MRSA, and MSSA events that were identified using a code and culture, code only, or culture only, overall and for septicemia hospitalizations.

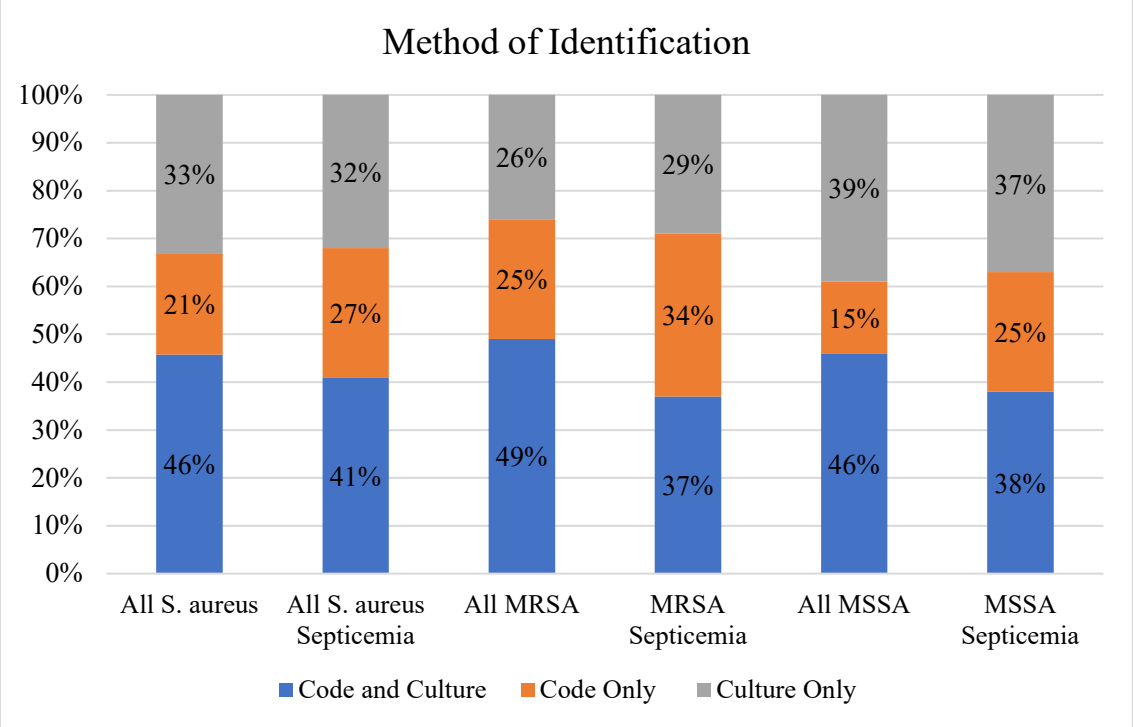


Table 2a. All *Staphylococcus aureus* hospitalizations, 2012-2017 (N= 306,991)						
	Code + Culture		Code Only		Culture Only	
	N	%	N	%	N	%
Total	140,468	45.8	65,077	21.2	101,446	33.1
Age (mean, standard deviation)	59.0	17.8	59.3	18.0	59.6	18.0
18 - 44	30,567	21.8	14,153	21.8	21,326	21.0
45 - 64	53,850	38.3	23,868	36.7	37,943	37.4
65 - 84	44,648	31.8	21,470	33.0	32,850	32.4
85+	11,403	8.1	5,586	8.6	9,327	9.2
Gender						
Female	59,816	42.6	29,764	45.7	44,870	44.2
Male	80,652	57.4	35,312	54.3	56,576	55.8
Unknown	0	0.0	1	0.0	0	0.0
Race/ethnicity						
White	105,092	74.8	51,059	78.5	75,072	74.0
Black	19,833	14.1	8,318	12.8	15,263	15.1
Other	14,712	10.5	5,297	8.1	10,411	10.3
Unknown/missing	831	0.6	403	0.6	700	0.7
Ethnicity						
Hispanic	6,453	4.6	2,308	3.6	4,745	4.7
Non-Hispanic	117,679	83.8	52,530	80.7	83,714	82.5
Unknown	16,336	11.6	10,239	15.7	12,987	12.8
Payer						
Medicare	75,099	53.5	36,281	55.8	55,268	54.5
Medicaid	25,037	17.8	11,492	17.7	18,200	17.9
Managed	19,607	14.0	9,063	13.9	13,776	13.6
Commercial/Employer	8,038	5.7	3,487	5.4	5,202	5.1
Other/Self-pay	12,687	9.0	4,754	7.3	9,000	8.9
Admission Source						
Non-healthcare facility	116,022	82.6	51,605	79.3	84,131	82.9
Clinic	10,451	7.4	5,221	8.0	7,390	7.3
Transfer from Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF) or born inside hospital	4,133	2.9	2,728	4.2	3,190	3.1
Transfer from health facility or born outside hospital	5,578	4.0	3,031	4.7	3,734	3.7
Court/Law enforcement	283	0.2	96	0.2	177	0.2
Transfer from Home Health Agency	1	0.0	1	0.0	0	0.0
Transfer from unit in same hospital	250	0.2	377	0.6	242	0.2
Transfer from Ambulatory Surgery Center	44	0.03	39	0.06	35	0.03
Transfer from Hospice	11	0.01	14	0.02	6	0.01
Information not available	3,695	2.6	1,965	3.0	2,541	2.5
Admission Type						
Emergency	108,939	77.6	47,570	73.1	77,653	76.6
Urgent	18,610	13.3	9,444	14.5	13,662	13.5
Elective	11,627	8.3	7,342	11.3	9,082	9.0
Trauma Center	645	0.5	343	0.5	669	0.7
Information not available	647	0.5	378	0.6	380	0.4
Length of stay (median, Q1, Q3)	7.0	(4.0, 12.0)	6.0	(3.0, 10.0)	5.0	(3.0, 9.0)
In-hospital mortality	10,805	7.7	4,395	6.8	12,212	12.0
POA indicator	130,228	92.7	61,900	95.1	---	---
Day of culture (mean, median)	3.0	1.0	---	---	3.2	2.0
Septicemia code	30,314	21.6	9,006	13.8	---	---
Blood culture	33,659	24.0	---	---	8,388	8.3

Table 2b. All MRSA hospitalizations, 2012-2017 (N= 168,634)						
	Code + Culture		Code Only		Culture Only	
	N	%	N	%	N	%
Total	82,194	48.7	42,447	25.2	43,993	26.1
Age (mean, standard deviation)	59.4	18.2	59.9	18.3	61.0	18.3
18 - 44	18,146	22.1	9,201	21.7	8,661	19.7
45 - 64	29,619	36.0	14,826	34.9	15,172	34.5
65 - 84	26,948	32.8	14,336	33.8	15,454	35.1
85+	7,481	9.1	4,084	9.6	4,706	10.7
Gender						
Female	36,400	44.3	20,177	47.5	20,239	46.0
Male	45,794	55.7	22,269	52.5	23,754	54.0
Unknown	0	0.0	1	0.0	0	0.0
Race/ethnicity						
White	61,492	74.8	33,650	79.3	32,692	74.3
Black	12,546	15.3	5,545	13.1	7,394	16.8
Other	7,690	9.4	3,018	7.1	3,647	8.3
Unknown/missing	466	0.6	234	0.6	260	0.6
Ethnicity						
Hispanic	3,371	4.1	1,329	3.1	1,734	3.9
Non-Hispanic	69,798	84.9	34,440	81.1	36,992	84.1
Unknown	9,025	11.0	6,678	15.7	5,267	12.0
Payer						
Medicare	46,294	56.3	24,649	58.1	26,533	60.3
Medicaid	14,794	18.0	7,494	17.7	7,789	17.7
Managed	9,646	11.7	5,258	12.4	4,565	10.4
Commercial/Employer	4,016	4.9	1,986	4.7	1,751	4.0
Other/Self-pay	7,444	9.1	3,060	7.2	3,355	7.6
Admission Source						
Non-healthcare facility	67,213	81.8	33,401	78.7	36,029	81.9
Clinic	5,696	7.6	3,222	7.6	2,871	6.5
Transfer from Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF)	3,220	3.9	2,116	5.0	2,197	5.0
Transfer from health facility	3,277	4.0	1,980	4.7	1,493	3.4
Court/Law enforcement	171	0.2	70	0.2	66	0.2
Transfer from Home Health Agency	1	0.0	0	0.0	0	0.0
Transfer from unit in same hospital	153	0.2	229	0.5	117	0.3
Transfer from Ambulatory Surgery Center	24	0.03	22	0.05	16	0.04
Transfer from Hospice	8	0.01	10	0.02	3	0.01
Information not available	2,431	3.0	1,397	3.3	1,201	2.7
Admission Type						
Emergency	64,040	77.9	31,340	73.8	34,276	77.9
Urgent	10,884	13.2	6,067	14.3	5,646	12.8
Elective	6,574	8.0	4,622	10.9	3,745	8.5
Trauma Center	309	0.4	173	0.4	170	0.4
Information not available	387	0.5	245	0.6	156	0.4
Length of stay (median, Q1, Q3)	7.0	(4.0, 12.0)	6.0	(3.0, 10.0)	5.0	(3.0, 9.0)
In-hospital mortality	9,652	8.5	3,060	7.2	5,755	13.1
POA indicator	76,531	93.1	40,567	95.6	---	---
Day of culture (mean, median)	2.9	1.0	---	---	3.5	2.0
Septicemia code	16,132	19.6	4,866	11.5	---	---
Blood culture	16,862	20.5	---	---	3,278	7.5

Table 2c. All MSSA hospitalizations, 2012-2017 (N= 148,776)						
	Code + Culture		Code Only		Culture Only	
	N	%	N	%	N	%
Total	67,817	45.6	22,930	15.4	58,029	39.0
Age (mean, standard deviation)	58.2	17.2	58.3	17.3	58.5	17.8
18 - 44	14,724	21.7	5,025	21.9	12,784	22.0
45 - 64	27,964	41.2	9,152	39.9	22,996	39.6
65 - 84	20,523	30.3	7,237	31.6	17,586	30.3
85+	4,606	6.8	1,516	6.6	4,663	8.0
Gender						
Female	27,422	40.4	9,716	42.4	24,865	42.9
Male	40,395	59.6	13,214	57.6	33,164	57.2
Race/ethnicity						
White	50,701	74.8	17,645	77.0	42,786	73.7
Black	8,760	12.9	2,811	12.3	7,964	13.7
Other	7,950	11.7	2,301	10.0	6,836	11.8
Unknown/missing	406	0.6	173	0.8	443	0.8
Ethnicity						
Hispanic	3,500	5.2	992	4.3	3,043	5.2
Non-Hispanic	55,870	82.4	18,324	79.9	47,181	81.3
Unknown	8,447	12.5	3,614	15.8	7,805	13.5
Payer						
Medicare	33,718	49.7	11,785	51.4	29,066	50.1
Medicaid	12,003	17.7	4,065	17.7	10,522	18.1
Managed	11,326	16.7	3,845	16.8	9,266	16.0
Commercial/Employer	4,565	6.7	1,511	6.6	3,485	6.0
Other/Self-pay	6,205	9.2	1,724	7.5	5,690	9.8
Admission Source						
Non-healthcare facility	56,747	83.7	18,450	80.5	48,574	83.7
Clinic	5,460	8.1	2,013	8.8	4,557	7.9
Transfer from Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF)	1,213	1.8	631	2.8	1,024	1.8
Transfer from health facility	2,607	4.0	1,061	4.6	2,259	3.9
Court/Law enforcement	126	0.2	27	0.1	114	0.2
Transfer from Home Health Agency	0	0.0	1	0.0	0	0.0
Transfer from unit in same hospital	113	0.2	149	0.7	128	0.2
Transfer from Ambulatory Surgery Center	21	0.03	18	0.1	19	0.03
Transfer from Hospice	4	0.01	4	0.02	3	0.01
Information not available	1,526	2.3	576	2.5	1,351	2.3
Admission Type						
Emergency	52,200	77.0	16,454	71.8	43,827	75.5
Urgent	9,063	13.4	3,425	14.9	8,093	14.0
Elective	5,854	8.6	2,745	12.0	5,374	9.3
Trauma Center	391	0.6	172	0.8	505	0.9
Information not available	309	0.5	134	0.6	230	0.4
Length of stay (median, Q1, Q3)	7.0	(4.0, 12.0)	6.0	(3.0, 10.0)	5.0	(3.0, 9.0)
In-hospital mortality	4,679	6.9	1,364	6.0	6,564	11.3
POA indicator	62,586	92.3	21,621	94.3	---	---
Day of culture (mean, median)	3.1	2.0	---	---	3.1	2.0
Septicemia code	16,422	24.2	4,247	18.5	---	---
Blood culture	19,170	28.3	---	---	5,203	9.0

