Institutional and Patient Level Predictors of Multi-Drug Resistant Healthcare-Associated Infections

Monika Pogorzelska

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ABSTRACT

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Healthcare-associated infections (HAI) caused by multi-drug resistant organisms (MDRO) are an important patient safety concern resulting in a substantial financial and clinical burden. This dissertation aims to contribute to the evidence base on institutional and patient level factors that predict multi-drug resistant infections in the hospital setting. In the first chapter, I review the evidence base on patient-level risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSI), system-level factors associated with implementation of infection control policies and MDRO rates, and the current knowledge on the use of infection control policies on the national level. In the second chapter, I use data from a national cross-sectional study to describe the range of MDRO screening and infection control policies in U.S. hospitals and identify predictors of their presence and implementation. In the third chapter, using data from a cross-sectional study of California hospitals, I assess the association between the presence and implementation of infection control policies for MDRO infections and rates of BSI caused by MRSA or vancomycin-resistant *Enterococcus* and infections caused by *Clostridium difficile.* Next, I identify risk factors for healthcare-associated MRSA BSI in a nested case control study using two sets of controls. In the last chapter, I conclude by summarizing the findings of these three studies.

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CHAPTER 1:

1.0 Introduction

Healthcare-associated infections (HAI) cause significant morbidity and mortality in acute care settings.[1] Part of this morbidity and mortality is due to increased resistance to antibiotics in HAI.[2-4] For these reasons and due to the increased focus on public reporting of these infections, the identification, prevention and control of MDRO is a major focus of infection prevention and control programs in acute care hospitals. Control measures most often utilized by hospitals to reduce MDRO rates include the use of active surveillance, isolation and contact precautions, antibiotic stewardship, and cohorting of colonized patients.[5] Although research studies have been conducted to explore the effectiveness of these different control measures, many of these studies are of poor quality and limited to single institutions and/or take place in outbreak settings.[6-7] To date, there is paucity of research on the use of these infection control policies at the national level and on the association between structural characteristics (e.g., infection control staffing, hospital teaching status) and the presence and implementation of these policies.[8-9] Data on the association between the presence and implementation of these policies, structural characteristics and MDRO HAI rates on the national level is also lacking. Furthermore, existing studies examining patient-level predictors of MDRO HAI are limited by small sample sizes and other methodological issues.

In this dissertation, I describe the range of policies related to screening for and control of MDRO infections, as well as adherence with these policies in intensive care units (ICU) across the nation using data from a national cross-sectional study. I identify structural predictors of the presence and implementation of these policies. I also assess

the association between structural characteristics, the presence and implementation of screening and infection control policies and MDRO HAI rates in a cross-sectional survey of California hospitals. Using a nested case control study, I then identify patient-level risk factors for Methicillin resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSI) using two sets of controls.

1.1 Background and Significance

In this section, I describe the burden of multidrug resistant HAI in U.S. hospitals. I discuss risk factors for MRSA infections in hospitalized patients and then focus specifically on risk factors for MRSA BSI, since Aim III of my dissertation (Chapter 4) focuses specifically on MRSA BSI. Next, I review the recommended infection control policies for reducing MDRO HAI in general in the acute care setting and the evidence base on the effectiveness of these interventions, which provides the foundation for my first two aims. Finally, I discuss the literature on the actual use of these interventions and on the factors that facilitate their use and implementation in acute care hospitals.

1.2 Multi-drug Resistant Healthcare-Associated Infections as a Significant Public Health Concern

Currently, it is estimated that more than 70% of bacteria that cause HAI are resistant to at least one antibiotic that is commonly used in treatment of the infection.[2] MRSA, vancomycin-resistant *Enterococcus* (VRE), extended-spectrum β-lactamase producing (ESBL) gram negative rods (GNR) such as *Klebsiella* species and *Escherichia coli* are some of the MDRO that have presented the greatest challenges.[3,4,10-12]

Although infections due to *Clostridium difficile* are not considered to be MDRO, they result in significant patient burden and are associated with the frequent use of antibiotics.[13-15] The importance of studying *C. difficile* is further underscored by the fact that several states including California have mandated public reporting of *C. difficile* infections. Therefore, infections due to *C. difficile* are also examined in this dissertation.

1.2.1 Morbidity, Mortality and Costs Associated with MRSA Infections in Hospitals

MRSA has been the focus of much research in the last several decades due to its major contribution to the morbidity and mortality in hospitalized patients. *Staphylococcus aureus* can cause serious infections at many body sites including the bloodstream, lung and skin and soft tissues. Since its introduction in 1960, methicillin represented a breakthrough in the treatment of infection due to *S. aureus*, however, resistance to methicillin was noted within two years of its introduction[16] and has increased rapidly from 2% in 1974 to 40% in 1997.[17, 18] More recent data from the National Healthcare Safety Network show that MRSA currently represents 56% of all *S. aureus* clinical isolates.[19] The overall MRSA prevalence rate in U.S. hospitals in 2006 was 46.3 per 1000 patients including an infection rate of 34 per 1000 patients and a colonization rate of 12 per 1000 patients as measured by a MRSA prevalence survey.[20] Traditionally, MRSA infections have occurred primarily in hospitals and other healthcare facilities[21] where transmission of MRSA is driven primarily by antibiotic selection pressures and facilitated by inadequate infection control processes.[22] However, in the last fifteen years, there has been an emergence of MRSA infections in community settings among patients without any healthcare associated risk factors.[4, 23]

Several studies have investigated the attributable morbidity, mortality and cost of methicillin resistance in HAI.[24-27] A recent study conducted by Filice and colleagues in Veterans Affairs (VA) hospitals showed that resistance to methicillin in *S. aureus* was independently associated with higher costs due to prolonged hospitalization resulting in additional laboratory and imaging tests, as well as increased number of invasive procedures provided to the MRSA infected patients. In addition, patients with MRSA infections as compared with methicillin-susceptible *Staphylococcus aureus* (MSSA) infections were much more likely to die.[24]

Bloodstream infections are commonly due to *Staphylococcus aureus.*[28] It is estimated that approximately one-third of patients with BSI caused by *S. aureus* develop local complications or distant septic metastases.[28] These infections are even more complicated when the *S. aureus* strain is resistant to methicillin or other semi-synthetic penicillins. Cosgrove et al. conducted a cohort study to specifically examine the impact of MRSA BSI as compared to MSSA BSI and estimated a median attributable length of stay of 2 days and a median attributable hospital charge of $6,016.[30] This same group of researchers conducted a meta-analysis to compare the mortality rate of MRSA BSI with MSSA BSI and showed a pooled odds ratio (OR) for mortality of 1.93 after controlling for age, severity of illness and other confounders.[31] The finding of increased mortality in patients with MRSA BSI as compared with MSSA BSI has been shown in other studies.[32-34] Differences in morbidity and mortality due to these two infections are posited to be the result of variations in virulence of the causative strains, vulnerabilities of the populations affected and delays in receiving drug therapies appropriate for the infection.[31,33]

One of the most common causes of BSI infections in hospitals after *S. aureus* is enterococcal species.[35] In the past two decades, resistance to vancomycin in clinical enterococcal isolates has been observed.[36] A recent meta-analysis of studies examining the attributable mortality associated with vancomycin resistant versus susceptible BSI showed that after controlling for severity of illness, patients with VRE BSI were more likely to die than patients with enterococcal BSI susceptible to vancomycin (pooled OR = 2.52, 95% CI = 1.9 – 3.4).[37]

1.3. Risk Factors for MRSA Colonization or Infection

Many researchers have investigated the risk factors associated with MRSA infections in hospitalized patients.[38-40] For example, Graffunder & Venezia conducted a case control study of 121 patients infected with MRSA compared with 123 patients infected with MSSA. Multivariate analysis identified levofloxacin, macrolides, previous hospitalization, enteral feeding, surgery and length of stay before culture as independently associated with MRSA infection.[39] In a study of U.S. veterans, McCarthy et al. described the risk factors associated with methicillin resistance among *S. aureus* infections at different anatomic sites. The adjusted odds ratios for methicillin resistance were higher among infections that occurred among patients who had a prior history of MRSA infection and resided in a long term care facility in the previous 12 months but were lower for infections that occurred among patients who had undergone a biopsy procedure in the past 12 months. The researchers also performed a subset analysis of BSI cases, which showed that the odds of resistance were highest in patients with chronic obstructive pulmonary disease (COPD), with a central venous catheter or with compromised skin.[40]

Several have attempted to assess risk factors for surgical site infections (SSI) caused by MRSA.[41-43] Chen et al. identified poor functional status as an independent predictor of SSI due to MRSA in older adults.[42] The researchers compared two sets of controls - 64 patients with MSSA SSI and 167 patients without SSI - with 84 patients with SSI due to MRSA, allowing the researchers to potentially differentiate between risk factors for MRSA SSI and SSI due to *S. aureus* in general. In this case the risk factors were the same. Using two separate multivariate models, the researchers showed that requiring assistance in three or more activities of daily living, Charlson comorbidity index and wound class were independently associated with MRSA BSI using both controls groups.

Research shows that *S. aureus* carriage in the anterior nares plays an important role in the pathogenesis of *S. aureus* infection.[44] Numerous studies have shown that patients colonized with *S. aureus* are at increased risk of infection, underscoring the importance of *S. aureus* carriage as an endogenous source of infection.[45-47] For example, Pujol et al. showed that nasal carriage of *S. aureus* places patients at higher risk for developing *S. aureus* infections. Furthermore, the researchers showed that MRSA colonization is a stronger predictor of BSI due to *S. aureus* than MSSA colonization.[47] A study conducted by Honda and colleagues showed a 2.5 to 4.7 fold increased risk of ICU-acquired *S. aureus* infections for those patients colonized with MSSA and MRSA, respectively, as compared to non-colonized patients.[48] These differences in infection rates may be due to differences in severity of illness between the two groups since patients who are colonized with MRSA often have greater co-morbidities, more frequent

hospitalizations and increased severity of illness[45] or due to a higher burden of bacteria at colonized sites or differences in virulence factors.[49]

Several studies have identified age as an independent predictor of BSI infection caused by *S. aureus*.[50,51] Additionally, elderly patients have higher incidence of MRSA colonization, increased utilization of catheters and other invasive devices and are less likely to acquire MRSA BSI through intravenous drug use.[52,53] Prior use of antimicrobial drugs has shown to be a strong risk factor for MDRO colonization and infection in several studies[39.54] regardless of the agent used.[47, 55] Longer length of stay is a well-known factor for antibiotic resistance and may represent chronic illness and increased opportunity for colonization with MDRO.[39] Ventilator dependency or enteral feeding, which have been identified as risk factors for MRSA HAI, may represent greater severity of illness in the MRSA infected patients. These differences in risk of infection underscore the need for carefully chosen comparison groups when studying infections, perhaps necessitating the use of matching procedures.

1.3.1. Patient-level Risk Factors for MRSA BSI

Due to the fact that MRSA BSI is a major contributor to the morbidity and mortality of hospitalized patients, it is important to identify risk factors that place patients at risk of developing this infection. Knowledge of the modifiable risk factors for MRSA BSI can help to identify patients at risk and can help hospitals institute appropriate infection control policies. Although other types of antibiotic resistant HAI such as VRE BSI are also important contributors to morbidity and mortality in hospitalized patients, this section and Aim III of this dissertation will focus specifically on BSI due to MRSA since this pathogen is the leading cause of BSI in acute care settings. Risk factors for

acquisition of HAI can be defined as intrinsic or extrinsic to the patient. Risk factors that are intrinsic to the patient are related to inherent characteristics of the patients such as age, sex and severity of illness and the patient's exposures before hospitalization. On the other hand, extrinsic factors are related to the procedures and therapies that the patient undergoes during the admission, as well as the structure and processes of care provided.[56]

Several case-control studies have attempted to identify predictors of MRSA BSI in hospitals. In a study conducted by Romero-Vivas and colleagues in a Spanish hospital, the researchers prospectively studied all cases of *S. aureus* BSI that occurred during a four-year outbreak of MRSA and compared the clinical characteristics and mortality rates of patients with nosocomial MRSA (n = 84) and MSSA (n=100) BSI. The researchers found that patients with MRSA BSI were more likely to be older, have prolonged hospitalization, prior antimicrobial therapy, urinary catheterization, nasogastric tube placement and prior surgery.[57] In a similar study, Libert and colleagues identified not living at home, prior antibiotic exposure, insulin-requiring diabetes and nosocomial BSI as the independent risk factors for MRSA BSI.[58] Furthermore, they found that nosocomial *S. aureus* BSI occurring more than 12.5 days after admission was more likely to be resistant to methicillin. Recent hospital admission and assisted living were also identified as independent predictors of MRSA BSI in a small study conducted in a single hospital in Seattle.[59] Blot et al. investigated the differences between patients with BSI due to methicillin-susceptible and resistant *S. aureus* in ICU patients and noted that patients with MRSA BSI had more acute renal failure and hemodynamic instability than patients with MSSA BSI, as well as longer ICU stay and ventilator dependency.[32] All of these studies compared patients with MRSA BSI to those with MSSA BSI.

Bakowski and colleagues conducted a case control study in a Brazilian hospital comparing 60 patients with MRSA BSI to 240 patients with no infection.[60] The independent predictors of MRSA BSI in this study were severity of illness indicators and the use of central venous catheters. The researchers chose an uninfected control group instead of a control group with methicillin-susceptible infections because they aimed to isolate and identify risk factors for BSI and not risk factors for methicillin resistance. In this study, the researchers randomly selected controls that were hospitalized on the same day or immediately after the results of the blood cultures for the cases were available. However, the researchers observed large differences in disease severity between the cases and controls, which masked other risk factors for infection. In order to evaluate the importance of control group selection in studies assessing the association between use of antibiotics and MRSA BSI, Ernst et al utilized two sets of controls: one group with MSSA BSI and another group without BSI.[61] The researchers hypothesized that using controls with MSSA BSI may overestimate the association between antibiotic use and MSSA BSI since prior use of antibiotics such as methicillin is likely to prevent infection with strains of bacteria that are susceptible to the particular antibiotic.[62] Indeed, the researchers observed a significant association between exposure to antibiotics and infections with MRSA BSI when compared with MSSA BSI controls but not when the non-infected control group was utilized. One of the major limitations of this study was the fact that the researchers matched cases and controls on age, gender, time at risk and hospital ward but did not utilize statistical methods appropriate for matched data. Since matching in a case control study introduced selection bias, proper control in the analysis stage is essential.

Researchers have also utilized the cohort design to identify risk factors for MRSA BSI. For example, Lodise et al. aimed to identify patients at risk for developing MRSA BSI at a trauma center.[55] The authors identified 494 cases of *S. aureus* BSI, only 45% of which were hospital onset. The majority of hospital onset *S. aureus* BSI were resistant to methicillin (69%), as opposed to community onset BSI (22%). The independent risk factors for MRSA BSI identified in this study were prior antibiotic exposure, hospital onset, history of hospitalization and presence of decubitus ulcers. Bader conducted a retrospective cohort study to identify predictors of 7-day mortality associated with *S. aureus* BSI in a cohort of older adults with this infection. In a secondary analysis, the author also identified previous hospitalization, residence in a long term care facility and altered mental status at the onset of BSI as independent predictors of MRSA BSI.[63]

A population based study of methicillin resistance in *S. aureus* BSI in Canada demonstrated a dramatic increase in cases of MRSA BSI and a steady rate of nosocomial and community acquired MSSA BSI cases from 2000 to 2006.[64] The authors identified dialysis, organ transplantation, HIV infection, cancer and diabetes as the most important risk factors for infection. Additionally, the authors noted that the overall case-fatality rate was significantly higher in persons with MRSA BSI (39%) as compared to persons with MSSA BSI (24%). The mortality rate presented in this study was 4.7 deaths/100,000 population/year for HAI and 2.0 deaths/100,000 population/year for community acquired infections. However, this study analyzed community and healthcare associated BSI cases together, which may mask some of the differences in risk factors between these two groups.

1.3.2. Limitations of Current Research on Risk Factors for MRSA BSI and Future Needs

Although several studies have set out to identify risk factors for MRSA BSI, they were limited by small sample sizes, single site settings and methodological issues such as inadequate control for severity of illness. Additionally, studies that utilized matching did not employ the correct statistical methods, which resulted in the use of control groups that were not selected independently of their exposure status. Several other studies reported independent predictors of MRSA BSI, however, this was not the primary aim of these studies, which set out to identify differences in outcomes in patients with MRSA vs. MSSA BSI.[33, 63] In addition, existing studies vary in the control group chosen. For example, some studies used control groups consisting of patients with antibiotic-susceptible BSI, which allows the researcher to identify predictors of resistance in BSI. However, other studies selected controls with no infection. In this instance, the predictors identified are predictors of BSI due to *S. aureus*. While most studies explored hospital-wide risk factors, one focused on ICU patients. Additionally, most studies did not focus specifically on healthcare-associated infections. In this dissertation, I explore the risk factors for MRSA BSI using a large sample of hospitalized patients (Chapter 4) and focus specifically on healthcare-associated infections. I compare cases with MRSA BSI to patients with MSSA BSI. In addition, I conduct a matched comparison (1:2) of MRSA BSI cases with non-infected controls.

1.4. System Level Factors Associated with MDRO Rates (Structures of Care)

The next two sections discuss MDRO in general, without focusing specifically on MRSA. In this section, I describe the literature on the impact of institutional factors on rates of MDRO infections in hospitals. The Study on the Efficacy of Nosocomial

Infection Control (SENIC) conducted by the Centers for Disease Control and Prevention (CDC) 30 years ago was the first study to show a link between effective infection control and lower HAI rates.[65] This national study of infection control departments measured infection control staffing ratios and intensity of infection control processes. The research team also measured the incidence of HAI in a stratified random sample of hospitals and showed that hospitals with better staffing and higher intensity of infection control processes had lower HAI rates. The authors identified several hospital level factors as significant predictors of HAI rates including hospital size, teaching status, region, nurse staffing ratios, infection preventionist (IP) staffing ratios, presence of hospital epidemiologists with training in infection control, and higher scores on surveillance and/or control indexes. Data for Aim I of this dissertation comes from the "Prevention of Nosocomial Infections and Cost Effectiveness" study,[66] which has been modeled after and undertaken to update the findings of the SENIC study. Importantly, there have been few recent multi-center studies to identify systems-level risk factors for MDRO HAI. The findings of the SENIC study guide the hypotheses examined in this dissertation that administrative and organizational factors such as the presence and higher implementation of policies will have an impact on rates of MDRO in the hospital setting.

A recent literature review on the association between staffing and rates of HAI suggests a link between higher level of nurse staffing and lower rates of HAI including MDRO.[67] However, this review identified only 3 studies, which examined the link between IP staffing and HAI rates and found mixed results. For example, Richet et al. found that having a higher mean number of beds per infection control nurse was the only independent predictor of high MRSA incidence rates.[68] However, a study exploring IP

and physician staffing on wound infections failed to observe any significant relationship between staffing and infection rates.[69] Other studies have found a link between high bed occupancy and high patient turnover and increased rates of MRSA[70] supporting the hypothesis that hospital specific factors influence rates of MDRO.

In recent years, there has been increased interest in the use of electronic surveillance systems (ESS) for tracking of HAI in order to improve case finding and decrease costs and time required for surveillance;[71] however, the impact of ESS use on MDRO HAI rates is not well described and necessitates further study. Additionally, many states have begun mandatory reporting of HAI rates including rates of MDRO HAI,[72, 73] although there is a paucity of research on the effect of mandatory reporting on HAI rates.[74] Aim II of this dissertation examines the relationship between institutional characteristics and rates of MDRO HAI (Chapter 3).

1.5. Types of Infection Control Practices to Reduce MDRO (Processes of Care)

Transmission of MDRO in hospitals has been attributed to inappropriate use of antibiotics, leading to selective pressure that drives resistance, and the lack of appropriate infection control measures in hospitals.[22] There is a range of different infection control measures utilized for reducing antibiotic resistant infections in hospitals. These include proper hand hygiene, isolation and contact precautions, active surveillance, antibiotic restriction or stewardship and cohorting of patients in the same room.[5] Although hand hygiene is one of the most effective and widely recognized infection control strategies for prevention of MDRO transmission,[75] the unreliability of self-reported compliance with hand hygiene is widely recognized;[76, 77] therefore, this dissertation does not specifically examine the role of hand hygiene in the prevention of MDRO.

Active surveillance testing to identify patients colonized or infected with MRSA is one infection control policy instituted in some hospitals to combat MDRO infections. The idea behind active surveillance is that routine laboratory-based testing will not identify a significant proportion of patients who are colonized with MDRO and that those who are colonized but not symptomatic will serve as a reservoir for transmission of the pathogen in the hospital.[78] Active surveillance is usually used to screen for MDRO in high-risk populations such as ICU patients, patients transferred from long-term facilities or other hospitals and those meeting other criteria for higher risk.[79] Clearly, timeliness of the screening culture is very important. Currently, the gold standard for screening patients for MDRO such as MRSA is with the use of cultures, but there is at least a 48-hour delay between the time the culture is taken and the availability of results. The use of rapid screening methods such as the use of polymerase chain reaction (PCR) assays have been suggested to allow for earlier identification and isolation of colonized or infected patients.[80] However, the utility of PCR as a stand-alone method of screening has not yet been established.[81,82]

Once a surveillance culture is taken, the patient may be placed on contact precautions pending the results of the screening culture or the hospital may choose to wait to institute contact precautions until a positive result is found. Contact precautions refer to a set of practices aimed at reducing either direct or indirect transmission of pathogens from infected patients. These include the use of barrier precautions such as the use of gowns and gloves, and isolation practices such as placing infected or colonized patients in single rooms. Another infection control practice, cohorting of patients, refers to the physical separation of patients who are colonized or infected with MRSA from

those who are negative to prevent cross transmission.[5] Antimicrobial stewardship is also used to prevent the development of MDRO and includes the use of automatic stop orders for antibiotics, the need for an infectious disease consult or pharmacy consult prior to prescribing certain antibiotics, and antibiotic prescribing policies developed by the hospital.[83]

1.5.1. Current Recommendations for Infection Control Practices to Reduce MDRO HAI in Hospitals

There is wide variation in published recommendations on infection control policies to reduce MDRO HAI. For example, the CDC guidelines written by the Healthcare Infection Control Practices Advisory Committee (HICPAC) recommends the use of barrier precautions for patients with confirmed MDRO colonization or infection. However, the guidelines do not recommend routine surveillance cultures in settings with low MDRO prevalence.[5] On the other hand, the Society for Healthcare Epidemiologists of America (SHEA) recommends surveillance cultures for all high risk patients upon hospital admission, as well as the use of preemptive barrier precautions for patients with pending surveillance culture results.[84-86] At the current time, the Association for Professionals in Infection Control and Epidemiology (APIC) suggests pre-emptive isolation and contact precautions pending a screen but acknowledges lack of evidence for a stronger recommendation.[87] Several European countries employ a search and destroy approach to combating MDRO, which includes screening for MDRO and isolation of patients found to be positive.[88] The 5 Million Lives Campaign conducted by the Institute for Healthcare Improvement (IHI) includes the following 5 components as part of an intervention to reduce MRSA: hand hygiene, decontamination of environment and

equipment, active surveillance, contact precautions for infected and colonized patients and use of central line and ventilator bundles.[89] Furthermore, active surveillance for MRSA and other MDRO is currently being mandated or pending legislation in several states.[71]

These wide variations in published recommendations underscore the need to identify effective surveillance and isolation strategies. Additionally, some researchers have raised concern about the adverse effects of using barrier and isolation precautions. A systematic review of the literature on the use of barrier precautions for patients with MDRO infections found evidence to show that the use of barrier precautions may be associated with less patient contact with healthcare providers, increased adverse events of noninfectious nature, delays in care as well as increased patient depression and dissatisfaction with received care.[90,91] These findings further necessitate the need for additional evidence on the effectiveness of these interventions.

1.5.2. Evidence on the Effectiveness of Infection Control Practices to Reduce MDRO HAI

Data on effective infection control policies aimed at reducing multi-drug resistant HAI is lacking. A systematic review of evidence on the effectiveness of barrier precautions and surveillance cultures to control transmission of MDRO identified 7 studies that solely examined the effectiveness of surveillance cultures.[7] The researchers found that although 5 of these studies showed decreased rates of colonization and infection following the implementation of the intervention, these studies were of poor quality. The authors noted the difficulty of conducting these studies due to ethical considerations as well as the potential for the Hawthorne effect whereby participants in

research studies change their behavior simply in response to being observed. Additionally, the researchers noted that most studies on the effectiveness of barrier precautions and surveillance cultures examined their impact on MRSA and VRE, underscoring the need for a broader focus. The finding of this literature review were in agreement with a review conducted by McGinigle and colleagues who investigated the role of active surveillance cultures in decreasing rates of MRSA.[92] Although the authors identified sixteen observational studies and the majority of these pointed to the effectiveness of active surveillance cultures in decreasing MRSA, they found the evidence base to be lacking due to the methodological flaws of the reviewed studies. Creamer et al. investigated the impact of rapid screening methods for MRSA in their hospital and noted that the use of PCR methods led to increased compliance with screening policies and allowed for earlier isolation of patients.[93] However, the results of other studies have been mixed.[94]

A study conducted by Weber et al. compared hospital wide versus targeted surveillance in ICUs for HAI and found that, although rates of infections due to MRSA and VRE were highest in the ICU, limiting surveillance to the ICU would result in missing 50% of infections due to MRSA or VRE.[95] Another study compared the use of active surveillance for VRE vs. laboratory-based surveillance and found that three-quarters of patients colonized with VRE would not be detected if the ICU relied solely on lab-based surveillance.[96] However, other studies investigating the comparative effectiveness of active surveillance systems for VRE generated equivocal results.[97, 98] Based on the lack of quality evidence and lack of data pointing to the cost effectiveness

of these measures, many have argued against routine screening of all admissions to the hospital.[54, 99,100]

Cooper et al. undertook a review of isolation precautions and rates of MRSA and noted the lack of well-designed studies to address the effectiveness of isolation precautions as a sole intervention. However, the authors did note some evidence pointing to the effectiveness of isolation precautions when combined with other infection control efforts.[101] A recent study on the use of infection control practices to reduce MRSA in Europe found an association between placement of MRSA patients in single rooms and lower MRSA prevalence.[102] The use of a search and destroy policy for MRSA in the Netherlands including the use of strict surveillance upon hospital admission and isolation of patient has been shown to be correlated with very low rates of MRSA colonization and infection.[88] Halcomb and colleagues performed a literature search to identify the evidence base on the effectiveness of isolation practices on transmission of MRSA in hospitals.[6] The researchers identified seven studies that focused solely on patient isolation practices and found the evidence for use of isolation in single rooms and cohorting of MRSA patients to be lacking. The authors noted evidence to suggest that improving the use of contact precautions could result in reduced MRSA rates; however, they cautioned on the interpretations of these finding since the quality of the studies was lacking and only a small number of studies were included in the review.

The use of policies restricting prescribing and use of antibiotics is considered to be of fundemental importance in efforts to reduce resistance.[83] Several studies have shown an association between inappropriate prescribing and use of antibiotic and increased resistance rates.[103-105] However, additional evidence is needed to confirm these

findings since most of the studies examining this relationship were small and limited to single site settings.[106, 107] Larson et al. conducted a study to assess the relationship between antimicrobial control policies, hospital and infection control characteristics and antimicrobial resistance rates in 33 U.S. hospitals.[108] The study found that only 30% of the hospitals had an antibiotic control policy. The researchers did not observe an association between the presence of an antibiotic control policy and rates of MRSA, VRE or ceftazidime-resistant *Klebsiella pneumoniae*. However, the researchers did observe an association between increased systems-level efforts to implement the CDC's hand hygiene guideline and lower MRSA and VRE rates.

