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Association of Electronic Health Records with Methicillin-Resistant Staphylococcus aureus Infection in a National Sample

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ASSOCIATION OF ELECTRONIC HEALTH RECORDS WITH METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS INFECTION IN A NATIONAL SAMPLE

BY

Eric Weaver

A doctoral project submitted to the faculty of the Medical University of South Carolina in partial fulfillment of the requirements for the degree of Doctor of Health Administration in the College of Health Professions

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Abstract

This study examined the relationship between advanced electronic health record (EHR) use in hospitals and rates of Methicillin-resistant *Staphylococcus aureus* (MRSA) infection in an inpatient setting. National Inpatient Sample (NIS) and Health Information Management Systems Society (HIMSS) Annual Survey are combined in the retrospective, cross-sectional analysis. A twenty percent simple random sample of the combined 2009 NIS and HIMSS datasets included a total of 1,032,905 patient cases of MRSA in 550 hospitals. Results of the propensity-adjusted logistic regression model revealed a statistically significant association between advanced EHR and MRSA, with patient cases from an advanced EHR being less likely to report a MRSA diagnosis code.

CHAPTER ONE

INTRODUCTION

Background and Need

Advancement of public health and medicine over the last century has led to the development and widespread use of antimicrobial agents (CDC, 1999) – one of the most important public health interventions in the history of mankind. Along with basic sanitation and global vaccination, antimicrobial agents have caused a substantial reduction in mortality from infectious microorganisms (MacDougall & Polk, 2005). Weaponized agents to fight disease are a human invention; however, antimicrobials have been naturally occurring in the environment for millennia in a form not visible to the human eye. It was not until the advent of modern medicine where humans were able to co-opt fungi and soil actinomycetes, on a molecular level to secure their ecologic niche in a world seething with predatory microorganisms (Davies, 1990).

The emergence of antimicrobial resistance was inevitable from an evolutionary and ecological perspective. According to Davies (2008), "Since the introduction of antibiotics in the late 1940's, there has been an inexorable propagation of antibiotic resistance genes in bacterial pathogens. The survival phenomenon was first characterized as the appearance of point mutations that altered drug targets, but in the mid-1950's transmissible antibiotic resistance genes were reported" (Davies, 2008, p. 3). In 1955, noted physician, psychiatrist, author, and publisher, Dr. Félix Martí-Ibáñez wrote about his concerns about the potential adverse effects of antibiotic resistance on society, "Antibiotic therapy, if indiscriminately used, may turn out to be a medicinal flood that temporarily cleans and heals, but ultimately destroys life itself." – an ominous prediction of how antimicrobial resistance could eventually overwhelm the human race (Harbarth & Samore, 2005, p. 794).

Antimicrobial resistance has likely been present for thousands of years. It is generally accepted that genetic encoding initially occurred as a countermeasure to the effects of naturally-occurring antimicrobials in the environment, and these mutations were incorporated into the genetic code of pathogenic flora immediately thereafter (Davies, 1997; Hawkey, 1998). MacDougall & Polk (2005) state that this evolutionary adaptation to enhance survival prospects in a biological ecosystem full of threats is "a testament to the impressive reproductive rate of most microorganisms, the tremendous selective pressure that antimicrobial agents apply to these populations, and the huge number of unculturable organisms in the environment that may be serving as reservoirs of antimicrobial resistance genes" (p. 638).

In the milieu of a modern-day hospital, antibiotic resistance is most likely to develop when there is a convergent coupling of extensive antimicrobial use with a high concentration of acutely ill patients at risk of infection. Avoidance of antibiotic misappropriation is the key to controlling antibiotic resistance since diagnostic uncertainty can lead to the rapid growth and proliferation of opportunistic pathogens due to antimicrobial selection pressure (Harbarth & Samore, 2005). Appropriateness of antibiotic selection in hospitals is an increasingly complex issue. Not only is there an effect on patient morbidity and mortality, there is also an economic impact of inappropriate therapy that includes costs of direct care, laboratory testing, isolation procedures, and provider education to improve infection control and antimicrobial decision algorithms (Davey & Marwick, 2008). The inherent difficulty of managing this public health problem has made it readily apparent to hospital administrators that physicians need assistance in selection of antibiotics for their sickest patients. Bioinformatics-assisted prescribing is the cornerstone of an effective program to manage the complexities of prescribing antimicrobials in the modern era of multi-drug resistance (Sintchenko, Coiera, & Gilbert, 2008); therefore, much attention placed on the role of electronic health records in combating drug-resistant pathogens.