Table 3a. *Staphylococcus aureus* Septicemia hospitalizations, 2012-2017 (N= 57,815)						
	Code + Culture		Code Only		Culture Only	
	N	%	N	%	N	%
Total	23,552	40.7	15,768	27.3	18,495	32.0
Age (mean, standard deviation)	61.6	16.8	59.9	17.2	61.3	17.2
18 - 44	3,818	16.8	3,106	19.7	3,215	17.4
45 - 64	8,936	37.9	6,034	38.3	7,061	38.2
65 - 84	8,684	36.9	5,415	34.3	6,388	34.5
85+	2,114	9.0	1,213	7.7	1,831	9.9
Gender						
Female	9,432	40.1	6,719	42.6	7,574	41.0
Male	14,120	60.0	9,049	57.4	10,921	59.1
Race/ethnicity						
White	16,519	70.1	11,796	74.8	13,445	72.7
Black	4,364	18.5	2,304	14.6	3,344	18.1
Other	2,535	10.8	1,557	9.9	1,615	8.7
Unknown/missing	134	0.6	111	0.7	91	0.5
Ethnicity						
Hispanic	1,031	4.4	606	3.8	704	3.8
Non-Hispanic	19,433	82.5	12,566	79.7	15,392	83.2
Unknown	3,088	13.1	2,596	16.5	2,399	13.0
Payer						
Medicare	14,571	61.9	9,117	57.8	10,870	58.8
Medicaid	3,902	16.6	2,905	18.4	3,022	16.3
Managed	2,622	11.1	1,834	11.6	2,331	12.6
Commercial/Employer	1,013	4.3	843	5.4	840	4.5
Other/Self-pay	1,444	6.1	1,069	6.8	1,432	7.7
Admission Source						
Non-healthcare facility	19,812	84.1	12,602	79.9	15,497	83.8
Clinic	1,127	4.8	909	5.8	1,006	5.4
Transfer from Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF)	847	3.6	764	4.9	588	3.2
Transfer from health facility	863	3.7	899	5.7	793	4.3
Court/Law enforcement	39	0.2	29	0.2	37	0.2
Transfer from unit in same hospital	27	0.1	70	0.4	33	0.2
Transfer from Ambulatory Surgery Center	9	0.04	4	0.03	3	0.02
Transfer from Hospice	4	0.02	7	0.04	2	0.01
Information not available	824	3.5	484	3.1	536	2.9
Admission Type						
Emergency	20,544	87.2	12,979	82.3	15,292	82.7
Urgent	2,133	9.1	1,728	11.0	2,188	11.8
Elective	739	3.1	973	6.2	873	4.7
Trauma Center	58	0.3	45	0.3	88	0.5
Information not available	78	0.3	43	0.3	54	0.3
Length of stay (median, Q1, Q3)	10.0	(6.0, 16.0)	8.0	(5.0, 14.0)	7.0	(4.0, 12.0)
In-hospital mortality	3,913	16.6	2,107	13.4	3,412	18.5
POA indicator	21,761	92.4	14,781	93.7	---	---
Day of culture (mean, median)	3.1	1.0	---	---	3.3	1.0
Septicemia code	23,552	100.0	15,768	100.0	---	---
Blood culture	23,552	100.0	---	---	18,495	100.0

Table 3b. MRSA Septicemia hospitalizations, 2012-2017 (N= 28,480)						
	Code + Culture		Code Only		Culture Only	
	N	%	N	%	N	%
Total	10,551	37.0	9,659	33.9	8,270	29.0
Age (mean, standard deviation)	62.4	16.9	60.5	12.2	62.1	17.4
18 - 44	1,658	15.7	1,867	19.3	1,404	17.0
45 - 64	3,795	36.0	3,564	36.9	2,965	35.9
65 - 84	4,069	38.6	3,404	35.2	2,993	36.2
85+	1,029	9.8	824	8.5	908	11.0
Gender						
Female	4,322	41.0	4,201	43.5	3,476	42.0
Male	6,229	59.0	5,458	56.5	4,794	58.0
Race/ethnicity						
White	7,220	68.4	7,246	75.0	5,860	70.9
Black	2,283	21.6	1,520	15.7	1,748	21.1
Other	987	9.4	828	8.6	620	7.5
Unknown/missing	61	0.6	65	0.7	42	0.5
Ethnicity						
Hispanic	412	3.9	334	3.5	251	3.0
Non-Hispanic	8,872	84.1	7,814	80.9	7,001	84.7
Unknown	1,267	12.0	1,511	15.6	1,018	12.3
Payer						
Medicare	6,929	65.7	5,828	60.3	5,249	63.5
Medicaid	1,811	17.2	1,816	18.8	1,367	16.5
Managed	861	8.2	948	9.8	789	9.5
Commercial/Employer	344	3.3	421	4.4	297	3.6
Other/Self-pay	606	5.7	646	6.7	568	6.9
Admission Source						
Non-healthcare facility	8,673	82.2	7,603	78.7	6,845	82.8
Clinic	439	4.2	550	5.7	419	5.1
Transfer from Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF)	569	5.4	566	5.9	398	4.8
Transfer from health facility	403	3.8	537	5.6	310	3.8
Court/Law enforcement	23	0.2	17	0.2	12	0.2
Transfer from unit in same hospital	13	0.1	39	0.4	15	0.2
Transfer from Ambulatory Surgery Center	2	0.02	3	0.03	1	0.01
Transfer from Hospice	1	0.01	4	0.04	2	0.02
Information not available	428	4.1	340	3.5	268	3.2
Admission Type						
Emergency	9,142	86.7	8,008	82.9	6,878	83.2
Urgent	999	9.5	995	10.3	963	11.6
Elective	345	3.3	603	6.2	375	4.5
Trauma Center	26	0.3	23	0.2	28	0.3
Information not available	39	0.4	30	0.3	26	0.3
Length of stay (median, Q1, Q3)	11.0	(7.0, 18.0)	8.0	(5.0, 14.0)	8.0	(4.0, 13.0)
In-hospital mortality	2,034	19.3	1,394	14.4	1,723	20.8
POA indicator	9,753	92.4	9,090	94.1	---	---
Day of culture (mean, median)	2.7	1.0	---	---	3.3	1.0
Septicemia code	10,551	100.0	9,659	100.0	---	---
Blood culture	10,551	100.0	---	---	8,270	100.0

Table 3c. MSSA Septicemia hospitalizations, 2012-2017 (N= 31,111)						
	Code + Culture		Code Only		Culture Only	
	N	%	N	%	N	%
Total	11,970	38.5	7,768	25.0	11,373	36.6
Age (mean, standard deviation)	61.0	16.7	59.4	16.9	60.6	17.1
18 - 44	1,990	16.6	1,525	19.6	2,004	17.6
45 - 64	4,751	39.7	3,099	39.9	4,537	39.9
65 - 84	4,237	35.4	2,613	33.6	3,810	33.5
85+	992	8.3	531	6.8	1,022	9.0
Gender						
Female	4,662	39.0	3,211	41.3	4,590	40.4
Male	7,308	61.1	4,557	58.7	6,783	59.6
Race/ethnicity						
White	8,585	71.7	5,730	73.8	8,375	73.6
Black	1,878	15.7	1,096	14.1	1,828	16.1
Other	1,444	12.1	884	11.4	1,111	9.8
Unknown/missing	63	0.5	58	0.8	59	0.5
Ethnicity						
Hispanic	579	4.8	328	4.2	498	4.4
Non-Hispanic	9,698	81.0	6,137	79.0	9,351	82.2
Unknown	1,693	14.1	1,303	16.8	1,524	13.4
Payer						
Medicare	7,007	58.5	4,292	55.3	6,321	55.6
Medicaid	1,929	16.1	1,371	17.7	1,848	16.3
Managed	1,645	13.7	1,077	13.9	1,668	14.7
Commercial/Employer	630	5.3	484	6.2	587	5.2
Other/Self-pay	759	6.3	544	7.0	949	8.3
Admission Source						
Non-healthcare facility	10,296	86.0	6,351	81.8	9,597	84.4
Clinic	626	5.2	454	5.8	650	5.7
Transfer from Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF)	239	2.0	268	3.5	233	2.1
Transfer from health facility	423	3.5	422	5.4	523	4.6
Court/Law enforcement	16	0.1	12	0.2	25	0.2
Transfer from unit in same hospital	13	0.1	33	0.4	19	0.2
Transfer from Ambulatory Surgery Center	7	0.06	2	0.03	2	0.02
Transfer from Hospice	2	0.02	4	0.05	1	0.01
Information not available	348	2.9	222	2.9	323	2.8
Admission Type						
Emergency	10,512	87.8	6,389	82.3	9,402	82.7
Urgent	1,039	8.7	892	11.5	1,336	11.8
Elective	354	3.0	440	5.7	539	4.7
Trauma Center	28	0.2	30	0.4	65	0.6
Information not available	37	0.3	17	0.2	31	0.3
Length of stay (median, Q1, Q3)	10.0	(6.0, 15.0)	8.0	(5.0, 14.0)	7.0	(4.0, 12.0)
In-hospital mortality	1,654	13.8	1,028	13.2	1,934	17.0
POA indicator	11,060	92.4	7,235	93.1	---	---
Day of culture (mean, median)	3.6	2.0	---	---	3.4	1.0
Septicemia code	11,970	100.0	7,768	100.0	---	---
Blood culture	11,970	100.0	---	---	11,373	100.0

Table 4a.			Overall		Community Onset (CO)		Hospital Onset (HO)		Discordant HO/CO	
	Code	Culture	N	%	N	%	N	%	N	%
Total *S. aureus*			283,577	100	234,107	83	29,906	11	19,564	7
True Positives	Any MRSA and/or MSSA Code	Culture Positive for MRSA and/or MSSA	130,451	46	103,463	79	7,424	6	19,564	15
False Positives	Any MRSA and/or MSSA Code	No Culture Positive for MRSA and/or MSSA	58,887	21	55,995	95	2,892	5	---	---
False Negatives	No Code for MRSA and/or MSSA	Culture Positive for MRSA and/or MSSA	94,239	33	74,649	79	19,590	21	---	---
S. aureus septicemia			52,902	100	43,212	82	5,807	11	3,883	7
True Positives	MRSA or MSSA septicemia code	Blood culture positive for MRSA or MSSA	21,802	41	16,567	76	1,352	6	3,883	18
False Positives	MRSA or MSSA septicemia code	No blood culture positive for MRSA/MSSA	14,024	27	13,117	94	907	6	---	---
False Negatives	No Code for MRSA or MSSA septicemia	Blood culture positive for MRSA or MSSA	17,076	32	13,528	79	3,548	21	---	---

Table 4b.			Overall		Community Onset (CO)		Hospital Onset (HO)		Discordant HO/CO	
	Code	Culture	N	%	N	%	N	%	N	%
Total MRSA			153,768	100	130,728	85	14,954	10	8,086	5
True Positives	Any MRSA Code	Culture Positive for MRSA	68,024	44	56,211	83	3,727	5	8,086	12
False Positives	Any MRSA Code	No Culture Positive for MRSA	42,173	27	40,253	95	1,920	5	---	---
False Negatives	No Code for MRSA	Culture Positive for MRSA	43,571	28	34,264	79	9,307	21	---	---
MRSA septicemia			25,617	100	22,772	89	2,240	9	605	2
True Positives	MRSA septicemia code	Blood culture positive for MRSA	9,563	37	8,364	87	594	6	605	6
False Positives	MRSA septicemia code	No blood culture positive for MRSA	8,510	33	7,988	94	522	6	---	---
False Negatives	No Code for MRSA septicemia	Blood culture positive for MRSA	7,544	29	6,420	85	1,124	15	---	---

Table 4c.			Overall		Community Onset (CO)		Hospital Onset (HO)		Discordant HO/CO	
	Code	Culture	N	%	N	%	N	%	N	%
Total MSSA			139,521	100	111,822	80	17,153	12	10,546	8
True Positives	Any MSSA Code	Culture Positive for MSSA	55,860	40	41,901	75	3,413	6	10,546	19
False Positives	Any MSSA Code	No Culture Positive for MSSA	24,546	18	23,110	94	1,436	6	---	---
False Negatives	No Code for MSSA	Culture Positive for MSSA	59,115	42	46,811	79	12,304	21	---	---
MSSA septicemia			28,920	100	21,923	76	3,885	13	3,112	11
True Positives	MSSA septicemia code	Blood culture positive for MSSA	11,286	39	7,470	66	704	6	3,112	28
False Positives	MSSA septicemia code	No blood culture positive for MSSA	7,039	24	6,546	93	493	7	---	---
False Negatives	No Code for MSSA septicemia	Blood culture positive for MSSA	10,595	37	7,907	75	2,688	25	---	---

Figure 2a. Trends in *S. aureus* code and culture rates, overall and for septicemia hospitalizations; observed rates shown as points, modeled trends shown as lines.

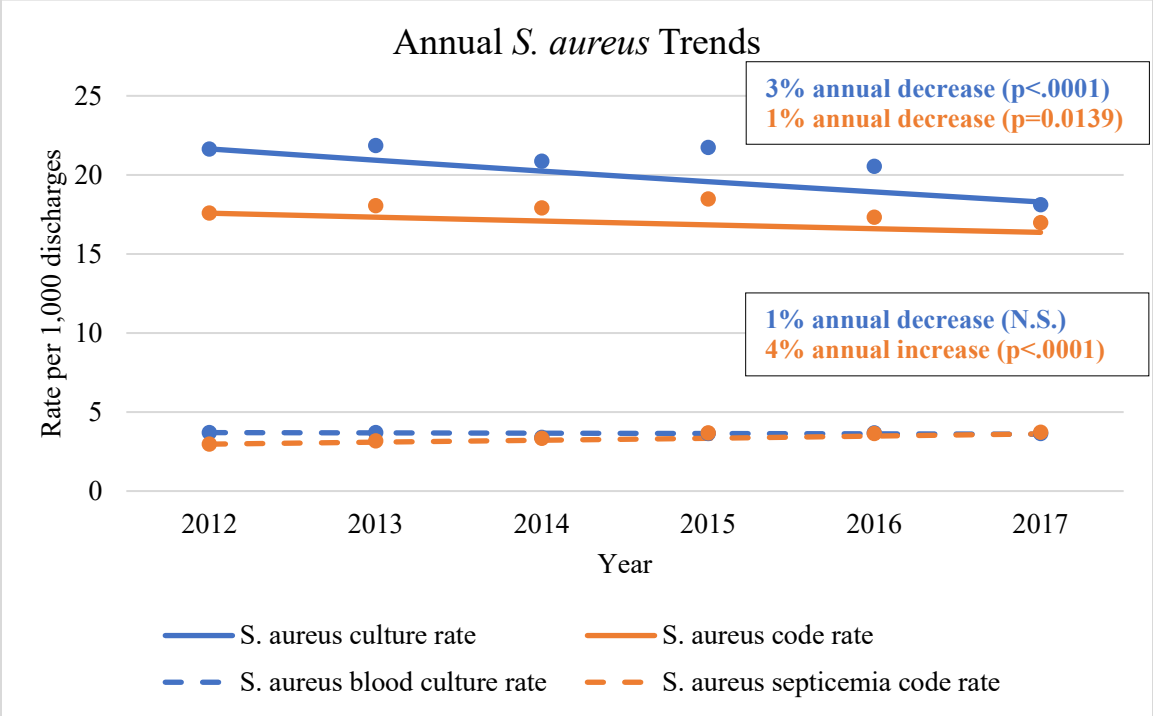


Figure 2b. Trends in MRSA code and culture rates, overall and for septicemia hospitalizations; observed rates shown as points, modeled trends shown as lines.