Numerous researchers have argued that one single policy will not solve the problem of MDRO HAI in hospitals and that a multi-pronged approach is needed to decrease rates. Through the use of mathematical modeling, Bootsma and colleagues showed evidence to suggest that the most effective infection control interventions to reduce MRSA were ones that included screening in combination with other interventions;[109] however, more research is needed to support these conclusions. Others have argued against focusing resources on a single resistant pathogen.[110] Instead, these authors suggest a population-based approach to infection control, which would impact rates of all antibiotic resistant pathogens. For example, the authors show that focusing on reducing rates of BSI will have an even bigger impact on MRSA BSI, where a decrease in BSI of 12.5% would equal a 50% reduction in rates of BSI due to MRSA. [110]

1.5.3. Implementation of Infection Control Practices to Reduce MDRO in Hospitals

There is paucity of data on the actual infection control practices implemented in hospitals in the United States. Jarvis and colleagues conducted a MRSA prevalence study

in 2006 where they surveyed members of the Association of Professionals in Infection Control & Epidemiology (APIC).[20] The researchers collected data on isolation measures taken for MRSA culture positive patients, whether active surveillance testing was done routinely to detect MRSA-colonized patients, the populations tested and the microbiologic methods used. This study showed that 45% of the 1237 surveyed hospitals performed hospital-wide HAI surveillance, whereas the rest targeted their surveillance methods. Less than a third of the hospitals (29%) reported the use of active MRSA surveillance testing; of these, half of the hospitals utilized routine media for testing (54%). The targeted populations included: long term care facility transfers (42%), other health care facility transfers (33%), readmissions (20%), patients on selected wards (18%), ICU (16%) or dialysis patients (14%). The majority of hospitals (72%) reported a policy for contact isolation for patients found to be colonized or infected with MRSA. These data show that less than one third of U.S. hospitals may engage in active surveillance for MRSA, which may have an impact on reported MRSA prevalence rates in the participating hospitals. Furthermore, of those that did perform active surveillance, the majority used non-selective media, which is less sensitive and may lead to underestimation of MRSA rates in this study. An important finding from this study is that the majority of MRSA cases were found on medical wards and not in the ICU resulting in serious implications for hospitals that target their screening programs to ICU patients. An important limitation of this study is its low response rate, which has an impact on the generalizability of the study results. According to the researchers, over 1200 health care facility respondents provided data, however, this only represents 24% of all U.S. hospitals.

Hansen et al. surveyed hospitals in 10 European countries to describe the range of policies employed for the prevention of MRSA in ICUs and surgical departments.[111] The researchers investigated the use of isolation precautions, decolonization and screening methods as well as the use and availability of alcohol based hand sanitizers at the patients' bedside. Data from 526 ICUs and 223 surgical departments were available. This study showed that the use of prevention measures related to MRSA varied widely between the countries. For example, the use of routine screening for newly admitted patients from other wards or hospitals ranged from 29% in Lithuanian ICUs and surgical departments to 100% in Slovakia. Isolation of MRSA patients in single rooms was another policy with a wide range of adoption (range = 41-100%). Differences in policies were also noted between the ICUs and surgical departments within the countries. Finally, the authors found that countries with the lowest MRSA rates were also the countries with the highest use of preventive policies but the authors could not investigate this relationship further using cross-sectional data. Richet and colleagues conducted a survey in 90 healthcare facilities in 30 countries in 1998 to determine the types of MRSA surveillance and control programs in these hospitals.[68] In this survey, hospitals reported routine use of the following infection control policies aimed at reducing MRSA: use of gloves and gowns (62% and 44%, respectively), hand washing (53%), use of an isolation sign on the patient's door (43%) and use of single rooms (34%). As did the study conducted by Hansen et al., this study noted a wide range of routine use of these policies between countries. One study surveyed infectious disease consults that participate in the Emerging Infections Network and determined that the majority of those surveyed (86%) reported the routine use of contact precautions in their hospital. Additionally, the survey

showed that although 50% of the respondents were in favor of the use of routine surveillance cultures for at least one MDRO, less than a third of them (30%) worked in a hospital where active surveillance cultures were performed routinely.[112]

In a study by Fridkin and colleagues, the researchers set out to identify predictors of vancomycin use in ICUs participating in the National Nosocomial Infection Surveillance System.[113] Data were obtained from 41 hospitals reporting on 108 ICU. The majority of hospitals (63%) reported that antimicrobial selection was based on diagnosis-based guidelines. A third of the hospitals reported the presence of a written guideline outlining appropriate vs. inappropriate use of vancomycin. However, less than a fifth of the hospitals stated that preapproval was required prior to the use of vancomycin in their ICU. Zillich et al. conducted a survey to explore the relationship between antimicrobial use control strategies and rates of resistant pathogens in U.S. hospitals.[114] This study found that more than half of the hospitals reported implementation of guidelines on the use and optimization of empirical antibiotic prophylaxis and found an association between the implementation of guidelines and reduced resistance rates. In a survey of laboratory directors from U.S. hospitals (n = 108), the range of policies related to antibiotic prescribing ranged widely from 85% for automated testing to 33% for offering molecular typing.[115]

Gravel et al. conducted a cross-sectional study of acute care hospitals in Canada participating in the Canadian Nosocomial Infection Surveillance Program to identify the infection control policies that these hospitals had in place to reduce *C. difficile* infections.[116] Thirty-three of 41 hospitals participated in the study. Half of the hospitals (55%) reported the use of infection control precautions for symptomatic patients prior to

availability of lab results. Respondents reported testing of liquid stool samples based on clinician's order (70%), testing all liquid stools submitted whether or not *C. difficile* testing was ordered (24%), use of single rooms or cohorting of patients (88%), use of equipment designated for infected patients (27%), and policies for use of contact precautions by visitors (70%). This study is limited by inclusion of only those hospitals that participated in this particular surveillance system which are more likely to be major hospitals affiliated with universities. Additionally, this study did not collect data on policies related to antibiotic stewardship, which is considered to be an important strategy in controlling *C. difficile* infection rates.[117]

Infection control departments were surveyed in another study conducted in Canada to examine the prevalence of infection surveillance and control activities.[118] The vast majority of hospitals reported the use of isolation precautions for VRE and MRSA (99%) as well as *C. difficile* (80%). Less than half of the hospitals (46%) reported the presence of guidelines recommending appropriate antimicrobial therapies including drug choices, timing and duration of perioperative antibiotics. The authors noted that very few hospitals (13%) reported compliance with at least 80% of recommended surveillance policies. These authors conducted another study using the same sample of hospitals to examine the association between infection control policies and MDRO rates.[119] Several infection control policies including reporting infection rates by specific risk groups and taking attendance at team meetings were independently associated with lower rates of MRSA. Higher rates of *C. difficile* infections were observed in larger hospitals and those hospitals reporting the authority to close wards in case of outbreaks, which may represent a higher prevalence rate of *C. difficile* in these hospitals. The authors noted that the rate

of MDRO seen in this study is lower than that reported in the U.S. which may impact the generalizability of the study results. Additionally, the authors did not investigate the infection control activities of interest in this dissertation including isolation/contact precautions, active surveillance and cohorting of patients. Although several studies have been conducted on the use of infection control practices in acute care hospitals, the extent to which infection policies related to MDRO are adopted by U.S. hospitals is not well described. This dissertation investigates the use of infection control policies using a national sample of National Healthcare Safety Network (NHSN) hospitals, as well as a separate sample of hospitals located in California.

1.5.4. Factors Associated with the Presence and Implementation of Infection Control Practices to Reduce MDRO HAI

Even when there is substantial evidence that certain policies are effective in reducing infection rates in hospitals and published guidelines recommend the adoption of these practices in the hospital setting, implementation is often lacking.[120] Research suggests that recommended care is provided to only half of adult patients.[121] However, there is paucity of research on the setting characteristics that influence the presence and/or implementation of infection control policies. The first aim of this study examines the relationship between structures of care and the presence and use of infection control policies in a national sample of hospitals.

One study conducted by Fukuda and colleagues examined factors associated with system level activities for patient safety and infection control in Japan.[122] The researchers noted an increased number of infection control activities in hospitals with a full time staff member dedicated to infection control or patient safety. Other factors associated with an

increased number of infection control activities included greater resources and higher profit margins in hospitals. A study by Chou et al. explored the relationship between implementation of infection control activities and formalization and standardization of protocols, centralization of decision making hierarchy, use of information technology, hospital culture, measures of effective communication and coordination between departments.[8] The researchers found a link between these structural characteristics and measures of appropriate use of antibiotics and implementation of policies such as feedback to providers. The study conducted by Zillich et al. described in the previous section found a link between hospital bed size and Veterans Affairs status and rates of antibiotic resistance in U.S. hospitals.[114] Flach and colleagues identified an association between the presence of several infection control policies and hospital teaching status, as well as high prevalence of at least one MDRO (defined as 10%) and the presence of the lab director on the hospital's infection control committee.[115] In their study, Zoutman et al. also noted a relationship between hospital bed size, teaching status, IP certification, computerization of surveillance and availability of references and the presence of infection control activities.[118] However, these studies did not specifically examine the factors associated with the presence and implementation of the screening and infection control policies of interest in this dissertation. Aim I of this dissertation fills this gap in the literature (Chapter 2).

1.6. Conceptual Framework:

The conceptual model used in this dissertation is based on the work of Donabedian who formulated a conceptual framework to define quality of care as consisting of the structure, processes and outcomes of care.[123] In this framework,

structures of care are defined as the conditions under which care is provided. Processes of care are the actions involved with the direct provision of care. Finally, outcomes of care are the consequences that can be attributed to the structures and processes of care.[124] In this model depicted in Figure 1, the structures of care include hospital characteristics such as bed size and teaching status, infection control department characteristics such as infection preventionist and epidemiologist staffing and unit characteristics such as ICU type. These structures of care variables were included in the conceptual model based on evidence literature indicating an association between these variables and HAI rates.[65] Processes of care include the presence and intensity of infection control interventions aimed at reducing MDRO HAI. Lastly, the outcomes of care of interest in this dissertation are organism specific HAI rates including MRSA BSI, VRE BSI and *C. difficile* infections. Patient characteristics have also been included in this model since they influence both the outcomes and structures of care.

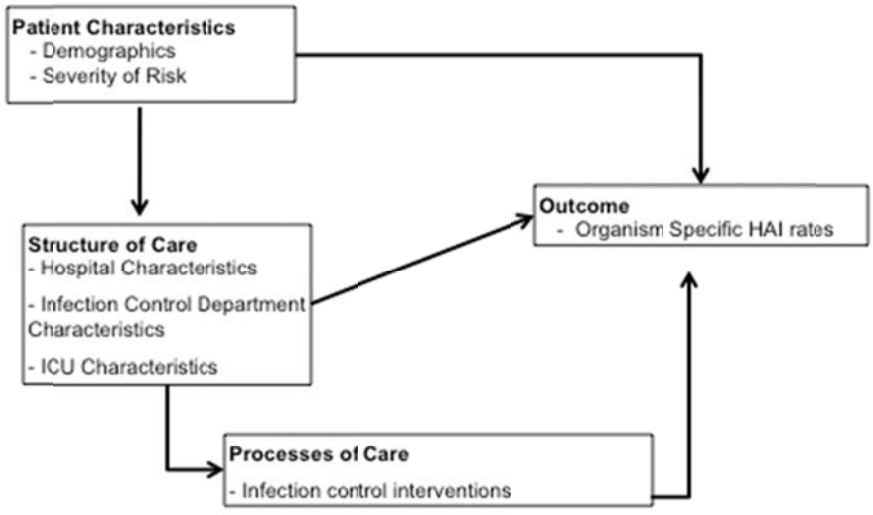

Figure 1. Conceptual Framework

1.7. Summary and Conclusion

As described in the sections above, multi-drug resistant HAI represent a major source of morbidity and mortality in hospitalized patients. Although bloodstream infections represent a significant proportion of HAI in hospitals and more than half of BSI are resistant to methicillin, studies conducted to explore the risk factors for MRSA BSI have been limited to single site settings, utilized a small number of patients and were limited by methodological issues. Additionally, there is paucity of data on the use of infection control policies aimed at MRSA and other MDRO in hospitals in the United States, as well as factors associated with the presence and implementation of these policies.

In this dissertation, I describe the use of infection control policies related to MDRO in a national sample of hospitals and the factors associated with their presence and implementation (Chapter 2). I examine the association between these infection control policies and rates of specific MDRO HAI (Chapter 3). Additionally, I explore risk factors for healthcare-associated MRSA BSI infections (Chapter 4). Finally, I summarize the results in the concluding chapter (Chapter 5).

CHAPTER 2

Implementation of Screening and Infection Control Interventions for Multi-Drug Resistant Organisms

2.1 Abstract

Infections caused by multi-drug resistant organisms (MDRO) cause significant morbidity and mortality in intensive care units (ICUs) in the U.S. and around the world. Hospitals utilize different interventions to combat MDRO; however, adoption of these interventions is not well described. In 2008, we conducted a cross-sectional survey of 250 infection control directors at National Healthcare Safety Network hospitals in order to describe adoption of MDRO screening and infection control interventions in U.S. ICUs and identify predictors of their presence, monitoring and implementation. Study ICUs routinely screened for methicillin-resistant *Staphylococcus aureus* (59%), vancomycin-resistant *Enterococcus* (22%), multi-drug resistant gram negative rods (12%) and *Clostridium difficile (11%)*. ICUs reported policies to screen all admissions for any MDRO (40%), screen periodically (27%), utilize presumptive isolation/contact precautions pending a screen (31%) and cohort colonized patients (42%). Several independent predictors of the presence and implementation of different interventions including mandatory reporting and teaching status were identified. This study found wide variation in adoption of MDRO screening and infection control interventions, which may reflect differences in published recommendations. Further research is needed to provide additional insight on effective strategies and how best to promote compliance.

Keywords: Healthcare-Associated Infections, Multi-Drug Resistant Infections, Antibiotic Resistance, Infection Control Policies

2.2 Introduction

Healthcare-associated infections (HAI) are one of the leading causes of death and a major source of morbidity in acute care hospitals.[1] Part of this morbidity and mortality is due to increased antibiotic resistance in HAI, which renders standard treatment ineffective and potentially requires more toxic treatment. It has been estimated that more than 70% of bacteria that cause HAI are resistant to at least one antibiotic commonly used in treatment.[2] Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and multi-drug resistant (MDR) gram negative rods (GNR) are several multi-drug resistant organisms (MDRO) that have presented serious challenges.[3-4] Additionally, although infections due to *Clostridium difficile* are not considered to be MDRO, they result in significant patient burden and are associated with frequent antibiotic use.[5] Furthermore, there is increased focus on mandated public reporting of *C. difficile* and MDRO rates.[6]

Due to the substantial burden caused by MDRO and *C. difficile*, identification and prevention of these infections remains a major component of infection control programs. Interventions often recommended to control MDRO and *C. difficile* include active surveillance, isolation/contact precautions, and cohorting of colonized/infected patients. However, there is wide variation in recommendations set forth by different organizations. For example, Centers for Disease Control and Prevention (CDC) guidelines recommend use of barrier precautions for confirmed cases, but do not recommend routine surveillance cultures in low MDRO prevalence settings.[7] Conversely, the Society for Healthcare Epidemiologists of America recommends surveillance cultures for all high risk admissions and use of preemptive barrier precautions for patients with pending

cultures.[8] Several European countries employ a more stringent 'search and destroy' approach that includes screening and isolation of patients considered high risk for MRSA carriage.[9]

Although several studies have been conducted on the use of different infection control practices,[10-15] adoption of specific MDRO and *C. difficile* screening and infection control policies in U.S. hospitals is not well described. Additionally, research on setting characteristics that influence implementation of these interventions in intensive care units (ICUs) is lacking. Therefore, the aims of this large, cross-sectional study of U.S. hospitals were to**:**

1) Describe adoption of MDRO and *C. difficile* screening and infection control interventions, as well as their implementation in ICUs.
2) Investigate whether screening for specific MDRO (i.e., MRSA, VRE, MDR GNR) and *C. difficile* in ICUs varies with setting characteristics (i.e., hospital, infection control department and ICU characteristics).
3) Examine whether presence, monitoring and/or implementation of screening and infection control interventions aimed at any MDRO vary with setting characteristics.

2.3 Methods

As part of a larger study, "Prevention of Nosocomial Infections and Cost Effectiveness Analysis," R01NR010107, select National Healthcare Safety Network hospitals (NHSN) were surveyed in 2008. Eligibility criteria included conducting NHSN HAI surveillance in 2007 and a minimum of 500 device days. A modified Dillman technique was used and recruitment is described in detail elsewhere.[16] The online survey

was designed to be answered by the infection control department director. Respondents provided data on each medical, medical/surgical and surgical ICU at their hospitals. Test-retest reliability of the survey was assessed (kappa = 0.88) and the survey was pilot tested by 3 infection preventionists (IPs) and 2 doctoral students.

2.3.1 Independent Variables:

Hospital characteristics examined included geographic region (Northeast, South, Midwest, West) and state mandatory reporting of HAI (yes/no). Teaching status and bedsize were obtained from public data sources and telephone calls to hospitals. Infection control department characteristics included: presence of hospital epidemiologist (full-time defined as 40 hours per week devoted to infection control, part-time defined as less than 40 hours and any [either part- or full-time]), proportion of IPs certified in infection control, number of IP full-time equivalents (FTE) per 100 beds, number of infection control staffing hours, number of IP staff and use of electronic surveillance systems for tracking of HAI (yes/no).

2.3.2 Dependent Variables:

To assess screening practices for specific organisms (Aim 2), respondents were asked whether each ICU routinely screened for: MRSA, VRE, *C. difficile,* and MDR GNR. Additionally, data were collected on 5 screening and infection control interventions (Aim 3): 1) screening ALL ICU admissions for any MDRO, 2) screening for any MDRO periodically after admission, 3) presumptive isolation/contact precautions pending a screen, 4) contact precautions for culture-positive patients and 5) cohorting of colonized patients. For each of these 5 interventions, we asked: Was a written policy in place? If yes, was it monitored? If monitored, what proportion of time was the policy

correctly implemented? Answer choices included: all the time (95-100%), usually (75-94%), sometimes (25-74%), rarely/never (less than 25%) and don't know. Fifteen outcomes were examined: presence, monitoring and correct implementation of each of the 5 interventions. Correct implementation was defined dichotomously as ≥75% versus <75% of the time based on distributions of responses.

2.3.3 Data Analysis**:**

Data were analyzed using Stata 11.1 (Stata Corporation, College Station, TX). Descriptive statistics were examined. We computed frequencies and percentages to determine adoption of different interventions (Aim 1). To explore differences in screening for specific MDRO and *C. difficile* by setting characteristics (Aim 2), we constructed bivariate logistic regression models for each outcome including screening for any MDRO, MRSA, VRE, *C. difficile* or MDR GNR. The independent variables were the hospital, infection control department and ICU characteristics outlined previously. Those variables with a p-value of ≤0.1 were entered into multivariable logistic regression models to estimate the independent effect of each predictor on the presence of screening for specific MDRO and *C. difficile*. Additionally, potential confounding variables were added one by one into the model, and if the coefficient of a covariate changed by 10% or more, the variable was considered a confounder and entered into the final model. Finally, to examine whether presence, monitoring and implementation of interventions for any MDRO varied with setting characteristics (Aim 3), we constructed bivariate logistic regression models. Again, variables with a p-value of ≤0.1 were entered into multivariable models and confounding variables were added as previously described. Since data were collected on more than one ICU, we calculated robust variance

estimators for all analyses to adjust for clustering at the hospital level.[17] Correlations among variables were examined to assess collinearity. A p-value of <0.05 was considered statistically significant.

2.4 Results

Of 441 eligible hospitals, 250 provided data on 413 ICUs (57% response rate). Table 1 provides demographic data of study hospitals. Almost half the hospitals were located in the Northeast (44%) and the majority was located in states with mandatory reporting of HAI (76%). Two-fifths reported presence of a part-time hospital epidemiologist (42%) while a full-time epidemiologist was present in only 6% of the hospitals. Of the independent variables, only total hours of infection control staffing and number of infection control staff were highly correlated (r = 0.90).

2.4.1 Aim 1: Describe adoption of MDRO and C. difficile screening and infection control interventions.

Study ICUs routinely screened for: MRSA (59%), VRE (22%), MDR GNRs (12%), and *C. difficile* (11%). A written policy to screen all admissions for any MDRO was reported for 40% of ICUs and 27% had a policy for periodic screening following admission (Table 2). Of those ICUs, the majority monitored implementation (80% and 79%, respectively) and correct implementation ≥75% of the time was reported for 96% and 91% of the ICUs, respectively. Approximately a third reported a policy requiring isolation/contact precautions for patients with pending screens; 98% and 42% reported a policy for contact precautions for culture-positive patients and cohorting of colonized patients, respectively. The reported monitoring and correct implementation of these interventions were not frequent.

2.4.2 Aim 2: Investigate whether screening for specific MDROs and C. difficile varies with setting characteristics.

In bivariate analyses, ICUs in mandatory reporting states were more likely to screen for any of the specific MDRO (OR = 2.56, p-value = 0.002) and MRSA (OR = 2.37, p-value = 0.004), whereas those located in the Midwest were less likely to screen for any MDRO (OR = 0.35, p-value = 0.012) and MRSA (OR = 0.32, p-value = 0.005). ICUs in hospitals with more than 500 beds were less likely to screen for *C. difficile* as compared to hospitals with 200 beds or less (OR = 0.21. p-value = 0.029).

Table 3 presents the multivariable results. Adjusting for region and percent of IPs certified in infection control, teaching status, hospital bedsize (201-500 beds versus less than 201) and mandatory reporting remained independent predictor of screening for MRSA (OR = 2.41, p-value = 0.008, OR = 2.62, p-value = 0.029 and OR = 2.24, p-value = 0.040, respectively). Controlling for total hours of infection control and mandatory reporting, ICUs in hospitals with a part-time hospital epidemiologist were more likely to have a policy to screen for *C. difficile* (OR = 4.26, p-value = 0.009), whereas ICUs in hospitals with 201-500 beds were less likely to screen as compared with smaller hospitals (OR = 0.24, p-value = 0.021).

2.4.3 Aim 3: *Examine whether presence, monitoring and/or implementation of screening and infection control interventions aimed at any MDRO vary with setting characteristics*.

In bivariate analysis, state mandatory reporting (OR = 2.52, p-value = 0.003), teaching status (OR = 1.80, p-value = 0.048), hospital bedsize of 201-500 beds (OR = 2.73, p-value = 0.009) and location in the Midwest (OR = 0.31, p-value = 0.015) were associated with a policy to screen all admissions for any MDRO. In the multivariable

model, mandatory reporting, teaching status and location in the West remained significant predictors of the presence of this policy (Table 4).

Mandatory reporting (OR = 2.25, p-value = 0.028), teaching status (OR = 2.68, p-value = 0.004) and use of electronic surveillance systems (OR = 1.95, p-value = 0.050) were positively associated with a policy to screen periodically after admission in bivariate analyses. Additionally, ICUs in hospitals with 201-500 beds were more likely to report this policy as compared to smaller hospitals (OR = 2.47, p-value = 0.043) and ICUs located in the Midwest and West were less likely to report this policy versus the Northeast (OR = 0.20, p-value = 0.001 and 0R = 0.28, p-value = 0.016, respectively). However, the presence of an electronic surveillance system, Midwest location and hospital size remained the only independent predictors of periodic screening in multivariable regression (OR = 2.45, p-value = 0.038, OR = 0.22, p-value = 0.040, and OR = 7.05, p = 0.037, respectively).

Mandatory reporting states were negatively associated with having a policy for presumptive isolation/contact precautions pending a screen (OR = 0.47, p-value = 0.012) and was the only significant predictor of this policy in bivariate analysis. Although mandatory reporting was significantly associated with a policy to cohort colonized patients in bivariate analysis (OR = 1.91, p-value = 0.031), it was not an independent predictor of having this policy after controlling for region and the number of infection control staff.

In bivariate analyses, ICUs in hospitals with a full-time epidemiologist were more likely to monitor compliance with cohorting of colonized patients (OR = 6.65, p-value = 0.041). Although approaching statistical significance, the presence of a hospital

epidemiologist was not significantly associated with monitoring the implementation of this policy (OR = 9.03, p-value = 0.067) after controlling for state mandatory reporting, region, number of infection control staff and proportion of IPs certified in infection control (data shown in Appendix 6.1.9).

Several setting characteristics predicted correct implementation of infection control policies ≥75% of the time. ICUs in hospitals with a greater proportion of certified IPs were less likely to report correct implementation of policy to screen new admissions (OR = 0.19, p-value = 0.008) after controlling for the number of infection control staff and region. In bivariate analyses, increasing infection control staffing hours were positively associated with correct implementation of periodic screening (OR = 1.01, p-value = 0.004) and the presence of any hospital epidemiologist approached statistical significance (OR = 6.11, p-value = 0.070). Increasing number of infection control staff, and infection control staffing hours were positive predictors of correct implementation of the policy to isolate culture-positive patients in bivariate analysis (OR = 1.32, p-value = 0.042, OR = 1.01, p-value = 0.017, respectively). Lastly, ICUs in the Midwest were significantly less likely to report correct implementation of a policy to cohort colonized patients (OR = 0.03, p-value = 0.008). However, we lacked sufficient power to assess these variables in multivariable analysis, or to assess the relationship between setting characteristics and contact precautions for patients with pending screens.

2.5 Discussion

To our knowledge, this is one of the first studies to examine adoption of these specific MDRO and *C. difficile* policies and to identify predictors of their presence and implementation. In our study, over half the ICUs routinely screened for MRSA; but only

a small proportion screened for VRE, MDR GNR and *C. difficile* (11-22%). The vast majority reported a policy for contact/isolation precautions for culture-positive patients, which is congruent with other studies that reported high use of barrier/isolation precautions for infected patients.[11,16,18] The presence of other MDRO-related infection control policies in our sample was low and may reflect wide variation in published recommendations on these interventions.

State mandatory reporting was a significant independent predictor of screening for MDRO, which is expected given that hospitals may have an incentive to screen new admissions for MDRO in order to identify infections not attributable to the hospital stay. Teaching status was an independent predictor of MRSA screening and screening all admissions for any MDRO. Other studies found similar relationships between teaching status, use of procedures to monitor antimicrobial resistance and greater surveillance scores.[12,14] Interestingly, ICUs in hospitals with higher percent of IPs certified in infection control were less likely to report correct implementation of policy to screen all admissions. One explanation is that more experienced IPs may be more accurate in reporting implementation, whereas less experienced IPs may over report adherence. Additionally, it may be the case that certified IPs are less strict about complying with policies for which the evidence-base is lacking.

Contrary to our hypothesis, except for the presence of a hospital epidemiologist as an independent predictor of screening for *C. difficile,* infection control staffing did not independently predict the presence and/or implementation of interventions. This suggests that factors other than staffing are influencing the likelihood of implementing these policies. Several studies have examined the role of organizational factors such as

institutional culture and suggest that these may be important in fostering adoption of infection control policies;[19,20] however, we did not assess these in this analysis. Future studies should investigate the relationship between staffing, organizational support and the effect both may have on policy implementation. Additionally, with the current increase in mandatory reporting, IPs may be focusing on fulfilling mandates rather than implementing policies based on their experience and hospital needs. Further studies are warranted to assess how mandatory reporting influences the role, activities and goals of the infection control department including policy implementation.

This study has several limitations. The data are cross-sectional preventing us from establishing temporality. Our study involved only NHSN hospitals, which in 2008 tended to be larger and more likely to be teaching. Eligibility criteria included a minimum number of device days, therefore, surveyed hospitals were on the larger end of the NHSN spectrum. Hospitals located in the Northeast were overrepresented, which may further limit generalizability. Additionally, data were self-reported by IPs which may be problematic in that IPs may have overestimated adoption of policies. Additionally, reported compliance may not be accurate since IPs do not spend substantial amounts of time in the ICU. Nonetheless, we were able to observe several significant predictors of full compliance with policies.

There is significant variation in adoption of screening and infection control interventions aimed at MDRO and *C. difficile* in U.S. ICUs, which is congruent with data from other studies and may reflect wide variation in published recommendations. Several setting characteristics hypothesized to be important in predicting these interventions did have an independent effect on their presence and implementation, specifically, mandatory

reporting, geographic region, bedsize, presence of a hospital epidemiologist, teaching status and presence of an electronic surveillance system. Further research is needed to confirm these findings and to identify additional factors that foster adoption of these interventions. Additional research is also needed to strengthen the evidence base on the effectiveness of these interventions and facilitate the development of more standardized guidelines to aid in implementing these interventions in the acute care setting.