Both the Centers for Disease Control and Prevention and the World Health Organization have identified antimicrobial resistance as a “major public health issue” and “one of the three greatest threats to human health” (So, Furlong & Heddini, 2010). To further illustrate this global health crisis, the theme of World Health Day 2011 was “Antimicrobial resistance: no action today and no cure tomorrow” with an international emphasis to raise awareness for resistance and the concern of having few new innovative antibiotics in the developmental pipeline (Chan, 2011). Antimicrobial resistance even took center stage at the 2016 meeting of the International Monetary Fund (IMF) because of its enormous projected economic cost to the world economy over the next few decades. At this meeting of the most prestigious international financial institution in the world, it was discussed how antimicrobial resistant pathogens could present a bigger threat to humankind than cancer by 2050, killing 10 million people per year and reducing global GDP by 3.5%, unless world leaders agree on international action (MacDonald, 2016). If this prediction is accurate, the doomsday scenario of antibiotic resistance would potentially make it a bigger threat to humanity than terrorist attacks, mass shootings, and global warming.

Antibiotics can be singled out as one of the most transformation discoveries in the field of medicine; however, due to antibiotic resistance, the golden age of antibiotic therapy to treat or prevent infections is likely coming to an end. Current antibiotics are failing, and they are not being replaced with new ones. Dr. Arjun Srinivasan, an associate director at the CDC states the following, "*For a long time, there have been newspaper stories and covers of magazines that talked about "The end of antibiotics, question mark?" Well, now I would say you can change the title to "The end of antibiotics, period." We're here. We're in the post-antibiotic era… we are literally in a position of having a patient in a bed who has an infection, something that five years ago even we could have treated, but now we can't.*" (Srinivasan, 2015, para. 17).

Antibiotic resistance contributed to one of the top healthcare stories in 2016 with the discovery of a strain of *E. coli* resistant to the antibiotic colistin – a last-resort antibiotic used only when all others have failed. This alarming development caused Tom Frieden, Centers for Disease Control and Prevention Director, to affirm that this example "*basically shows us that the end of the road isn't very far away for antibiotics – that we may be in a situation where we have patients in our intensive care units, or patients getting urinary tract infections for which we do not have antibiotics*" (Sun & Dennis, 2016, May 27, para. 6).

The prospects of a post-antibiotic world and its implication of the future healthcare system are alarming. A typical American in his or her lifetime will have nine surgeries (Lee, Regenbogen, & Gawande, 2008), and this number will certainly go down as antibiotics become obsolete. For example, that means that commonplace surgeries such as joint replacement and life-saving organ transplants would no longer be able to be performed due to the likelihood of infection. Furthermore, stem cell transplants, bone marrow transplantation, and cancer chemotherapy would be largely impossible because the affect these procedures have on weakening a patient's immune system to the point where a physician would not be able to treat the sequelae of life-threatening infection. This grim scenario is all the more likely because of the dearth of new antibiotics being developed that are able to combat anti-resistant pathogens. "As of May an estimated 37 new antibiotics were in clinical development, according to the Pew Charitable Trusts, with 13 in Phase 3 clinical trials. Historically, only one in five products that reach Phase 3 win approval" (Johnson, 2016, para. 11).