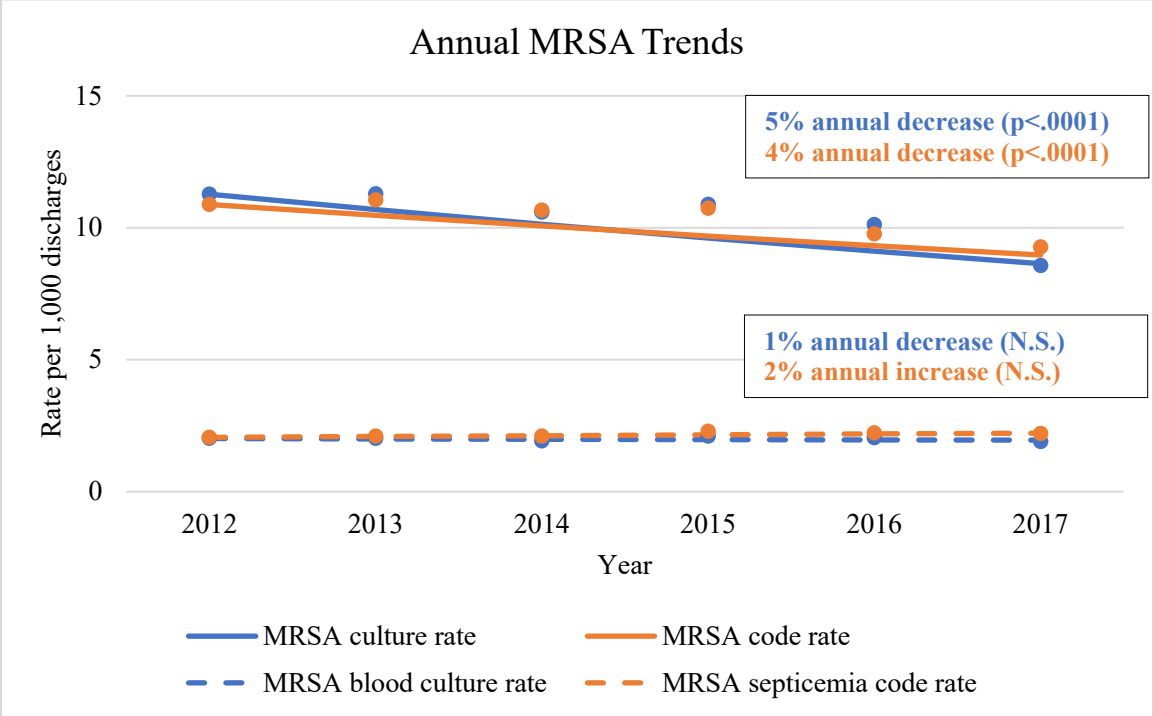


Figure 2c. Trends in MSSA code and culture rates, overall and for septicemia hospitalizations; observed rates shown as points, modeled trends shown as lines.

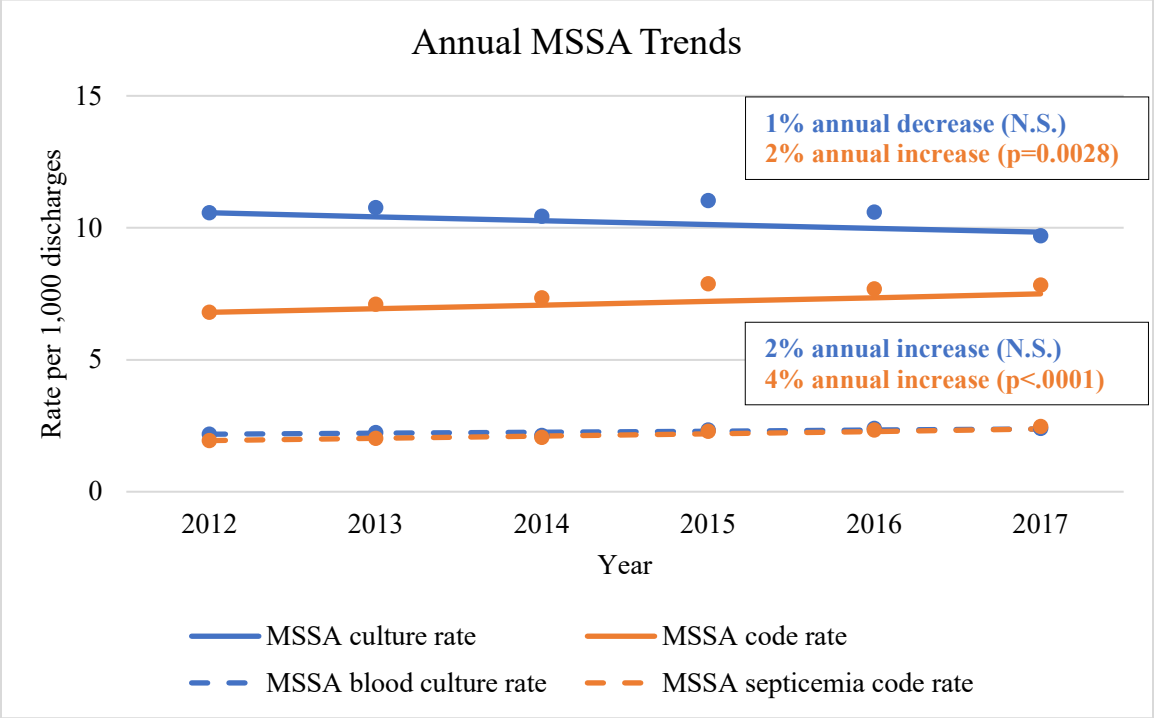


Table 5a. Logistic regression results for MRSA code only and MRSA culture only.

Factor	Code Only OR (95% CI)	Culture Only OR (95% CI)
Age	1.04 (1.04, 1.04)	1.04 (1.03, 1.04)
Gender		
Female vs. Male*	0.91 (0.84, 0.98)	0.96 (0.90, 1.01)
Race		
Black vs. White	1.01 (0.89, 1.14)	1.08 (1.00, 1.17)
Other vs. White	1.28 (1.12, 1.47)	1.23 (1.11, 1.36)
Ethnicity		
Hispanic vs. Non-Hispanic	1.08 (0.85, 1.37)	0.92 (0.78, 1.08)
Admission Source		
Clinic vs. Non-healthcare facility*	0.92 (0.77, 1.08)	0.81 (0.70, 0.93)
Court/law enforcement vs. Non-healthcare facility	0.57 (0.08, 4.18)	0.78 (0.28, 2.20)
Information not available vs. Non-healthcare facility	1.21 (0.99, 1.48)	1.00 (0.84, 1.19)
Transfer vs. Non-healthcare facility	1.26 (1.14, 1.41)	1.34 (1.23, 1.46)
Payer		
Commercial vs. Self/Other	1.06 (0.80, 1.42)	0.88 (0.71, 1.10)
Managed vs. Self/Other	1.06 (0.83, 1.34)	0.80 (0.67, 0.96)
Medicaid vs. Self/Other	0.95 (0.76, 1.20)	0.91 (0.77, 1.07)
Medicare vs. Self/Other*	0.96 (0.77, 1.18)	0.79 (0.68, 0.92)
Admission Type		
Urgent vs. Emergency	0.74 (0.65, 0.83)	0.76 (0.69, 0.84)
Elective vs. Emergency	0.73 (0.63, 0.84)	0.56 (0.49, 0.64)
Trauma Center vs. Emergency*	1.11 (0.68, 1.80)	1.53 (1.04, 2.26)
Information not available vs. Emergency	1.11 (0.65, 1.89)	0.97 (0.59, 1.59)
Comorbidity		
Human Immunodeficiency virus (HIV)*	1.27 (0.84, 1.90)	1.44 (1.07, 1.92)
Hematologic malignancy*	1.07 (0.80, 1.42)	1.57 (1.23, 1.99)
Hematopoietic stem cell transplant	1.74 (0.70, 4.33)	1.21 (0.55, 2.66)
Solid organ transplant	1.09 (0.85, 1.39)	1.06 (0.87, 1.30)
Solid organ malignant tumor*	1.14 (1.04, 1.26)	1.06 (0.98, 1.15)
Rheumatologic Disorders	0.94 (0.77, 1.14)	1.09 (0.94, 1.27)
Diabetes mellitus*	0.93 (0.86, 1.01)	0.91 (0.86, 0.96)
Congestive heart failure	1.28 (1.17, 1.41)	1.28 (1.19, 1.39)
Chronic pulmonary disease*	0.96 (0.89, 1.04)	0.85 (0.80, 0.90)
End stage renal disease	1.56 (1.38, 1.76)	1.63 (1.47, 1.80)
Drug Abuse	0.88 (0.73, 1.07)	0.92 (0.80, 1.07)
Infection Type		
Osteomyelitis	0.83 (0.70, 0.97)	0.52 (0.44, 0.61)
Endocarditis	2.85 (2.37, 3.43)	1.81 (1.28, 2.55)
Skin & soft tissue infection (SSTI)	0.56 (0.51, 0.62)	0.32 (0.29, 0.34)
Urinary tract infection (UTI)*	1.28 (1.18, 1.40)	1.03 (0.97, 1.11)
Intra-abdominal infection	2.15 (1.93, 2.40)	1.79 (1.64, 1.95)
Pulmonary infection	2.67 (2.46, 2.90)	1.87 (1.75, 1.99)
Epidemiology Classification		
Hospital-Onset vs. Community-Onset	2.03 (1.79, 2.31)	1.50 (1.41, 1.59)

*Difference in statistical significance between models (i.e., a parameter was significantly associated in one model, but not significantly associated in the other)

Table 5b. Logistic regression results for MRSA septicemia code only and MRSA blood culture only.

Factor	Code Only OR (95% CI)	Culture Only OR (95% CI)
Age	1.04 (1.04, 1.05)	1.04 (1.03, 1.04)
Gender		
Female vs. Male*	1.12 (0.99, 1.27)	1.21 (1.07, 1.36)
Race		
Black vs. White	0.90 (0.75, 1.08)	0.91 (0.78, 1.06)
Other vs. White	1.16 (0.94, 1.44)	1.18 (0.95, 1.47)
Ethnicity		
Hispanic vs. Non-Hispanic	1.05 (0.73, 1.52)	0.98 (0.68, 1.41)
Admission Source		
Clinic vs. Non-healthcare facility	0.77 (0.57, 1.04)	0.82 (0.61, 1.09)
Court/law enforcement vs. Non-healthcare facility	0.60 (0.38, 0.97)	1.54 (0.19, 12.3)
Information not available vs. Non-healthcare facility	0.99 (0.71, 1.38)	1.09 (0.79, 1.50)
Transfer vs. Non-healthcare facility*	1.09 (0.92, 1.30)	1.29 (1.07, 1.55)
Payer		
Commercial vs. Self/Other*	0.60 (0.38, 0.97)	0.91 (0.59, 1.40)
Managed vs. Self/Other	1.00 (0.70, 1.42)	0.94 (0.67, 1.33)
Medicaid vs. Self/Other	0.84 (0.60, 1.17)	1.05 (0.76, 1.44)
Medicare vs. Self/Other	0.75 (0.55, 1.03)	0.94 (0.70, 1.26)
Admission Type		
Urgent vs. Emergency*	1.07 (0.87, 1.32)	0.75 (0.61, 0.91)
Elective vs. Emergency*	1.13 (0.88, 1.46)	0.71 (0.53, 0.96)
Trauma Center vs. Emergency	1.66 (0.64, 4.27)	1.11 (0.46, 2.64)
Information not available vs. Emergency	2.26 (0.94, 5.48)	0.68 (0.22, 2.14)
Comorbidity		
Human Immunodeficiency virus (HIV)*	1.55 (0.87, 2.74)	2.09 (1.32, 3.31)
Hematologic malignancy*	0.93 (0.60, 1.45)	1.80 (1.15, 2.80)
Hematopoietic stem cell transplant	1.57 (0.33, 7.57)	0.49 (0.10, 2.36)
Solid organ transplant	0.87 (0.57, 1.32)	1.10 (0.76, 1.59)
Solid organ malignant tumor	1.15 (0.97, 1.36)	1.10 (0.93, 1.30)
Rheumatologic Disorders	1.33 (0.98, 1.80)	1.00 (0.73, 1.35)
Diabetes mellitus*	0.92 (0.81, 1.05)	0.85 (0.75, 0.96)
Congestive heart failure*	1.23 (1.05, 1.43)	1.13 (0.96, 1.33)
Chronic pulmonary disease	0.94 (0.83, 1.07)	0.89 (0.78, 1.00)
End stage renal disease*	1.37 (1.15, 1.62)	1.01 (0.85, 1.19)
Drug Abuse*	0.82 (0.62, 1.08)	0.63 (0.48, 0.83)
Infection Type		
Osteomyelitis	0.77 (0.60, 0.99)	0.38 (0.28, 0.51)
Endocarditis**	2.01 (1.59, 2.53)	0.73 (0.54, 0.99)
Skin & soft tissue infection (SSTI)	0.62 (0.53, 0.72)	0.34 (0.29, 0.39)
Urinary tract infection (UTI)	0.99 (0.87, 1.14)	0.93 (0.81, 1.06)
Intra-abdominal infection	1.74 (1.47, 2.06)	1.35 (1.13, 1.62)
Pulmonary infection	1.91 (1.68, 2.17)	1.93 (1.70, 2.18)
Epidemiology Classification		
Hospital-Onset vs. Community-Onset	2.22 (1.81, 2.73)	1.81 (1.56, 2.10)

*Difference in statistical significance between models (i.e., a parameter was significantly associated in one model, but not significantly associated in the other)

**Difference in directionality (i.e., a parameter was positively associated with in-hospital mortality in one model and negatively associated in the other).

Table 5c. Logistic regression results for MSSA code only and MSSA culture only.