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Table 1. Description of Hospitals and Intensive Care Units

Hospital Characteristics (N = 250)			
Region		**N**	**%**
	Northeast	109	44
	South	66	26
	Midwest	40	16
	West	35	14
Mandatory Reporting (State)		189	76
Bed Count			
	< 201	50	20
	201 - 500	145	58
	> 501	55	22
Length in NHSN/NNIS (years)			
	< 1	33	13
	1-3	78	31
	< 3	134	54
	Missing	5	2
Electronic Surveillance System			
	Yes	63	25
	No	183	73
	Missing	4	2
Presence of Hospital Epidemiologist			
	Full-time	15	6
	Part-time	105	42
		Median	**Range**
Proportion of IPs certified in infection control		50%	0 – 100%
Number of IP FTE per 100 beds		0.61	0 – 4.75
ICU Characteristic (N = 413)			
ICU Type		**N**	**%**
	Medical	102	25
	Medical/Surgical	222	54
	Surgical	89	22

FTE = Full Time Equivalent, ICU = Intensive Care Unit, IP = Infection Preventionist, NHSN = National Healthcare Safety Network, NNIS = National Nosocomial Infection Surveillance

Table 2. Extent to which ICUs have written infection control policies related to MDRO, monitor their implementation and proportion of time these policies are correctly implemented (N = 413)

	Presence of Written Policy		Presence of Monitoring for Implementation*		ICUs Reporting Correct Implementation At Least 75% of the Time*	
	N	%	N	%	N	%
Screen ALL patients for any MDRO upon admission	164	40	131	80	126	96
Screen periodically after admission	110	27	87	79	79	91
Presumptive isolation pending screen results	128	31	61	48	59	97
Contact precautions for culture positive patients	404	98	264	65	255	97
Cohorting of colonized patients	175	42	87	50	50	57

ICU = Intensive Care Unit, MDRO = Multi-Drug Resistant Organism

*Monitoring of Implementation was assessed among those ICUs that reported the presence of a written policy and correct implementation was assessed among those ICUs that reported monitoring of implementation of the written policy.

Table 3. Multivariable Logistic Regressions Examining Predictors of Screening for Specific MDRO

	OR	95% CI	P-value
Predictors of Screening for any MDRO (n = 296)			
Mandatory reporting	3.53	1.54 – 8.08	0.003
Region (vs.Northeast)			
South	0.91	0.35 – 2.36	0.849
Midwest	0.53	0.16 – 1.74	0.296
West	0.70	0.23 – 2.09	0.524
Number of infection control staff	1.14	0.89 – 1.46	0.301
Bedsize (vs. < 201)			
201 – 500	4.18	1.45 – 11.99	0.008
> 500	0.96	0.23 – 4.02	0.959
Predictors of Screening for MRSA (n = 359)			
Mandatory reporting	2.24	1.04 - 4.84	0.040
Teaching	2.41	1.26 – 4.61	0.008
Region (vs.Northeast)			
South	0.71	0.32 – 1.55	0.386
Midwest	0.47	0.16 – 1.40	0.175
West	0.52	0.18 – 1.50	0.228
Bedsize (vs. < 201)			
201 – 500	2.62	1.10 – 6.24	0.029
> 500	1.11	0.43 – 2.88	0.836
Percent IP Certified	0.62	0.26 – 1.50	0.288
Predictors of Screening for *Clostridium difficile* (n = 367)			
Total hours of infections control	1.00	0.98 – 1.01	0.614
Bedsize (vs. < 201)			
201 – 500	0.24	0.07 – 0.81	0.021
> 500	0.11	0.01 – 1.83	0.123
Presence of part-time HE	4.26	1.43 – 12.68	0.009
Mandatory reporting	1.21	0.36 – 4.04	0.753

All variables entered into each model are presented in the table.

MDRO = Multi-Drug Resistant Organism, MRSA = Methicillin-Resistant *Staphylococcus aureus*

Table 4. Predictors of Presence of Infection Control Policies in Multivariable Analysis

	OR	95 % CI	P-value
Screening All Patients on Admission for Any MDRO (n = 361)			
Mandatory reporting	3.34	1.51 – 7.38	0.003
# of FTE IPs per 100 beds	1.01	0.54 – 1.88	0.987
Teaching	2.30	1.18 – 4.46	0.014
Region (vs.Northeast)			
South	1.38	0.64 – 2.97	0.413
Midwest	0.97	0.34 – 2.78	0.949
West	0.28	0.10 – 0.78	0.015
Bedsize (vs. < 201)			
201 – 500	2.74	0.93 – 8.10	0.068
> 500	1.78	0.56 – 5.78	0.326
Screening Periodically After Admission (n = 411)			
Mandatory reporting	1.62	0.56 – 4.67	0.375
Electronic surveillance system	2.45	1.05 – 5.71	0.038
Teaching	2.44	0.95 – 6.24	0.063
Region (vs.Northeast)			
South	1.64	0.65 – 4.12	0.294
Midwest	0.22	0.05 – 0.93	0.040
West	0.37	0.11 – 1.31	0.123
Percent IP certified	1.67	0.53 – 5.01	0.397
Number of infection control staff	1.00	0.76 – 1.32	0.988
Bedsize (vs. < 201)			
201 – 500	7.05	1.12 – 44.40	0.037
> 500	4.43	0.61 – 31.88	0.139
Contact Precautions for Culture Positive Patients (n = 355)			
Mandatory Reporting	0.73	0.13 – 4.16	0.725
# of FTE IPs per 100 beds	0.63	0.32 – 1.22	0.172
Percent of IPs certified	0.02	0.01 – 1.18	0.060
Cohorting of Patients			
Mandatory reporting	1.16	0.51 – 2.62	0.727
Region (vs.Northeast)			
South	0.52	0.21 – 1.29	0.157
Midwest	0.30	0.10 – 0.92	0.035
West	0.47	0.17 – 1.32	0.154
Number of infection control staff	1.14	0.96 – 1.35	0.127

All variables entered into each model are presented in the table.
FTE = Full Time Equivalent, IP = Infection Preventionist, MDRO = Multi-Drug Resistant Organism

CHAPTER 3

Impact of Infection Control & Surveillance Policies on Rates of Multi-Drug Resistant Infections

3.1 Abstract

Background:

The study objective is to describe the use of infection control policies aimed at multi-drug resistant organisms (MDRO) in California and assess the relationship between these policies, structural characteristics and rates of methicillin resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococcus* (VRE) bloodstream infections (BSI) and *Clostridium difficile* infections.

Methods:

Data on infection control policies, structural characteristics, and MDRO rates were collected through a 2010 survey of California infection control departments. Bivariate and multivariable Poisson and negative binomial regressions were conducted.

Results:

180 hospitals provided data (response rate=54%). Targeted MRSA screening upon admission was reported by the majority of hospitals (87%); however, few reported targeted admission screening for VRE and *C. difficile*. The majority of hospitals implemented contact precautions for confirmed MDRO and *C. difficile* patients; presumptive isolation/contact precautions for patients with pending screens were less frequently implemented. Hospitals with a certified infection control director had significantly lower rates of MRSA BSI ($P<0.05$).

Conclusions:

Although most California hospitals are involved in activities to decrease MDRO, there is variation in specific activities utilized with the most focus placed on MRSA. This study highlights the importance of certification and its significant impact on infection rates. Additional research is needed to confirm these findings.

Key Words*:*

Antibiotic resistance, infection control policies, multi-drug resistant infections, Methicillin-resistant *Staphylococcus aureus,* Vancomycin-resistant *Enterococcus, Clostridium difficile*

3.2 Introduction:

Healthcare associated infections (HAI) due to multi-drug resistant organisms (MDRO) are an important patient safety concern. Multiple studies have shown that MDRO infections are associated with greater patient morbidity and mortality, as well as increased healthcare costs.[1-4] Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) species are two MDRO that have presented some of the greatest challenges in the healthcare setting.[5-6] In fact, surveillance for and reporting of MRSA and other MDRO is currently being mandated or pending legislation in several states (Association of Professionals in Infection Control & Epidemiology, 2010), underscoring the importance of these infections. In addition, although not specifically considered MDRO, infections caused by *Clostridium difficile* are associated with the frequent use of antibiotics and also result in significant patient burden.[7-8]

Transmission of both MDRO and *C. difficile* in hospitals has been attributed in part to inappropriate use of antibiotics, leading to selective pressure that drives resistance, and the lack of appropriate infection control measures in hospitals.[9] Infection prevention programs utilize a range of infection control measures to reduce antibiotic resistant infections in the hospital setting. These include encouraging proper hand hygiene, isolation and contact precautions, active surveillance, antibiotic restriction or stewardship, and cohorting of colonized or infected patients.[10] However, there is wide variation in published recommendations on the actual use of these measures.[10-14]

This variation underscores the need to identify effective strategies, but such data are currently scant. Several recent systematic reviews have been conducted to summarize the evidence on the effectiveness of barrier/isolation precautions, active surveillance and

other infection control policies to control transmission of MDRO.[15-18] Although the reviews noted some evidence of effectiveness, all of the authors pointed to the overall poor quality and methodological flaws of the reviewed studies.[15-18] Based on the lack of quality evidence and lack of data regarding the cost effectiveness of these measures, many have argued against routine screening of all admissions to the hospital.[19-20] Through the use of mathematical modeling, Bootsma and colleagues showed evidence to suggest that the most effective infection control interventions to reduce MRSA were ones that included screening in combination with other interventions;[21] however, more research is needed to support these conclusions. Others have argued against focusing resources on a single resistant pathogen.[22] Instead, these authors suggest a population-based approach to infection control, which could result in reduced transmission of a number of antibiotic resistant pathogens.

In addition to the gaps in the evidence regarding effective infection control policies directed at MDRO infections, there is also lack of data on the actual implementation of infection control policies in hospitals in the United States. Although several studies have been conducted on the use of different infection control practices in acute care hospitals,[23-25] the extent to which infection control strategies related to MDRO are adopted is not well described. Furthermore, there is paucity of data exploring structural (i.e. hospital and infection control department) characteristics that influence MDRO and *C. difficile* rates. Therefore the aims of this study were to:

1) describe the use of infection control policies aimed at reducing MDRO and *C. difficile* in the State of California, and

2) assess the relationship between the presence and/or correct implementation of infection control policies for multi-drug resistant infections, structural characteristics and rates of BSI caused by MRSA or VRE and infections caused by *Clostridium difficile*.

We hypothesized that increased intensity of infection control policies is associated with decreased rates of MRSA and VRE BSI and *C. difficile* infection, controlling for potential confounders or structures of care characteristics.

3.3 Methods:

Data for this study are from a large cross-sectional study of California hospitals. The aim of this larger study funded by the Blue Shield of California Foundation (Grant # 2490932) was to explore the impact of mandatory reporting on the role of infection preventionists (IPs) and HAI rates. The analysis presented in this paper included data from the 2010 survey of California hospitals.

3.3.1 Recruitment and Enrollment

All non-specialty acute care facilities in California were eligible to participate; psychiatric facilities, drug/alcohol rehabilitation centers, nursing homes, outpatient units, and children's hospitals were excluded. In total, 331 hospitals were eligible to participate in this study. Participants were recruited by the Association for Professionals in Infection Control and Epidemiology, Inc. (APIC) and the Columbia University School of Nursing research staff during an eight-week period from April to June 2010. A modified Dillman technique was used including electronic and print invitation letters as well as emails and telephone calls encouraging incomplete responders to participate in the survey.[26] Electronic and print invitations were sent directly to the hospital infection prevention and

control department and the director or coordinator from each hospital's infection prevention and control department, was asked to complete this web-based survey. Survey announcements were also included in APIC e-newsletters to facilitate recruitment. As an incentive to participate, eight weekly lotteries to win an APIC textbook were offered to participants who completed the survey.

3.3.2 Conceptual Framework & Data Elements

The conceptual framework used in this study was based on the quality of care definition developed by Donabedian.[27] It is defined as being comprised of the structures, processes and outcomes of care (Figure 1).

Structures of Care

The structures of care characteristics of interest in this study are hospital characteristics such as number of beds, teaching status, hospital setting (urban/suburban/rural) and hospital participation in quality improvement (California Hospital Assessment and Reporting Task Force [CHART], Institute for Healthcare Improvement's (IHI) Five Million Lives Campaign, California Healthcare-Associated Infections Prevention Initiative (CHAIPI) and others). Structures of care also included infection control department characteristics such as infection control staffing defined as the number of full-time equivalent (FTE) IPs per 100 beds (presuming a 40-hour work week), presence of a full-time and part-time Physician hospital epidemiologist, total hours of infection control staffing hours, total number of IPs and the use of electronic surveillance systems for tracking of HAI.

Processes of Care

The processes of care examined in this study were infection control and surveillance policies aimed at reducing MDRO including: 1) screening all new patients for the specific MDRO upon admission, 2) screening select patients for the specific MDRO upon admission, 3) screening all patients for the specific MDRO periodically after admission, 4) implementing presumptive isolation/contact precautions pending results of a screen, 5) implementing contact precautions for patients with positive cultures, and 6) conducting surveillance of microbiology results for new cases of the specific MDRO. Data on these policies were collected for MRSA, VRE and *C. difficile* hospital-wide surveillance separately. If respondents indicated that they screened select patients for the specific MDRO upon admission, they were prompted to indicate what population was being screened: readmissions within 30 days of discharge, transfers from nursing homes/long term healthcare facilities, ICU patients, dialysis patients and/or other. Those respondents who indicated that their hospital screened select patients periodically after admission were asked whether the populations screened included ICU, dialysis and/or other patients.

Respondents who indicated the presence of written infection policies outlined above for hospital-wide MRSA surveillance were asked about the intensity with which the policy was implemented and the possible answer choices were: all of the time (95-100%), usually (75-94%), sometimes (25-74%), rarely/never (<25%), monitor but don't know the proportion, and no monitoring. Questions about intensity were asked only about MRSA in order to reduce respondent burden. For the analysis, intensity of each of the policies was assessed as a dichotomous variable: 95% of the time or greater vs. other. In addition, in the MRSA hospital-wide surveillance section, respondents were also asked

about the method used to collect surveillance cultures for MRSA including standard culture, polymerase chain reaction (PCR) or other rapid diagnostic test, MRSA selective agar, other, or do not collect surveillance culture. Respondents were also asked whether the hospital promoted the use of soap and water handwashing after caring for patients with *C. difficile*-associated diarrhea. Finally, participants were also asked whether their hospital had a policy regarding antibiotic restriction (yes/no/don't know) and if yes, they were asked to describe the policy in an open-ended question.

Although hand hygiene is one of the most effective and widely recognized infection control strategies for prevention of MDRO transmission,[28] the lack of reliability of self-reported compliance with hand hygiene is widely recognized,[29-30] therefore, we did not collect data on hand hygiene compliance.

Outcomes of Care

The outcomes of care assessed were rates of MRSA BSI, VRE BSI and *C. difficile* infections. Therefore, respondents were asked to provide the following hospital-wide data for the first quarter of 2010: total number of inpatient days, total number of central line days, number of healthcare-associated MRSA BSI, number of healthcare-associated VRE BSI, and number of healthcare-associated *C. difficile* infections. In addition to entering the rates, the respondents were also allowed to select the following answer choices: 'don't monitor', 'prefer not to answer' and 'no hospital level data.' For VRE BSI and MRSA BSI rates, the numerator was the number of BSI events caused by the specific organism and the denominator was the total number of central line days. For the *C. difficile* infection rate, the numerator was the number of *C. difficile* infections and the denominator was the total number of inpatient days.

3.3.3 Statistical Analysis

Data analysis was conducted using Stata Version 11.1 (Stata Corporation, College Station, Texas). Descriptive analyses included frequencies, percentages, medians and interquartile ranges. The three sets of dependent variables explored in this study were healthcare-associated MRSA BSI, VRE BSI, and *C. difficile* infection rates. The independent variables included the structures and processes of care variables described previously; the unit of analysis was the hospital. We used two methods to examine predictors of MRSA BSI rates. Since the variance of these outcome measures was greater than their respective means indicating over-dispersion,[31-32] and examination of the dispersion parameter alpha in the likelihood ratio chi-squared test showed that the dispersion parameter of the count model differed significantly from zero, providing further evidence of over-dispersion,[32] we used negative binomial regression. In addition, we also examined predictors of MRSA BSI rates by conducting bivariate Poisson regression with a dispersion parameter. Poisson regressions were conducted to examine predictors of VRE BSI and *C. difficile* rates as the assumption of mean equal to variance was met. Expected incidence rate ratios (IRR) were calculated for all models.

To test the hypothesis that increased intensity of infection control policies is associated with decreased rates of MRSA and VRE BSI and *C. difficile* infection, we first explored whether simply having a policy in place was associated with decreased rates. Then we explored the association between full compliance with policies defined as 95% of the time or more (versus other) and infection rates. For all of the analysis, we first conducted bivariate regressions to identify the infection control policies and structural characteristics that predicted MRSA BSI, VRE BSI and *C. difficile* infection rates.

Multivariable regressions were only conducted for MRSA BSI as we lacked a sufficient sample to identify independent predictors of VRE BSI and *C. difficile* rates. Those variables significant in bivariate analysis with a p-value < 0.2 were entered into a multivariable model to assess the independent predictors of MRSA BSI rates. All of these variables were checked for confounding and were considered confounders if the coefficients of the other selected variables changed by more than 10% when the assessed variable was removed from the model. Those variables that met this criteria were kept in the final model.

3.4 Results

3.4.1 Hospital Demographics

In total, 203 hospitals completed the overall survey for a response rate of 61%. Of those, 180 completed questions in the MDRO section of the survey (response rate 54%). Table 1 provides the demographic data for study hospitals. Less than half of the hospitals reported the presence of a hospital epidemiologist (n = 96, 44.8%), with a full-time hospital epidemiologist reported by only 6 hospitals (3.4%). Half of hospitals reported that the director in charge of the infection control department was certified in infection control (n = 89, 51.2%); in the majority of the cases the infection control director was a member of APIC or the Society for Healthcare Epidemiologists of America (SHEA). The median IP staffing ratio was 0.53 FTE IP per 100 beds in the study sample (interquartile range = 0.35 – 0.87). The mean MRSA BSI rate provided by 91 hospitals was 0.43 MRSA BSI per 1000 central line days (median = 0, range = 0, 8) and the mean VRE BSI rate was 0.21 VRE BSI per 1000 central line days (median = 0, range 0, 3.2). Finally, the *C. difficile* rate provided by 105 hospitals was 0.50 *C. difficile* infections per 1000

inpatient days (median = 0.41, range = 0, 2.3).

3.4.2 Adoption of MDRO Infection Control Policies

Table 2 presents data on the adoption of infection control policies aimed at MDRO in California hospitals. The vast majority of hospitals reported that a surveillance culture (n = 174, 97.2%) was collected at admission; the specific populations cultured included transfers from nursing homes (n = 140, 77.8%), readmissions within 30 days (n = 136, 75.6%), ICU patients (n = 131, 72.8%), dialysis patients (n = 114, 63.3%), all admissions excluding labor and delivery (n = 36, 20%). Less than a third of hospitals reported screening all patients for MRSA upon admission (n = 52, 29.4%). The use of targeted screening for MRSA upon admission was reported more frequently (n = 151, 87.3%); however, few hospitals reported targeted screening upon admission for VRE and *C. difficile* (6.7% and 3.9%, respectively). The most frequently screened groups for MRSA included readmissions within 30 days (89.4%), transfers from nursing homes (96.0%), ICU patients (86.8%), dialysis patients (76.8%) and patients with specific medical conditions (55.0%). The vast majority of hospitals reported policies to implement contact precautions for patients positive for MRSA (n = 166, 93.3%), VRE (n = 117, 65%), and *C. difficile* (n = 151, 83.9%). Policies for presumptive isolation/contact precautions for patients with pending screens were less frequently implemented. Only a third of hospitals had a policy regarding antibiotic restriction (n = 64, 36.4%) including the use of pre-approvals, stop orders or use of formularies.

The most frequently used method for MRSA surveillance was standard culture (36.7%), MRSA selective agar (32.2%) and PCR (23.9%). The reported compliance with MRSA infection control policies varied depending on the policy: 83.5% and 81.3% of

hospitals reported that the policy to implement contact precautions for patients with positive MRSA cultures and to perform surveillance of microbiology results for new MRSA cases was correctly implemented 95% of the time or more, (n = 86 and 65, respectively). Full compliance with the other infection control policies aimed at MRSA was less frequently reported by the hospitals (data shown in Appendix 6.2.1).

3.4.3 Predictors of MRSA BSI

In bivariate analysis, hospitals participating in the IHI campaign and those reporting the presence of an infection control director certified in infection control had significantly lower rates of MRSA BSI (IRR = 0.30 and 0.32, p-values = 0.01 and 0.02, respectively). The only MRSA infection control policies significantly associated with lower MRSA BSI rates in bivariate analysis was surveillance of microbiology results for new MRSA cases (IRR = 10.02, p = 0.05). Moreover, due to the lack of variation in hospitals reporting the presence of policies for periodic MRSA screening of all patients, we were unable to assess the association between the presence of this policy and MRSA BSI rates.

In the multivariable models presented in Table 3, we assessed the association between each of the infection control policies aimed at MRSA and MRSA BSI rates, controlling for structural characteristics. The adjusted IRR for hospitals that reported the presence of a policy to screen all patients for MRSA upon admission was 10.2 times higher compared with hospitals that did not report this policy (p-value = 0.01). Conversely, those hospitals with a policy to target new admissions for MRSA screening showed a significantly lower MRSA BSI rates as compared to hospitals that did not report this policy (IRR = 0.03, p-value = 0.01), controlling for the infection control department characteristics. However, we did not see an association between the

remaining MRSA infection control policies and MRSA BSI rates. The presence of an infection control director certified in infection control was a significant predictor of lower MRSA BSI rates in the first two models ($p < 0.01$, respectively) and approached statistical significance in the last two models ($p = 0.06$ and 0.05, respectively). The total number of infection control hours did not have an independent effect on MRSA rates in the multivariable model and the IP per beds staffing ratio was an independent predictor of MRSA BSI rates in only one model (adjusted IRR = 0.13, p-value = 0.05). The results of the Poisson regressions with a dispersion parameter were very similar to the results obtained with negative binomial regressions (data shown in Appendix 6.2.8 & 6.2.9). We show the results of the negative regression, as this approach allowed us to calculate incidence rate ratios and was a more conservative approach. The presence of a certified infection control director was an independent predictor of lower MRSA BSI rates in all four models.

An examination of the association between full compliance (all of the time vs. other) with infection control policies related to MRSA and MRSA BSI rates, revealed no statistically significant results (results shown in Appendix 6.2.7).

3.4.4 Predictors of VRE BSI

Several setting characteristics were significant predictors of lower VRE BSI rates in bivariate analysis (Table 4). Presence of a full-time hospital epidemiologist and total hospital epidemiologist hours were both highly statistically associated with higher VRE BSI rates (IRR = 11.9 and 1.03, p-values 0.004 and 0.009, respectively). Participation in CHART and in any initiative was associated with lower VRE BSI rates (IRR = 0.29 and 0.22, p-values 0.01 and 0.001, respectively). Only one infection control policy, targeted

screening of new admissions, approached statistical significance (IRR = 3.31, p-value = 0.08). Since very few hospitals reported the presence of the two policies for periodic screening, we lacked sufficient power to assess the relationship between these two policies and VRE BSI rates.

3.4.5 Predictors of C. difficile

In bivariate analyses, hospitals located in rural settings showed a significantly lower *C. difficile* rate (IRR = 0.41, p-value = 0.05) as compared to hospitals located in the urban setting (Table 4). Higher total number of infection control director hours was associated with higher *C. difficile* rates (IRR = 1.02, p-value = 0.05). None of the infection control policies aimed at *C. difficile* were associated with *C. difficile* rates.

3.5 Discussion

This study is one of the few to explore the relationship between the presence and implementation of infection control policies, structural characteristics and rates of MDRO infections in a large group of hospitals in the United States. One of the major strengths of this analysis is a large sample of California hospitals and the use of standard National Healthcare Safety Network (NHSN) definitions for healthcare-associated infections.[33]

This study was conducted more than a year after the institution of mandatory reporting of MRSA and VRE BSI and *C. difficile* rates, as well as legislation requiring targeted screening for MRSA,[34] and the majority, but not all, hospitals (87%) reported the presence of a policy to target new admissions for MRSA screening. A survey of Los Angeles County hospitals conducted in 2008 prior to the institution of legislation for MRSA screening showed that 79% of the hospitals reported a policy for targeted

screening.[35] Our data demonstrate greater adoption of this policy but indicate a definite lag between implementation of regulations and implementation of policies in the hospitals.

The data also indicate that MRSA remains the main focus of infection control programs as most hospitals reported activities aimed at preventing MRSA infections whereas less attention was placed on surveillance and control of VRE and *C. difficile*. These data are consistent with results presented by Peterson and colleagues who also found that MRSA was the most frequently screened organism, followed by VRE, methicillin-susceptible *S. aureus* and *C. difficile.*[35] Since targeted MRSA screening is mandated by the State of California, it appears that infection control departments are potentially reacting to legislation and focusing on fulfilling mandates, which may or may not be in line with the infection control priorities of their hospital. This poses a potential risk that the additional time and resources required to fulfill mandates may prevent IPs from proactively determining the most important infection control priorities in their individual setting and instituting policies aimed at these emerging issues. Additional research is needed to determine the degree to which these types of mandates are aligned with the actual needs of the hospitals and the degree to which they impact infection rates and the role of infection control personnel.

The most frequently reported methods for MRSA surveillance in our sample of hospitals were standard culture or use of MRSA selective agar in more than two-thirds of hospitals; PCR was used in almost one-fourth. This differs slightly from what was reported by a national study conducted by APIC in 2006, in which only 8% reported the use of PCR methods.[23] Although the majority of hospitals were obtaining admission

cultures for at least certain high-risk groups, the majority used standard cultures for which results are available only after 1-3 days. Importantly, since few hospitals report the use of presumptive isolation or contact precautions for patients with pending results and institute isolation only when culture results are positive, the usefulness of screening at admission is greatly diminished as these patients remain a potential reservoir for transmission.

In our study, having an infection control director who was certified in infection control was a significant independent predictor of lower MRSA BSI rates. A study conducted by Krein and colleagues reported an association between the presence of a certified IP and use of policies aimed at reducing catheter-related BSI[36] but to our knowledge, this is the first study that has demonstrated a link between staff certification and lower MDRO rates. It is possible that infection control director certification may directly influence MRSA BSI rates through the adoption of evidence-based practices instituted by a potentially more experienced and knowledgeable director, or that certification is an indicator of the overall quality of the organization and a more supportive organizational climate. The impact of certification on quality of care and patient outcomes merits further investigation.

Few infection control policies were shown to be significant predictors of infection rates in our study, which may be due to a lack of statistical power to detect small differences. In this study, we did observe a significant relationship between universal screening policies upon admission (as opposed to no active surveillance screening or targeted screening) and higher rates of MRSA BSI. This is not surprising since expanding surveillance and reporting to other areas is likely to identify additional cases and results

in higher reported rates of infections.

3.5.1 Limitations

One limitation of this study is its cross-sectional nature, which prevents us from determining temporality. Data on the timing of the policies and how long these policies were in place prior to the observation of the infection rates was not collected. An additional weakness is reliance on self-reported data regarding the presence and intensity of infection control processes and infection rates. However, collection of these data through direct observation or review of medical records would be extremely costly in time and resources and would prohibit the use of a large sample. The estimates reported in this study are likely to be, if anything, over-reported. There is a possibility of selection bias in that hospitals with high intensity of infection control processes and low healthcare-associated infection rates may have been more likely to participate in this study. However, since this analysis was not the primary aim of the study, the potential for this selection bias should be minimal. Additionally, when we compared hospitals that provided data with those that did not, there were no significant differences between the two groups in terms of location, participation in initiatives or infection control staffing levels (data not shown). Although there is the possibility of slight variation in definitions of infections across settings, this variation should be minimal since this study includes only California hospitals that are mandated by law to report their BSI and *C. difficile* rates to the NHSN and are therefore using NHSN definitions. An additional limitation is the lack of data on MDRO rates from all of the participating hospitals. Lastly, this study is restricted to acute care hospitals in California, which may limit the generalizability of these results.