Multidrug-resistant organisms account for more than 70% of all hospital-associated infections, with limited antimicrobial treatment options and consequently higher mortality rates in comparison to "normal" strains of bacteria (APIC, 2010). There are six 'superbugs' that are among the most deadly antibiotic-resistant bacteria, identified as urgent or serious threats by CDC: CRE (carbapenem-resistant Enterobacteriaceae), MRSA (methicillin-resistant *Staphylococcus aureus*), ESBL-producing Enterobacteriaceae (extended-spectrum ß-lactamases), VRE (vancomycin-resistant enterococci), multi-drug resistant pseudomonas, and multi-drug resistant *Acinetobacter* (CDC, 2016a). Of all these resistant bacterial microorganisms that cause infection, MRSA is considered to be one of the most virulent and prevalent, as it is the most commonly identified multidrug-resistant pathogen in Europe, the Middle East, and

Africa, Asia-Pacific, and the Americas (APIC, 2010). Clinicians and epidemiologists now see MRSA as a major public health threat because of its "rising rate of occurrence in both hospital and community settings and the dearth of proven treatment options available" (Lodise & McKinnon, 2007, p. 1002).

The reasons for the emergence of MRSA are multifactorial; attributed causes of the epidemic are infection control practices and various host factors that can lead to insusceptibility from antimicrobial pressures (Graffunder & Venezia, 2002). Although the medical research community will never know with exact certainty how MRSA has evolved to its current state, one thing is known for sure: MRSA infections are creating a national health crisis. As a matter of comparison, more people in the U.S. now actually die from MRSA infections than from AIDS, Parkinson's disease, emphysema, and homicide combined (IDSA et al., 2011). Adverse events in hospitals leading to MRSA infection can have tragic patient outcomes, as well as far-reaching economic impacts on the healthcare industry and society. The main reason methicillin-resistant *S. aureus* has become a massive public health problem is due to ineffective institutional programs to combat antimicrobial resistance. If prevention of these adverse outcomes is not improved, the scope of staphylococcal antimicrobial resistance will extend to new antimicrobial agents and settings. Based on epidemiological projections, the prevalence of MRSA in the US community is now at over 25%; with rates that are alarmingly triple that in hospitals (Chambers, 2001).

Electronic health records (EHRs) and clinical decision support systems (CDSSs) are the main technologies used to enhance existing antimicrobial stewardship programs within hospitals (Forrest et al., 2014). Technological development – in the form of advanced EHR implementation – will not singularly eradicate the epidemic of institutional MRSA, but it is the foundational component of an effective antimicrobial resistance program to combat this deadly pathogen. Although it is generally accepted that electronic health records improve care quality, research evaluating the impact of EHRs and CDSSs on antimicrobial stewardship program effectiveness is lacking (Forrest et al., 2014). This study attempts to evaluate the relationship between advanced EHR implementation and MRSA infection in order to meet a critical need for additional research in this area.

International evidence supports the premise that the U.S. healthcare system is underinvested in clinical information systems. The United States lags Europe in clinical investments in health information technology (McCullough, 2008). Perpetual underinvestment in health information technology that can improve patient outcomes, such as healthcare-associated infections due to MRSA, is likely a contributing factor why the U.S. continues to rank so low in the World Health Organization's rankings of the countries with the highest quality healthcare systems. In recognition of America's fallen stature, President Bush set as a goal in 2004 that every American would have an electronic health record by 2014. Within three years of that pronouncement, the Department of Health and Human Services (HHS) established the Office of the National Coordinator for Health Information Technology (ONC) to oversee policy to promote the adoption of electronic health records (Simborg, 2008). The U.S. government then created a federal program to infuse billions of dollars of capital investment into hospitals for purposes of building a national infrastructure of electronic health records.

The Health Information Technology for Economic and Clinical Health Act (HITECH), as part of the American Reinvestment & Recovery Act (ARRA) of 2009, was created to accelerate the pace of technology diffusion in the American healthcare system. The promulgation of this health policy led to the Meaningful Use incentive program – a $30 billion initiative to transform healthcare delivery in hospitals through the advanced implementation of electronic health records system technology. With this program, the Centers for Medicare & Medicaid Services (CMS) provides eligible hospitals and professionals with financial incentives to implement systems that demonstrate "meaningful use" of certified electronic health records systems. By providing incentives to individual providers for using EHR systems in specific ways, CMS has attempted to motivate a fragmented customer base to behave more like a single customer with coherent demands (Tripathi, 2012). Diana, Kazley, Ford, & Menachemi (2012) have actually found, however, that there is potential for the HITECH Act to inadvertently increase the digital divide between hospitals with certain characteristics and their counterparts without those characteristics. In their estimation, policy makers should consider ways to alleviate adoption barriers, especially for nonusers of EHRs, to realize the anticipated impact of the HITECH Act.