Factor	Code Only OR (95% CI)	Culture Only OR (95% CI)
Age	1.04 (1.04, 1.05)	1.03 (1.03, 1.04)
Gender		
Female vs. Male*	0.94 (0.84, 1.04)	0.90 (0.85, 0.95)
Race		
Black vs. White*	1.10 (0.94, 1.30)	1.09 (1.01, 1.18)
Other vs. White*	1.15 (0.96, 1.37)	1.28 (1.18, 1.38)
Ethnicity		
Hispanic vs. Non-Hispanic	0.85 (0.62, 1.17)	0.92 (0.81, 1.05)
Admission Source		
Clinic vs. Non-healthcare facility*	0.79 (0.62, 1.00)	0.74 (0.65, 0.84)
Court/law enforcement vs. Non-healthcare facility	0.00 (0.00, 0.00)	0.70 (0.33, 1.48)
Information not available vs. Non-healthcare facility	1.31 (0.97, 1.76)	1.00 (0.84, 1.19)
Transfer vs. Non-healthcare facility	1.47 (1.26, 1.73)	1.39 (1.26, 1.53)
Payer		
Commercial vs. Self/Other*	0.97 (0.68, 1.40)	0.79 (0.68, 0.92)
Managed vs. Self/Other	0.69 (0.50, 0.95)	0.68 (0.60, 0.76)
Medicaid vs. Self/Other*	1.02 (0.76, 1.38)	0.70 (0.62, 0.79)
Medicare vs. Self/Other*	0.96 (0.73, 1.26)	0.65 (0.58, 0.72)
Admission Type		
Urgent vs. Emergency	0.78 (0.66, 0.93)	0.75 (0.69, 0.82)
Elective vs. Emergency	0.54 (0.43, 0.68)	0.48 (0.43, 0.55)
Trauma Center vs. Emergency*	0.99 (0.59, 1.69)	1.28 (1.02, 1.61)
Information not available vs. Emergency	0.75 (0.37, 1.50)	1.15 (0.79, 1.67)
Comorbidity		
Human Immunodeficiency virus (HIV)*	1.91 (1.19, 3.09)	1.10 (0.84, 1.45)
Hematologic malignancy	1.03 (0.70, 1.53)	1.14 (0.90, 1.44)
Hematopoietic stem cell transplant*	2.93 (1.06, 8.12)	1.57 (0.76, 3.23)
Solid organ transplant	1.69 (1.30, 2.19)	1.11 (0.91, 1.36)
Solid organ malignant tumor	1.17 (1.02, 1.35)	1.15 (1.07, 1.24)
Rheumatologic Disorders*	1.13 (0.86, 1.48)	0.83 (0.71, 0.98)
Diabetes mellitus*	0.99 (0.88, 1.10)	0.82 (0.77, 0.87)
Congestive heart failure	1.39 (1.22, 1.59)	1.39 (1.29, 1.50)
Chronic pulmonary disease*	0.98 (0.88, 1.10)	0.83 (0.78, 0.88)
End stage renal disease	1.43 (1.21, 1.68)	1.58 (1.43, 1.75)
Drug Abuse	0.71 (0.55, 0.92)	1.16 (1.03, 1.30)
Infection Type		
Osteomyelitis	0.64 (0.52, 0.80)	0.36 (0.30, 0.43)
Endocarditis	1.98 (1.61, 2.43)	1.71 (1.31, 2.24)
Skin & soft tissue infection (SSTI)	0.50 (0.44, 0.57)	0.20 (0.18, 0.21)
Urinary tract infection (UTI)	1.22 (1.07, 1.38)	0.90 (0.84, 0.96)
Intra-abdominal infection	2.25 (1.94, 2.60)	1.60 (1.47, 1.75)
Pulmonary infection	2.93 (2.62, 3.29)	1.60 (1.51, 1.70)
Epidemiology Classification		
Hospital-Onset vs. Community-Onset	2.02 (1.72, 2.37)	1.62 (1.53, 1.72)

*Difference in statistical significance between models (i.e., a parameter was significantly associated in one model, but not significantly associated in the other)

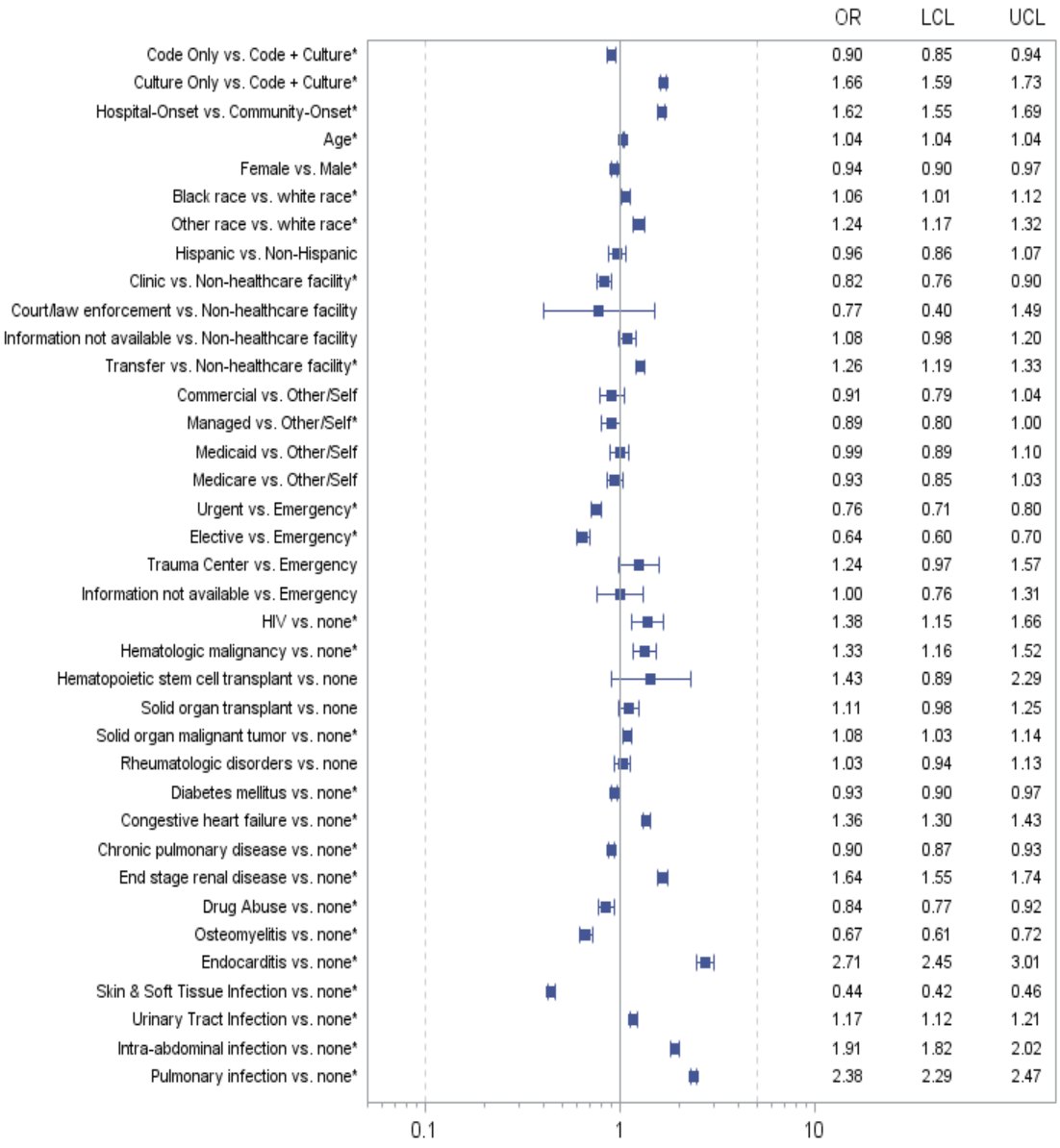
Table 5d. Logistic regression results for MSSA septicemia code only and MSSA blood culture only.

Factor	Code Only OR (95% CI)	Culture Only OR (95% CI)
Age	1.04 (1.04, 1.05)	1.04 (1.03, 1.04)
Gender		
Female vs. Male	0.94 (0.81, 1.08)	1.01 (0.90, 1.12)
Race		
Black vs. White	1.18 (0.96, 1.46)	1.17 (1.01, 1.37)
Other vs. White	1.24 (0.99, 1.55)	1.14 (0.95, 1.36)
Ethnicity		
Hispanic vs. Non-Hispanic	0.84 (0.56, 1.26)	1.01 (0.76, 1.34)
Admission Source		
Clinic vs. Non-healthcare facility*	0.85 (0.60, 1.20)	0.61 (0.47, 0.81)
Court/law enforcement vs. Non-healthcare facility	0.00 (0.00, 0.00)	1.45 (0.47, 4.51)
Information not available vs. Non-healthcare facility*	1.55 (1.07, 2.26)	1.13 (0.83, 1.53)
Transfer vs. Non-healthcare facility	1.41 (1.14, 1.75)	1.25 (1.03, 1.52)
Payer		
Commercial vs. Self/Other	0.95 (0.60, 1.50)	0.82 (0.59, 1.15)
Managed vs. Self/Other	0.78 (0.53, 1.16)	0.79 (0.60, 1.02)
Medicaid vs. Self/Other	0.94 (0.65, 1.38)	0.93 (0.72, 1.21)
Medicare vs. Self/Other	0.96 (0.67, 1.36)	0.88 (0.70, 1.12)
Admission Type		
Urgent vs. Emergency	1.01 (0.80, 1.27)	0.89 (0.75, 1.06)
Elective vs. Emergency	0.76 (0.54, 1.07)	0.96 (0.74, 1.26)
Trauma Center vs. Emergency	1.13 (0.43, 2.96)	0.97 (0.50, 1.90)
Information not available vs. Emergency	1.81 (0.47, 6.92)	1.50 (0.57, 3.91)
Comorbidity		
Human Immunodeficiency virus (HIV)*	2.79 (1.57, 4.98)	1.52 (0.96, 2.42)
Hematologic malignancy	1.14 (0.71, 1.83)	1.23 (0.84, 1.80)
Hematopoietic stem cell transplant	2.69 (0.83, 8.75)	2.96 (0.95, 9.25)
Solid organ transplant*	1.48 (1.06, 2.06)	1.04 (0.74, 1.47)
Solid organ malignant tumor*	1.09 (0.89, 1.33)	1.30 (1.13, 1.51)
Rheumatologic Disorders	1.24 (0.85, 1.83)	1.11 (0.83, 1.48)
Diabetes mellitus*	0.94 (0.81, 1.09)	0.81 (0.72, 0.90)
Congestive heart failure	1.37 (1.14, 1.64)	1.29 (1.11, 1.49)
Chronic pulmonary disease	0.88 (0.75, 1.03)	0.96 (0.85, 1.08)
End stage renal disease	1.07 (0.87, 1.31)	0.95 (0.81, 1.12)
Drug Abuse	0.89 (0.65, 1.21)	0.91 (0.72, 1.15)
Infection Type		
Osteomyelitis	0.55 (0.41, 0.75)	0.25 (0.18, 0.34)
Endocarditis*	1.96 (1.54, 2.49)	0.90 (0.70, 1.15)
Skin & soft tissue infection (SSTI)	0.50 (0.42, 0.59)	0.31 (0.27, 0.36)
Urinary tract infection (UTI)*	1.02 (0.87, 1.20)	0.84 (0.74, 0.95)
Intra-abdominal infection	2.38 (1.97, 2.87)	1.50 (1.28, 1.77)
Pulmonary infection	1.92 (1.65, 2.23)	1.63 (1.45, 1.83)
Epidemiology Classification		
Hospital-Onset vs. Community-Onset	2.11 (1.68, 2.65)	1.29 (1.15, 1.46)

* Difference in statistical significance between models (i.e., a parameter was significantly associated in one model, but not significantly associated in the other)

Figure 3a. Multivariable Logistic Regression Analysis of Characteristics Associated with Mortality of Patients with a MRSA Code, Culture or both, 2012-2017