3.6 Conclusion

There is still much to be learned about the factors that influence a hospital's adoption of infection control policies and rates of MDRO. This study highlights the importance of infection control certification as an important predictor of healthcare-associated infection rates. It also demonstrates the continued focus placed on MRSA as evidenced by policies instituted by infection control departments, potentially in response to state mandates. Also evident is the use of screening using standard culture techniques without concurrent implementation of contact precautions for potentially infected/colonized patients, which may diminish the utility of these policies. Further research is needed to confirm these findings and to generate quality data on the most effective infection prevention and control policies aimed at MDRO healthcare-associated infections in order to strengthen the evidence base and facilitate the development of more standardized infection prevention and control guidelines.

3.7 References

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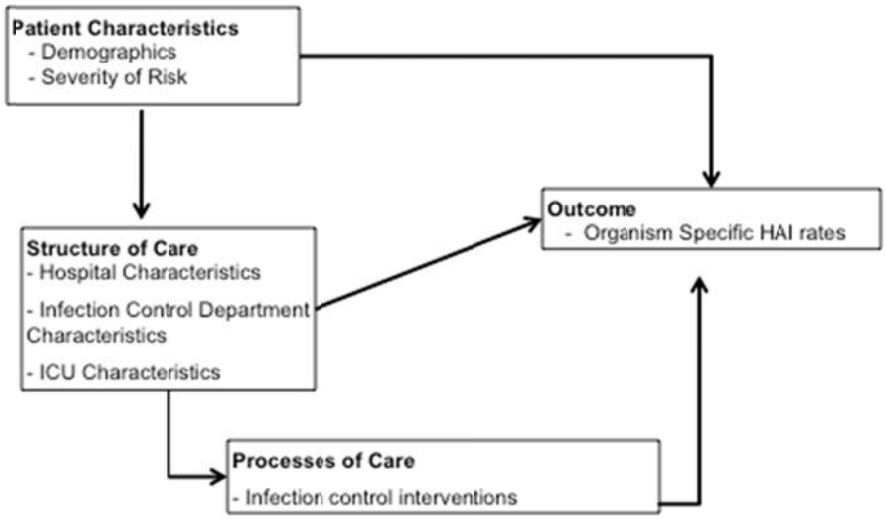

Figure 1. Conceptual Framework

Table 1. Hospital Demographic Data (N = 180)

		N	%
Teaching		48	26.8
Presence of Hospital Epidemiologist			
	Any	96	44.8
	Full-time	6	3.4
	Missing	6	3.4
Participation in CHAIPI		36	20.0
Participation in CHART		105	58.3
Participation in IHI		99	55.0
Participation in other initiative		58	32.2
Participation in any initiative		150	83.3
Infection Control Director certified in infection control (n = 174)		89	51.2
Infection Control Director member of SHEA/APIC (n = 175)		157	89.7
Electronic Surveillance System (n = 179)		53	29.6
		Median	**Interquartile Range**
Hospital Bedsize		173	100 - 340
Infection Control Director hours		40	25 - 50
# of Hospital Epidemiologists*		2	1 - 2
Hospital Epidemiologist hours		4	1 - 8
# of Infection Preventionists		1	0 - 2
Total Infection Preventionist hours		52	40 - 81
Proportion of Infection Preventionists certified in infection control		0.25	0 - 1
# of FTE Infection Preventionists per 100 beds		0.53	0.35 - 0.87
Total infection control hours (Infection Preventionist + Director)		94.5	80 - 137

*either full time or part time

APIC = Association of Professionals in Infection Control & Epidemiology, Inc., CHAIPI = California Healthcare-Associated Infections Prevention Initiative, CHART = California Hospital Assessment and Reporting Taskforce, FTE = Full-time Equivalents, IHI = Institute for Healthcare Improvement, SHEA = Society for Healthcare Epidemiology of America

Table 2. MDRO Infection Control Policies in California Hospitals (N = 180)	N	%
Collection of a surveillance culture upon hospital admission for any group of patients	174	97.2
All admissions	36	20
Readmissions within 30 days of discharge	136	75.6
Transfers from nursing homes	140	77.8
ICU patients	131	72.8
Dialysis patients	114	63.3
Other	83	46.1
Screen all patients for MRSA upon admission	52	29.4
Target new admissions for MRSA screening	151	87.3
Screen all patients for MRSA periodically after admission	5	2.8
Screen select patients for MRSA periodically after admission	22	12.6
Implement presumptive isolation/contact precautions pending a MRSA screen	61	34.3
Implement contact precautions for patients with positive MRSA cultures	166	93.3
Perform surveillance of microbiology results for new cases of MRSA	130	73
Screen all new patients for VRE upon admission	1	0.6
Screen select patients for VRE upon admission	12	6.7
Screen all patients for VRE periodically after ICU admission	1	0.6
Screen select patients for VRE periodically after ICU admission	2	1.1
Implement presumptive isolation/contact precautions pending a VRE screen	21	11.7
Implement contact precautions for patients with positive VRE cultures	117	65
Surveillance of microbiology results for new VRE cases	95	52.8
Screen all new cases for *C. difficile* upon admission	1	0.6
Screen select patients for *C. difficile* upon admission	7	3.9
Screen all patients for *C. difficile* periodically after admission	0	0
Screen select patients periodically for *C. difficile* after admission	2	1.1
Implement presumptive isolation/contact precautions pending a *C. difficile* screen	84	46.7
Implement contact precautions for patients with positive test	151	83.9
Conduct surveillance of microbiology results for new *C. difficile* cases	119	66.1
Promote the use of soap and water after caring for patients with *C. difficile* associated diarrhea	136	75.6
Policy regarding antibiotic restriction	64	36.4

Table 3. Predictors of MRSA BSI rate per 1,000 central line days in multivariable analysis (N = 36)

	Coef	p-value	IRR*	95% CI+
Model 1				
Screen all patients for MRSA upon admission	2.33	0.01	10.23	1.62 – 64.5
Infection Control Director hours	0.09	0.07	1.09	0.99 – 1.20
Infection Control Director certified in infection control	-2.01	<0.01	0.13	0.03 – 0.58
# of IP FTE per 100 beds	-3.71	0.05	0.02	0.001 – 0.95
Participation in IHI	-0.74	0.27	0.48	0.13 – 1.78
Model 2				
Target new admissions for MRSA screening	-3.51	0.01	0.03	0.01 – 0.43
Infection Control Director hours	0.08	0.18	1.08	0.96 – 1.22
Infection Control Director certified in infection control	-2.29	<0.01	0.10	0.03 – 0.39
# of IP FTE per 100 beds	-2.17	0.09	0.11	0.01 – 1.43
Participation in CHART	0.89	0.34	2.43	0.39 – 15.27
Model 3				
Screen select patients for MRSA periodically after admission	-1.07	0.24	0.34	0.06 – 2.02
Infection Control Director hours	0.05	0.17	1.05	0.98 – 1.13
Infection Control Director certified in infection control	-1.21	0.06	0.30	0.09 – 1.03
# of IP FTE per 100 beds	-1.43	0.27	0.24	0.02 – 2.95
Participation in IHI	-0.73	0.26	0.48	0.14 – 1.71
Model 4				
Implement presumptive isolation/contact precautions pending a MRSA screen	-0.16	0.84	0.85	0.18 – 4.02
Infection Control Director hours	0.05	0.21	1.05	0.97 – 1.13
Infection Control Director certified in infection control	-1.35	0.05	0.26	0.07 – 1.00
# of IP FTE per 100 beds	-1.60	0.27	0.20	0.01 – 3.25
Participation in IHI	-0.73	0.25	0.48	0.14 – 1.67

*All of the variables entered into the model are shown in the table.

CHART = California Hospital Assessment and Reporting Taskforce, CI = Confidence Interval, FTE = Full-time Equivalents, IHI = Institute for Healthcare Improvement, IRR = Incidence Rate Ratio

Table 4. Significant Structural Predictors of VRE BSI rates and *C. difficile infections* in bivariate analysis

	Coef	p-value	IRR	95% CI
VRE BSI*(N = 91)				
Participation in CHART	-1.26	0.01	0.29	0.11 – 0.75
Participation in any initiative	-1.52	<0.01	0.22	0.09 – 0.54
Physician Hospital Epidemiologist hours	0.03	<0.01	1.03	1.01 – 1.06
Presence of a Full-time Hospital Epidemiologist	2.48	<0.01	11.9	2.22 – 63.90
***C. difficile*† (N = 105)**				
Setting (reference group = urban)				
Suburb	-0.33	0.27	0.72	0.40 – 1.29
Rural	-0.89	0.05	0.41	0.17 – 1.00
Infection Control Director hours	0.02	0.05	1.02	1.00 – 1.04

*per 1,000 central line days

†per 1,000 inpatient days

CHART = California Hospital Assessment and Reporting Taskforce, IHI = Institute for Healthcare Improvement

CHAPTER 4

Risk Factors for Bloodstream Infections with methicillin-resistant *Staphylococcus aureus*: A Nested Case-Control Study

4.1 Abstract

Background:

The study objective is to compare risk factors for hospital-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSI) using two sets of controls-- controls with methicillin-susceptible *Staphylococcus aureus* (MSSA) BSI and non-infected controls-- in a large sample of hospitalized patients.

Methods:

A nested case control study was conducted utilizing three years of administrative, clinical and infection control data from four hospitals. Cases were compared to unmatched controls with MSSA BSI. Additionally, cases were 1:2 matched with non-infected controls. Traditional and conditional logistic regressions were conducted.

Results:

A total of 204 cases with MRSA BSI and 301 controls were identified during the study period. 201 cases were matched to 402 non-infected controls. The independent risk factors differed between the two comparison groups and also depending on whether antibiotic exposure was used in the model. The three independent risk factors for MRSA BSI as compared to MSSA BSI were older age ($p = 0.048$), major organ transplant ($p = 0.016$) and quinolone use ($p = 0.016$). Cases were more likely than non-infected controls to have renal failure ($p = 0.003$), cirrhosis ($p = 0.013$), and a central venous catheter ($p = 0.003$), after controlling for other risk factors.

Conclusions:

This large case-control study allowed us to assess risk factors for MRSA BSI using two sets of controls and showed that risk factors for MRSA BSI differed greatly depending on the control group chosen. More importantly, these results confirm the need for careful selection of appropriate controls groups, especially when studying antibiotics as potential risk factors for MRSA BSI, as well as the need to carefully adjust for underlying severity of illness. Further research is needed to identify proper controls in these types of studies.

Key Words:

Antibiotic resistance, multi-drug resistant infections, methicillin-resistant *Staphylococcus aureus*, bloodstream infections.

4.2 Introduction

Healthcare-associated infections (HAI) cause significant morbidity and mortality in acute care settings (1). Part of this morbidity and mortality is due to increased resistance to antibiotics in HAI. Currently, it is estimated that more than 70% of bacteria that cause HAI are resistant to at least one antibiotic that is commonly used in treatment of the infection (2). Methicillin-resistant *Staphylococcus aureus* (MRSA) has been the focus of much research in the last several decades due to its major contribution to the morbidity and mortality of hospitalized patients (3-6).

Staphylococcus aureus can cause serious infections at many body sites; it is the most common cause of bloodstream infections (BSI) (7). It is estimated that approximately one-third of patients with BSI caused by *S. aureus* develop local complications or distant septic metastases (8). These infections are even more complicated when the *S. aureus* strain is resistant to methicillin or other semi-synthetic penicillins and result in increased mortality, length of stay, as well as higher hospital costs for patients with resistant infections as compared to those with a BSI that is caused by methicillin-susceptible *Staphylococcus aureus* (MSSA) (9-13). Differences in morbidity and mortality due to these two infections are posited to be the result of variations in virulence of the causative strains, vulnerabilities of the populations affected and delays in receiving drug therapies appropriate for the infection (10, 13).

Due to the fact that MRSA BSI is a major contributor to the morbidity and mortality of hospitalized patients, it is important to identify factors that place patients at risk of developing MRSA BSI. Knowledge of the modifiable risk factors for MRSA BSI can help to identify patients at risk and can help hospitals institute appropriate infection

control policies. Several researchers have attempted to identify predictors of MRSA BSI in hospitals (12, 14-20). However, the majority of these studied were limited by small sample sizes, single site settings and methodological issues such as inadequate control for severity of illness. Additionally, studies that utilized matching failed to employ statistical methods to adjust for the lack of independence among cases and matched controls.

Several researchers reported independent predictors of MRSA BSI, however, this was not the primary aim of these studies, which set out to identify differences in outcomes in patients with MRSA vs. MSSA BSI (13, 19). In addition, existing studies varied in the control group chosen. For example, most studies used control groups consisting of patients with antibiotic-susceptible BSI, which allows the researcher to identify predictors of resistance in BSI. However, researchers have hypothesized that using controls with MSSA BSI may overestimate the association between antibiotic use and MRSA BSI since prior use of antibiotics such as oxacillin is likely to prevent infection with strains of bacteria that are susceptible to that particular antibiotic (21). On the other hand, other studies selected controls with no infection. In this comparison, the predictors identified are predictors of BSI due to *S. aureus*. Many of these studies did not adequately control for severity of illness. Additionally, most studies did not focus specifically on healthcare-associated infections but grouped community-acquired and healthcare-associated infections together which may mask some important hospital-related risk factors.

4.3 Objective

The objective of this study was to identify risk factors for healthcare-associated MRSA BSI in a nested case control study using three years of data (2006-8) from the

NewYork Presbyterian Hospital (NYPH) System. Specifically, the aim was to compare risk factors for hospital-acquired MRSA BSI using two sets of controls-- controls with MSSA BSI and non-infected controls-- in a large sample of hospitalized patients. This study involves a secondary analysis of a dataset compiled as part of the "Distribution of the Costs of Antimicrobial Resistant Infection" study funded by the National Institute of Nursing Research (R01NR010822).

4.4 Methods

Data were obtained from four New York City hospitals that make up the NewYork Presbyterian Hospital System, the largest hospital system in New York. It is comprised of Milstein Hospital, a tertiary academic health center (642 beds) located in a low-income, immigrant community of Washington Heights, and Weill Cornell (866 beds), which is also a tertiary hospital, located in an affluent neighborhood. Morgan Stanley Children's Hospital of New York (CHONY) (282 beds) is a pediatric hospital located in Washington Heights, and Allen Hospital (205 beds) is a community hospital in Inwood with a significant population of patients transferred from skilled nursing facilities. As part of NYPH, the four hospitals share one Clinical Data Warehouse (CDW), which integrates data from over 20 clinical databases including laboratory, radiology, pathology, diagnostic data sources among many others. As part of the larger study, a database was created, which linked data from the CDW with operating room, administrative, cost accounting and electronic health records data that were routinely collected. The linkage between the different data sources was performed using medical records numbers unique to each patient.

4.4.1 Case and Control Selection

This study used de-identified data from the four hospitals for the years 2006 through 2008, including data on all patients admitted to NYPH in these three years. In order to be considered hospital-associated in our study, we defined BSI as those that manifested at least 48 hours after admission. Case and controls were defined using an algorithm defined for the larger study and based on the National Healthcare Safety Network (NHSN) definitions for primary BSI (22). NHSN is a surveillance network through which hospital report HAI rates to the Centers for Disease Control and Prevention and NHSN definitions have become the recognized standard for defining infections around the world (23). For the purposes of this study, the NHSN definitions were modified to focus on electronically available data, given the large number of potential cases to evaluate.

Case (MRSA BSI)

- Positive blood culture for methicillin-resistant *Staphylococcus aureus*

  AND

- No positive culture with methicillin-resistant *Staphylococcus aureus* at other body sites within 14 days prior to positive blood culture

We used two sets of controls. Patients with MRSA BSI were compared to patients with MSSA BSI to determine the risk factors for methicillin resistance (unmatched). In addition, non-infected controls were matched to cases on age (± 5 years), minimum length of exposure (number of days hospitalized prior to development of BSI in cases), hospital, early ICU stay (defined as having been admitted to an ICU in the first 3 calendar

days of hospital stay) and hospital to determine the risk factors for MRSA BSI (using 2:1 matching). The two sets of controls were defined using the following criteria:

Control (MSSA BSI)

- Positive blood culture with methicillin-susceptible *Staphylococcus aureus*

  AND

- No positive culture with methicillin-susceptible *Staphylococcus aureus* at other body sites within 14 days prior to positive blood culture

Non-Infected Control

- No positive blood culture for ANY organism

4.4.2 Data Elements

The risk factors examined in this study are presented below and were based on a review of the existing literature.

Patient Characteristics

Demographic Characteristics

The demographic factors considered were gender (male/female) and age (continuous variable defined as age at discharge). Age was used as a matching factor for the comparison of cases to non-infected controls and gender was investigated as a potential risk factor for MRSA BSI using MSSA BSI controls.

Intrinsic Risk Factors Prior to Hospitalization

Prior hospitalization and stay in a skilled nursing facility (SNF) have been identified as risk factors for MRSA BSI in several studies (14-15, 17). To investigate the specific role that prior hospitalization plays in increasing risk for BSI, we examined history of hospitalization in the prior year, length of stay during the last hospitalization

and days since the hospitalization in the prior year. History of stay at a SNF within the prior year was also examined and defined based on the admission source from administrative data and by matching admission addresses to known SNF in the area.

Clinical Risk Factors

Data on the following risk factors were also collected (yes/no): diabetes mellitus, malignancy, trauma, open wound, chronic dermatitis, renal failure, burns (involving 10 % or more of the body or 3rd degree), history of major organ transplant, history of substance abuse, asthma, chemotherapy, congestive heart failure, cirrhosis, chronic obstructive pulmonary disease (COPD), cardiovascular disease, decubitus ulcer, hepatitis B and C infection, HIV infection, neurological disease, rheumatoid arthritis and tracheostomy. These risk factors were identified using ICD 9 codes and present on admission indicators. A Charlson co-morbidity score was also calculated as a measure of the patient's health status at admission using ICD-9-CM diagnostic codes for conditions present on admission (25).

Encounter-Specific Variables:

Antibiotic & Immunosuppressive Medication Use

History of antibiotic use has also been implicated as a risk factor for the development of resistant infections (26-28). In this data set, the following variables were available on medication use: medications administered during the hospital stay, day when medication was first and last administered, and total number of days medication was administered. Using these variables, we defined exposure to antibiotics and immunosuppressive drugs for cases and the two comparison groups in the time period at risk for infection. Exposure to immunosuppressive drugs in the time period at risk was

also examined as a potential risk factor for infection with MRSA BSI. Antibiotic exposure was assessed in two ways: overall exposure to an antibiotic in the time period at risk, exposure to specific classes of antibiotics including aminoglycosides, carbapenems, cephalosporins, glycylcylines, macrolides, monobactams, penicillins, polypeptides, quinolones, sulfonamides, tetracyclines and other antibiotics. Exposure to medications was examined as a dichotomous variable and defined as occurring during the period at risk for the cases and MSSA BSI controls. For non-infected controls, exposure was assessed during the corresponding period at risk for their matched case.

Procedure-based Risk Factors

The use of central venous and urinary catheters prior to infection was investigated as potential risk factors for infection in this study. Data on the total days of central venous lines and urinary catheters prior to infection (or during the matched time at risk for the non-infected controls) were available and allowed us to investigate prolonged use of these devices as potential risk factors for infection. In addition, the occurrence of each of the following procedures in the patient's period of risk were assessed as potential risk factors: specialized cardiac procedure (either cardiac catheterization, coronary angioplasty, cardiac angiography, or vascular stenting), intubation, dialysis (hemodialysis), insertion of feeding tube, major organ transplant, general anesthesia, open biopsy, any operating room procedure performed in encounter lasting 30 minutes or more, major operating room diagnostic or therapeutic procedure defined according to the Healthcare Cost and Utilization Project (HCUP) classifications. For the comparison of cases with MSSA BSI controls, the occurrence of these procedure- based risk factors was defined before the development of BSI in the cases and controls. For the comparison of

cases with matched non-infected controls, exposure to these risk factors was defined as during the period of risk for each index case and during the corresponding period at risk for the matched control.

Outcome Variable

The following variables were utilized to define cases and the two sets of controls using the algorithm described previously: BSI, BSI with MRSA, hospital day when MRSA BSI was detected, MSSA BSI, hospital day when MSSA BSI was detected, year of admission, day of discharge, length of stay.

4.4.3 Statistical Analysis

Data were entered and analyzed in STATA 11.1 (Stata Corporation, College Station, Texas). In the first analysis, we assessed risk factors for MRSA resistance in BSI by comparing MRSA BSI cases to controls with MSSA BSI. Mann-Whitney tests for continuous non-parametric variables and Chi-squared tests or Fisher's exact tests for categorical variables were used in bivariate analysis as appropriate. Multivariable logistic regression models were used to assess the independent effect of these variables on the risk of developing a resistant BSI. The second analysis assessed risk factors for MRSA BSI by comparing cases with MRSA BSI and non-infected matched controls using conditional logistic regression. Specifically, we used conditional logistic regressions to account for matching on age, period at risk, early ICU stay and hospital.

For both analyses, variables with a p-value ≤ 0.1 in bivariate analysis were included in multivariable analysis to estimate the probability of MRSA BSI. In addition, all predictors were checked for confounding, effect modification and colinearity. Possible confounding variables were added one by one into the model, and if the coefficient

estimates of a covariate changed by 10% or more, the variable was considered to be a confounder and added to the model. Effect modification between covariates was evaluated by testing of interaction terms for variables that were conceptually potential effect modifiers. Due to the fact that antibiotic exposure data was not electronically recorded at two hospital sites for the whole length of the study resulting in antibiotic exposure data missing for a substantial number of cases, multivariable models for both analysis were run two ways: including and excluding antibiotic risk factors. Multi-colinearity was assessed by examining tolerance and variance inflation factors (VIF) of the variables in the models. The goodness of fit of the models was assessed using the Hosmer-Lemeshow goodness of fit test for logistic regression and the Akaike Information Criterion (AIC) for conditional logistic regression. A p-value of < 0.05 was considered statistically significant.

4.5 Results

4.5.1 Comparison of MRSA BSI and MSSA BSI patients

A total of 204 cases with MRSA BSI and 301 controls with MSSA BSI were identified during the study period. Patient demographic, clinical and encounter-based risk factors are summarized in Table 1. Bivariate analysis identified five risk factors that differed significantly between cases and controls. Cases were more likely than controls to be older ($p < 0.001$), have renal failure ($p < 0.001$) and a tracheostomy ($p = 0.02$) present on admission, as well as have a urinary catheter ($p = 0.001$), dialysis ($p = 0.009$) and a major organ transplant ($p = 0.018$) during their encounter prior to the development of BSI. In addition MRSA BSI cases had a higher Charlson severity of illness measure than MSSA BSI controls ($p = 0.051$). Immunosuppressive medication was identified as a

partial mediator of the relationship between organ transplant and the outcome. Cases were more likely than controls to have had a major organ transplant (OR = 3.4, 95% CI = 1.04 – 11.24) and this association was diminished when adjusted for immunosuppressive medication use prior to BSI (OR = 3.02, 95% CI = 0.90 – 10.12).

Cases and controls were also compared in terms of exposure to antibiotics prior to the development of BSI (Table 2); quinolone exposure was the only class of antibiotics that was significantly associated with an increased risk of BSI with MRSA (p = 0.001). Overall antibiotic exposure and exposure to monobactams approached statistical significance (p-values of 0.059 and 0.056, respectively).

In the multivariable logistic regression model excluding antibiotic risk factors (N = 504), three independent risk factors for MRSA BSI were identified: older age (OR = 1.01, p = 0.001), renal failure (OR = 1.58, p = 0.029) and major operating room therapeutic procedure (OR = 1.68, p = 0.032). In addition, major organ transplant approached statistical significance as an independent risk factor (OR = 4.90, p = 0.052). When antibiotic risk factors were added to the model (N = 330), the three independent risk factors for MRSA BSI were older age (OR = 1.01, p = 0.048), major organ transplant (OR = 14.0, p = 0.016) and quinolone use prior to development of BSI (OR = 3.41, p = 0.016). No differences in the models were seen whether urinary catheter exposure was assessed as a dichotomous variable or as the number of catheter days prior to development of BSI (data shown in Appendix 6.3.4 and 6.3.5).

4.5.2 Comparison of MRSA BSI cases and non-infected matched controls

Overall, 1:2 matching on early ICU stay, age, hospital and minimum time at risk was successful for 201 out of 204 MRSA BSI cases. Table 1 shows the bivariate

comparison of MRSA BSI cases and their matched non-infected controls. Cases and controls differed significantly on a variety of factors including gender ($p = 0.016$), hospitalization in the prior year ($p = 0.008$), severity of illness as measured by the Charlson score ($p = 0.001$), history of malignancy ($p = 0.020$), renal failure ($p < 0.001$), cirrhosis ($p = 0.009$), tracheostomy ($p = 0.026$), central venous catheter use ($p <0.001$), major OR therapeutic procedure ($p = 0.005$) and the number of days spent in the ICU ($p = 0.005$). Bivariate analysis of differences in antibiotic use between cases and controls is summarized in Table 2. As in the comparison of cases with MSSA BSI controls, cases were significantly more likely to have been exposed to quinolones in the period at risk than their corresponding non-infected controls (OR = 4.2, $p = 0.003$).

Multiple independent risk factors for MRSA BSI were identified in a multivariable logistic regression model excluding antibiotic risk factors (N = 595). These included male gender (OR = 1.62, $p = 0.017$), malignancy (OR = 1.87, $p = 0.047$), renal failure (OR = 2.71, $p < 0.001$), cirrhosis (OR = 3.63, $p = 0.008$), HIV infection (OR = 4.53, $p = 0.029$), and central venous catheter use (OR =2.36, $p = 0.001$). Cases were less likely than their matched controls to have a major OR procedure in their time period at risk (OR = 0.64, $p = 0.042$). In the smaller multivariable model including antibiotic use (N = 358), cases were more likely than controls to have renal failure (OR = 2.74, $p = 0.003$), cirrhosis (OR = 4.03, $p = 0.013$), and a central venous catheter (OR = 3.08, $p = 0.003$). After controlling for the other risk factors, quinolone exposure was no longer a significant predictor of MRSA BSI infection ($p = 0.206$). As in the previous model, controlling for the other risk factors, cases were less likely than controls to have a major OR therapeutic procedure in the time at risk although the association was not statistically

significant (OR = 0.57, p = 0.055). Central venous catheter use had the same independent impact on the risk of BSI, whether it was assessed as a continuous days variable or as a dichotomous variable (data shown in Appendix 6.3.6 and 6.3.7).

4.6 Discussion

We performed a large case-control study to evaluate risk factors for MRSA BSI and utilized two sets of controls. Although we improved upon the design of the previous studies by employing a large sample, using two control groups, and adjusting for underlying differences between cases and uninfected controls through the use of matching, we found similar results to what has been published previously in the literature verifying the validity of previously published studies.

We found that the risk factors for MRSA BSI differed depending on the control group chosen. This is in contrast to a study assessing risk factors for MRSA surgical site infections (SSI) in older adults where the researchers utilized two sets of controls; 84 patients with SSI due to MRSA were compared to 64 patients with MSSA SSI and 167 patients without SSI, potentially allowing to differentiate between risk factors for MRSA SSI and SSI due to any *S. aureus* (29). Using two separate multivariate models, the researchers showed that requiring assistance in three or more activities of daily living, and wound class were independently associated with MRSA BSI using both controls groups.