The potential of advanced EHR technology to transform healthcare delivery and patient outcomes is being demonstrated in innumerable case studies. The implications of how health information technology can impact medical expenditures are also immense. Effective implementation of electronic health records could save more than $81 billion annually – by improving health care efficiency and safety, and the adoption of interoperable EHR systems could produce efficiency and safety savings of $142–$371 billion (Hillestad et al., 2005). We are currently in a vibrant era of discovery and technological innovation, and dissemination of this newfound knowledge will ultimately allow clinicians to improve patient outcomes. Over the last two decades, health services research has shown mounting evidence of a positive association between use of health IT and quality of care; nonetheless "the gap between the postulated and empirically demonstrated benefits of health IT is still significant" (Appari, Carian, Johnson, & Anthony, 2012, p. 360). There is also recent evidence of potential disadvantages in using health IT systems such as computerized physician order-entry when they are not implemented effectively or used meaningfully; this potentially may lead to unintended medication errors that cause harm to patients. In the case of the meaningful use program being used to catalyze higher performance in the healthcare system, it must be realized that it is not simply the EHR technology alone that will unlock potential; it is also experience and application in using the technology that matters for quality. Due to the complex role played by information technology in healthcare service delivery, the application of further research is necessary to evaluate health IT against a comprehensive set of operational performance measures and patient outcomes.

Given the challenges associated with health IT implementation, it is important to recognize the value of the perceived benefit with the barriers to adoption. McCullough (2008) describes three classes of mechanisms to describe the adoption and diffusion of new technologies within a hospital: "First, structural differences across individual adopters may change the value of the technology adoption. Second, environmental factors, such as competitions and reimbursement mechanisms, may affect technology adoption decisions. Third, interactions between providers may influence the diffusion of new technologies" (p. 650). Ultimately, health services research must seek to determine whether technology diffusion is socially efficient to meet the overall objectives of population health.

Understanding how MRSA infection prevention fits into an overarching health IT adoption strategy cannot be overstated. Given that there never really was an economic motive to pursue societal welfare as part of an EHR implementation project – until recent transitioning to a more evolved value-based reimbursement model – hospitals have traditionally adopted information technology only in ways that would maximize utility functions that increase profits within a fee-for-service reimbursement model. The ensuing unfortunate outcome of this delay in technology diffusion was a rampant epidemic of healthcare-associated infections in the U.S. due to unsophisticated, non-IT leveraged antimicrobial stewardship programs – with MRSA leading this pathogenic scourge.

Problem Statement

There has been little research on the overall effectiveness of advanced EHRs on rates of healthcare-associated infections in an inpatient setting. Various studies have attempted to show the value of various aspects of EHR technology on other key quality performance indicators, but no comprehensive research exists that evaluates the relationship between advanced EHR use and healthcare-associated MRSA infection. This study adds to the body of knowledge by investigating this untested relationship.

The purpose of this study was to examine the relationships among electronic health record adoption stage and hospitalized patients' rate of MRSA infection. Knowing that MRSA infection is already directly linked to adverse outcomes (i.e., readmissions, prolonged length of stay), the intent of this study is to contribute meaningful knowledge to the improvement of patient safety. As reported by the Institute of Medicine (IOM) in their agenda for comparative-effectiveness research priorities, research aimed at improving patient safety and the quality of care tops the list of 100 healthcare research priorities for the nation (Iglehart, 2009).

Research Question

Is there a significant relationship between the advanced use of electronic health records in acute care hospitals and the rate of Methicillin-resistant *Staphylococcus aureus* infections acquired by patients during a recent hospitalization?

Hypothesis

Hospitals with advanced EHR adoption have lower rates of MRSA compared to hospitals without advanced EHRs.