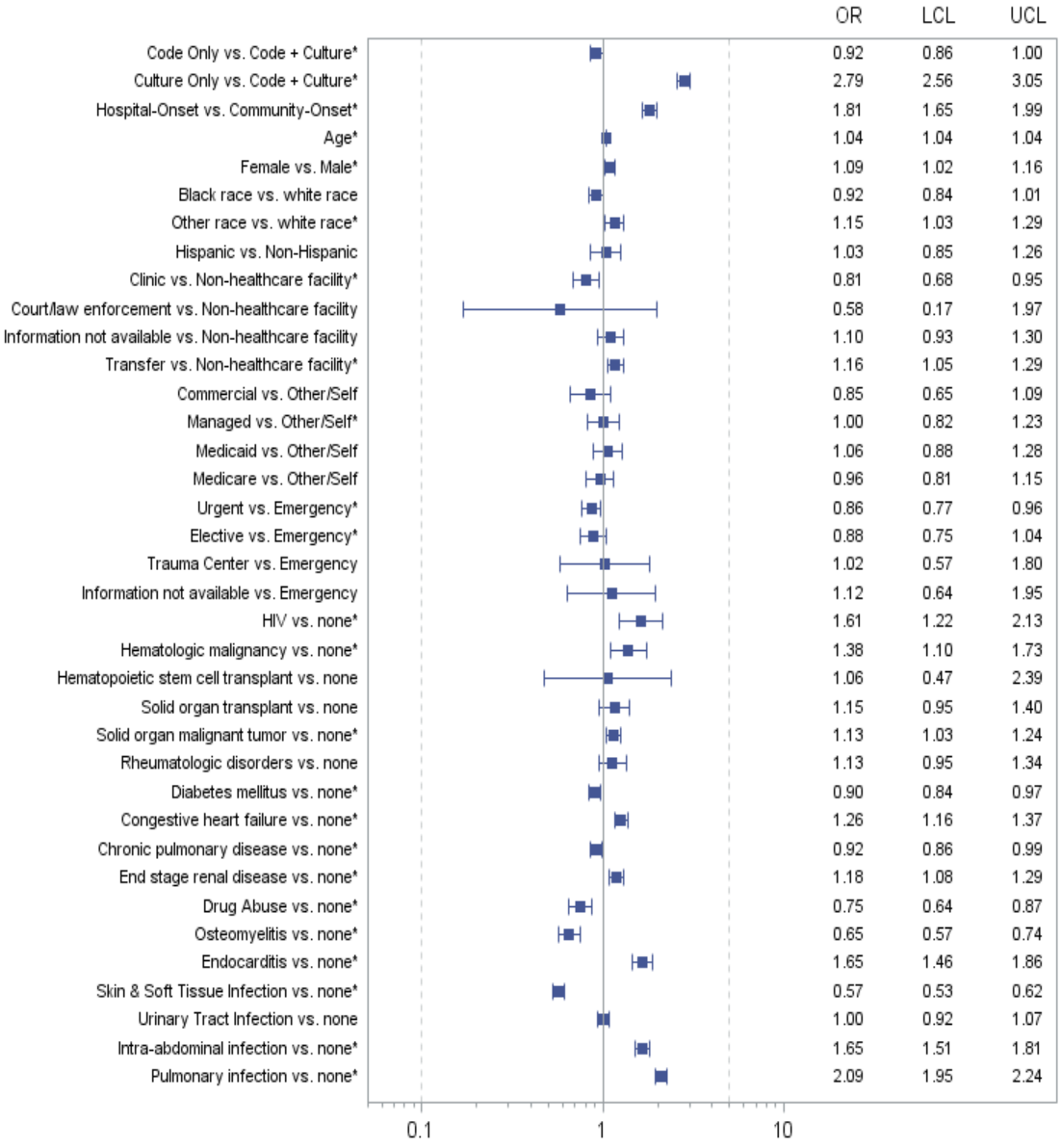
Odds Ratio and 95% Confidence Limit



*signifies statistically significant result

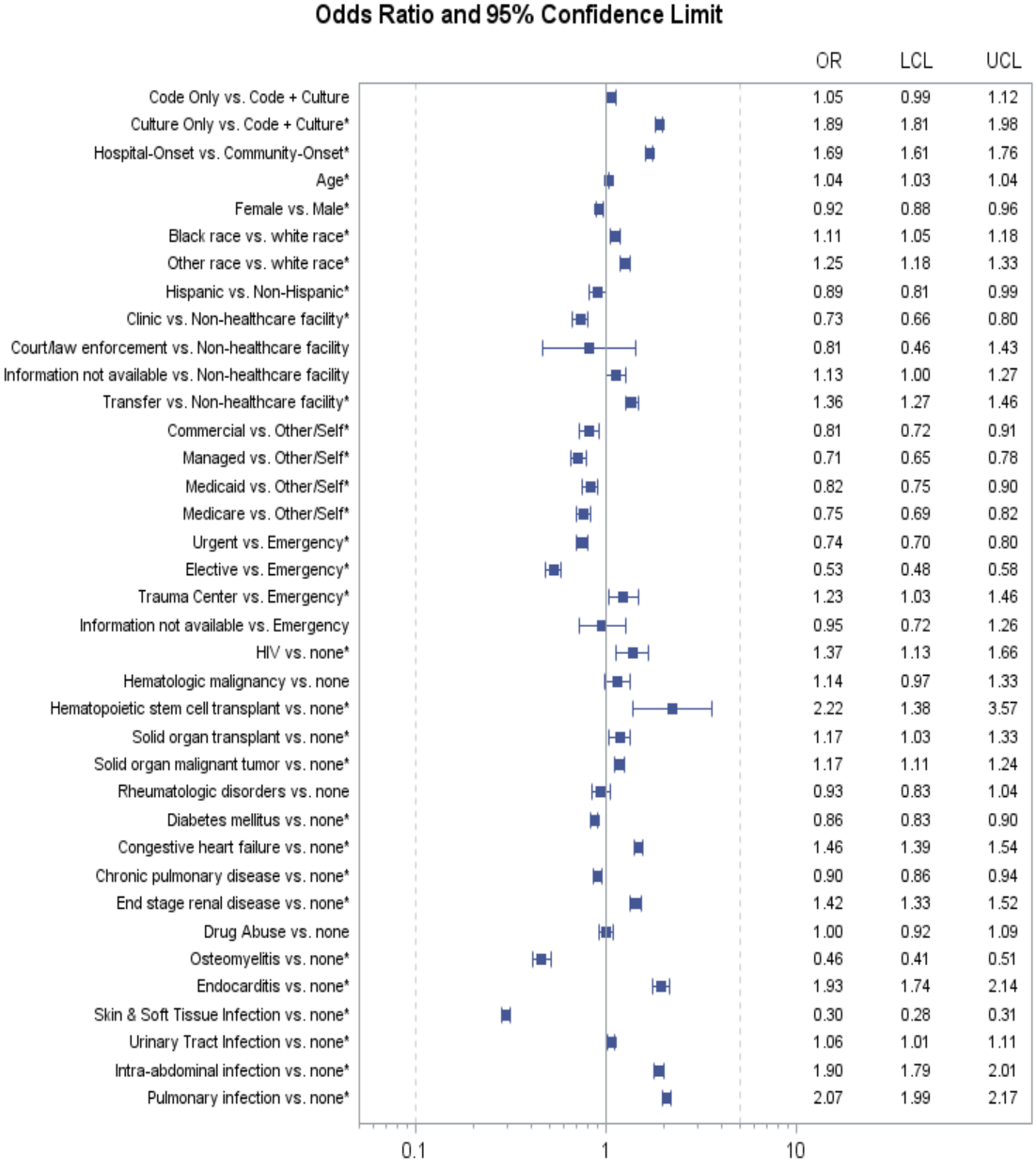
Figure 3b. Multivariable Logistic Regression Analysis of Characteristics Associated with Mortality of Patients with a MRSA Septicemia Code, Blood Culture or both, 2012-2017

Odds Ratio and 95% Confidence Limit



*signifies statistically significant result

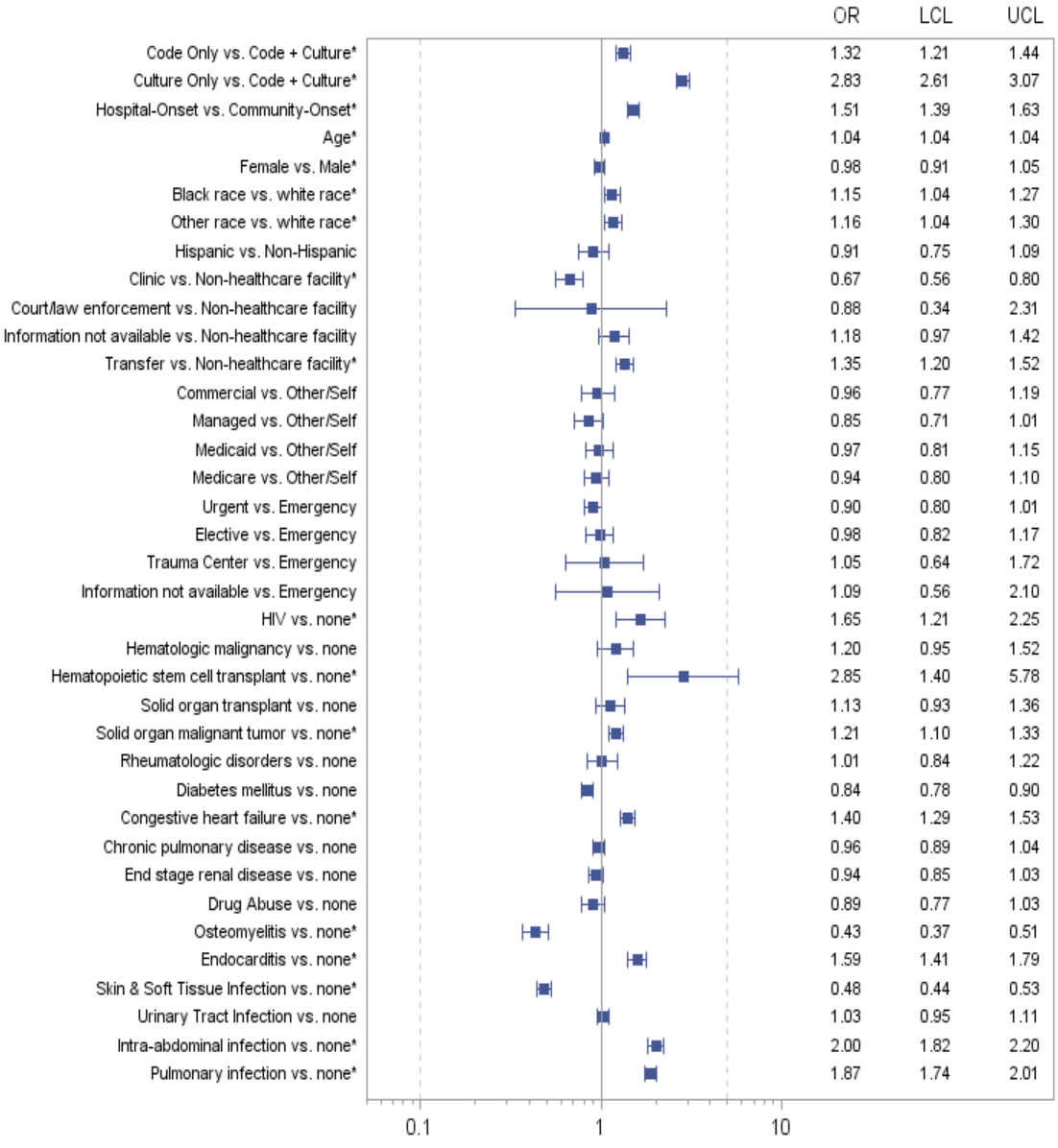
Figure 3c. Multivariable Logistic Regression Analysis of Characteristics Associated with Mortality of Patients with a MSSA Code, Culture or both, 2012-2017



*signifies statistically significant result

Figure 3d. Multivariable Logistic Regression Analysis of Characteristics Associated with Mortality of Patients with a MSSA Septicemia Code, Blood Culture or both, 2012-2017

Odds Ratio and 95% Confidence Limit



*signifies statistically significant result

Appendix

Table A1. ICD-9-CM and ICD-10-CM diagnosis codes included in analysis.

ICD Code	Description	ICD Version
038.11	Methicillin-susceptible *Staphylococcus aureus* septicemia	9
038.12	Methicillin-resistant *Staphylococcus aureus* septicemia	9
041.11	Methicillin-susceptible *Staphylococcus aureus* in conditions classified elsewhere and of unspecified site	9
041.12	Methicillin-resistant *Staphylococcus aureus* in conditions classified elsewhere and of unspecified site	9
482.41	Methicillin-susceptible *Staphylococcus aureus* pneumonia	9
482.42	Methicillin-resistant *Staphylococcus aureus* pneumonia	9
A41.01	Sepsis due to Methicillin-susceptible *Staphylococcus aureus*	10
A41.02	Sepsis due to Methicillin-resistant *Staphylococcus aureus*	10
A49.01	Methicillin-susceptible *Staphylococcus aureus* infection, unspecified site	10
A49.02	Methicillin-resistant *Staphylococcus aureus*, unspecified site	10
B95.61	Methicillin-susceptible *Staphylococcus aureus* infection as the cause of diseases classified elsewhere	10
B95.62	Methicillin-resistant *Staphylococcus aureus* infection as the cause of diseases classified elsewhere	10
J15.211	Pneumonia due to Methicillin-susceptible *Staphylococcus aureus*	10
J15.212	Pneumonia due to Methicillin-resistant *Staphylococcus aureus*	10

Table A2. ICD-9-CM and ICD-10-CM administrative codes used to identify infection type.

ICD-9-CM Code	ICD-10-CM Code
Urinary Tract	
590.00, 590.01, 590.10, 590.11, 590.2, 590.3, 590.80, 590.81, 590.9, 595.0, 595.2, 595.3, 595.4, 595.89, 595.9, 597.0,597.80, 597.89, 598.00, 598.01, 599.0, 996.64	A56.01, N10, N11.0, N11.1, N11.8, N11.9, N12, N13.6, N15.1, N15.9, N16, N28.84, N28.85, N28.86, N30.00, N30.01, N30.20, N30.21, N30.30, N30.31, N30.80, N30.81, N30.90, N30.91, N34.0, N34.1, N34.2, N35.111, N35.112, N35.113, N35.114, N35.119, N35.12, N37, N39.0, T83.510A, T83.511A, T83.512A, T83.518A
Pulmonary	
480.0–480.9, 481, 482.0–482.9, 483.0–483.8, 484.1–484.8, 485, 486, 487.0, 510.9, 513.0, 997.31, 415.12	A22.1, A37.01, A37.11, A37.81, A37.91, A48.1, B25.0, B44.0, B77.81, I26.01, I26.90, J10.00, J10.01, J10.08, J11.00, J11.08, J12.0, J12.1, J12.2, J12.3, J12.81, J12.89, J12.9, J13, J14, J15.0, J15.1, J15.20, J15.211, J15.212, J15.29, J15.3, J15.4, J15.5, J15.6, J15.7, J15.8, J15.9, J16.0, J16.8, J17, J18.0, J18.1, J18.8, J18.9, J85.0, J85.1, J85.2, J86.91, J95.851
Skin and Soft Tissue	
566, 680, 681, 682, 683, 684, 685,686, 728.86, 785.4, 958.3, 996.62, 997.62, 998.5	K61.0, K61.1, K61.2, K61.3, K61.4, L02.02, L02.03, L02.12, L02.13, L02.221, L02.222, L02.223, L02.224, L02.225, L02.226, L02.229, L02.231, L02.232, L02.233, L02.234, L02.235, L02.236, L02.239, L02.421, L02.422, L02.423, L02.424, L02.429, L02.431, L02.432, L02.433, L02.434, L02.439, L02.521, L02.522, L02.529, L02.531, L02.532, L02.539, L02.32, L02.33, L02.425, L02.426, L02.429, L02.435, L02.436, L02.439, L02.621, L02.622, L02.629, L02.631, L02.632, L02.639, L02.821, L02.828, L02.831, L02.838, L02.92, L02.93, L02.511, L02.512, L02.519, L03.011, L03.012, L03.019, L03.021, L03.022, L03.029, L02.611, L02.612, L02.619, L03.031, L03.032, L03.039, L03.041, L03.042, L03.049, K12.2, L02.01, L03.211, L03.212, L03.213, L02.11, L03.221, L03.222, L02.211, L02.212, L02.213, L02.214, L02.215, L02.216, L02.219, L03.311, L03.312, L03.313, L03.314, L03.315, L03.316, L03.319, L03.321, L03.322, L03.323, L03.324, L03.325, L03.326, L03.329, L02.411, L02.412, L02.413, L02.414, L02.419, L03.111, L03.112, L03.113, L03.114, L03.119, L03.121, L03.122, L03.123, L03.124, L03.129, L02.511, L02.512, L02.519, L02.31, L03.317, L03.327, L02.415, L02.416, L03.115, L03.116, L03.125, L03.126, L02.611, L02.612, L02.619, L02.811, L02.818, L03.811, L03.818, L03.891, L03.898, L02.91, L03.90, L03.91, L98.3, L04.0, L04.1, L04.2, L04.3, L04.8, L04.9, L01.00, L01.01, L01.02, L01.03, L01.09, L01.1, L05.01, L05.02, L05.91, L05.92, L08.0, L88, L08.81, L08.89, L92.8, L98.0, B78.1, E83.2, L08.82, L08.89, L08.9, E08.52, E09.52, E10.52, E11.52, E13.52, I70.361, I70.362, I70.363, I70.368, I70.369, I70.461, I70.462, I70.463, I70.468, I70.469, I70.561, I70.562, I70.563, I70.568, I70.569, I70.661, I70.662, I70.663, I70.668, I70.669, I70.761, I70.762, I70.763, I70.768, I70.769, I73.01, I96, T79.8XXA, T82.7XXA, T87.40, T87.41, T87.42, T87.43, T87.44, T81.4XXA, K68.11, M72.6