A study by Graffunder and colleagues of 121 MRSA patients and 123 MSSA controls, identified levofloxacin, belonging to the class of quinolones, and macrolides as independent risk factors for MRSA infection as compared to MSSA infection (although this study did not specifically look at BSI) (26). We also identified macrolides as risk

factors in bivariate analysis but macrolide use failed to remain an independent predictor of MRSA BSI when entered into a multivariable model in our study. Importantly, in our study exposure to quinolones was an independent predictor of MRSA BSI as compared to MSSA BSI but not in the comparison of MRSA BSI patients and non-infected controls. This confirms the results obtained by Ernst and colleagues who evaluated the importance of control group selection in studies assessing the association between use of antibiotics and MRSA BSI and utilized two sets of controls: one group with MSSA BSI and another group without BSI (18). Specifically, the researchers argued that the appropriate control group to be used when assessing antibiotic exposure as a potential risk factor in a case control study is a non-infected control group, since those patients who take an antibiotic effective in treatment of a MSSA would be much less likely to develop an infection with a susceptible organism. Therefore, patients with antibiotic exposure may be less likely to end up as controls in the case-control study, leading to selection bias and an overestimation of the effect that antibiotic exposure has on the development of MRSA BSI. Indeed, as in our study, the researchers observed a significant association between exposure to antibiotics and infections with MRSA BSI when compared with MSSA BSI controls but not when the non-infected control group was utilized. One of the flaws of this study, in addition to a small sample size, was the fact that the researchers matched cases and controls on age, gender, time at risk and hospital ward but did not utilize statistical methods appropriate for matched data. Despite this limitation, the results of the Ernst study are confirmed by our findings, which underscore the importance of choosing appropriate controls depending on the risk factors that are under examination.

In a study of 60 MRSA BSI patients with 240 non-infected controls, Bakowski and colleagues identified severity of illness indicators and the use of central venous catheters as independent risk factors for MRSA BSI (20). In addition, the authors found prior surgery as protective against acquiring a MRSA BSI. The researchers chose an uninfected control group instead of a control group with methicillin-susceptible infections because they aimed to isolate and identify risk factors for BSI and not risk factors for methicillin resistance. However, the researchers observed large differences in disease severity between the cases and controls, which they believe masked other risk factors for infection. Our study identified similar results in that the comparison of MRSA BSI with non-infected controls identified central venous catheter use as the only independent encounter-based risk factor for MRSA BSI and identified 'Major OR therapeutic procedure' as a protective factor, after controlling for other demographic and clinical risk factors. Even after matching cases and controls on age, early ICU stay and minimum time at risk, important differences in underlying severity of illness seem to be present as evidenced by the appearance of 'major OR therapeutic procedure' as protective in terms of development of infections. A potential explanation for this observation is that those patients who are admitted to the hospital specifically to undergo a major therapeutic procedure may be healthier than those who are admitted for another reason and therefore may be less likely to develop MRSA BSI. This finding underscores the need for carefully chosen comparison groups when studying infections and the importance of careful consideration of the underlying differences in severity of illness between comparison groups, perhaps necessitating the use of more stringent matching procedures such as reason for admission.

In this study, we identified immunosuppressive medication use as a potential mediating risk factor, revealing the biological path through which organ transplant acts to increase the risk of infection. Patients who undergo transplants are at higher risk for developing MRSA BSI and our data suggest that exposure to immunosuppressive medication is a partial mediator of this relationship. Additional investigations of the specific relationships between demographic, clinical and encounter-based risk factors identified in the literature, would allow us to better understand the mechanisms that place patients at increased risk for MRSA BSI.

4.6.1 Limitations

One of the limitations of this analysis was dependence upon data available in the electronic medical record. Numerous studies have shown that patients colonized with *S. aureus* are at increased risk of infection, underscoring the importance of *S. aureus* carriage as an endogenous source of infection (28, 30-31). However, since this was a retrospective study, data on certain potential risk factors such as previous colonization with MRSA or MSSA were not available. Moreover, in order to utilize a data set of this magnitude, it was necessary to modify NHSN definitions to focus on electronically available data. Thus it is possible that secondary BSIs were mistakenly misclassified as primary BSIs and vice versa, because only microbiologic data was used to determine whether an infection existed at another site. Another limitation is the lack of complete data on antibiotic use in two of the four hospital sites for part of the study period. Furthermore, although this is a large study focusing on risk factors for MRSA BSI, it was limited to four hospitals in NYC, which may limit the generalizability of the results.

4.6.2 Strengths

One of the major strengths of this analysis was the large sample size of MRSA and MSSA BSI, which gives sufficient power to identify pertinent risk factors. Since this study included all cases of MRSA and MSSA BSI in a three-year period it should not be subject to selection bias. Data were obtained from four hospitals which served very different patient populations, increasing the generalizability of the results. In addition, the use of two control groups allowed for the identification and comparison of risk factors for MRSA BSI and resistance in BSI.

4.7 Conclusions

We performed a case-control study to assess risk factors for MRSA BSI using two sets of controls; risk factors for MRSA BSI differed greatly depending on the control group chosen. Additionally, whether antibiotic use was included in the analysis influenced the results but to a lesser degree. More importantly, our results confirm the need for careful selection of appropriate control groups, especially when studying antibiotics as potential risk factors for MRSA BSI, as well as the need to carefully adjust for underlying severity of illness. Further research is needed to identify proper controls in these types of studies. Moreover, additional research to further uncover the inter-relationships between different risk factors for MRSA BSI would aid in our understanding of the mechanisms through which these infections are acquired.

4.8 References

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Table 1. Bivariate comparison of characteristics of MRSA BSI cases with MSSA BSI controls and Uninfected controls†							
	MRSA (N = 204)	**MSSA (N = 301)**	**P-value**	**MRSA BSI (N = 201)**	**Uninfected Controls (N = 402)**	**OR (95% CI)**	**P-value**
	N (%) or Mean (Median)	**N (%) or Mean (Median)**		**N (%) or Mean (Median)**	**N (%) or Mean (Median)**		
Demographic							
Male Gender	120 (58.8)	171 (56.8)	0.653	118 (58.7)	195 (48.5)	1.6 (1.1 – 2.2)	0.016
Age	54.7 (57.5)	42.4 (50.0)	<0.001	54.6 (58)*	54.9 (58)*	--	--
Intrinsic Risk Factors Prior to Hospitalization							
Stay in Skilled Nursing Facility	9 (4.4)	13 (4.3)	0.960	9 (4.5)	8 (2.0)	2.6 (0.9 – 7.4)	0.077
Hospitalization in Prior Year	92 (45.1)	113 (37.5)	0.090	91 (45.3)	140 (34.8)	1.7 (1.1 – 2.5)	0.008
Length of Stay in Prior Hospitalization	16.4 (11.0)	14 (7.0)	0.063	16.5 (11)	13.6 (7)	1.0 (1.0 – 1.0)	0.233
Days Since Prior Hospitalization	90.0 (28.0)	94.1 (46.0)	0.119	151.5 (28)	106.9 (24.5)	1.0 (1.0 – 1.0)	0.936
Clinical Risk Factors (Based on Present on Admission Indicators)							
Charlson Severity of Illness Measure	2.6 (2.0)	2.4 (2.0)	0.051	2.6 (2.0)	2.0 (1.0)	1.1 (1.1 – 1.2)	0.001
Diabetes Mellitus	52 (25.5)	58 (19.3)	0.097	51 (25.4)	82 (20.4)	1.4 (0.9 – 2.0)	0.156
Malignancy	52 (25.5)	78 (25.9)	0.915	52 (25.9)	73 (18.2)	1.7 (1.1 – 2.7)	0.020
Open Wound	2 (1.0)	4 (1.3)	1.000	2 (1.0)	3 (0.8)	1.3 (0.2 – 8.0)	0.753
Chronic Dermatitis	27 (13.2)	35 (11.6)	0.589	27 (13.4)	38 (9.5)	1.5 (0.9 – 2.4)	0.150
Renal Failure	102 (50.0)	200 (33.5)	<0.001	99 (49.3)	115 (28.6)	3.1 (2.0 – 4.6)	<0.001
Any Burn	7 (3.4)	7 (2.3)	0.458	6 (3.0)	16 (4.0)	0.7 (0.2 – 2.0)	0.495
3rd Degree Burn	7 (3.4)	4 (1.3)	0.102	6 (3.0)	9 (2.2)	1.4 (0.4 – 4.7)	0.542
History of Major Organ Transplant	8 (3.9)	9 (3.0)	0.569	8 (4.0)	14 (3.5)	1.1 (0.5 – 2.7)	0.763
History of Substance Abuse	20 (9.8)	18 (6.0)	0.110	20 (10.0)	36 (9.0)	1.1 (0.6 – 2.1)	0.670
Asthma	15 (7.4)	13 (4.3)	0.144	15 (7.5)	26 (6.5)	0.2 (0.6 – 2.4)	0.628
Chemotherapy	7 (3.4)	3 (1.0)	0.098	7 (3.5)	7 (1.7)	2.0 (0.7 – 5.7)	0.195
Congestive Heart Failure	51 (25.0)	59 (19.6)	0.149	50 (24.9)	74 (18.4)	1.5 (1.0 – 2.4)	0.054
Cirrhosis	15 (7.4)	17 (5.7)	0.440	15 (7.5)	11 (2.7)	3.1 (1.3 – 7.0)	0.009

COPD	12 (5.9)	15 (5.0)	0.659	11 (5.5)	25 (6.2)	0.9 (0.4 – 1.8)	0.720
Cardiovascular Disease	9 (4.4)	17 (5.7)	0.537	9 (4.5)	22 (5.5)	0.8 (0.4 – 1.8)	0.6
Decubitus Ulcer	14 (6.9)	12 (4.0)	0.151	13 (6.5)	19 (4.7)	1.4 (0.7 – 3.1)	0.352
Hepatitis B	1 (0.5)	5 (1.7)	0.409	1 (0.5)	4 (1.0)	0.5 (0.1 – 4.5)	0.535
Hepatitis C	7 (3.4)	9 (3.0)	0.781	7 (3.5)	9 (2.2)	1.6 (0.6 – 4.2)	0.381
HIV Infection	11 (5.4)	12 (4.0)	0.457	11 (5.5)	11 (2.7)	2.6 (0.9 – 7.3)	0.067
Neurological Disease	12 (5.9)	13 (4.3)	0.427	12 (6.0)	16 (4.0)	1.6 (0.7 – 3.7)	0.252
Rheumatoid Arthritis	2 (1.0)	1 (0.3)	0.568	2 (1.0)	1 (0.3)	4.0 (0.4 – 44.1)	0.258
Tracheostomy	25 (12.3)	19 (6.3)	0.020	23 (11.4)	28 (7.0)	2.3 (1.1 – 5.0)	0.026
Encounter-Specific Risk Factors (prior to development of BSI)							
Immunosuppressive Medication	73 (35.8)	89 (29.7)	0.149	71 (35.3)	115 (29.0)	1.4 (0.9 – 2.0)	0.100
Central Venous Catheter Use	84 (41.2)	124 (41.3)	0.972	81 (40.3)	106 (26.6)	2.4 (1.6 – 3.8)	<0.001
Central Venous Catheter Days	9.0 (0)	8.5 (0)	0.896	8.0 (0)	4.9 (0)	1.0 (1.0 – 1.0)	0.003
Urinary Catheter Use	102 (50.0)	107 (35.7)	0.001	101 (50.3)	201 (50.9)	1.0 (0.7 – 1.4)	0.994
Urinary Catheter Days	8.1 (0.5)	4.1 (0)	< 0.001	7.8 (1)	6.5 (1)	1.0 (1.0 – 1.0)	0.145
Cardiac Procedure**	25 (12.3)	23 (7.8)	0.085	24 (12.0)	60 (15.4)	0.8 (0.4 – 1.2)	0.227
Intubation	37 (18.1)	60 (20.0)	0.603	35 (17.4)	65 (16.4)	1.1 (0.7 – 1.8)	0.696
Mechanical Ventilation	46 (22.6)	71 (23.7)	0.771	43 (21.4)	71 (17.9)	1.4 (0.8 – 2.3)	0.202
Biopsy	11 (5.4)	17 (5.7)	0.895	11 (5.5)	21 (5.3)	1.1 (0.5 – 2.3)	0.896
Insertion of Feeding Tube	11 (5.4)	14 (4.7)	0.713	10 (5.0)	22 (5.5)	0.9 (0.4 – 1.9)	0.739
Organ Transplant	8 (3.9)	2 (0.7)	0.018	8 (4.0)	10 (2.5)	1.6 (0.6 – 4.1)	0.322
Major OR Therapeutic Procedure	54 (26.5)	59 (19.7)	0.072	52 (25.9)	147 (37.1)	0.6 (0.4 – 0.8)	0.005
Major OR Diagnostic Procedure	8 (3.9)	11 (3.7)	0.833	8 (4.0)	21 (5.3)	0.8 (0.3 – 1.7)	0.513
Early ICU Stay	78 (38.2)	121 (40.2)	0.658	75 (37.3)*	150 (37.3)*	--	--
ICU Days	11.0 (0)	11.9 (0)	0.723	11.5 (0)	8.7 (0)	1.0 (1.0 - 1.0)	0.005
Length of Stay	22.9 (11)	20.7 (9)	0.145	--	--	--	--

†(For matched analysis, defined exposure for controls within period at risk for matched case)

*Variable used in matching MRSA BSI cases to non-infected controls

** Cardiac Procedure defined as either cardiac catheterization, coronary angioplasty, catheter angiography and vascular stenting

Table 2. Comparison of Antibiotic Use between MRSA BSI cases with Controls with MSSA BSI or No-Infection†							
	MRSA (N = 123)	**MSSA (N = 207)**		**MRSA BSI (N = 122)**	**Uninfected Controls (N = 240)**		
	N (%)	N (%)	P-value	N (%)	N (%)	OR (95% CI)	P-value
Overall Antibiotic Exposure	60 (48.8)	79 (38.2)	0.059	57 (47.1)	102 (42.5)	1.2 (0.8 – 2.0)	0.412
Aminoglycosides	1 (0.8)	3 (1.5)	1.000	0 (0.0)	4 (1.7)	--	--
Carbapenems	6 (4.9)	6 (2.9)	0.353	5 (4.1)	9 (3.8)	0.6 (0.2 – 2.5)	0.505
Cephalosporins	16 (13.0)	29 (14.0)	0.798	16 (13.1)	37 (15.4)	0.8 (0.4 – 1.6)	0.577
Glycylcyclines	2 (1.6)	1 (0.5)	0.558	1 (0.8)	2 (0.8)	--	--
Macrolides	9 (7.3)	13 (6.3)	0.715	9 (7.4)	18 (7.5)	1 (0.4 – 2.4)	1.000
Monobactams	6 (4.9)	2 (0.97)	0.056	6 (4.9)	2 (0.8)	6.6 (0.7 – 60.9)	0.096
Penicillins	14 (11.4)	19 (9.2)	0.519	14 (11.5)	19 (7.9)	1.7 (0.7 – 3.9)	0.207
Polypeptides	0 (0.0)	0 (0.0)	---	0 (0.0)	0 (0.0)	--	--
Quinolones	16 (13.0)	7 (3.4)	0.001	16 (13.1)	8 (3.3)	4.2 (1.6 – 11.8)	0.003
Sulfonamides	0 (0.0)	5 (2.4)	0.162	0 (0.0)	2 (0.8)	--	--
Tetracyclines	0 (0.0)	0 (0.0)	---	0 (0.0)	0 (0.0)	--	--
Other antibiotics	34 (27.6)	54 (26.1)	0.797	33 (27.1)	49 (20.4)	1.5 (0.8 – 2.8)	0.178

†For matched analysis, defined exposure for controls within period at risk for matched case

Table 3. Multivariable Analysis of Risk Factors for MRSA BSI Using Controls with MSSA BSI excluding antibiotic use (N= 504)					
	β	**S.E.**	**OR**	**95% CI**	**P-value**
Age	0.015	0.004	1.01	1.01 – 1.02	0.001
Hospitalization in Prior Year	0.298	0.201	1.35	0.90 – 2.00	0.138
Charlson Severity of Illness Measure	-0.056	0.041	0.95	0.87 – 1.02	0.171
Diabetes Mellitus	0.008	0.245	1.01	0.62 – 1.63	0.975
Renal Failure	0.457	0.210	1.58	1.05 – 2.38	0.029
3rd Degree Burn	1.268	0.689	3.55	0.92 – 13.70	0.066
Chemotherapy	1.138	0.715	3.12	0.77 – 12.67	0.111
Tracheostomy	0.375	0.351	1.46	0.73 – 2.90	0.285
Urinary Catheter Use	0.214	0.207	1.24	0.83 – 1.86	0.302
Major Organ Transplant	1.589	0.819	4.90	0.98 – 24.37	0.052
Major OR Therapeutic Procedure	0.516	0.241	1.68	1.06 – 2.69	0.032

Table 4. Multivariable Analysis of Risk Factors for MRSA BSI Using MSSA BSI Controls including antibiotic use (N= 330)					
	β	**S.E.**	**OR**	**95% CI**	**P-value**
Age	0.011	0.006	1.01	1.00 – 1.02	0.048
Hospitalization in Prior Year	0.322	0.253	1.38	0.84 – 2.27	0.204
Charlson Severity of Illness Measure	-0.052	0.050	0.95	0.86 – 1.05	0.302
Diabetes Mellitus	0.050	0.302	1.05	0.58 – 1.90	0.869
Renal Failure	0.438	0.269	1.55	0.92 – 2.63	0.104
3rd Degree Burn	0.396	1.570	1.49	0.07 – 32.25	0.801
Chemotherapy	1.588	1.187	4.89	0.48 – 50.10	0.181
Tracheostomy	-0.287	0.472	0.75	0.30 – 1.89	0.544
Urinary Catheter Use	0.094	0.277	1.10	0.64 – 1.89	0.735
Major Organ Transplant	2.639	1.097	13.99	1.63 – 120.07	0.016
Major OR Therapeutic Procedure	0.552	0.347	1.74	0.88 – 3.43	0.112
Monobactam Use	1.094	0.891	2.99	0.52 – 17.15	0.220
Quinolone Use	1.226	0.308	3.41	1.26 – 9.21	0.016

Table 5. Multivariable Analysis of Risk Factors for MRSA BSI Using Non-Infected Controls excluding antibiotic use (N = 595)					
	β	**S.E.**	**OR**	**95% CI**	**P-value**
Male Gender	0.486	0.204	1.62	1.10 – 2.42	0.017
Stay in Skilled Nursing Facility	0.597	0.630	1.82	0.53 – 6.25	0.343
Hospitalization in the Prior Year	0.319	0.225	1.38	0.88 – 2.14	0.157
Charlson Severity of Illness Measure	-0.046	0.064	0.96	0.84 – 1.08	0.469
Malignancy	0.625	0.314	1.87	1.01 – 3.46	0.047
Renal Failure	0.995	0.248	2.71	1.66 – 4.40	<0.001
Congestive Heart Failure	0.100	0.266	1.11	0.66 – 1.86	0.705
Cirrhosis	1.290	0.485	3.63	1.40 – 9.40	0.008
HIV Infection	1.511	0.692	4.53	1.17 – 17.58	0.029
Tracheostomy	0.330	0.445	1.39	0.58 – 3.34	0.460
Central Venous Catheter Use	0.857	0.268	2.36	1.39 – 3.98	0.001
Major OR Therapeutic Procedure	-0.449	0.220	0.64	0.41 – 0.98	0.042
ICU Days	0.021	0.012	1.02	1.00 – 1.04	0.064
Immunosuppressive Medication	-0.015	0.222	0.99	0.64 – 1.52	0.947

Table 6. Multivariable Analysis of Risk Factors for MRSA BSI Using Non-Infected Controls including antibiotic use (N = 358)					
	β	**S.E.**	**OR**	**95% CI**	**P-value**
Male Gender	0.451	0.269	1.57	0.93 – 2.66	0.093
Stay in Skilled Nursing Facility	0.437	0.822	1.55	0.31 – 7.76	0.595
Hospitalization in the Prior Year	0.350	0.285	1.42	0.81 – 2.48	0.220
Charlson Severity of Illness Measure	0.030	0.087	1.03	0.87 – 1.22	0.733
Malignancy	0.345	0.458	1.41	0.58 – 3.47	0.451
Renal Failure	1.007	0.344	2.74	1.39 – 5.38	0.003
Congestive Heart Failure	-0.198	0.341	0.82	0.42 – 1.60	0.562
Cirrhosis	1.384	0.559	4.03	1.35 – 12/06	0.013
HIV Infection	1.353	0.870	3.87	0.70 – 21.28	0.120
Tracheostomy	0.666	0.832	1.95	0.38 – 9.93	0.423
Central Venous Catheter Use	1.126	0.384	3.08	1.45 – 6.54	0.003
Major OR Therapeutic Procedure	-0.563	0.294	0.57	0.32 – 1.01	0.055
ICU Days	-0.003	0.020	1.00	0.96 – 1.04	0.866
Immunosuppressive Medication	-0.020	0.294	0.98	0.55 – 1.74	0.945
Monobactam Use	0.711	0.980	2.03	0.30 – 13.89	0.468
Quinolone Use	0.644	0.509	1.90	0.70 – 5.17	0.206

CHAPTER 5: CONCLUSIONS

Although much focus has been placed on controlling healthcare-associated infections (HAI) due to multi-drug resistant organisms in acute care hospitals, important gaps in the literature persist. Recommendations on the use of effective surveillance and infection control policies vary widely,[5,84-86] reflecting gaps in quality of evidence on the effectiveness of these interventions. In addition, data on the use of these policies at the national level, and on the association between structural characteristics, the presence and implementation of these policies and rates of MDRO HAI were lacking.

In this dissertation, I used data from two cross-sectional studies to address these gaps. Specifically, in Chapter 2, I used data from a national cross-sectional study to examine the adoption of MDRO surveillance and infection control policies in U.S. hospitals and to identify structural predictors of these policies. The majority of hospitals in this study screened for MRSA reflecting the continuing focus on this organism, while only a small proportion of hospitals reported screening for other MDRO. Aside from the widely adopted policy for isolation/contact precautions for patients with confirmed cultures, other infection control policies were present infrequently (42-27%), potentially reflecting the wide variation in published recommendations on the use of these practices. Not surprisingly, state mandatory reporting of infections was identified as a significant predictor of screening for MDRO at admission, which may reflect the hospitals' attempt to identify infections not attributable to the patient's hospital stay. An interesting inverse relationship between infection preventionist certification and compliance with a policy to cohort colonized or infected patients was also identified, which may reflect more accurate reporting of policy implementation on the part of more experienced IPs. It is also possible

that these IPs may be less likely to comply with policies for which the evidence base is lacking.

Although I hypothesized that infection control staffing would be an important structural predictor of the adoption of these policies, the only infection control staffing characteristic identified as an independent predictor of an infection control policy was the presence of a hospital epidemiologist, which was associated with a policy to screen for *C. difficile*. The lack of an observed association between infection control staffing and the presence and/or implementation of infection control policies may suggest that factors other than staffing may influence the adoption of these policies. Future studies are needed to explore the relationship between other structural factors that may influence adoption of these infection control policies, such as the hospital's organizational climate, which has been shown to influence adoption of policies.[8.125] In addition, this study did not explore how state mandatory reporting of infections impacts the work of the infection control department and the adaption and implementation of infection control policies; future studies should address this gap.

In Chapter 3 of this dissertation, I explored the association between structural characteristics, the presence, monitoring and/or implementation of screening and infection control policies and rates of specific MDRO in a cross-sectional study of California hospitals. As in the national study (described in Chapter 2), the major focus of infection control departments in terms of surveillance was MRSA, which is consistent with other published studies. [126] Although this study was conducted more than a year after the state of California required hospitals to target new admissions for MRSA screening, the presence of this policy was reported by only 79% of the hospitals, indicating a lag

between legislative action and implementation of policies in the hospitals. This study did not explore the degree to which state and federal mandates align with the infection control polices of hospitals across the country nor the way in which they impact the activities and priorities of infection control programs. Since mandatory reporting and other mandates are increasing in number across the U.S., evaluations of the impact and effectiveness of these mandates on the role of the infection control departments and HAI rates in hospitals is needed.

One important finding in this study is the use of standard culture or MRSA selective agar as the most frequently used method for MRSA surveillance (69%), coupled with the infrequent presence of a policy for contact/isolation precautions for patients with pending screens (34%). Since culture results with the use of these methods are available in 1-3 days and, in the meantime, these patients are most likely not placed on contact precautions and serve as a potential reservoir of transmission to other patients and hospital staff, the utility of screening patients at admission without concurrent placement of patients on contact precautions is greatly diminished.

To my knowledge this is the first study to show a link between infection control certification and lower MDRO rates, controlling for other setting characteristics. Hospitals with an infection control director certified in infection controls were shown to have lower MRSA BSI rates. It is not clear whether infection control director certification is a marker of overall quality of the hospital, which in turn leads to lower rates or whether an infection control director who is certified in infection control may be more likely to adopt effective evidence-based infection control strategies which in turn lead to lower

rates. Future studies are needed to confirm these findings and further elucidate this relationship.

In this study, few infection control policies were shown to be associated with lower MDRO rates, which may be due to an inadequate sample size to observe significant associations. Although power calculations conducted prior to the study indicated sufficient power to assess the relationship between infection control policies, almost half of the study hospitals did not provide infection rate data resulting in a smaller sample available for analysis. In addition, the data came from a cross-sectional study and it is unclear when the adoption of the individual surveillance control policies occurred in relation to the when the rate data were collected and whether the timing of the policy adoption had an impact on the effectiveness of the policy. To effectively answer this question, additional studies that collect longitudinal data on the adoption and implementation of these policies and rates of infections over time are needed.

Having explored institutional predictors of MDRO infections, I then examined patient-level risk factors for MRSA BSI using two different control groups (controls with MSSA BSI and non-infected controls) to determine whether the risk factors for MRSA BSI would differ depending on the choice of the control group (Chapter 4). In addition, since previous studies using a non-infected control group were limited by great differences between the cases and controls in terms of severity of illness,[60] which may have masked important risk factors, I attempted to alleviate this issue by matching cases and controls on early ICU stay, age and minimum period at risk. Despite the methodological improvements made, the results of the study largely confirmed the findings of previously published reports.

The risk factors identified differed based on the control group examined and n whether antibiotic exposure was included in the models. The three independent risk factors for MRSA BSI as compared to MSSA BSI were older age, major organ transplant, and quinolone use. Cases were more likely than non-infected controls to have renal failure, cirrhosis and a central venous catheter, after controlling for other factors. One of the major findings of this study is the identification of quinolone as an independent risk factor for MRSA BSI when compared to controls with a susceptible BSI but not when an uninfected control group was utilized. This confirms the findings of a study by Ernst and colleagues[61] and underscores the importance of appropriate control group selection when examining antibiotic use as a potential risk factor for antibiotic resistant infection. Researchers conducting studies to identify risk factors for antibiotic resistant infections should carefully examine which control group is most appropriate to answer the specific question posited by the researchers.

Immunosuppressive medication use was identified as a potential partial mediator of the association between major organ transplant and risk of MRSA BSI. Future studies should explore the specific relationships between the demographic, clinical and encounter-based risk factors already identified in the literature in order to describe the specific mechanisms that lead patients to develop MRSA BSI. Knowledge of the specific pathways can help to inform effective control and prevention strategies.

In this dissertation I explored institutional and patient-level predictors of MDRO HAI. I showed that MRSA remains the focus of infection control programs and that there is variation in the infection control policies employed in U.S. hospitals. I identified several structural characteristics as independent predictors of these infection control

policies and HAI rates, although few infection control policies had an impact on HAI rates. Lastly, by comparing patients with MRSA BSI with two sets of controls, I confirmed the need for careful selection of appropriate control groups in studies of individual level risk factors for antibiotic resistant HAI. Longitudinal studies are needed to further elucidate the relationship between setting characteristics, infection control policies and HAI rates. Additional studies of individual level risk factors should be conducted to further examine the interrelationships between different clinical and encounter-based factors to provide a clear description for the mechanisms through which patients acquire antibiotic resistant infections.