EHR Adoption Model

EHRs in our sample was grouped by stage of use, a model previously used by Kazley (2014), based on individual application reported to be in use by the hospitals. The EHR usage level was classified into four stages based on various components of an EHR reported to be in use at the time of reporting. These measures were grouped into categories to measure the level EHR functionality of each hospital. This allowed us to measure the effects on MRSA infection rates for each hospital as the hospital adopts additional components of an EHR. The categories we used are Stage 0 (no EHR applications installed), Stage 1 (EHR with ancillary services including a clinical data repository, pharmacy, laboratory, and radiology information systems), Stage 2 (Stage 1 plus EHR with nursing workflow including electronic nursing documentation and medication administration records), and Stage 3 (EHR with Stage 1 and 2 components, plus CPOE and clinical decision support). A hospital with Stage 3 EHR has reported successful implementation all of all Stage 1 and Stage 2 applications plus CPOE and CDS. Teufel et al. (2012) point out that many of the functions present in advanced Stage 3 would be considered minimal functions required to meet Meaningful Use objectives. Since Stage 3 consists of more advanced automated features, Stage 3 hospitals should possess enhanced capabilities to handle the demands of providing high quality care, which in turn will affect the patient safety capabilities of those hospitals.

Definitions

Key definitions in this study are:

1) HAI: Healthcare-associated infections
2) MRSA: Methicillin-resistant *Staphylococcus aureus*
3) ASP: Antimicrobial stewardship program
4) EHR: Electronic Health Record
5) Advanced EHR: hospital has met Stage 3 criteria for EHR adoption.
6) CPOE: Computerized Physician Order Entry
7) CDSS: Clinical Decision Support System
8) CMS: Centers for Medicare and Medicaid Services
9) HITECH: Health Information Technology for Economic & Clinical Health Act.
10) ACO: Accountable Care Organization

CHAPTER TWO

REVIEW OF THE LITERATURE

Healthcare-Associated Infections

Healthcare-associated infections (HAIs) are among the most frequent causes of morbidity and mortality among patients receiving medical care. The Centers for Disease Control (CDC) estimates there are over 2.7 million HAIs per year in acute care hospitals within the United States, resulting in 99,000 deaths and an estimated $28-33 billion in preventable healthcare expenditures annually (Henderson, et al., 2012). At any given time, approximately 1 in 20 admitted patients will contract an HAI during their stay in an American hospital, with HAIs being the most common type of complication for patients who are hospitalized (Jeeva & Wright, 2014). Patrick Conway, M.D., Chief Medical Officer at Centers for Medicare and Medicaid Services affirmed for the nation in congressional testimony that, "despite the significant burden of HAIs in the United States and the growing threat of antibiotic resistant pathogens, most HAIs are preventable" (Department of Health and Human Services, 2013, para. 3).

In 1999, the Institute of Medicine issued *To Err is Human: Building a Safer Health System* which brought national attention to "the nation's epidemic of medical errors" that included preventable nosocomial infection deaths related to poor hygienic protocols (Kohn, Corrigan, & Donaldson, 1999, p. 1). Interestingly, healthcare–associated infections were only briefly mentioned in *To Err Is Human* (Kohn et al., 1999), reflecting their relatively low initial priority in the safety field at the time. Elevation of HAIs as today's leading patient safety concern occurred because of additional epidemiological studies of prevalence that were performed by the CDC and state health departments in the wake of the *To Err Is Human* shockwave (Gerberding, 2002) as well as by the influential 2001 Agency for Healthcare Research and Quality evidence report *Making Healthcare Safer* (Shojania, Duncan, McDonald, Wachter, & Markowitz, 2001).