Intra-abdominal	
008.45, 009.0–009.3, 540.0–540.9, 541, 542, 543.9, 562.01, 562.03, 562.11, 562.13, 567.0–567.9, 569.5, 569.61, 569.71, 569.83, 572.0–572.8, 574.00–574.91, 575.0–575.9, 576.0–576.9, 614.0–614.9 and 008.8, 003.0	A02.0, A04.71, A04.72, A08.4, A08.8, A09, A56.11, K35.2, K35.3, K35.80, K35.89, K36, K37, K38.1, K38.2, K38.3, K38.8, K38.9, K50.014, K50.114, K50.814, K50.914, K51.014, K51.214, K51.314, K51.414, K51.514, K51.814, K51.914, K57.00, K57.01, K57.12, K57.13, K57.20, K57.21, K57.32, K57.33, K57.40, K57.41, K57.52, K57.53, K57.80, K57.81, K57.92, K57.93, K63.0, K63.1, K65.0, K65.1, K65.2, K65.3, K65.4, K65.8, K65.9, K67, K68.12, K68.19, K68.9, K70.41, K71.11, K72.01, K72.10, K72.11, K72.90, K72.91, K75.0, K75.1, K76.6, K76.7, K80.00, K80.01, K80.10, K80.11, K80.12, K80.13, K80.18, K80.19, K80.20, K80.21, K80.30, K80.31, K80.32, K80.33, K80.34, K80.35, K80.36, K80.37, K80.40, K80.41, K80.42, K80.43, K80.44, K80.45, K80.46, K80.47, K80.50, K80.51, K80.60, K80.61, K80.62, K80.63, K80.64, K80.65, K80.66, K80.67, K80.70, K80.71, K80.80, K80.81, K81.0, K81.1, K81.2, K81.9, K82.0, K82.1, K82.2, K82.3, K82.4, K82.8, K82.9, K83.0, K83.1, K83.2, K83.3, K83.4, K83.5, K83.8, K83.9, K87, K91.5, K91.850, K94.02, K94.12, N70.01, N70.02, N70.03, N70.11, N70.12, N70.13, N70.91, N70.92, N70.93, N73.0, N73.1, N73.2, N73.3, N73.4, N73.5, N73.6, N73.8, N73.9, N74
Endocarditis	
421, 421.1, 421.9	I33.0, I33.9, I39
Osteomyelitis	
730, 730.01, 730.02, 730.03, 730.04, 730.05, 730.06, 730.07, 730.08, 730.09, 730.2, 730.21, 730.22, 730.23, 730.24, 730.25, 730.26, 730.27, 730.28, 730.29	M86.00 M86.10 M86.20, M86.011 M86.012 M86.019 M86.111 M86.112 M86.119 M86.211 M86.212 M86.219, M86.021 M86.022 M86.029 M86.121 M86.122 M86.129 M86.221 M86.222 M86.229, M86.031 M86.032 M86.039 M86.131 M86.132 M86.139 M86.231 M86.232 M86.239, M86.041 M86.042 M86.049 M86.141 M86.142 M86.149 M86.241 M86.242 M86.249, M86.051 M86.052 M86.059 M86.151 M86.152 M86.159 M86.251 M86.252 M86.259, M86.061 M86.062 M86.069 M86.161 M86.162 M86.169 M86.261 M86.262 M86.269, M86.071 M86.072 M86.079 M86.171 M86.172 M86.179 M86.271 M86.272 M86.279, M86.08 M86.18 M86.28, M86.09 M86.19 M86.29, M86.9, M46.20 M46.21 M46.22 M46.23 M46.24 M46.25 M46.26 M46.27 M46.28

Table A3. ICD-9-CM and ICD-10-CM administrative codes used to identify comorbidities.

ICD-9-CM Code	ICD-10-CM Code
Human immunodeficiency virus infection (HIV)	
042, V08, 079.53	B20, B97.35, Z21
Hematologic malignancy (lymphoma, leukemia, and myelodysplastic syndrome)	
200, 201, 202.0, 202.1, 202.2, 202.4, 202.7, 202.8, 202.9, 203, 204, 205, 206, 207.0, 207.2, 207.8, 208, 238.7, V10.6, V10.7	C81.00, C81.01, C81.02, C81.03, C81.04, C81.05, C81.06, C81.07, C81.08, C81.09, C81.10, C81.11, C81.12, C81.13, C81.14, C81.15, C81.16, C81.17, C81.18, C81.19, C81.20, C81.21, C81.22, C81.23, C81.24, C81.25, C81.26, C81.27, C81.28, C81.29, C81.30, C81.31, C81.32, C81.33, C81.34, C81.35, C81.36, C81.37, C81.38, C81.39, C81.40, C81.41, C81.42, C81.43, C81.44, C81.45, C81.46, C81.47, C81.48, C81.49, C81.70, C81.71, C81.72, C81.73, C81.74, C81.75, C81.76, C81.77, C81.78, C81.79, C81.90, C81.91, C81.92, C81.93, C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, C82.00, C82.01, C82.02, C82.03, C82.04, C82.05, C82.06, C82.07, C82.08, C82.09, C82.10, C82.11, C82.12, C82.13, C82.14, C82.15, C82.16, C82.17, C82.18, C82.19, C82.20, C82.21, C82.22, C82.23, C82.24, C82.25, C82.26, C82.27, C82.28, C82.29, C82.30, C82.31, C82.32, C82.33, C82.34, C82.35, C82.36, C82.37, C82.38, C82.39, C82.40, C82.41, C82.42, C82.43, C82.44, C82.45, C82.46, C82.47, C82.48, C82.49, C82.50, C82.51, C82.52, C82.53, C82.54, C82.55, C82.56, C82.57, C82.58, C82.59, C82.60, C82.61, C82.62, C82.63, C82.64, C82.65, C82.66, C82.67, C82.68, C82.69, C82.80, C82.81, C82.82, C82.83, C82.84, C82.85, C82.86, C82.87, C82.88, C82.89, C82.90, C82.91, C82.92, C82.93, C82.94, C82.95, C82.96, C82.97, C82.98, C82.99, C83.00, C83.01, C83.02, C83.03, C83.04, C83.05, C83.06, C83.07, C83.08, C83.09, C83.10, C83.11, C83.12, C83.13, C83.14, C83.15, C83.16, C83.17, C83.18, C83.19, C83.30, C83.31, C83.32, C83.33, C83.34, C83.35, C83.36, C83.37, C83.38, C83.39, C83.50, C83.51, C83.52, C83.53, C83.54, C83.55, C83.56, C83.57, C83.58, C83.59, C83.70, C83.71, C83.72, C83.73, C83.74, C83.75, C83.76, C83.77, C83.78, C83.79, C83.80, C83.81, C83.82, C83.83, C83.84, C83.85, C83.86, C83.87, C83.88, C83.89, C83.90, C83.91, C83.92, C83.93, C83.94, C83.95, C83.96, C83.97, C83.98, C83.99, C84.00, C84.01, C84.02, C84.03, C84.04, C84.05, C84.06, C84.07, C84.08, C84.09, C84.10, C84.11, C84.12, C84.13, C84.14, C84.15, C84.16, C84.17, C84.18, C84.19, C84.40, C84.41, C84.42, C84.43, C84.44, C84.45, C84.46, C84.47, C84.48, C84.49, C84.60, C84.61, C84.62, C84.63, C84.64, C84.65, C84.66, C84.67, C84.68, C84.69, C84.70, C84.71, C84.72, C84.73, C84.74, C84.75, C84.76, C84.77, C84.78, C84.79, C84.90, C84.91, C84.92, C84.93, C84.94, C84.95, C84.96,

	C84.97, C84.98, C84.99, C84.A0, C84.A1, C84.A2, C84.A3, C84.A4, C84.A5, C84.A6, C84.A7, C84.A8, C84.A9, C84.Z0, C84.Z1, C84.Z2, C84.Z3, C84.Z4, C84.Z5, C84.Z6, C84.Z7, C84.Z8, C84.Z9, C85.10, C85.11, C85.12, C85.13, C85.14, C85.15, C85.16, C85.17, C85.18, C85.19, C85.20, C85.21, C85.22, C85.23, C85.24, C85.25, C85.26, C85.27, C85.28, C85.29, C85.80, C85.81, C85.82, C85.83, C85.84, C85.85, C85.86, C85.87, C85.88, C85.89, C85.90, C85.91, C85.92, C85.93, C85.94, C85.95, C85.96, C85.97, C85.98, C85.99, C86.0, C86.1, C86.2, C86.3, C86.4, C86.5, C86.6, C88.2, C88.3, C88.4, C88.8, C88.9, C90.00, C90.01, C90.02, C90.10, C90.11, C90.20, C90.21, C90.22, C90.30, C90.31, C90.32, C90.12, C91.00, C91.01, C91.02, C91.10, C91.11, C91.12, C91.30, C91.31, C91.32, C91.40, C91.41, C91.42, C91.50, C91.51, C91.52, C91.60, C91.61, C91.62, C91.90, C91.91, C91.92, C91.A0, C91.A1, C91.A2, C91.Z0, C91.Z1, C91.Z2, C92.00, C92.01, C92.02, C92.10, C92.11, C92.12, C92.20, C92.21, C92.22, C92.30, C92.31, C92.32, C92.40, C92.41, C92.42, C92.50, C92.51, C92.52, C92.60, C92.61, C92.62, C92.90, C92.91, C92.92, C92.A0, C92.A1, C92.A2, C92.Z0, C92.Z1, C92.Z2, C93.00, C93.01, C93.02, C93.10, C93.11, C93.12, C93.30, C93.31, C93.32, C93.90, C93.91, C93.92, C93.Z0, C93.Z1, C93.Z2, C94.00, C94.01, C94.02, C94.20, C94.21, C94.22, C94.30, C94.31, C94.32, C94.40, C94.41, C94.42, C94.6, C94.80, C94.81, C94.82, C95.00, C95.01, C95.02, C95.10, C95.11, C95.12, C95.90, C95.91, C95.92, C96.4, C96.9, C96.Z, D46.0, D46.1, D46.20, D46.21, D46.22, D46.4, D46.9, D46.A, D46.B, D46.C, D46.Z, D47.1, D47.3, D47.4, D47.9, D47.Z1, D47.Z2, D47.Z9, Z85.6, Z85.72, Z85.71, Z85.79, Z85.831
Hematopoietic stem cell transplant	
V42.81, V42.82, 996.85, 996.88	T86.00, T86.01, T86.02, T86.03, T86.09, T86.5, Z48.290, Z94.81, Z94.84
Solid organ transplant (heart, liver, kidney, lung, pancreas, and intestine)	
V42.0, V42.1, V42.2, V42.4, V42.6, V42.7, V42.83, V42.84, V42.89, 996.80, 996.81, 996.82, 996.83, 996.84, 996.86, 996.87	T86.10, T86.11, T86.12, T86.13, T86.19, T86.20, T86.21, T86.22, T86.23, T86.290, T86.298, T86.30, T86.31, T86.32, T86.33, T86.39, T86.40, T86.41, T86.42, T86.43, T86.49, T86.810, T86.811, T86.812, T86.818, T86.819, T86.850, T86.851, T86.852, T86.858, T86.859, T86.890, T86.891, T86.892, T86.898, T86.899, T86.90, T86.91, T86.92, T86.93, T86.99, Z48.22, Z48.21, Z48.23, Z48.24, Z48.280, Z48.298, Z94.0, Z94.1, Z94.2, Z94.3, Z94.4, Z94.6, Z94.82, Z94.83, Z94.89, Z95.2, Z95.3, Z95.4
Solid organ malignant tumor (excluding skin tumor)	
140-171, 174-199, V10.0-5,8,9	C00.0, C00.1, C00.2, C00.3, C00.4, C00.5, C00.6, C00.8, C00.9, C01, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.9, C05.0, C05.1, C05.2, C05.8, C05.9, C06.0, C06.1, C06.2, C06.80, C06.89, C06.9, C07,