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APPENDICES

6.1 Appendix 1: Chapter 2 Appendix

Table 6.1.1 Tabular Analysis of Setting Characteristics and Presence of Screening Policies for Specific MDRO and *C. difficile* (N = 413)										
Screening for:	**Any MDRO**		**MRSA**		**VRE**		***C. difficile***		**MDR GNR**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Mandatory Reporting	186 (71)	65 (49)	166 (72)	85 (52)	59 (67)	192 (63)	28 (68)	223 (63)	32 (71)	219 (63)
Teaching	206 (75)	90 (65)	184 (76)	112 (66)	67 (75)	229 (71)	28 (64)	268 (73)	34 (71)	262 (72)
Region										
Northeast	125 (45)	44 (32)	117 (48)	52 (30)	34 (38)	135 (42)	22 (50)	147 (40)	26 (54)	143 (39)
South	79 (29)	40 (29)	65 (27)	54 (32)	28 (32)	91 (28)	7 (16)	112 (30)	10 (21)	109 (30)
Midwest	31 (11)	31 (23)	26 (11)	36 (21)	4 (4)	58 (18)	2 (5)	60 (16)	2 (4)	60 (16)
West	40 (15)	23 (17)	34 (14)	29 (17)	23 (26)	40 (12)	13 (30)	50 (14)	10 (21)	53 (15)
Bedsize										
<201	36 (13)	27 (20)	31 (13)	32 (19)	15 (17)	48 (15)	14 (32)	49 (13)	12 (25)	51 (14)
201 – 500	166 (60)	61 (44)	150 (62)	77 (45)	49 (55)	178 (55)	23 (52)	204 (55)	21 (44)	206 (56)
>500	73 (27)	50 (36)	61 (25)	62 (36)	25 (28)	98 (30)	7 (16)	116 (31)	15 (31)	108 (30)
ESS	86 (32)	32 (24)	77 (32)	41 (24)	26 (30)	92 (29)	10 (23)	108 (30)	12 (25)	106 (30)
Any HE	162 (61)	72 (53)	141 (60)	93 (55)	60 (71)	174 (54)	30 (73)	204 (57)	31 (69)	203 (57)
Part-Time HE	122 (46)	61 (45)	105 (45)	78 (46)	49 (58)	134 (42)	24 (59)	159 (44)	22 (49)	161 (45)
ICU Type										
Medical	70 (26)	32 (23)	64 (27)	38 (22)	23 (26)	79 (24)	10 (23)	92 (25)	13 (27)	89 (24)
Medical/Surgical	144 (52)	78 (57)	125 (52)	97 (57)	49 (55)	173 (53)	27 (61)	195 (53)	23 (48)	199 (55)
Surgical	61 (22)	28 (20)	53 (22)	36 (21)	17 (19)	72 (22)	7 (16)	82 (22)	12 (25)	77 (21)
% of IPs Certified*	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.4)	0.5 (0.5)	0.6 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)
Number of Staff*	3 (3.7)	3.0 (3.6)	3 (3.7)	3 (3.6)	4 (4.1)	3 (3.5)	2 (2.9)	3 (3.7)	3 (2.3)	3 (3.7)
Total IP Hours*	100 (121)	100.0 (114)	100 (120)	100 (116)	98 (135)	102 (114)	82 (89)	106 (122)	92 (120)	102 (119)
# of FTE IP/100 beds*	0.6 (0.7)	0.5 (0.8)	0.7 (0.7)	0.6 (0.8)	0.7 (0.7)	0.6 (0.7)	0.7 (0.7)	0.6 (0.7)	0.7 (0.7)	0.6 (0.7)

Frequencies (percentages) provided for categorical variables. *Medians (means) provided for continuous variables.

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.2 Tabular Analysis of Setting Characteristics and Presence of MDRO Infection Control Policies (N = 413)										
	Screening ALL ICU admissions		**Screening periodically after admission**		**Presumptive precautions pending screen**		**Contact precautions for positive patients**		**Cohorting of patients**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Mandatory Reporting	186 (71)	65 (49)	166 (72)	85 (52)	59 (67)	192 (63)	28 (68)	223 (63)	32 (71)	219 (63)
Teaching	206 (75)	90 (65)	184 (76)	112 (66)	67 (75)	229 (71)	28 (64)	268 (73)	34 (71)	262 (72)
Region										
Northeast	125 (45)	44 (32)	117 (48)	52 (30)	34 (38)	135 (42)	22 (50)	147 (40)	26 (54)	143 (39)
South	79 (29)	40 (29)	65 (27)	54 (32)	28 (32)	91 (28)	7 (16)	112 (30)	10 (21)	109 (30)
Midwest	31 (11)	31 (23)	26 (11)	36 (21)	4 (4)	58 (18)	2 (5)	60 (16)	2 (4)	60 (16)
West	40 (15)	23 (17)	34 (14)	29 (17)	23 (26)	40 (12)	13 (30)	50 (14)	10 (21)	53 (15)
Bedsize										
<201	36 (13)	27 (20)	31 (13)	32 (19)	15 (17)	48 (15)	14 (32)	49 (13)	12 (25)	51 (14)
201 – 500	166 (60)	61 (44)	150 (62)	77 (45)	49 (55)	178 (55)	23 (52)	204 (55)	21 (44)	206 (56)
>500	73 (27)	50 (36)	61 (25)	62 (36)	25 (28)	98 (30)	7 (16)	116 (31)	15 (31)	108 (30)
ESS	86 (32)	32 (24)	77 (32)	41 (24)	26 (30)	92 (29)	10 (23)	108 (30)	12 (25)	106 (30)
Any HE	162 (61)	72 (53)	141 (60)	93 (55)	60 (71)	174 (54)	30 (73)	204 (57)	31 (69)	203 (57)
Part-Time HE	122 (46)	61 (45)	105 (45)	78 (46)	49 (58)	134 (42)	24 (59)	159 (44)	22 (49)	161 (45)
ICU Type										
Medical	70 (26)	32 (23)	64 (27)	38 (22)	23 (26)	79 (24)	10 (23)	92 (25)	13 (27)	89 (24)
Medical/Surgical	144 (52)	78 (57)	125 (52)	97 (57)	49 (55)	173 (53)	27 (61)	195 (53)	23 (48)	199 (55)
Surgical	61 (22)	28 (20)	53 (22)	36 (21)	17 (19)	72 (22)	7 (16)	82 (22)	12 (25)	77 (21)
% of IPs Certified*	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.4)	0.5 (0.5)	0.6 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)
Number of Staff*	3 (3.7)	3.0 (3.6)	3 (3.7)	3 (3.6)	4 (4.1)	3 (3.5)	2 (2.9)	3 (3.7)	3 (2.3)	3 (3.7)
Total IP Hours*	100 (121)	100.0 (114)	100 (120)	100 (116)	98 (135)	102 (114)	82 (89)	106 (122)	92 (120)	102 (119)
# of FTE IP/100 beds*	0.6 (0.7)	0.5 (0.8)	0.7 (0.7)	0.6 (0.8)	0.7 (0.7)	0.6 (0.7)	0.7 (0.7)	0.6 (0.7)	0.7 (0.7)	0.6 (0.7)

Frequencies (percentages) provided for categorical variables. *Medians (means) provided for continuous variables.

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.3 Tabular Analysis of Setting Characteristics and Monitoring of MDRO Infection Control Policies (N = 413)										
Monitoring of Policy for:	**Screening ALL ICU admissions (N = 164)**		**Screening periodically after admission (N = 110)**		**Presumptive precautions pending screen (N = 128)**		**Contact precautions for positive patients (N = 404)**		**Cohorting of patients (N = 175)**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Mandatory Reporting	92 (76)	25 (76)	58 (73)	20 (87)	31 (53)	32 (50)	166 (65)	79 (60)	66 (80)	54 (64)
Teaching	100 (76)	29 (88)	76 (87)	17 (74)	40 (66)	52 (78)	190 (72)	99 (71)	59 (68)	62 (70)
Region										
Northeast	60 (46)	20 (61)	50 (57)	8 (35)	26 (43)	28 (42)	102 (39)	62 (44)	41 (47)	41 (47)
South	43 (33)	8 (24)	26 (30)	12 (52)	14 (23)	23 (34)	77 (29)	42 (30)	21 (24)	24 (27)
Midwest	14 (11)	5 (15)	4 (5)	2 (9)	10 (16)	12 (18)	38 (14)	21 (15)	8 (9)	13 (15)
West	14 (11)	0 (0)	7 (8)	1 (4)	11 (18)	4 (6)	47 (18)	15 (11)	17 (20)	10 (11)
Bedsize										
<201	13 (10)	2 (6)	6 (7)	3 (13)	10 (16)	12 (18)	36 (14)	24 (17)	15 (17)	15 (17)
201 – 500	82 (63)	22 (67)	54 (62)	12 (52)	37 (61)	38 (57)	161 (61)	62 (44)	42 (48)	42 (48)
>500	36 (27)	9 (27)	27 (31)	8 (35)	14 (23)	17 (25)	67 (25)	54 (39)	30 (34)	31 (35)
ESS	47 (36)	10 (31)	32 (37)	11 (48)	14 (24)	18 (27)	78 (30)	39 (28)	31 (36)	17 (20)
Any HE	77 (60)	18 (55)	55 (63)	11 (48)	34 (56)	34 (53)	149 (58)	81 (60)	50 (58)	50 (60)
Part-Time HE	54 (42)	14 (42)	40 (46)	8 (35)	22 (36)	29 (45)	109 (42)	70 (52)	29 (34)	41 (49)
ICU Type										
Medical	35 (27)	8 (24)	26 (30)	5 (22)	15 (25)	16 (24)	62 (23)	38 (27)	22 (25)	21 (24)
Medical/Surgical	66 (50)	18 (55)	41 (47)	12 (52)	30 (49)	38 (57)	142 (54)	73 (52)	40 (46)	51 (58)
Surgical	30 (23)	7 (21)	20 (23)	6 (26)	16 (26)	13 (19)	60 (23)	29 (21)	25 (29)	16 (18)
% of IPs Certified*	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)
Number of Staff*	3 (4.2)	3 (3.5)	3 (3.9)	3 (3.9)	3 (3.3)	3 (3.2)	3 (3.6)	3 (3.8)	4 (4.3)	3 (3.5)
Total IP Hours*	105 (119)	96 (124)	110 (128)	96 (125)	100 (114)	100 (111)	100 (115)	120 (125)	129 (138)	100 (114)
# of FTE IP/100 beds*	0.6 (0.6)	0.7 (0.7)	0.6 (0.6)	0.5 (0.7)	0.7 (0.7)	0.7 (0.7)	0.6 (0.7)	0.7 (0.8)	0.6 (0.7)	0.6 (0.7)

Frequencies (percentages) provided for categorical variables. *Medians (means) provided for continuous variables.

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.4 Tabular Analysis of Setting Characteristics and Correct Implementation (Defined as ≥75% of the time) of MDRO Infection Control Policies										
Correct Implementation of Policy for:	**Screening ALL ICU admissions (N = 131)**		**Screening periodically after admission (N = 87)**		**Presumptive precautions pending screen (N = 70)**		**Contact precautions for positive patients (N = 264)**		**Cohorting of patients (N = 75)**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Mandatory Reporting	88 (76)	4 (80)	56 (76)	2 (40)	30 (53)	6 (55)	158 (64)	8 (89)	41 (84)	17 (68)
Teaching	98 (78)	2 (40)	68 (86)	8 (100)	42 (71)	6 (55)	186 (73)	4 (44)	35 (70)	16 (64)
Region										
Northeast	59 (47)	1 (20)	45 (57)	5 (63)	27 (46)	1 (9)	100 (39)	2 (22)	27 (54)	6 (24)
South	43 (34)	0 (0)	24 (30)	2 (25)	13 (22)	4 (36)	72 (28)	5 (56)	11 (22)	8 (32)
Midwest	14 (11)	0 (0)	3 (4)	1 (13)	9 (15)	2 (18)	37 (15)	1 (11)	1 (2)	7 (28)
West	10 (8)	4 (80)	7 (9)	0 (0)	10 (17)	4 (36)	46 (18)	1 (11)	11 (22)	4 (16)
Bedsize										
<201	13 (10)	0 (0)	6 (8)	0 (0)	8 (14)	2 (18)	36 (14)	0 (0)	9 (18)	2 (8)
201 – 500	78 (62)	4 (80)	50 (63)	4 (50)	36 (61)	9 (82)	152 (60)	9 (100)	20 (40)	15 (60)
>500	35 (28)	1 (20)	23 (29)	4 (50)	15 (25)	0 (0)	67 (26)	0 (0)	21 (42)	8 (32)
ESS	46 (37)	1 (20)	31 (40)	1 (13)	14 (24)	1 (10)	75 (30)	3 (33)	17 (34)	10 (40)
Any HE	77 (63)	0 (0)	53 (67)	2 (25)	37 (63)	5 (45)	143 (57)	6 (67)	33 (67)	12 (48)
Part-Time HE	54 (44)	0 (0)	39 (49)	1 (13)	24 (41)	4 (36)	105 (42)	4 (44)	23 (47)	5 (20)
ICU Type										
Medical	34 (27)	1 (20)	24 (30)	2 (25)	16 (27)	5 (45)	61 (24)	1 (11)	13 (26)	6 (24)
Medical/Surgical	64 (51)	2 (40)	36 (46)	5 (63)	28 (47)	4 (36)	136 (53)	6 (67)	24 (48)	9 (36)
Surgical	28 (22)	2 (40)	19 (24)	1 (13)	15 (25)	2 (18)	58 (23)	2 (22)	13 (26)	10 (40)
% of IPs Certified*	0.5 (0.5)	0.8 (0.8)	0.5 (0.5)	0.7 (0.7)	0.5 (0.4)	0.3 (0.5)	0.5 (0.5)	0.5 (0.4)	0.6 (0.5)	0.4 (0.4)
Number of Staff*	3 (3.6)	3 (2.6)	3 (4.0)	3 (3.0)	3 (3.8)	3 (2.4)	3 (3.6)	3 (2.7)	5 (4.4)	4 (4.3)
Total IP Hours*	102 (120)	130 (110)	120 (132)	86 (82)	102 (121)	130 (106)	100 (117)	89 (85)	138 (141)	129 (158)
# of FTE IP/100 beds*	0.6 (0.6)	0.7 (0.7)	0.6 (0.7)	0.4 (0.4)	0.7 (0.6)	0.7 (0.7)	0.6 (0.7)	0.5 (0.6)	0.7 (0.7)	0.7 (0.8)

Frequencies (percentages) provided for categorical variables. *Medians (means) provided for continuous variables.

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.5. Bivariate Analysis of Relationship Between Setting Characteristics and Screening Policies (N = 413)									
	Screening for Any MDRO			Screening for MRSA			Screening for VRE		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Mandatory Reporting	2.56	1.39 - 4.70	0.002	2.37	13.2 - 4.28	0.004	1.22	0.56 - 2.65	0.618
Yes									
Teaching	1.59	0.88 - 2.89	0.125	1.67	0.96 - 2.92	0.071	1.26	0.63 - 2.53	0.510
Region (vs. Northeast)									
South	0.7	0.34 - 1.42	0.318	0.53	0.27 - 1.04	0.066	1.22	0.56 - 2.67	0.615
Midwest	0.35	0.16 - 0.79	0.012	0.32	0.15 - 0.71	0.005	0.27	0.06 - 1.25	0.095
West	0.61	0.25 - 1.49	0.28	0.521	0.21 - 1.28	0.155	2.28	0.82 - 6.38	0.116
Bedsize (vs. <201)									
201 – 500	2.04	0.94 – 4.42	0.070	2.01	0.96 – 4.23	0.065	0.88	0.36 – 2.19	0.784
>500	1.10	0.47 – 2.56	0.834	1.02	0.44 – 2.32	0.971	0.82	0.27 – 2.43	0.715
ESS	1.51	0.80 - 2.87	0.206	1.49	0.81 - 2.77	0.203	1.03	0.46 - 2.31	0.934
Any HE	1.35	0.75 - 2.43	0.318	1.22	0.69 - 2.15	0.486	1.97	0.88 - 4.43	0.100
Presence of Full-Time HE	1.64	0.55 - 4.91	0.377	1.48	0.53 - 4.14	0.454	2.32	0.74 - 7.26	0.149
Presence of Part-Time HE	1.02	0.57 -1.83	0.945	0.94	0.54 - 1.64	0.826	1.86	0.89 - 3.91	0.101
Proportion of IPs Certified	0.82	0.36 - 1.85	0.631	0.75	0.35 - 1.64	0.477	0.53	0.19 - 1.44	0.211
Number of Staff	1.02	0.87 - 1.21	0.780	1.01	0.87 - 1.18	0.904	1.13	0.92 - 1.41	0.264
Total IP Hours	1.00	1.00 - 1.01	0.552	1.00	1.00 - 1.00	0.737	1.00	1.00 - 1.01	0.236
# of FTE IP/100 beds	0.75	0.44 - 1.25	0.269	0.76	0.48 - 1.20	0.241	0.96	0.60 - 1.53	0.863
ICU Type (vs. Medical)									
Medical/Surgical	0.84	0.50 - 1.43	0.526	0.77	0.46 - 1.26	0.294	0.97	0.55 - 1.71	0.924
Surgical	1.00	0.67 - 1.49	0.984	0.87	0.62 - 1.24	0.453	0.81	0.53 - 1.25	0.341

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.5. Bivariate Analysis of Relationship Between Setting Characteristics and Screening Policies Cont'd (N = 413)						
	Screening for *C. difficile*			**Screening for MDR GNR**		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Mandatory Reporting	1.27	0.40 - 3.99	0.688	1.47	0.51 - 4.23	0.473
Teaching	0.66	0.26 - 1.65	0.375	0.95	0.39 - 2.34	0.920
Region (vs. Northeast)						
South	0.42	0.13 - 1.35	0.144	0.50	0.15 - 1.68	0.265
Midwest	0.22	0.03 - 1.82	0.161	0.18	0.02 - 1.47	0.111
West	1.74	0.51 - 5.92	0.377	1.04	0.34 - 3.18	0.948
Bedsize (vs. <201)						
201 – 500	0.39	0.14 – 1.14	0.086	0.43	0.15 – 1.28	0.130
>500	0.21	0.05 – 0.86	0.029	0.59	0.17 – 2.09	0.413
ESS	0.69	0.24 - 1.98	0.496	0.80	0.30 - 2.12	0.647
Any HE	2.10	0.70 - 6.28	0.185	1.68	0.62 - 4.55	0.308
Presence of Full-Time HE	1.65	0.42 - 6.47	0.471	2.87	0.68 - 12.20	0.153
Presence of Part-Time HE	1.79	0.67 - 4.79	0.244	1.16	0.46 - 2.93	0.746
Proportion of IPs Certified	1.44	0.38 - 5.52	0.594	1.35	0.33 - 5.62	0.677
Number of Staff	0.79	0.53 - 1.18	0.249	0.91	0.62 - 1.34	0.634
Total IP Hours	0.99	0.99 - 1.00	0.068	1.00	0.99 - 1.01	0.948
# of FTE IP/100 beds	0.88	0.43 - 1.81	0.725	0.83	0.41 - 1.70	0.611
ICU Type (vs. Medical)						
Medical/Surgical	1.27	0.64 - 2.53	0.489	0.79	0.39 - 1.61	0.520
Surgical	0.79	0.47 - 1.32	0.361	1.07	0.72 - 1.58	0.746

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.6. Bivariate Analysis of Relationship Between Setting Characteristics and Presence of Infection Control Policies (N = 412)						
	Screening ALL ICU admissions			**Screening periodically after admission**		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Mandatory Reporting	2.52	1.36 - 4.66	0.003	2.25	1.09 - 4.64	0.028
Teaching	1.80	1.01 - 3.21	0.048	2.68	1.36 - 5.29	0.004
Region (vs. Northeast)						
South	0.84	0.43 - 1.62	0.598	0.91	0.44 - 1.84	0.774
Midwest	0.49	0.22 - 1.07	0.072	0.20	0.08 - 0.53	0.001
West	0.31	0.12 - 0.80	0.015	0.28	0.10 - 0.79	0.016
Bedsize (vs. <201)						
201 – 500	2.73	1.28 – 5.79	0.009	2.47	1.03 – 5.94	0.043
>500	1.87	0.78 – 4.49	0.161	2.41	0.90 – 6.49	0.081
ESS	1.68	0.89 - 3.18	0.111	1.95	1.00 - 3.82	0.050
Any HE	1.06	0.60 - 1.88	0.831	1.11	0.59 - 2.09	0.737
Presence of Full-Time HE	1.45	0.53 - 4.00	0.476	1.36	0.44 - 4.19	0.594
Presence of Part-Time HE	0.81	0.46 - 1.43	0.464	0.91	0.49 - 1.70	0.760
Proportion of IPs Certified	1.02	0.48 - 2.19	0.955	0.97	0.41 - 2.27	0.942
Number of Staff	1.00	0.86 - 1.17	0.963	1.08	0.91 - 1.28	0.385
Total IP Hours	1.00	1.00 - 1.00	0.804	1.00	1.00 - 1.01	0.374
# of FTE IP/100 beds	0.70	0.45 - 1.07	0.099	0.71	0.44 - 1.16	0.171
ICU Type (vs. Medical)						
Medical/Surgical	0.83	0.50 - 1.36	0.456	0.71	0.43 - 1.19	0.195
Surgical	0.96	0.69 - 1.33	0.804	0.93	0.66 - 1.32	0.694

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.6 Cont'd. Bivariate Analysis of Relationship Between Setting Characteristics and Presence of Infection Control Policies (N = 412)									
	Presumptive precautions pending screen			Contact precautions for positive patients			Cohorting of patients		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Mandatory Reporting	0.47	0.26 - 0.85	0.012	0.69	0.13 - 3.61	0.661	1.91	1.06 - 3.42	0.031
Teaching	1.02	0.56 - 1.87	0.950	0.84	0.16 - 4.28	0.831	0.81	0.44 - 1.49	0.501
Region (vs. Northeast)									
South	0.95	0.48 - 1.89	0.890	--	--	--	0.64	0.31 - 1.30	0.216
Midwest	1.16	0.51 - 2.65	0.723	0.48	0.10 - 2.21	0.346	0.54	0.24 - 1.19	0.125
West	0.66	0.25 - 1.75	0.404	1.51	0.16 - 14.27	0.360	0.79	0.34 - 1.80	0.570
Bedsize (vs. <201)									
201 – 500	0.92	0.45 – 1.89	0.819	2.79	0.59 – 13.09	0.194	0.65	0.31 – 1.34	0.241
>500	0.63	0.26 – 1.53	0.310	6.05	0.62 – 59.40	0.122	1.10	0.46 – 2.60	0.828
ESS	0.79	0.42 - 1.50	0.476	--	--	--	0.93	0.47 - 1.82	0.823
Any HE	0.80	0.45 - 1.44	0.461	2.35	0.55 - 10.11	0.251	1.05	0.59 - 1.87	0.861
Presence of Full-Time HE	1.49	0.47 - 4.71	0.501	--	--	--	2.24	0.72 - 6.99	0.166
Presence of Part-Time HE	0.76	0.42 - 1.37	0.367	1.39	0.32 - 6.00	0.656	1.74	0.42 - 1.32	0.309
Proportion of IPs Certified	1.01	0.45 - 2.27	0.986	0.11	0.01 - 1.35	0.084	0.98	0.47 - 2.03	0.951
Number of Staff	0.87	0.73 - 1.05	0.145	1.34	1.00 - 1.81	0.053	1.09	0.93 - 1.28	0.275
Total IP Hours	1.00	0.99 - 1.00	0.461	1.00	0.99 - 1.01	0.393	1.00	1.00 - 1.01	0.296
# of FTE IP/100 beds	0.90	0.56 - 1.45	0.661	0.53	0.27 - 1.05	0.067	1.05	0.60 - 1.83	0.862
ICU Type (vs. Medical)									
Medical/Surgical	1.00	0.59 - 1.67	0.991	0.31	0.04 - 2.56	0.276	0.94	0.57 - 1.53	0.794
Surgical	1.09	0.74 - 1.60	0.654	--	--	--	1.15	0.80 - 1.66	0.447

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.7. Bivariate Analysis of Relationship Between Setting Characteristics and Monitoring of Infection Control Policies						
	Screening ALL ICU admissions (N = 164)			Screening periodically after admission (N = 110)		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Mandatory Reporting	1.02	0.37 - 2.77	0.977	0.41	0.07 - 2.33	0.317
Teaching	0.44	0.11 - 1.78	0.253	2.44	0.63 - 9.50	0.199
Region (vs. Northeast)						
South	1.79	0.56 - 5.74	0.326	0.35	0.09 - 1.36	0.128
Midwest	0.93	0.24 - 3.59	0.920	0.32	0.04 - 2.32	0.260
West	--	--	--	1.12	0.13 - 9.34	0.917
Bedsize (vs. <201)						
201 – 500	0.57	0.11 – 2.92	0.503	2.25	0.42 – 12.19	0.347
>500	0.62	0.10 – 3.77	0.599	1.69	0.27 – 10.52	0.575
ESS	1.26	0.40 - 3.95	0.690	0.65	0.19 - 2.22	0.488
Any HE	1.26	0.46 - 3.43	0.654	1.88	0.56 - 6.27	0.307
Presence of Full-Time HE	0.75	0.14 - 4.06	0.739	0.68	0.06 - 7.39	0.748
Presence of Part-Time HE	0.99	0.37 - 2.65	0.985	1.60	0.49 - 5.19	0.437
Proportion of IPs Certified	1.54	0.52- 2.61	0.436	1.36	0.40 - 4.62	0.618
Number of Staff	0.84	0.64 - 1.11	0.224	0.99	0.70 - 1.40	0.963
Total IP Hours	1.00	0.99 - 1.01	0.802	1.00	0.99 - 1.01	0.935
# of FTE IP/100 beds	0.64	0.14 - 2.92	0.568	0.94	0.18 - 4.80	0.938
ICU Type (vs. Medical)						
Medical/Surgical	1.02	0.50 - 2.09	0.955	1.56	0.65 - 3.76	0.322
Surgical	0.86	0.29 - 2.52	0.777	1.03	0.31 - 3.44	0.968

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.7 Bivariate Analysis of Relationship Between Setting Characteristics and Monitoring of Infection Control Policies Cont'd.									
	Presumptive precautions pending screen (N = 128)			Contact precautions for positive patients (N = 404)			Cohorting of patients (N = 175)		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Mandatory Reporting	1.11	0.44 - 2.78	0.829	1.21	0.66 - 2.22	0.529	2.37	0.92 - 6.13	0.076
Teaching	0.55	0.22 - 1.37	0.199	1.06	0.59 - 1.93	0.840	0.88	0.35 - 2.25	0.795
Region (vs. Northeast)									
South	0.66	0.23 - 1.88	0.433	1.11	0.57 - 2.19	0.753	0.88	0.27 - 2.79	0.822
Midwest	0.90	0.23 - 3.46	0.875	1.10	0.47 - 2.55	0.824	0.62	0.19 - 1.98	0.416
West	2.96	0.64 - 13.79	0.167	1.90	0.72 - 5.02	0.192	1.70	0.49 - 5.90	0.403
Bedsize (vs. <201)									
201 – 500	1.17	0.38 – 3.59	0.786	1.73	0.81 – 3.70	0.157	1.00	0.34 – 2.98	1.000
>500	0.99	0.24 – 4.15	0.987	0.83	0.35 – 1.98	0.671	0.97	0.27 – 3.46	0.960
ESS	0.83	0.31 - 2.24	0.712	1.09	0.56 - 2.12	0.804	2.29	0.82 - 6.41	0.115
Any HE	1.11	0.45 - 2.76	0.820	0.91	0.51 - 1.63	0.754	0.94	0.40 - 2.24	0.897
Presence of Full-Time HE	2.60	0.45 - 15.01	0.287	2.05	0.54 - 7.82	0.294	6.65	1.08 - 40.96	0.041
Presence of Part-Time HE	0.68	0.27 - 1.74	0.422	0.68	0.38 - 1.22	0.193	0.53	0.22 - 1.36	0.173
Proportion of IPs Certified	0.55	0.16 - 1.87	0.338	1.04	0.48 - 2.24	0.929	0.82	0.26 - 2.56	0.733
Number of Staff	1.05	0.77 - 1.43	0.779	0.94	0.80 - 1.12	0.502	1.16	0.92 - 1.47	0.206
Total IP Hours	1.00	0.99 - 1.01	0.871	1.00	0.99 - 1.00	0.435	1.00	1.00 - 1.01	0.201
# of FTE IP/100 beds	0.66	0.27 - 1.65	0.377	0.75	0.44 - 1.27	0.280	1.12	0.44 - 2.85	0.733
ICU Type (vs. Medical)									
Medical/Surgical	0.76	0.39 - 1.50	0.430	0.79	0.54 - 1.16	0.230	0.75	0.36 – 1.58	0.447
Surgical	0.64	0.27 - 1.57	0.329	0.94	0.55 - 1.61	0.822	1.49	0.81 – 2.73	0.195