Despite the disease burden and resultant costs associated with HAIs, infections associated with medical treatment were once considered to be "an acceptable and unavoidable cost of doing business in the United State healthcare system" (Jeeva & Wright, 2014, p. S4). However, since the issuance of the IOM report over 15 years ago, experts in the field of patient safety have begun to think differently about HAIs. Since HAIs are preventable with the right systems in place, there are even some that are looking to eliminate HAIs altogether through the alignment of payment systems that will force hospitals to accept financial risk for adverse outcomes. The groundbreaking IOM report has also inspired numerous patient safety initiatives to prevent HAIs, including the Institute of Healthcare Improvement's 100,000 Lives Campaign in 2004 and Protecting 5 Million Lives Campaign in 2006, the Surgical Infection Prevention Project implemented in 2002, subsequently expanded to the Surgical Care Improvement Project in 2006, and the Comprehensive Unit-Based Safety Program (Henderson et al., 2012). As the American healthcare industry is now transitioning to value-based care and pay-for-performance initiatives, HAI reductions continue to be a prime focus in reducing prolonged hospitalizations and avoidable readmissions. Sadly, there has been minimal improvement in patient safety since the release of *To Err is Human*, (Leape, et al., 2009; Wachter, 2010; Landrigan et al., 2010).

Rigorous infection prevention and control programs have been shown to have lower infection rates in hospitals, and the backbone of these programs is technology-enabled surveillance systems (Evans et al., 2009). The use of health information technology surveillance systems have shown a 14-percentage point absolute increase in identification of healthcare- associated infections and a 65% relative decrease in identification time (from 130 to 46 hours) (Chaudhry et al., 2006). In recognition of the strong research-basis for surveillance technology effectiveness, the CDC created a 'voluntary, secure, internet-based surveillance system' called the National Healthcare Safety Network (NHSN) as a way to facilitate the tracking of HAIs.

The NHSN began collecting voluntarily-reported data in 2005 as a national surveillance system for patient and healthcare personnel safety; consequently, there is much more known about HAIs than there was when *To Err is Human* was issued in 1999. Of all HAIs (i.e., central line–associated bloodstream infections, catheter-associated urinary tract infections, ventilator-associated pneumonia, and surgical site infections) reported by acute care hospitals in the National Healthcare Safety Network, *Staphylococcus aureus* is one of the biggest threats to patients undergoing treatment in acute care hospitals. It is the primary cause of lower respiratory tract and surgical site infections and the second leading cause of nosocomial bacteremia, pneumonia, and cardiovascular infections (Richards, Edwards, Culver, & Gaynes, 1999).

Government Action to Prevent MRSA Infection

Prevention of HAIs has also become a policy priority on both the state and federal level. At the state level, there have been considerable federal investments to develop systems to address HAIs, including MRSA. The American Recovery and Reinvestment Act (ARRA) of 2009 provided a total of $50 million in funding for state-level HAI-related activities (Jeeva & Wright, 2014). State activities to build capacity for HAI prevention attempt to control HAIs across four prevention areas: “1) building and maintaining partnerships (e.g., collaborating with quality improvement organizations or hospital associations), 2) supporting HAI-related outbreak response by building infrastructure to identify and respond to reports of outbreaks in healthcare settings, 3) conducting or supporting HAI training, and 4) validating HAI data (i.e., analyzing data for quality and completeness and/or reviewing medical records to check data accuracy)” (CDC, 2016a, para. 4). Indicative of varying degrees of state involvement in HAI prevention, there are some pockets of success emerging throughout the country. For example, a regional collaboration known as the Pittsburgh Regional Health Initiative has shown to reduce healthcare–associated bloodstream infections by as much as 68% through the use of targeted approaches in HAI prevention (Jeeva & Wright, 2014).

On the national level, improving health care through HAI surveillance, prevention, and control are priorities for CDC, The U.S. Department of Health and Human Services, and the White House. Federal government involvement in HAI prevention ostensibly began when the Government Accountability Office (GAO) released a 2008 report critical of the Department of Health and Human Services’ leadership on the issue of HAIs and of coordination of HAI-related activities across operating divisions within the department. This report was followed by congressional hearings on the subject. In response, the HHS Action Plan to Prevent Healthcare-associated Infections (later named the HAI National Action Plan), an interdepartmental national strategy to address the HAI epidemic was launched and implemented (Kahn, Mendel, Leuschner, Hiatt, Gall, Siegel, &Weinberg, 2014).