	C08.0, C08.1, C08.9, C09.0, C09.1, C09.8, C09.9, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C11.0, C11.1, C11.2, C11.3, C11.8, C11.9, C12, C13.0, C13.1, C13.2, C13.8, C13.9, C14.0, C14.2, C14.8, C15.3, C15.4, C15.5, C15.8, C15.9, C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, C16.9, C17.0, C17.1, C17.2, C17.3, C17.8, C17.9, C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19, C20, C21.0, C21.1, C21.2, C21.8, C22.0, C22.1, C22.2, C22.3, C22.4, C22.7, C22.8, C22.9, C23, C24.0, C24.1, C24.8, C24.9, C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, C26.0, C26.1, C26.9, C30.0, C30.1, C31.0, C31.1, C31.2, C31.3, C31.8, C31.9, C32.0, C32.1, C32.2, C32.3, C32.8, C32.9, C33, C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.2, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90, C34.91, C34.92, C37, C38.0, C38.1, C38.2, C38.3, C38.4, C38.8, C39.0, C39.9, C40.00, C40.01, C40.02, C40.10, C40.11, C40.12, C40.20, C40.21, C40.22, C40.30, C40.31, C40.32, C40.80, C40.81, C40.82, C40.90, C40.91, C40.92, C41.0, C41.1, C41.2, C41.3, C41.4, C41.9, C45.0, C45.1, C45.2, C45.7, C45.9, C46.0, C46.1, C46.2, C46.3, C46.4, C46.50, C46.51, C46.52, C46.7, C46.9, C47.0, C47.10, C47.11, C47.12, C47.20, C47.21, C47.22, C47.3, C47.4, C47.5, C47.6, C47.8, C47.9, C49.20, C49.21, C49.22, C48.0, C48.1, C48.2, C48.8, C49.0, C49.10, C49.11, C49.12, C49.3, C49.4, C49.5, C49.6, C49.8, C49.9, C49.A0, C49.A1, C49.A2, C49.A3, C49.A4, C49.A5, C49.A9, C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329, C50.411, C50.412, C50.419, C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, C51.0, C51.1, C51.2, C51.8, C51.9, C52, C53.0, C53.1, C53.8, C53.9, C54.0, C54.1, C54.2, C54.3, C54.8, C54.9, C55, C56.1, C56.2, C56.9, C57.00, C57.01, C57.02, C57.10, C57.11, C57.12, C57.20, C57.21, C57.22, C57.3, C57.4, C57.7, C57.8, C57.9, C58, C60.0, C60.1, C60.2, C60.8, C60.9, C61, C62.00, C62.01, C62.02, C62.10, C62.11, C62.12, C62.90, C62.91, C62.92, C63.00, C63.01, C63.02, C63.10, C63.11, C63.12, C63.2, C63.7, C63.8, C63.9, C64.1, C64.2, C64.9, C65.1, C65.2, C65.9, C66.1, C66.2, C66.9, C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.7, C67.8, C67.9, C68.0, C68.1, C68.8, C68.9, C69.00, C69.01, C69.02, C69.10, C69.11, C69.12, C69.20, C69.21, C69.22, C69.30, C69.31, C69.32, C69.40, C69.41, C69.42, C69.50, C69.51, C69.52, C69.60, C69.61, C69.62, C69.80, C69.81, C69.82, C69.90, C69.91, C69.92, C70.0, C70.1, C70.9, C71.0, C71.1, C71.2,

	C71.3, C71.4, C71.5, C71.6, C71.7, C71.8, C71.9, C72.0, C72.1, C72.20, C72.21, C72.22, C72.30, C72.31, C72.32, C72.40, C72.41, C72.42, C72.50, C72.59, C72.9, C73, C74.00, C74.01, C74.02, C74.10, C74.11, C74.12, C74.90, C74.91, C74.92, C75.0, C75.1, C75.2, C75.3, C75.4, C75.5, C75.8, C75.9, C76.0, C76.1, C76.2, C76.3, C76.40, C76.41, C76.42, C76.50, C76.51, C76.52, C76.8, C77.0, C77.1, C77.2, C77.3, C77.4, C77.5, C77.8, C77.9, C78.00, C78.01, C78.02, C78.1, C78.2, C78.30, C78.39, C78.4, C78.5, C78.6, C78.7, C78.80, C78.89, C79.00, C79.01, C79.02, C79.10, C79.11, C79.19, C79.2, C79.31, C79.32, C79.40, C79.49, C71.51, C79.52, C79.60, C79.61, C79.62, C79.70, C79.71, C79.72, C79.81, C79.82, C79.89, C79.9, C80.0, C80.1, C80.2, Z85.00, Z85.01, Z85.020, Z85.028, Z85.030, Z85.038, Z85.040, Z85.048, Z85.05, Z85.060, Z85.068, Z85.07, Z85.09, Z85.110, Z85.12, Z85.118, Z85.20, Z85.21, Z85.22, Z85.230, Z85.238, Z85.29, Z85.3, Z85.40, Z85.41, Z85.42, Z85.43, Z85.44, Z85.45, Z85.46, Z48.47, Z85.48, Z85.49, Z85.50, Z85.51, Z85.520, Z85.528, Z85.53, Z85.54, Z85.59, Z85.810, Z85.818, Z85.819, Z85.820, Z85.821, Z85.828, Z85.830, Z85.831, Z85.840, Z85.841, Z85.848, Z85.850, Z85.858, Z85.89, Z85.9
Rheumatologic disorders (systemic lupus erythematosus, systemic sclerosis, dermatomyositis, polymyositis, rheumatoid arthritis, giant cell arteritis)	
446.5, 710.0-4, 714.0-2, 714.8, 725	M05.00, M05.011, M05.012, M05.019, M05.021, M05.022, M05.029, M05.031, M05.032, M05.039, M05.041, M05.042, M05.049, M05.051, M05.052, M05.059, M05.061, M05.062, M05.069, M05.071, M05.072, M05.079, M05.09, M05.10, M05.111, M05.112, M05.119, M05.121, M05.122, M05.129, M05.131, M05.132, M05.139, M05.141, M05.142, M05.149, M05.151, M05.152, M05.159, M05.161, M05.162, M05.169, M05.171, M05.172, M05.179, M05.19, M05.20, M05.211, M05.212, M05.219, M05.221, M05.222, M05.229, M05.231, M05.232, M05.239, M05.241, M05.242, M05.249, M05.251, M05.252, M05.529, M05.261, M05.262, M05.269, M05.271, M05.727, M05.279, M05.29, M05.30, M05.311, M05.312, M05.319, M05.321, M05.322, M05.329, M05.331, M05.332, M05.339, M05.341, M05.342, M05.349, M05.351, M05.352, M05.359, M05.361, M05.362, M05.369, M05.371, M05.372, M05.379, M05.39, M05.60, M05.611, M05.612, M05.619, M05.40, M05.411, M05.412, M05.419, M05.421, M05.422, M05.429, M05.431, M05.432, M05.439, M05.441, M05.442, M05.449, M05.451, M05.452, M05.459, M05.461, M05.462, M05.469, M05.471, M05.472, M05.479, M05.49, M05.50, M05.511, M05.512, M05.519, M05.521, M05.522, M05.529, M05.531, M05.532, M05.539, M05.541, M05.542, M05.549, M05.551, M05.552, M05.559, M05.561, M05.562, M05.569, M05.571, M05.572, M05.579, M05.59, M05.70, M05.711, M05.712, M05.719, M06.4, M31.5, M31.6, M32.0, M32.10,

	M32.11, M32.12, M32.13, M32.14, M32.15, M32.19, M32.8, M32.9, M33.00, M33.01, M33.02, M33.03, M33.09, M33.10, M33.11, M33.12, M33.13, M33.19, M33.20, M33.21, M33.22, M33.29, M33.90, M33.91, M33.92, M33.93, M33.99, M34.0, M34.1, M34.2, M34.81, M34.82, M34.83, M34.89, M34.9, M35.00, M35.01, M35.02, M35.03, M35.04, M35.09, M35.3, M36.0
Diabetes mellitus	
250.0-9	E10.10, E10.11, E10.21, E10.22, E10.29, E10.311, E10.319, E10.3211, E10.3212, E10.3213, E10.3219, E10.3291, E10.3292, E10.3293, E10.3299, E10.3311, E10.3312, E10.3313, E10.3319, E10.3391, E10.3392, E10.3393, E10.3399, E10.3411, E10.3412, E10.3413, E10.3419, E10.3491, E10.3492, E10.3493, E10.3499, E10.3511, E10.3512, E10.3513, E10.3519, E10.3521, E10.3522, E10.3523, E10.3529, E10.3531, E10.3532, E10.3533, E10.3539, E10.3541, E10.3542, E10.3543, E10.3549, E10.3551, E10.3552, E10.3553, E10.3559, E10.3591, E10.3592, E10.3593, E10.3599, E10.641, E10.65, E10.69, E10.9, E11.00, E11.01, E11.10, E11.11, E11.21, E11.22, E11.29, E11.311, E11.319, E11.3211, E11.3212, E11.3213, E11.3219, E11.3291, E11.3292, E11.3293, E11.3299, E11.3311, E11.3312, E11.3313, E11.3319, E11.3391, E11.3392, E11.3393, E11.3399, E11.3411, E11.3412, E11.3413, E11.3419, E11.3491, E11.3492, E11.3493, E11.3499, E11.3511, E11.3512, E11.3513, E11.3519, E11.3521, E11.3522, E11.3523, E11.3529, E11.3531, E11.3532, E11.3533, E11.3539, E11.3541, E11.3542, E11.3543, E11.3549, E11.3551, E11.3552, E11.3553, E11.3559, E11.3591, E11.3592, E11.3593, E11.3599, E11.641, E11.65, E11.69, E11.9, E13.00, E13.01, E13.10, E13.11, E13.21, E13.22, E13.29, E13.641, E13.9
Congestive heart failure	
398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4-9, 428	A18.84, E63.9, I09.81, I11.0, I13.0, I13.2, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9, I43, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.814, I50.9
Chronic pulmonary disease	
416.8-9, 490–505, 506.4, 508.1, 508.8	I27.20, I27.21, I27.22, I27.23, I27.24, I27.29, I27.81, I27.89, I27.9, J40, J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9, J45.20, J45.21, J45.22, J45.30, J45.31, J45.32, J45.40, J45.41, J45.42, J45.50, J45.51, J45.52, J45.901, J45.902, J45.909, J45.990, J45.991, J45.998, J47.0, J47.1, J47.9, J60, J61, J62.0, J62.8, J63.0, J63.1, J63.2, J63.3, J63.4, J63.5, J63.6, J64, J65, J66.0, J66.1, J66.2, J66.8, J67.0, J67.1, J67.2, J67.3, J67.4, J67.5, J67.6, J67.7, J67.8, J67.9, J68.4, J70.1, J70.2, J70.3, J70.4, J70.8
End stage renal disease (stage 5 or dependence on dialysis)	
403.01, 403.11, 403.91, 404.02-3, 404.12-3, 404.92-3, 585.5-6	I12.0, I13.11, I13.2, N18.5, N18.6
Drug abuse	

304.0-9, 305.2-9	F11.10, F11.11, F11.120, F11.129, F11.20, F11.21, F11.220, F11.221, F11.222, F11.229, F11.23, F11.24, F11.250, F11.251, F11.259, F11.281, F11.282, F11.288, F11.29, F11.90, F12.10, F12.11, F12.20, F12.21, F12.220, F12.221, F12.222, F12.229, F12.250, F12.251, F12.259, F12.280, F12.288, F12.29, F12.90, F13.10, F13.11, F13.120, F13.20, F13.21, F13.220, F13.221, F13.229, F13.230, F13.231, F13.232, F13.239, F13.24, F13.250, F13.251, F13.259, F13.26, F13.27, F13.280, F13.281, F13.282, F13.288, F13.29, F13.90, F14.10, F14.11, F14.120, F14.20, F14.21, F14.220, F14.221, F14.222, F14.229, F14.23, F14.24, F14.250, F14.251, F14.259, F14.280, F14.281, F14.282, F14.288, F14.29, F14.90, F15.10, F15.11, F15.120, F15.20, F15.21, F15.220, F15.221, F15.222, F15.229, F15.23, F15.24, F15.250, F15.251, F15.259, F15.280, F15.281, F15.282, F15.288, F15.29, F15.90, F16.10, F16.11, F16.120, F16.20, F16.21, F16.220, F16.221, F16.229, F16.24, F16.250, F16.251, F16.259, F16.280, F16.283, F16.288, F16.29, F16.90, F18.10, F18.11, F18.120, F18.20, F18.21, F18.220, F18.221, F18.229, F18.24, F18.250, F18.251, F18.259, F18.27, F18.280, F18.288, F18.29, F18.90, F19.10, F19.11, F19.120, F19.20, F19.21, F19.220, F19.221, F19.222, F19.229, F19.230, F19.231, F19.232, F19.239, F19.24, F19.250, F19.251, F19.259, F19.26, F19.27, F19.280, F19.281, F19.282, F19.288, F19.29, F19.90, F55.0, F55.1, F55.2, F55.3, F55.4, F55.8

Table A4a. Negative binomial regression results for *S. aureus* code and culture rates, overall and septicemia.

	***S. aureus* culture**	***S. aureus* code**	***S. aureus* blood culture**	***S. aureus* septicemia code**
	IRR (95% CI)	**IRR (95% CI)**	**IRR (95% CI)**	**IRR (95% CI)**
Discharge Year	0.97 (0.95, 0.98)	0.99 (0.97, 1.00)	0.99 (0.98, 1.01)	1.04 (1.02, 1.06)
Discharge Month				
January	1.02 (0.99, 1.05)	1.02 (0.99, 1.04)	0.95 (0.90, 1.00)	0.99 (0.94, 1.04)
February	0.99 (0.95, 1.02)	1.04 (1.01, 1.06)	0.97 (0.92, 1.02)	0.98 (0.94, 1.03)
March	0.97 (0.94, 1.00)	1.01 (0.99, 1.04)	0.92 (0.87, 0.96)	0.98 (0.93, 1.02)
April	1.01 (0.98, 1.04)	1.03 (1.00, 1.05)	0.96 (0.91, 1.02)	1.02 (0.97, 1.07)
May	1.01 (0.98, 1.05)	1.03 (1.01, 1.06)	0.99 (0.95, 1.04)	1.03 (0.98, 1.08)
June	1.05 (1.02, 1.09)	1.05 (1.02, 1.08)	0.99 (0.94, 1.05)	1.00 (0.95, 1.05)
July	1.08 (1.04, 1.11)	1.09 (1.06, 1.12)	1.03 (0.98, 1.09)	1.05 (1.00, 1.10)
August	1.08 (1.05, 1.11)	1.09 (1.06, 1.12)	1.00 (0.95, 1.06)	1.06 (1.01, 1.11)
September	1.08 (1.05, 1.11)	1.11 (1.08, 1.14)	1.02 (0.97, 1.08)	1.05 (1.00, 1.10)
October	1.04 (1.02, 1.07)	1.07 (1.05, 1.10)	0.98 (0.93, 1.04)	1.05 (1.00, 1.11)
November	1.00 (0.97, 1.02)	1.01 (0.98, 1.03)	0.94 (0.89, 0.99)	0.97 (0.92, 1.02)
December	Reference	Reference	Reference	Reference
Region				
New England	0.56 (0.45, 0.70)	0.64 (0.51, 0.79)	0.76 (0.61, 0.94)	0.75 (0.59, 0.95)
Mid-Atlantic	0.77 (0.66, 0.90)	0.69 (0.60, 0.80)	1.00 (0.83, 1.21)	0.80 (0.66, 0.97)
South Atlantic	0.67 (0.56, 0.81)	0.69 (0.56, 0.85)	0.81 (0.60, 1.09)	0.70 (0.56, 0.89)
Northeast Central	0.67 (0.59, 0.76)	0.72 (0.63, 0.82)	0.72 (0.61, 0.85)	0.64 (0.53, 0.79)
Southeast Central	0.79 (0.55, 1.13)	0.96 (0.78, 1.18)	1.06 (0.67, 1.69)	0.83 (0.61, 1.13)
Northwest Central	0.71 (0.62, 0.82)	0.84 (0.74, 0.95)	0.99 (0.84, 1.17)	0.84 (0.70, 1.01)
Southwest Central	0.69 (0.58, 0.83)	0.74 (0.63, 0.87)	0.82 (0.70, 0.98)	0.72 (0.57, 0.91)
Mountain	0.83 (0.64, 1.07)	0.90 (0.71, 1.14)	0.92 (0.76, 1.11)	0.93 (0.72, 1.22)
Pacific	Reference	Reference	Reference	Reference
No. of beds, <300	1.10 (0.98, 1.22)	1.03 (0.95, 1.13)	1.13 (1.02, 1.26)	1.03 (0.93, 1.15)
No. of beds, ≥300	Reference	Reference	Reference	Reference
Rural	0.93 (0.82, 1.06)	0.99 (0.91, 1.08)	0.85 (0.71, 1.01)	0.97 (0.84, 1.12)
Urban	Reference	Reference	Reference	Reference
Non-Teaching	0.92 (0.84, 1.02)	0.91 (0.83, 0.99)	0.96 (0.85, 1.09)	0.88 (0.78, 1.00)
Teaching	Reference	Reference	Reference	Reference
Percent of Discharges by Age Group				