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.8. Bivariate Analysis of Relationship Between Setting Characteristics and Compliance with Infection Control Policies						
	Screening ALL ICU admissions (N = 131)			Screening periodically after admission (N = 87)		
	OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Mandatory Reporting	0.79	0.06 - 10.25	0.199	4.67	0.54 - 40.44	0.162
Teaching	5.25	0.45 - 61.40	0.186	--	--	--
Region (vs. Northeast)						
South	--	--	--	1.33	0.11 - 16.00	0.821
Midwest	--	--	--	0.33	0.02 - 4.80	0.419
West	0.04	0.01 - 0.57	0.017	--	--	--
Bedsize (vs. <201)						
201 – 500	--	--	--	--	--	--
>500	--	--	--	--	--	--
ESS	2.36	0.18 - 30.61	0.512	4.62	0.44 - 48.65	0.203
Any HE	--	--	--	6.12	0.86 - 43.47	0.070
Presence of Full-Time HE	--	--	--	--	--	--
Presence of Part-Time HE	--	--	--	6.83	0.66 - 71.05	0.108
Proportion of IPs Certified	0.06	0.01 - 1.59	0.092	0.30	0.03 - 3.17	0.318
Number of Staff	1.39	0.98 - 1.97	0.062	1.27	0.84 - 1.93	0.260
Total IP Hours	1.00	0.99 - 1.01	0.644	1.01	1.00 - 1.02	0.004
# of FTE IP/100 beds	--	--	--	--	--	--
ICU Type (vs. Medical)						
Medical/Surgical	2.43	0.59 - 10.06	0.221	0.63	0.15 - 2.66	0.532
Surgical	2.29	0.52 - 0.98	0.272	0.38	0.06 - 2.67	0.330

Compliance defined as usually or all of the time (at least 75% of the time) vs. other

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.8. Bivariate Analysis of Relationship Between Setting Characteristics and Compliance with Infection Control Policies Cont'd									
	Presumptive precautions pending screen (N = 70)			Contact precautions for positive patients (N = 264)			Cohorting of patients (N = 75)		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Mandatory Reporting	0.93	0.14 - 6.06	0.936	0.22	0.03 - 1.90	0.169	2.41	0.49 - 11.94	0.281
Teaching	2.06	0.32 - 13.45	0.451	3.37	0.77 - 14.78	0.107	1.31	0.31 - 5.50	0.710
Region (vs. Northeast)									
South	0.12	0.01 - 1.79	0.124	0.29	0.05 - 1.71	0.171	0.31	0.05 - 1.98	0.213
Midwest	0.17	0.01 - 1.97	0.155	0.74	0.06 - 8.66	0.810	0.03	0.01 - 0.40	0.008
West	0.09	0.01 - 1.56	0.099	0.92	0.08 - 10.89	0.947	0.61	0.09 - 4.12	0.613
Bedsize (vs. <201)									
201 – 500	1.00	0.13 – 7.49	1.000	--	--	--	0.30	0.05 – 1.93	0.203
>500	--	--	--	--	--	--	0.58	0.07 – 5.19	0.629
ESS	2.86	0.27 - 30.57	0.384	0.85	0.15 - 4.70	0.854	0.77	0.18 - 3.41	0.733
Any HE	2.02	0.31 - 12.97	0.459	0.67	0.15 - 3.01	0.606	2.23	0.54 - 9.25	0.267
Presence of Full-Time HE	--	--	--	--	--	--	0.30	0.07 - 1.29	0.105
Presence of Part-Time HE	1.20	0.16 - 9.00	0.859	0.91	0.20 - 4.21	0.906	3.54	0.80 - 15.66	0.096
Proportion of IPs Certified	0.60	0.07 - 4.85	0.631	2.78	0.47 - 16.44	0.259	2.69	0.39 - 18.38	0.313
Number of Staff	1.54	1.04 - 2.28	0.030	1.32	1.01 - 1.71	0.042	1.01	0.69 - 1.49	0.948
Total IP Hours	1.00	0.99 - 1.01	0.539	1.01	1.00 - 1.01	0.017	1.00	0.99 - 1.01	0.600
# of FTE IP/100 beds	0.45	0.05 - 4.20	0.486	2.40	0.48 - 12.04	0.288	0.7	0.14 - 3.48	0.660
ICU Type (vs. Medical)									
Medical/Surgical	0.43	0.16 - 1.12	0.083	2.10	0.19 - 23.90	0.549	1.67	0.65 - 4.28	0.288
Surgical	0.93	0.20 - 4.33	0.930	0.78	0.14 - 4.33	0.778	2.05	0.44 - 9.51	0.359

Compliance defined as usually or all of the time (at least 75% of the time) vs. other

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Table 6.1.9. Predictors of Monitoring of Policy to Cohort Patients, Multivariable Logistic Regression (N = 122)			
	OR	**95% CI**	**P-value**
Mandatory Reporting	1.52	0.46 – 5.06	0.495
# of Full-time HE	9.03	0.85 – 95.54	0.067
Region (vs. Northeast)			
South	0.44	0.09 – 2.17	0.310
Midwest	0.83	0.13 – 5.20	0.843
West	2.89	0.65 – 12.65	0.162
Number of Staff	1.22	0.87 – 1.44	0.365
Proportion of IPs Certified	1.14	0.27 – 4.77	0.862

Table 6.1.10. Predictors of Correct Implementation of Screening All Upon Admission Policy Usually or All of the time, Multivariable Logistic Regression (N = 47)			
	OR	**95% CI**	**p-value**
Number of IC Staff	1.69	0.93 - 3.06	0.086
Percent of Staff CIC Certified	0.19	0.05 - 0.64	0.008
Region (vs. Northeast)			
South	--	--	--
Midwest	--	--	--
West	0.84	0.08 - 8.85	0.887

Compliance defined as usually or all of the time (at least 75% of the time) vs. other

ESS = Electronic Surveillance System, FTE = Full Time Equivalent, HE = Hospital Epidemiologist, ICU = Intensive Care Unit, IP = Infection Preventionist

Appendix 6.1.11. Relevant Sections of Questionnaire Used in Aim I

Survey Sections
I: HOSPITAL AND RESPONDENT DEMOGRAPHICS
II: INFECTION CONTROL DEPARTMENT STAFF
III: INFECTION CONTROL PROFESSIONAL TIME&
IV: ORGANIZATION & SUPPORT FOR INFECTION CONTROL DEPARTMENT
V: ICU SPECIFIC POLICIES
VI: HOSPITAL-WIDE INFECTION PREVENTION AND CONTROL
VII: REPORTING OF INFECTIONS
VIII: PHASE II interest

I: HOSPITAL AND RESPONDENT DEMOGRAPHICS

Facility Name: _____
Facility Mailing Address: _____
_____
City: _____
County: _____
State: _____
Zip Code: _____

Please provide one of the identifiers below or check "Don't know" if you do not have this information:
American Hospital Association ID#: _____
CMS Provider #:_____

How long has your hospital been part of the CDC Network (National Healthcare Safety Network (NHSN) and/or NNIS)?
___ Less than 1 year ___ 1-3 years ___ More than 3 years

What is your ethnic background?
___ Asian-Pacific Islander ___ Native American ___ Latino ___ African-American (non-Latino origin) ___ Caucasian (non-Latino origin)

What is your highest educational level?
___ Diploma ___ 1 year technical __ Associate degree ___ Bachelors degree ___ Masters degree ___ PhD __ MD

II: INFECTION CONTROL DEPARTMENT STAFF
Does your hospital have an Infection Control Director position?
1 – No 2 – Yes

Please indicate the total number of hours the Infection Control Director actually works (including overtime) for the Infection Control Department each week._____

Is the Infection Control Director certified in infection control (CIC)?

For the Infection Control Director, what is the highest qualification attained?
___ MD with infectious disease specialty ___ MD without infectious disease specialty
___ RN with graduate degree (e.g., MPH, MSN) ___ RN without graduate degree
___ LPN ___ Masters in Epidemiology, non-nurse
___ Med Tech ___ Other ___ DON'T KNOW
If Other, please specify: _____

For the Infection Control Director, how many years experience does he/she have?_____

For the Infection Control Director, is this person a member of SHEA or APIC? 1 – No
2 – Yes 3 – DK

To whom does the Infection Control Director report? (Check all that apply).
___ Medical Director
___ Nursing Director
___ Quality Mgt Director
Other _____

Please indicate the number of Hospital Epidemiologists, other than the Infection Control Director at your hospital. _____

Please indicate the number of Infection Control Professionals (ICPs), other than the Infection Control Director and Hospital Epidemiologists at your hospital. _____

Does your department have help with data management? 1 – No 2 – Yes 3 – DK
If yes, how many hours? _____
Does your department have help with secretarial functions? 1 – No 2 – Yes 3 – DK
If yes, how many hours? _____
Does your department have other help (e.g., statistician or operations manager)?
1 – No 2 – Yes 3 – DK If yes, how many hours? _____

What is your role in the Infection Control Department?
___ Infection control department Director/Coordinator
___ Hospital epidemiologist, other than Director/Coordinator
___ ID Physician, other than Director/Coordinator/Hospital Epide
___ ICP other than Director/Coordinator
___ Data Analyst/Manager
___ Administrative Assistant/Secretary ___ Other

<u>Infection Control Professional or Hospital Epidemiologist – individual staff information</u>
Please indicate the total number of hours that this Infection Control Professional/ Hospital Epidemiologist actually works (including overtime) for the Infection Control Department each week.

Is this ICP/HE certified in infection control (CIC)? 1 – No 2 – Yes 3 – DK

For this ICP/HE, what is the highest qualification attained?
___ MD with infectious disease specialty ___ MD without infectious disease specialty
___ RN with graduate degree (e.g., MPH, MSN) ___ RN without graduate degree
___ LPN ___ Masters in Epidemiology, non-nurse
___ Med Tech ___ Other ___ DON'T KNOW

For this ICP/HE, how many years experience does he/she have?
___ less than 2 years ___ 2-5 years ___ 6-10 years
___ 11-15 years ___ more than 15 years ___ DON'T KNOW

For this ICP/HE, is this person a member of SHEA or APIC? 1 – No 2 – Yes 3 – DK

IV: ORGANIZATION & SUPPORT FOR INFECTION CONTROL DEPARTMENT
The following questions are about the institutional organization and support for the department. For each item in the following section, please indicate which answer best represents your work environment.

1 – Never 2 – Rarely 3 – Sometimes 4 - Most of the time 5 - Always
___ I have access to key decision makers in my hospital for planning the Infection Control Program.

___ The Hospital Epidemiologist or the Director of the Infection Control Department has the authority to close beds in the event of an outbreak.
___ My hospital or department funds continuing education activities for Infection Control staff.
___ I have access to key decision makers in my hospitals if I have a problem.
___ Does your institution use an electronic surveillance system for tracking Healthcare Associated Infections?

If yes, what system does it use? (Check all that apply).
- ___ Custom system developed at the hospital
- ___ AICE
- ___ MedMined
- ___ Theradoc
- ___ SafetySurveillor
- Other _____

VII: REPORTING OF INFECTIONS

Screening of Organisms

Does this ICU routinely screen for the following organisms? Please check all that apply.
- a. MRSA
- b. VRE
- c. C. difficile
- d. Multi-drug resistant GNRs
- e. Other _____
- f. Does not screen for any MDRO

Policies and Interventions: Multi-Drug Resistant Organisms (MDROs)

Please mark whether in this ICU the following policies/measures are implemented.

1 – No	2 – Yes	3 – DON'T KNOW	
1 - All of the time (95-100%)		2 - Usually (75-94%)	3 - Sometimes (25-74%)
4 - Rarely/Never (less than 25%)		5 – DON'T KNOW	

Does your ICU have a written policy in place to screen ALL patients for MDROs upon ICU admission?
If yes, does your ICU monitor whether ALL patients are screened for MDROs upon ICU admission?
If yes, please estimate the proportion of patients that are screened for MDROs upon ICU admission:

Does your ICU have a written policy in place to screen patients for MDROs periodically after ICU admission?
If yes, does your ICU monitor whether patients are screened for MDROs periodically after ICU admission?
If yes, please estimate the proportion of time that patients are screened for MDROs periodically after ICU admission:

Does your ICU have a written policy in place to implement presumptive isolation/contact precautions pending a MDRO screen?
If yes, does your ICU monitor whether presumptive isolation/contact precautions are implemented pending a MDRO screen?
If yes, please estimate the proportion of time that presumptive isolation/contact precautions are implemented pending a MDRO screen:

Does your ICU have a written policy in place to implement contact precautions for patients with positive cultures for MDROs?

If yes, does your ICU monitor whether contact precautions are implemented for patients with positive cultures for MDROs?
If yes, please estimate the proportion of time that contact precautions are implemented for patients with positive cultures for MDROs:

Does your ICU have a written policy in place to cohort infected patients with MDROs in the same room?
If yes, does your ICU track whether patients infected with MDROs are cohorted in the same room?
If yes, please estimate the proportion of patients infected with MDROs that are cohorted in the same room:

Does your ICU have a written policy in place to cohort patients colonized with MDROs in the same room?
If yes, does your ICU track whether patients colonized with MDROs are cohorted in the same room?
If yes, please estimate the proportion of patients colonized with MDROs that are cohorted in the same room:

6.2 Appendix 2: Chapter 3 Appendix

Table 6.2.1. Compliance with MRSA Policies

	All of the time	Usually	Sometimes	Rarely/ Never	Monitor but Don't Know	No Monitoring
Screening all patients for MRSA upon admission (N = 46)	22 (48)	15 (33)	2 (4)	0 (0)	3 (7)	4 (9)
Target new admissions for MRSA screening (N = 103)	34 (33)	42 (41)	8 (8)	1 (1)	13 (13)	5 (5)
Screen all patients for MRSA periodically after admission (N = 5)	2 (40)	2 (40)	0 (0)	0 (0)	1 (20)	0 (0)
Screen select patients for MRSA periodically after admission (N = 13)	7 (54)	4 (31)	1 (8)	0 (0)	0 (0)	1 (8)
Implement presumptive isolation/contact precautions pending a MRSA screen (N = 38)	20 (53)	6 (16)	5 (13)	0 (0)	3 (8)	4 (11)
Implement contact precautions for patients with positive MRSA cultures (N = 103)	86 (84)	8 (8)	0 (0)	0 (0)	6 (6)	3 (3)
Perform surveillance of microbiology results for new cases of MRSA (N = 80)	65 (81)	10 (13)	0 (0)	0 (0)	2 (3)	3 (1)

Table 6.2.2. Infection Rates by Different Hospital Characteristics and Infection Control Policies			
	MRSA BSI Rate (N = 91)	VRE BSI Rate (N = 91)	*C. Difficile* Infection Rate (N = 105)
	Median (Interquartile range)		
Teaching			
Yes	0 (0 – 0.31)	0 (0 – 0.42)	0.49 (0.29 – 0.56)
No	0 (0 – 0.35)	0 (0 – 0.09)	0.37 (0 – 0.75)
Region			
Urban	0 (0 – 0.41)	0 (0 – 0.42)	0.53 (0.25 – 0.91)
Suburban	0 (0 – 0.59)	0 (0 – 0.18)	0.49 (0.17 – 0.71)
Rural	0 (0 – 0)	0 (0 – 0)	0 (0 – 0.28)
Presence of Hospital Epidemiologist			
Any	0 (0 – 0.06)	0 (0 – 0.41)	0.43 (0.19 – 0.71)
None	0 (0 – 0.04)	0 (0 – 0.18)	0.38 (0 – 0.78)
Participation in CHAIPI			
Yes	0 (0 – 0.09)	0 (0 – 0.19)	0.49 (0.11 – 0.64)
No	0 (0 – 0.41)	0 (0 – 0.17)	0.41 (0.12 – 0.75)
Participation in CHART			
Yes	0 (0 – 0.42)	0 (0 – 0.14)	0.15 (0.49 – 0.74)
No	0 (0 – 0.34)	0 (0 – 0.44)	0.37 (0 – 0.73)
Participation in IHI			
Yes	0 (0 – 0)	0 (0 – 0.19)	0.41 (0 – 0.70)
No	0 (0 – 0.57)	0 (0 – 0.15)	0.52 (0.18 – 0.79)
Participation in Other Initiative			
Yes	0 (0 – 0.42)	0 (0 – 0.09)	0.49 (0.15 – 0.71)
No	0 (0 – 0.31)	0 (0 – 0.23)	0.41 (0.11 – 0.75)
Participation in Any Initiative			
	0 (0 – 0.34)	0 (0 – 0.93)	0.41 (0.12 – 0.74)
	0 (0 – 0.62)	0 (0 – 0.15)	0.47 (0.11 – 0.96)
Infection Control Director Certified in Infection Control			
Yes	0 (0 – 0.42)	0 (0 – 0.21)	0.51 (0.35 – 0.68)
No	0 (0 – 0.15)	0 (0 – 0.03)	0.23 (0 – 0.61)
Infection Control Director member of SHEA/APIC			
Yes	0 (0 – 0.41)	0 (0 – 0.21)	0.43 (0.15 – 0.74)
No	0 (0 – 0.15)	0 (0 – 0.03)	0.14 (0 – 0.67)
Electronic Surveillance System			
Yes	0 (0 – 0.74)	0 (0 – 0.21)	0.49 (0.31 – 0.74)
No	0 (0 – 0)	0 (0 – 0.14)	0.36 (0 – 0.74)
Screen All Patients Upon Admission*			
Yes	0 (0 – 0.44)	--	--
No	0 (0 – 0)	--	--
Target New Admissions for Screening*			
Yes	0 (0 – 0.34)	0 .31 (0.17 – 1.10)	0.11 (0 – 0.52)
No	0.10 (0 – 0.75)	0 (0 – 0.15)	0.42 (0.12 – 0.74)
Screen All Patients Periodically After Admission*			
Yes	0 (0 – 0)	--	--
No	0 (0 – 0.41)	--	--

Screen Select Patients Periodically After Admission*			
Yes	0 (0 – 0.15)	--	--
No	0 (0 – 0.44)	--	--
Implement Presumptive Isolation/Contact Precautions Pending A Screen*			
Yes	0 (0 – 0.21)	0 (0 – 0)	0.37 (0.15 – 0.68)
No	0 (0 – 0.35)	0 (0 – 0.18)	0.51 (0 – 0.78)
Implement Contact Precautions for Patients with Positive Cultures*			
Yes	0 (0 – 0.35)	0 (0 – 0.22)	0.42 (0.15 – 0.74)
No	0 (0 – 0)	0 (0 – 0)	0.17 (0 – 0.78)
Conduct Surveillance of Microbiology Results for New Cases*			
Yes	0 (0 – 0.51)	0 (0 – 0.18)	0.46 (0.15 – 0.73)
No	0 (0 – 0)	0 (0 – 0.21)	0.35 (0 – 0.78)
Promote the use of soap and water after caring for patients with *C. difficile*-associated diarrhea			
Yes	--	--	0.41 (0.12 – 0.73)
No	--	--	0.48 (0 – 0.76)

*For the particular organism of interest (MRSA BSI, VRE BSI or *C. diff)* for which the infection rate was given

MRSA and VRE BSI rates calculated as the number of infections/1,000 central line days. *C. difficile* rate calculated as the number of infections/1,000 inpatients days.

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Table 6.2.3. Bivariate Analysis of Relationship between Structural Characteristics and MRSA BSI Rate												
	MRSA BSI Rate (N = 91)				VRE BSI Rate (N = 91)				*C. difficile* Rate (N = 105)			
	Coef	p-value	IRR	95% CI	Coef	p-value	IRR	95% CI	Coef	p-value	IRR	95% CI
Teaching Status	0.02	0.971	1.02	0.37-2.83	0.398	0.420	1.49	0.57-3.92	-0.043	0.894	0.96	0.51-1.82
Bedsize	0.00	0.374	1.00	1.00-1.00	<0.001	0.941	1.00	1.00-1.00	0.001	0.217	1.00	1.00-1.00
Setting (vs. urban)												
Suburban	0.50	0.327	1.64	0.61-4.44	-0.390	0.439	0.68	0.25-1.82	-0.334	0.267	0.72	0.40-1.29
Rural	-0.75	0.342	0.47	0.10-2.22	-1.364	0.141	0.26	0.04-1.57	-0.890	0.049	0.41	0.17-1.00
CHAIPI	0.27	0.591	1.31	0.49-3.56	-0.659	0.298	0.52	0.15-1.79	0.032	0.918	1.03	0.56-1.92
CHART	-0.87	0.060	0.42	0.17-1.04	-1.260	0.012	0.29	0.11-0.75	-0.102	0.723	0.90	0.51-1.59
IHI	-1.21	0.010	0.30	0.12-0.75	-0.574	0.235	0.56	0.22-1.45	-0.264	0.338	0.77	0.45-1.32
Other Initiative	0.74	0.117	2.09	0.83-5.26	-0.931	0.141	0.39	0.11-1.36	-0.008	0.978	0.99	0.57-1.73
Any Initiative	-0.47	0.414	0.63	0.20-1.93	-1.518	0.001	0.22	0.09-0.54	-0.246	0.508	0.78	0.38-1.62
ICD Hours	0.03	0.138	1.03	0.99-1.08	-0.017	0.321	0.98	0.95-1.02	0.020	0.052	1.02	1.00-1.04
Certified ICD	-1.50	0.015	0.32	0.13-0.80	0.083	0.871	1.09	0.40-2.93	0.363	0.223	1.44	0.80-2.58
ICD Member of SHEA/APIC	1.21	0.312	3.36	0.32-35.08	2.014	0.338	7.49	0.12-462.53	0.455	0.471	1.58	0.46-5.44
ESS	0.55	0.251	1.73	0.68-4.40	-0.458	0.415	0.63	0.21-1.90	0.174	0.545	1.19	0.68-2.09
HE*	0.30	0.537	1.34	0.53-3.43	-0.607	0.204	0.54	0.21-1.39	-0.211	0.453	0.81	0.47-1.41
Full-time HE	-0.55	0.791	0.58	0.01-33.95	2.477	0.004	11.90	2.22-63.90	0.679	0.525	1.97	0.24-16.00
# of HE	0.07	0.871	1.07	0.46-2.50	-0.111	0.780	0.89	0.41-1.95	-0.129	0.538	0.88	0.58-1.32
HE hours	0.01	0.554	1.01	0.97-1.06	0.032	0.009	1.03	1.01-1.06	0.009	0.517	1.01	0.98-1.04
# of IP	-0.17	0.478	0.84	0.53-1.35	-0.030	0.768	0.97	0.79-1.19	-0.006	0.902	0.99	0.91-1.09
Total IP hours	-0.01	0.482	0.99	0.98-1.01	-0.006	0.492	0.99	0.98-1.01	0.005	0.337	1.00	1.00-1.01
% IP Certified	0.45	0.486	1.56	0.45-5.46	-0.818	0.244	0.44	0.11-1.75	0.304	0.444	1.36	0.62-2.96
# IP per 100 beds	-1.55	0.155	0.21	0.02-1.80	--	--	--	--	--	--	--	--
Total IC hours**	0.00	0.767	1.00	0.99 - 1.01	-0.004	0.587	1.00	0.98 - 1.01	0.005	0.267	1.00	1.00-1.01

*either full-time or part-time **Infection Preventionist + Infection Control Director Hours

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Table 6.2.4. Relationship Between Infection Control Policies and MRSA BSI Rates, Bivariate Analysis Using Negative Binomial Regression				
	Coef	**p-value**	**IRR**	**95% CI**
Screening all patients for MRSA upon admission	0.48	0.361	1.61	0.58 - 4.47
Target new admissions for MRSA screening	-0.49	0.444	0.61	0.18 - 2.15
Screen all patients for MRSA periodically after admission	--	--	--	--
Screen select patients for MRSA periodically after admission	-1.46	0.140	0.23	0.30 - 1.62
Implement presumptive isolation/ contact precautions pending a MRSA screen	0.36	0.466	1.43	0.54 - 3.78
Implement contact precautions for patients with positive cultures	-0.50	0.570	0.61	0.11 - 3.41
Perform surveillance of micro results for new cases of MRSA	2.30	0.049	10.02	1.01 - 99.27

Table 6.2.5. Relationship Between Infection Control Policies and VRE BSI Rates, Bivariate Analysis Using Poisson Regression				
	Coef	**p-value**	**IRR**	**95% CI**
Screening all patients for VRE upon admission	--	--	--	--
Target new admissions for VRE screening	1.20	0.076	3.31	0.88 - 12.40
Screen all patients for VRE periodically after admission	--	--	--	--
Screen select patients for VRE periodically after admission	--	--	--	--
Implement presumptive isolation/ contact precautions pending a VRE screen	-1.23	0.411	0.29	0.02 - 5.52
Implement contact precautions for patients with positive cultures	0.69	0.285	2.00	0.56 - 7.14
Perform surveillance of micro results for new cases of VRE	-0.18	0.712	0.83	0.33 - 2.15

Table 6.2.6. Relationship Between Infection Control Policies and *C. difficile* Rates, Bivariate Analysis Using Poisson Regression				
	Coef	**p-value**	**IRR**	**95% CI**
Screening all patients for *C. difficile* upon admission	--	--	--	--
Target new admissions for *C. difficile* screening	--	--	--	--
Screen all patients for *C. difficile* periodically after admission	--	--	--	--
Screen select patients for *C. difficile* periodically after admission	--	--	--	--
Implement presumptive precautions pending a screen	-0.20	0.465	0.82	0.47 - 1.41
Implement precautions for patients with positive cultures	0.07	0.886	1.07	0.43 - 2.63
Surveillance of microbiology results for new cases	-0.07	0.817	0.93	0.51 - 1.71
Promote the use of soap and water	-0.04	0.910	0.96	0.46 - 2.01

Table 6.2.7. Effect of Full Compliance with MRSA BSI Policies on MRSA BSI Rate per 100 Central Line Days in Bivariate Analysis† (All of the Time vs. Other)					
	Coef	**S.E.**	**p-value**	**IRR**	**95% CI**
Screening all patients for MRSA upon admission	0.38	0.83	0.65	1.46	0.29 – 7.45
Target new admissions for MRSA screening	-1.33	0.89	0.14	0.26	0.05 -1.52
Screen all patients for MRSA periodically after admission	--	--	--	--	--
Screen select patients for MRSA periodically after admission	--	--	--	--	--
Implement presumptive isolation/contact precautions pending a MRSA screen	-0.90	1.37	0.51	0.41	0.03 – 5.97
Implement contact precautions for patients with positive MRSA cultures	-0.95	0.71	0.18	0.39	0.10 – 1.54
Perform surveillance of microbiology results for new cases of MRSA	0.48	0.81	0.55	1.62	0.33 – 8.01