The HAI National Action Plan stresses the judicious use of antibiotics to prevent transmission of infections due to antibiotic-resistant microorganisms such as MRSA. A major goal of the current version of the National Action Plan is to "reduce by at least 50% overall methicillin-resistant *Staphylococcus aureus* bloodstream infections by 2020 as compared to 2011" (The White House, 2015, p. 6). Another objective of the HAI Action Plan is to align and standardize data definitions across as many healthcare information systems as possible, as these standardized data definitions can improve HAI data analysis, reporting, and interpretation (Jeeva & Wright, 2014). Consequently, advanced implementation of electronic health records will play a major role in the stated national objective to lower MRSA bloodstream infections by 2020.

In response to societal demands from numerous constituencies, the federal government is also addressing patient safety concerns associated with MRSA infection through reforms of the Medicare fee-for-service payment system and diagnosis-related groups (DRGs) system that allows reclassifying to a higher DRG when complications occur. Historically, Medicare and other payers have provided reimbursement to hospitals for treating infections or errors even when they could have been prevented, thus providing "little financial incentive for health care organizations and providers to improve safety and quality" (Kohn et al., 1999, p. 1). Now Medicare – with state

Medicaid programs and many private sector health plans following suit – are moving rapidly to change payment systems to reward better outcomes instead of volume of services. Three separate pay-for-performance programs affect the amount of Medicare payment for inpatient services to about 3,400 US hospitals (Kahn et al., 2015). These programs will put a growing share of Medicare hospital payments (6 percent by 2017) at risk, depending how well the hospitals perform under the Hospital-Acquired Conditions Reduction Program, the Value-Based Purchasing Program, and the Hospital Readmissions Reduction Program. All of these programs have a pay-for-performance measure directly related to MRSA infection.

The Deficit Reduction Act of 2005 (DRA) has directed CMS to reduce payments to hospitals for conditions associated with complications of care that stem from certain hospital-acquired conditions through the Hospital-acquired Conditions (HAC) Reduction program. Beginning in October 2008, provisions of the DRA stipulate that hospitals no longer receive additional payment for 10 selected conditions, 3 of which are HAIs (Lee et al., 2012). This approach of nonpayment for preventable complications is intended to remove the perverse incentive by which hospitals received additional payments for care complicated by preventable adverse events, including certain HAIs such as catheter-associated bloodstream infections and catheter-associated urinary tract infections related to MRSA and other pathogens (Lee et al., 2012). Research has shown that the national effect of the HAC Program to reduce additional payments for preventable hospital complications is negligible; it has not been shown there is any effect on rates of targeted healthcare–associated infections as measured with the use of clinical data (Lee et al., 2012).

Recent healthcare reform efforts associated with the Affordable Care Act (ACA) of 2010 established the Hospital Value Based Purchasing (VBP) program, a CMS initiative that rewards acute-care hospitals with incentive payments for the quality of care provided. VBP aims to incentivize inpatient providers to deliver higher value healthcare by placing "2-percent of hospital Medicare reimbursement at risk by metrics of quality, outcomes, and experiences of care" (Blumenthal & Jena, 2013, para. 8). In its efforts to curtail MRSA infection rates, CMS is implementing a patient safety measure in fiscal 2017 that will process scoring for hospital-onset methicillin-resistant *Staphylococcus aureus* infection (Kahn et al., 2015).

The Affordable Care Act also established the Hospital Readmissions Reduction Program (HRRP), which reduces Medicare payments to hospitals that have excess readmissions beginning in October 2012. The federal government's interest in readmission rates is driven by the recognition that a significant proportion of readmissions are avoidable. Overall, infection-related readmissions comprise nearly 30% of all-cause readmissions, and high hospital infection-related readmissions are associated with serving a high proportion of patients with comorbidities, long lengths of stay, discharge to skilled nursing facility, and those living in federal poverty areas (Gohil et al., 2015). Initially, HRRP measured only readmissions rates for three very common and expensive conditions for Medicare beneficiaries -- heart attack, heart failure, and pneumonia. However, CMS recently finalized expansion of the readmissions program with measures for two more common conditions – chronic obstructive pulmonary disease and joint replacements of the knee and hip that were added to the program in FY 2015. The new condition in the HRRP pertaining to joint replacement surgery readmissions is directly related to MRSA, as *Staphylococcus aureus* accounts for the majority of periprosthetic joint infections post-surgery (Garvin & Konigsberg, 2011). Building upon the efforts of HRRP, the federal government also announced recently it will launch a new series of Hospital Improvement and Innovation Networks (HIINs) aimed at enhancing hospital patient safety and reducing hospital readmissions due to healthcare-associated infections (Conway, 2016, May 25).