Percent of discharges aged 0	0.04 (0.02, 0.08)	0.11 (0.04, 0.29)	0.11 (0.03, 0.38)	0.19 (0.04, 0.96)
Percent of discharges aged 1-17	0.24 (0.07, 0.84)	0.19 (0.08, 0.46)	0.30 (0.03, 2.70)	0.09 (0.005, 1.81)
Percent of discharges aged 45-64	0.67 (0.33, 1.36)	0.72 (0.29, 1.77)	0.86 (0.13, 5.50)	0.97 (0.14, 6.56)
Percent of discharges aged 65-84	0.43 (0.21, 0.89)	0.64 (0.24, 1.71)	0.50 (0.10, 2.51)	0.49 (0.07, 3.24)
Percent of discharges aged 85+	1.02 (0.64, 1.60)	1.87 (1.04, 3.38)	1.16 (0.59, 2.30)	2.47 (1.12, 5.45)
Percent of discharges aged 18-44	Reference	Reference	Reference	Reference
Percent of discharges White race	1.09 (0.93, 1.29)	1.20 (1.02, 1.40)	0.77 (0.63, 0.94)	0.94 (0.73, 1.21)
Percent of discharges Male gender	1.50 (1.01, 2.24)	2.82 (1.70, 4.69)	4.85 (1.73, 13.59)	9.39 (3.20, 27.56)

Table A4b. Negative binomial regression results for MRSA code and culture rates, overall and septicemia.

	MRSA culture	MRSA code	MRSA blood culture	MRSA septicemia code
	IRR 95% CI	**IRR 95% CI**	**IRR 95% CI**	**IRR 95% CI**
Discharge Year	0.95 (0.93, 0.97)	0.96 (0.95, 0.98)	0.99 (0.97, 1.01)	1.02 (1.00, 1.03)
Discharge Month				
January	1.03 (0.99, 1.07)	1.03 (1.00, 1.07)	0.99 (0.93, 1.06)	1.00 (0.93, 1.06)
February	1.00 (0.97, 1.04)	1.04 (1.01, 1.08)	0.96 (0.90, 1.03)	0.99 (0.93, 1.05)
March	0.98 (0.94, 1.02)	1.03 (1.00, 1.06)	0.93 (0.86, 0.99)	0.95 (0.90, 1.01)
April	1.03 (0.99, 1.06)	1.04 (1.01, 1.07)	0.99 (0.92, 1.05)	1.00 (0.94, 1.06)
May	1.02 (0.98, 1.06)	1.04 (1.00, 1.07)	1.01 (0.94, 1.07)	1.04 (0.97, 1.11)
June	1.03 (1.00, 1.07)	1.04 (1.01, 1.07)	0.97 (0.90, 1.04)	0.97 (0.91, 1.04)
July	1.07 (1.02, 1.11)	1.08 (1.04, 1.11)	1.00 (0.93, 1.08)	1.03 (0.96, 1.10)
August	1.06 (1.03, 1.10)	1.07 (1.04, 1.11)	1.01 (0.95, 1.08)	1.04 (0.97, 1.11)
September	1.09 (1.05, 1.13)	1.11 (1.07, 1.15)	0.97 (0.91, 1.04)	1.01 (0.95, 1.07)
October	1.04 (1.01, 1.07)	1.07 (1.03, 1.10)	0.99 (0.92, 1.06)	1.00 (0.94, 1.08)
November	1.00 (0.96, 1.03)	1.00 (0.97, 1.03)	0.93 (0.87, 0.99)	0.95 (0.89, 1.01)
December	Reference	Reference	Reference	Reference
Region				
New England	0.52 (0.40, 0.68)	0.61 (0.48, 0.78)	0.73 (0.52, 1.03)	0.79 (0.60, 1.05)
Mid-Atlantic	0.83 (0.71, 0.98)	0.69 (0.59, 0.81)	0.98 (0.80, 1.20)	0.85 (0.71, 1.02)
South Atlantic	0.72 (0.57, 0.92)	0.70 (0.52, 0.92)	0.80 (0.59, 1.09)	0.63 (0.50, 0.81)
Northeast Central	0.77 (0.67, 0.90)	0.77 (0.66, 0.89)	0.78 (0.64, 0.95)	0.76 (0.62, 0.93)
Southeast Central	1.09 (0.76, 1.58)	1.21 (0.96, 1.52)	1.32 (0.81, 2.14)	1.29 (0.94, 1.76)
Northwest Central	0.90 (0.78, 1.04)	0.96 (0.84, 1.10)	1.17 (0.96, 1.42)	1.13 (0.94, 1.36)
Southwest Central	0.81 (0.67, 0.97)	0.83 (0.70, 1.00)	0.87 (0.71, 1,06)	0.90 (0.72, 1.12)
Mountain	0.97 (0.67, 1.40)	0.95 (0.67, 1.35)	1.09 (0.82, 1.45)	1.06 (0.77, 1.45)
Pacific	Reference	Reference	Reference	Reference
No. of beds, <300	1.09 (0.96, 1.23)	1.02 (0.92, 1.13)	1.16 (1.03, 1.31)	1.05 (0.94, 1.17)
No. of beds, ≥300	Reference	Reference	Reference	Reference
Rural	0.92 (0.80, 1.06)	1.01 (0.91, 1.12)	0.85 (0.70, 1.03)	0.94 (0.82, 1.08)
Urban	Reference	Reference	Reference	Reference
Non-Teaching	0.93 (0.83, 1.04)	0.95 (0.86, 1.05)	0.90 (0.78, 1.05)	0.92 (0.81, 1.04)
Teaching	Reference	Reference	Reference	Reference
Percent of Discharges by Age Group				
Percent of discharges aged 0	0.02 (0.01, 0.07)	0.08 (0.02, 0.31)	0.04 (0.01, 0.22)	0.11 (0.02, 0.62)
Percent of discharges aged 1-17	0.23 (0.06, 0.97)	0.26 (0.08, 0.83)	0.24 (0.02, 2.39)	0.18 (0.02, 2.05)

Percent of discharges aged 45-64	0.70 (0.27, 1.83)	0.97 (0.33, 2.87)	0.87 (0.10, 7.26)	1.49 (0.19, 11.37)
Percent of discharges aged 65-84	0.34 (0.13, 0.84)	0.55 (0.18, 1.74)	0.30 (0.05, 1.78)	0.22 (0.04, 1.38)
Percent of discharges aged 85+	1.23 (0.69, 2.17)	2.27 (1.04, 4.93)	0.96 (0.40, 2.30)	1.95 (0.81, 4.73)
Percent of discharges aged 18-44	Reference	Reference	Reference	Reference
Percent of discharges White race	1.05 (0.86, 1.29)	1.26 (1.03, 1.55)	0.76 (0.60, 0.98)	0.90 (0.71, 1.15)
Percent of discharges Male gender	1.44 (0.80, 2.58)	2.01 (1.06, 3.83)	4.38 (1.16, 16.53)	7.93 (2.16, 29.11)

Table A4c. Negative binomial regression results for MSSA code and culture rates, overall and septicemia.

	MSSA culture	MSSA code	MSSA blood culture	MSSA septicemia code
	IRR 95% CI	**IRR 95% CI**	**IRR 95% CI**	**IRR 95% CI**
Discharge Year	0.99 (0.97, 1.00)	1.02 (1.01, 1.03)	1.02 (1.00, 1.04)	1.04 (1.02, 1.06)
Discharge Month				
January	1.01 (0.97, 1.04)	0.99 (0.96, 1.03)	0.94 (0.88, 1.00)	0.96 (0.91, 1.02)
February	0.98 (0.94, 1.02)	1.03 (1.00, 1.07)	0.95 (0.90, 1.01)	1.03 (0.96, 1.09)
March	0.97 (0.93, 1.00)	1.00 (0.97, 1.03)	0.92 (0.86, 0.98)	0.99 (0.93, 1.05)
April	1.00 (0.96, 1.04)	1.02 (0.99, 1.06)	0.96 (0.90, 1.03)	1.01 (0.95, 1.09)
May	1.02 (0.98, 1.06)	1.04 (1.01, 1.08)	0.99 (0.93, 1.05)	1.02 (0.96, 1.08)
June	1.06 (1.02, 1.10)	1.07 (1.03, 1.10)	1.00 (0.94, 1.06)	1.02 (0.96, 1.09)
July	1.09 (1.05, 1.13)	1.11 (1.07, 1.15)	1.05 (0.99, 1.12)	1.08 (1.01, 1.14)
August	1.09 (1.05, 1.13)	1.12 (1.08, 1.17)	1.02 (0.95, 1.09)	1.08 (1.01, 1.16)
September	1.07 (1.03, 1.11)	1.11 (1.07, 1.16)	1.07 (1.00, 1.13)	1.10 (1.03, 1.17)
October	1.04 (1.01, 1.08)	1.09 (1.05, 1.13)	1.00 (0.93, 1.07)	1.08 (1.01, 1.15)
November	1.00 (0.97, 1.04)	1.03 (1.00, 1.07)	0.95 (0.90, 1.00)	1.00 (0.95, 1.06)
December	Reference	Reference	Reference	Reference
Region				
New England	0.61 (0.50, 0.73)	0.68 (0.54, 0.73)	0.77 (0.63, 0.93)	0.81 (0.65, 1.01)
Mid-Atlantic	0.75 (0.63, 0.88)	0.70 (0.59, 0.82)	0.91 (0.76, 1.08)	0.86 (0.71, 1.04)
South Atlantic	0.66 (0.56, 0.79)	0.71 (0.60, 0.84)	0.82 (0.67, 1.02)	0.81 (0.66, 0.99)
Northeast Central	0.61 (0.53, 0.71)	0.68 (0.58, 0.80)	0.63 (0.53, 0.74)	0.64 (0.54, 0.77)
Southeast Central	0.58 (0.40, 0.83)	0.67 (0.52, 0.85)	0.72 (0.46, 1.13)	0.68 (0.53, 0.87)
Northwest Central	0.60 (0.52, 0.70)	0.72 (0.63, 0.84)	0.79 (0.67, 0.94)	0.81 (0.68, 0.97)
Southwest Central	0.64 (0.53, 0.77)	0.65 (0.54, 0.77)	0.71 (0.60, 0.85)	0.68 (0.56, 0.83)
Mountain	0.75 (0.63, 0.90)	0.87 (0.73, 1.03)	0.83 (0.69, 1.01)	0.86 (0.69, 1.08)
Pacific	Reference	Reference	Reference	Reference
No. of beds, <300	1.11 (1.00, 1.24)	1.05 (0.95, 1.16)	1.11 (1.00, 1.22)	1.05 (0.96, 1.16)
No. of beds, ≥300	Reference	Reference	Reference	Reference
Rural	0.93 (0.81, 1.07)	0.96 (0.87, 1.05)	0.87 (0.74, 1.02)	0.92 (0.82, 1.02)
Urban	Reference	Reference	Reference	Reference
Non-Teaching	0.92 (0.84, 1.02)	0.86 (0.78, 0.95)	0.96 (0.86, 1.07)	0.90 (0.82, 0.99)
Teaching	Reference	Reference	Reference	Reference
Percent of Discharges by Age Group				
Percent of discharges aged 0	0.08 (0.04, 0.20)	0.33 (0.11, 0.97)	0.16 (0.04, 0.65)	0.46 (0.10, 2.13)
Percent of discharges aged 1-17	0.17 (0.04, 0.72)	0.13 (0.03, 0.59)	0.19 (0.02, 2.10)	0.18 (0.02, 2.08)

Percent of discharges aged 45-64	0.54 (0.20, 1.42)	0.48 (0.14, 1.60)	0.39 (0.05, 3.04)	0.93 (0.11, 7.50)
Percent of discharges aged 65-84	0.43 (0.16, 1.12)	0.86 (0.23, 3.22)	0.62 (0.10, 3.90)	0.74 (0.09, 5.87)
Percent of discharges aged 85+	1.17 (0.70, 1.94)	2.18 (1.18, 4.03)	1.17 (0.56, 2.43)	2.15 (1.04, 4.43)
Percent of discharges aged 18-44	Reference	Reference	Reference	Reference
Percent of discharges White race	1.04 (0.87, 1.24)	1.10 (0.93, 1.29)	0.92 (0.76, 1.11)	0.94 (0.76, 1.16)
Percent of discharges Male gender	2.71 (1.57, 4.66)	10.02 (5.02, 19.99)	12.19 (4.10, 36.23)	21.88 (6.92, 69.17)