† Using negative binomial regression

Table 6.2.8. Predictors of MRSA BSI Rate per 1000 Central Line Days in Bivariate Poisson Analysis†			
	Coef	**S.E.**	**p-value**
Setting Characteristics			
Setting (reference group = urban)			
Suburb	0.50	0.59	0.40
Rural	0.75	1.09	0.49
Participation in CHAIPI	0.27	0.61	0.65
Participation in CHART	-0.87	0.51	0.09
Participation in IHI	-1.21	0.56	0.03
Participation in other initiative	0.74	0.54	0.17
Participation in any initiative	-0.47	0.66	0.45
ICD hours	0.02	0.02	0.33
ICD certified in infection control	-1.14	0.50	0.02
ICD member of SHEA/APIC	1.21	1.79	0.50
ESS	0.55	0.59	0.36
Presence of Hospital Epidemiologist*	0.30	0.62	0.63
Presence of full-time Hospital Epidemiologist	-0.55	2.56	0.83
# of Hospital Epidemiologists*	0.06	0.49	0.90
Hospital Epidemiologist hours	0.01	0.02	0.59
# of Infection Preventionists	-0.13	-0.26	0.61
Total Infection Preventionist hours	-0.01	0.01	0.49
Proportion of Infection Preventionists certified in infection control	0.45	0.68	0.51
# of FTE IP per 100 beds	--	--	--
Total infection control hours (IP + Director)	-0.01	0.01	0.78
MRSA Infection Control Policies			
Screen all patients for MRSA upon admission	0.48	0.60	0.43
Target new admissions for MRSA screening	-0.49	0.72	0.50
Screen all new patients for MRSA periodically after admission	--	--	--
Target MRSA screening periodically after admission	-1.46	1.48	0.32
Implement presumptive isolation/contact precautions pending a MRSA screen	0.36	0.57	0.53
Implement contact precautions for patients with positive cultures	-0.50	0.97	0.61
Perform surveillance of microbiology results for new cases of MRSA	2.30	1.82	0.21

*Either part-time or full-time †Poisson regression with dispersion parameter used

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T**able 6.2.9. Predictors of MRSA BSI Rate per 1,000 Central Line Days in Multivariable Poisson Regression**			
	Coef	**S.E.**	**P-value**
Model 1			
Screen all patients for MRSA upon admission	2.33	0.91	0.10
Infection Control Director hours	0.09	0.05	0.06
Infection Control Director certified in infection control	-2.01	0.72	0.01
# of IP FTE per 100 beds	-3.71	0.65	0.04
Participation in IHI	-0.74	0.07	0.25
Model 2			
Target new admissions for MRSA screening	-3.51	0.95	<0.01
Infection Control Director hours	0.08	0.04	0.06
Infection Control Director certified in infection control	-2.29	0.48	<0.01
# of IP FTE per 100 beds	-2.17	0.91	0.02
Participation in CHART	0.89	0.66	0.18
Model 3			
Screen select patients for MRSA periodically after admission	-1.07	0.75	0.15
Infection Control Director hours	0.05	0.03	0.10
Infection Control Director certified in infection control	-1.21	0.52	0.02
# of IP FTE per 100 beds	-1.43	1.06	0.18
Participation in IHI	-0.73	0.53	0.18
Model 4			
Implement presumptive isolation/contact precautions pending a MRSA screen	-0.16	0.69	0.82
Infection Control Director hours	0.05	0.03	0.15
Infection Control Director certified in infection control	-1.35	0.60	0.03
# of IP FTE per 100 beds	-1.60	1.24	0.20
Participation in IHI	-0.73	0.55	0.19

†Poisson regression with dispersion parameter used

CHAIPI = California Healthcare-Associated Infections Prevention Initiative, CHART = California Hospital Assessment and Reporting Taskforce, FTE = Full-time Equivalents, IHI = Institute for Healthcare Improvement

Appendix 6.2.10. Relevant Sections of California Survey used in Aim II

Survey Sections
I: HOSPITAL AND RESPONDENT DEMOGRAPHICS
II: INFECTION PREVENTION AND CONTROL DEPARTMENT STAFF
III: IP STAFF TIME USE and PROGRAMS AFFECTING DEPTARTMENT
V: ELECTRONIC SURVEILLANCE SYSTEM
VII: POLICIES ON INFECTIOUS AGENTS

I: HOSPITAL AND RESPONDENT DEMOGRAPHICS

What is your role in the Infection Prevention and Control Department ?
1– Infection Prevention and Control Department Director/Coordinator
2– Physician hospital epidemiologist, other than Director/Coordinator
3– Physician with infectious disease specialty, other than Director/ Coordinator/ Hospital epidemiologist
4– IP other than Director/Coordinator
5– Data Analyst/Manager
6– Administrative Assistant/Secretary
7– Other (txt)

Is your hospital a teaching hospital? ? 1 – yes, 0 – no

How would you describe the hospital setting at which you practice?
1 – Urban setting / Large city more than 200,000
2 – Suburb / medium sized town
3 – Rural setting/ town less than 50,000

Is your hospital participating in any of the following programs? (check all that apply)
1....Yes, 0....No
_____ California Hospital Assessment and Reporting Task Force
_____ Five Million Lives Campaign
_____ other

How many licensed bed does your hospital have, not including long term care or rehab facilities?

Does your infection control program provide service to outpatient clinics?
1 – yes, 0 – no, 3 – DK
Does your infection control program provide service to long term care facilities?
1 – yes, 0 – no, 3 – DK If yes, how many beds?

Does your infection control program provide service to rehab facilities? 1 – yes, 0 – no, 3 – DK
If yes, how many beds?

II: INFECTION CONTROL DEPARTMENT STAFF

Please answer these questions based on the personnel resources available at this time in your infection control department. There will be separate questions about the Infection Control Director, Hospital Epidemiologists, Infection Preventionists, and support staff.

INFECTION CONTROL DEPARTMENT MANAGEMENT

Does your hospital have an Infection Control Director position (include yourself)? 1 – yes, 0 – no, 3 – DK

Please indicate the total number of hours the Infection Control Director actually works (including overtime) for the Infection Control Department each week.

Please answer the following questions for the Infection Control Director or, if there is no director, the person who oversees the day-to-day operations of the infection control department

Is he/she certified in infection control (CIC)? 1 – yes, 0 – no, 3 – DK

Is this person a member of SHEA or APIC? 1 – yes, 0 – no, 3 – DK

Is he/she on the local Infection Control Committee?
1=Chair/Cochair, 2=Participant, 3=Not on committee, 4=No committee

HOSPITAL EPIDEMIOLOGISTS / INFECTION PREVENTIONISTS

Please indicate the number of Hospital Epidemiologists **(MD only)**, other than the department Director/ manager entered above (enter whole numbers only, including part time staff)
If your hospital epidemiologist is not a physician, please consider that person an infection preventionist for the purposes of this survey.

Please indicate the number of Infection Preventionists (IPs), other than the Infection Control Director and Hospital Epidemiologist entered above. (enter whole numbers only, including part time staff) _____

OTHER STAFFING

Does your department have help with data management? 1 – yes, 0 – no, 3 – DK
If yes, how many hours?

Does your department have help with secretarial functions? 1 – yes, 0 – no, 3 – DK
If yes, how many hours?

Does your department have other help (e.g., statistician or operations manager)?
1 – yes, 0 – no, 3 – DK If yes, how many hours?

V: ELECTRONIC SURVEILLANCE SYSTEM (ESS)

___ Does your institution use an electronic surveillance system for tracking healthcare associated infections? 1....Yes 0....No 3 .. DK
If yes, when did your hospital begin using this surveillance system? _____

We have and utilize the following features (1....Yes 0....No 3 .. DK)
_____ Data mining (system is integrated with clinical, laboratory, and pharmacy
_____ Automatic alerts
_____ Use built-in templates to create reports and data summaries
_____ Integration of infection data with CDC definitions and/ or reporting requirements
_____Share reports with key committees and hospital administration

Total number of hours per day the surveillance system is used by all IP staff _____

VII: POLICIES ON INFECTIOUS AGENTS (Hospital Wide Policies)
These questions pertain to hospital policies and are not specific to the ICU described in the previous section.

Does your hospital collect a surveillance culture upon admission for any group of patients?
0 = no 1 = yes 3 = don't know
If yes, for which patients?
0 = no 1 = yes
All admissions (excluding L&D)
Readmissions within 30 days of discharge
Transfers from nursing homes
ICU patients
Dialysis patients
Other _____ (txt)

Methicillin Resistant *Staphylococcus Aureus* (MRSA) (Hospital wide surveillance)		
For Jan – March 2010	Does your hospital have a written policy to: 0 = no 1 = yes 3 = dk	During the last period monitored, what proportion of time was this policy was correctly implemented? 1 - All of the time (95-100%) 2 - Usually (75-94%) 3 - Sometimes (25-74%) 4 - Rarely/Never (less than 25%) 5 - We monitor implementation but don't know the proportion 6 - No Monitoring
Screen **all** patients for MRSA upon admission?		
Target **new** admissions for MRSA screening? (e.g., readmissions, transfers from nursing homes, ICU patients, etc)		
drop down If you target **new** admissions, which populations do you target? Check all that apply. Readmissions within 30 days of discharge Transfers from skilled nursing facilities/long term health care ICU patients Dialysis patients Surgical patients with documented medical conditions that make them susceptible to infection Other, specify: _____(txt)		
Screen <u>all</u> patients for MRSA **periodically** after admission?		
Screen <u>select</u> patients for MRSA **periodically** after admission?		
drop down If you screen **select** patients for MRSA **periodically after admission**, which populations are targeted? Check all that apply. ICU		

Dialysis Other, specify: _____ (txt)		
Implement **presumptive** isolation/contact precautions pending a MRSA screen?		
Implement contact precautions for patients with positive cultures for MRSA?		
Perform surveillance of microbiology results for new cases of MRSA?		
If your hospital collects surveillance culture for MRSA, which method is used? (Check all that apply). Standard culture PCR or other rapid diagnostics MRSA Selective agar (e.g. CHROMager) Other Other, specify: _____ (txt) Do not collect surveillance cultures		
What other activities does your hospital use to decrease MRSA?_____		

Vancomycin-resistant Enterococci (VRE) infections **Hospital wide surveillance**
Is your <u>hospital</u> involved in any activities to decrease healthcare associated **Vancomycin-resistant Enterococci (VRE) infections**? 0 = no 1 = yes 3 = dk
drop down **If yes**, please check which activities your hospital is involved in to decrease VRE: (Check all that apply). Screen **ALL new** patients for VRE upon admission Screen **select** patients for VRE upon admission (e.g., readmissions, transfers, ICU patients) Screen **all** patients for VRE **periodically** after ICU admission Screen **select** patients for VRE **periodically** after ICU admission Implement **presumptive** isolation/ contact precautions pending a screen Implement contact precautions for patients with positive cultures Surveillance of microbiology results for new cases Other, specify: _____ (txt)
*drop down * If your hospital **screens select patients for VRE** upon **admission**, which populations are screened? Readmissions within 30 days of discharge Transfers from nursing homes/long term healthcare facilities ICU patients Dialysis patients Other, specify: _____(txt)
*drop down * If your hospital **screens select patients for VRE periodically after admissions**, which populations are screened? ICU Dialysis Other, specify _____(txt)

***Clostridium difficile* hospital wide surveillance**
Is your <u>hospital</u> involved in any activities to decrease healthcare associated **C. difficile-associated infections**? 0 = no 1 = yes 3 = dk

*drop down * **If yes**, please check which activities your hospital is involved in to decrease C. difficile: (Check all that apply). Screen **ALL new** patients upon admission Screen **select** patients upon admission (e.g., readmissions, transfers from nursing homes) Screen **all** patients **periodically** after ICU admission Screen **select** patients **periodically** after ICU admission Implement **presumptive** isolation/ contact precautions pending a screen Implement contact precautions for patients with positive cultures Surveillance of microbiology results for new cases Promote the use of soap and water after caring for patients with C. difficile associated diarrhea Other, specify: _____(txt)
*drop down * If your hospital **screens select patients** for C. difficile **upon admission**, which populations are screened? Readmissions within 30 days of discharge Transfers from nursing homes/long term healthcare facilities ICU patients Dialysis patients Other, specify: _____(txt)
*drop down * If your hospital **screens select patients** for C. difficile **periodically after admissions**, which populations are screened? ICU Dialysis Other Other, specify: _____ (txt)

Do you routinely screen for any other organism(s)? 0 = no 1 = yes 3 = dk

If yes, please specify which organism(s) your hospital routinely screens for (other than MRSA, VRE and C. difficile): (txt)_____

Does your hospital have a policy regarding antibiotic restriction? 0 = no 1 = yes 3 = dk

If yes, please describe the policy: (txt)_____

Please report the following:	**1st quarter of 2010 (Jan – March)**
	1 -Don't monitor 2 -Prefer not to answer 3-Do not have ICU level data
Total number of hospital admissions	
Total number of inpatient days	
Total number of central line days (hospital-wide)	
Number of health-care-associated **MRSA -Blood Stream Infections** (hospital-wide)	
Number of health-care-associated **VRE -Blood Stream Infections** (hospital-wide)	
Number of health-care-associated ***C. difficile*** infections (hospital-wide)	

6.3 Appendix 3: Chapter 4 Appendix

Appendix 6.3.1. List of classes of antibiotics used to define antibiotic exposure

Aminoglycocides
- Amikacin
- Gentamicin Sulfate
- Tobramycin Sulfate

Carbapenems
- Imipenem Cilastatin
- Meropenem

Cephalosporins and Related
- Cefaclor
- Cefadroxil
- Cefazolin
- Cefepime
- Cefixime
- Cefotaxime Sodium
- Cefoxitin
- Cefpodoxime
- Cefprozil
- Caftazidime
- Ceftriaxone
- Cefuroxime Axetil
- Cefuroxime Sodium
- Cephalexin

Glycylcyclines
- Tigecycline

Macrolides
- Azithromycin
- Clarithromycin
- Erythromycin Base
- Erythromycin Ethylsuccinate
- Erythromycin Lactobionate
- Erythromycin Stearate

Monobactams
- Aztreonam

Sulfonamides
- Sulfasalazine
- Sulfamethoxazole Trimethoprim
- Sulfadiazine

Penicillins
- Amoxicillin Clavulante
- Amoxicillin
- Ampicillin Sodium
- Ampicillin Sulbactam
- Dicloxacillin Sodium
- Oxacillin
- Penicillin G Benzathine
- Penicillin G Potassium
- Penicillin G Procaine
- Penicillin G Sodium
- Penicillin V Potassium
- Pipercillin Tazobactam

Polypeptides
- Polymyxin B Sulfate

Quinolones
- Ciprofloxacin
- Levofloxacin

Tetracyclines
- Demeclocycline
- Doxycycline Calcium
- Doxycyline Hyclate
- Minocycline HCL
- Tetracycline HCL

Other
- Vancomycin
- Clindamycin
- Daptomycin
- Chloramphenicol
- Linezolid
- Rifabutin
- Rifampin
- Nitrofurantoin
- Trimethoprim

Appendix 6.3.2. List of medication administered used to define exposure to immunosuppressive medication

Abciximab
Adalimumab
Aldesleukin
Altretamine
Aminoglutethimide
Anakinra
Anastrozole
Asparaginase
Azathioprine
Basiliximab
Betamethasone
Bleomycin
Busulfan
Capecitabine
Carboplatin
Carmustine
Chlorambucil
Cisplatin
Cladribine
Cortisone
Cyclophosphamide
Cyclosporine
Cytarabine
Dacarbazine
Daclizumab
Dactinomycin
Daunorubicin
Delavirdine
Denileukin diftitox
Dexamethasone
Docetaxel
Doxoru bicin
Doxorubicin
Epirubicin
Estramustine
Etanercept
Etoposide
Exemestane
Floxuridine
Fludarabine
Fluorouracil
Flutamide
Gemcitabine
Gemtuzumab Ozogamicin
Hydrocortisone
Hydroxychloroquine
Hydroxyurea
Idarubicin
Ifosphamide
Infliximab
Interferon alfa-2a
Interferon alfa-2b
Interferon beta-la
Interferon beta-lb
Interferon gamma-lb
Irinotecan
Isotretinoin
Leflunomide
Letrozole
Leuprolide
lnterleukin-2
Lomustine
Mechlorethamine HCI
Melphalan
Mercaptopurine
Methotrexate
Methylprednisolone
Mitomycin
Mitotane
Mitoxantrone
Muromonab-CD3
Mycophenolate
Paclitaxel
Pegaspargase
Penicillamine
Pentostatin
Pimecrolimus
Pipobroman
Plicamycin
Prednisolone
Prednisone
Priliximab
Procarbazine
Rituximab
Sargramostim
Streptozocin
Tacrolimus
Temozolomide
Teniposide
Testolactone
Thioguanine
Thiotepa
Trastuzumab
Tretinoin
Triamcinolone
Uracil mustard
Valrubicin
Vinblastine
Vincristine
Vinorelbine

Table 6.3.3. Matched Comparison of MRSA BSI Cases and Non-infected Controls Using Mantel-Haenszel Methods

	Cases (n=201)	Controls (n=402)			
	N (%)	N (%)	MH OR	95% CI	p-value
Gender					
Female	83 (41.3)	207 (51.5)	1.55	1.08 – 2.26	0.015
Male	118 (58.7)	195 (48.5)			
Stay in skilled nursing facility					
Yes	9 (4.5)	8 (2.0)	2.43	0.91 – 6.50	0.068
No	192 (95.5)	394 (98.0)			
Prior Hospitalization					
Yes	91 (45.3)	140 (34.8)	1.68	1.14 – 2.46	0.007
No	110 (54.7)	262 (65.2)			
Diabetes					
Yes	51 (25.4)	82 (20.4)	1.34	0.89 – 2.03	0.156
No	150 (74.6)	320 (79.6)			
Any Burn					
Yes	6 (3.0)	16 (4.0)	0.69	0.24 – 1.99	0.493
No	195 (97.0)	386 (96.0)			
Burns of >10% of body					
Yes	3 (1.5)	7 (1.7)	0.83	0.20 – 3.49	0.803
No	198 (98.5)	395 (98.3)			
3rd degree burns					
Yes	6 (3.0)	9 (2.2)	1.43	0.45 – 4.50	0.540
No	195 (97.0)	393 (97.8)			
Renal failure					
Yes	99 (49.3)	115 (28.6)	3.02	1.99 – 4.59	<0.001
No	102 (50.8)	287 (71.4)			
Open wound					
Yes	2 (1.0)	3 (0.8)	1.33	0.22 – 7.98	0.752
No	199 (99.0)	399 (99.3)			
Malignancy					
Yes	52 (25.9)	73 (18.2)	1.65	1.08 – 2.50	0.019
No	149 (74.1)	329 (81.8)			
Chronic dermatitis					
Yes	27 (13.4)	38 (9.5)	1.47	0.87 – 2.49	0.148
No	174 (86.6)	364 (90.6)			
History of major organ transplant					
Yes	8 (4.0)	14 (3.5)	1.14	0.48 – 2.72	0.763
No	193 (96.0)	388 (96.5)			
History of substance abuse					

Yes	20 (10.0)	36 (9.0)	1.14	0.62 – 2.11	0.670
No	181 (90.0)	366 (91.0)			
Intubation					
Yes	35 (17.4)	65 (16.4)	1.10	0.67 – 1.82	0.696
No	166 (82.6)	332 (83.6)			
Mechanical ventilation during encounter					
Yes	43 (21.4)	71 (17.9)	1.39	0.84 – 2.31	0.200
No	158 (78.6)	326 (82.1)			
Insertion of feeding tube					
Yes	10 (5.0)	22 (5.5)	0.87	0.39 – 1.95	0.739
No	191 (95.0)	375 (94.5)			
Any Cardiac Procedure					
Yes	24 (12.0)	60 (15.4)	0.72	0.41 – 1.23	0.225
No	176 (88.0)	330 (84.6)			
Biopsy performed					
Yes	11 (5.5)	21 (5.3)	1.05	0.49 – 2.26	0.900
No	190 (94.5)	376 (94.7)			
Dialysis performed					
Yes	22 (11.0)	30 (7.6)	1.52	0.84 – 2.75	0.164
No	179 (89.0)	367 (92.4)			
Major organ transplant performed					
Yes	8 (4.0)	10 (2.5)	1.60	0.63 – 4.05	0.317
No	193 (96.0)	387 (97.5)			
Major or diagnostic procedures performed in encounter as per HCUP classification					
Yes	8 (4.0)	21 (5.3)	0.76	0.34 – 1.72	0.512
No	193 (96.0)	376 (94.7)			
Major or therapeutic procedure performed in encounter as per HCUP classification					
Yes	52 (25.8)	147 (37.1)	0.56	0.37 – 0.84	0.005
No	149 (74.1)	249 (62.9)			
Central venous catheter inserted					
Yes	81 (40.3)	106 (26.6)	2.41	1.55 – 3.75	<0.001
No	120 (59.7)	292 (73.4)			
Asthma					
Yes	15 (7.5)	26 (6.5)	1.18	0.60 – 2.32	0.628
No	186 (92.5)	376 (93.5)			
Chemotherapy					
Yes	7 (3.5)	7 (1.7)	2.00	0.70 – 5.70	0.186
No	194 (96.5)	395 (98.3)			
Congestive Heart Failure					
Yes	50 (24.9)	74 (18.4)	1.54	0.99 – 2.40	0.053
No	151 (75.1)	328 (81.6)			
Cirrhosis					

Yes	15 (7.5)	11 (2.7)	3.11	1.32 – 7.32	0.006
No	186 (92.5)	391 (97.3)			
COPD					
Yes	11 (5.5)	25 (6.2)	0.88	0.44 – 1.77	0.720
No	190 (94.5)	377 (93.8)			
Decubitus Ulcers					
Yes	13 (6.5)	19 (4.7)	1.44	0.67 – 3.09	0.350
No	188 (93.5)	383 (95.3)			
Hepatitis B					
Yes	1 (0.5)	4 (1.0)	0.50	0.06 – 4.47	0.527
No	200 (99.5)	398 (99.0)			
Hepatitis C					
Yes	7 (3.5)	9 (2.2)	1.56	0.58 – 4.18	0.377
No	194 (96.5)	393 (97.8)			
HIV					
Yes	11 (5.5)	11 (2.7)	2.57	0.93 – 7.12	0.059
No	190 (94.5)	391 (97.3)			
Neurological Disease					
Yes	12 (6.0)	16 (4.0)	1.67	0.69 – 4.00	0.248
No	189 (94.0)	386 (96.0)			
Rheumatoid Arthritis					
Yes	2 (1.0)	1 (0.3)	4.00	0.36 – 44.11	0.221
No	199 (99.0)	401 (99.8)			
Tracheostomy					
Yes	23 (11.4)	28 (7.0)	2.29	1.10 – 4.74	0.022
No	178 (88.6)	374 (93.0)			

COPD = Chronic Obstructive Pulmonary Disease, HIV = Human Immunodeficiency Virus

Table 6.3.4. Multivariable Analysis of Risk Factors for MRSA BSI Using Controls with MSSA BSI Using Catheter Days (Excluding Antibiotic Use)					
	B	**S.E.**	**OR**	**95% CI**	**P-value**
Age	0.015	0.004	1.02	1.01 – 1.02	<0.001
Hospitalization in Prior Year	0.288	0.201	1.33	0.90 – 1.98	0.153
Charlson Severity of Illness Measure	-0.057	0.041	0.94	0.87 – 1.02	0.168
Diabetes Mellitus	0.004	0.246	1.00	0.62 – 1.61	0.988
Renal Failure	0.446	0.210	1.56	1.04 – 2.36	0.033
3rd Degree Burn	1.258	0.702	3.52	0.89 – 13.93	0.073
Chemotherapy	1.114	0.712	3.05	0.75 – 12.30	0.118
Tracheostomy	0.251	0.375	1.29	0.62 – 2.68	0.503
Urinary Catheter Days	0.011	0.008	1.01	0.99 – 1.03	0.197
Major Organ Transplant	1.611	0.818	5.01	1.01 – 24.86	0.049
Major OR Therapeutic Procedure	0.513	0.241	1.67	1.04 – 2.68	0.033

This analysis used catheter days instead of dichotomous variable for catheter use.

OR = Operating Room

Table 6.3.5. Multivariable Analysis of Risk Factors for MRSA BSI Using Controls with MSSA BSI Using Catheter Days (Including Antibiotic Use)					
	β	**S.E.**	**OR**	**95% CI**	**P-value**
Age	0.012	0.005	1.01	1.00 – 1.02	0.026
Hospitalization in Prior Year	0.316	0.254	1.37	0.84 – 2.26	0.212
Charlson Severity of Illness Measure	-0.053	0.050	0.95	0.86 – 1.05	0.294
Diabetes Mellitus	0.042	0.302	1.04	0.58 – 1.88	0.890
Renal Failure	0.457	0.270	1.58	0.93 – 2.68	0.090
3rd Degree Burn	0.640	1.557	1.90	0.09 – 40.11	0.681
Chemotherapy	1.531	1.181	4.62	0.46 – 46.81	0.195
Tracheostomy	-0.186	0.493	0.83	0.32 – 2.18	0.705
Urinary Catheter Days	0.006	0.010	0.99	0.97 – 1.01	0.569
Major Organ Transplant	2.766	1.109	15.90	1.81 – 139.70	0.013
Major OR Therapeutic Procedure	0.626	0.338	1.87	0.96 – 3.63	0.064
Monobactam Use	1.085	0.884	2.96	0.52 – 16.74	0.220
Quinolone Use	1.269	0.309	3.56	1.30 – 9.74	0.014

This analysis used catheter days instead of dichotomous variable for catheter use.

OR = Operating Room

Table 6.3.6. Multivariable Analysis of Risk Factors for MRSA BSI vs. Non-Infected Controls Using Catheter Days (Excluding Antibiotic Use)					
	β	**S.E.**	**OR**	**95% CI**	**P-value**
Male Gender	0.446	0.201	1.56	1.95 – 2.32	0.027
Stay in Skilled Nursing Facility	0.382	0.643	1.47	0.42 – 5.17	0.552
Hospitalization in the Prior Year	0.325	0.223	1.38	0.89 – 2.15	0.145
Charlson Severity of Illness Measure	-0.061	0.063	0.94	0.83 – 1.06	0.331
Malignancy	0.680	0.308	1.97	1.08 – 3.61	0.027
Renal Failure	1.001	0.245	2.72	1.68 – 4.40	<0.001
Congestive Heart Failure	0.162	0.263	1.18	0.70 – 1.96	0.538
Cirrhosis	1.338	0.488	3.82	1.46 – 9.93	0.006
HIV Infection	1.489	0.691	4.43	1.14 – 17.16	0.031
Tracheostomy	0.396	0.442	1.49	0.63 – 3.53	0.369
Central Venous Catheter Days	0.026	0.012	1.03	1.00 – 1.05	0.027
Major OR Therapeutic Procedure	-0.443	0.224	0.64	0.41 – 1.00	0.048
ICU Days	0.023	0.012	1.02	1.00 – 1.05	0.054
Immunosuppressive Medication	-0.043	0.216	1.04	0.68 – 1.60	0.841

This analysis used catheter days instead of dichotomous variable for catheter use.

ICU = Intensive Care unit, OR = Operating Room

Table 6.3.7. Multivariable Analysis of Risk Factors for MRSA BSI vs. Non-Infected Controls Using Catheter Days (Including Antibiotic Use)					
	β	**S.E.**	**OR**	**95% CI**	**P-value**
Male Gender	0.461	0.271	1.59	0.93 – 2.70	0.089
Stay in Skilled Nursing Facility	0.206	0.869	1.23	0.22 – 6.75	0.813
Hospitalization in the Prior Year	0.364	0.288	1.44	0.82 – 2.53	0.206
Charlson Severity of Illness Measure	0.021	0.085	1.02	0.86 – 1.22	0.804
Malignancy	0.363	0.439	1.44	0.61 – 3.40	0.409
Renal Failure	0.988	0.345	2.69	1.37 – 5.28	0.004
Congestive Heart Failure	-0.199	0.345	0.82	0.42 – 1.61	0.565
Cirrhosis	1.268	0.559	3.55	1.19 – 10.63	0.023
HIV Infection	1.212	0.882	3.56	0.60 – 18.91	0.169
Tracheostomy	0.857	0.838	3.36	0.46 – 12.18	0.306
Central Venous Catheter Days	0.033	0.018	1.03	1.00 – 1.07	0.066
Major OR Therapeutic Procedure	-0.594	0.304	0.52	0.30 – 1.00	0.050
ICU Days	-0.020	0.025	0.98	0.93 – 1.03	0.431
Immunosuppressive Medication	-0.100	0.287	1.11	0.63 – 1.94	0.728
Monobactam Use	1.975	1.258	7.20	0.62 – 84.85	0.117
Quinolone Use	0.920	0.597	2.51	0.78 – 8.09	0.123

This analysis used catheter days instead of dichotomous variable for catheter use.

ICU = Intensive Care Unit, OR = Operating Room