In addition to action plans and payment reforms, the federal government is also looking to prevent MRSA infection by creating transparency for consumers of healthcare through the Hospital Compare website. Healthcare facility rankings, such as those generated through hospital public reporting and the Hospital Compare Web site, have recently gained momentum through the Affordable Care Act. The stated goal of these rankings is "to encourage hospitals to monitor and improve quality and to increase transparency of hospital performance to payers, consumers, and regulatory bodies" (Schweizer & Rubin, 2012, p, 122). By having patients more informed about a hospital's quality of care, HAIs can potentially be prevented by creating competition based on outcomes transparency in the marketplace. The Hospital Compare website includes the CDC's NHSN HAI measure results and data, showing a hospital's performance on a wide variety of quality measures, including methicillin-resistant *Staphylococcus aureus* bloodstream infections (Schweizer & Rubin, 2012).

Elimination of methicillin-resistant *Staphylococcus aureus* is a national priority of the highest magnitude, and was directly addressed by a 2014 Executive Order from President Obama in his declaration of war against antibiotic-resistant bacteria (Birnbaum, 2015). This American executive order, however, might be a more realistic statement of the problem than it is actually creating a war against MRSA that many in the scientific and medical research community feel that we can win. As stated by Birnbaum (2015), "*It remains to be seen how well those in the front lines of healthcare epidemiology and infection control shape framing of this problem before American federal and state agencies respond to their presidential directive by relaying marching orders through laws, rules, regulations, financial incentives and penalties. It remains to be seen whether the next decade will be more successful than the last given a more recent emphasis on the strategy of bundling small sets of practical key measures into effect, and the involvement of public health departments in support of antimicrobial stewardship. Unlike a generation ago, it also is clear that international trade and travel make this a global problem. America cannot be expected to resolve emerging drug resistance alone even if containment efforts within its own borders are successful, but like other developed countries it can be expected to have vested self-interests in promoting global solutions to this complex problem. Framing this problem as combat, in an American war to win with victory defined as eliminating all future public health threat from emerging antimicrobial resistance, could prove to be an unfortunate choice*" (p. 34).

History and Overview of MRSA

Healthcare-associated infections with *S. aureus* are especially difficult to treat because of evolved resistance to pharmacological treatment. Of the 10 most common pathogens causing healthcare-associated infections (accounting for 84% of any HAIs), *S. aureus* has the highest prevalence which equates to fifteen-percent of all HAI-causing microorganisms. Furthermore, as many as 16% of all HAIs are associated with multidrug-resistant pathogens, including methicillin-resistant *Staphylococcus aureus*

(MRSA) which comprises 8% of all healthcare-associated infections (Hidron, Edwards, Patel, Horan, Sievert, Pollock, & Fridkin, 2008). *Staphylococcus aureus* is the most commonly isolated bacterial pathogen causing everything from superficial skin and soft-tissue infections to invasive infections such as pneumonia, endocarditis, and sepsis. Penicillin is the drug of choice if the isolate is sensitive to it; however, MRSA strains are not affected by the antibiotic (Lowy, 1998).

Methicillin-resistant *Staphylococcus aureus* is the best-known example of an antibiotic-resistant 'superbug' and has been intensely scrutinized and investigated by political and scientific communities throughout world (Darzi, 2007). MRSA as a major cause of healthcare- associated infections is becoming increasingly difficult to combat because of emerging resistance to all current antibiotic classes. Infections with MRSA are untreatable with the customary antibiotics prescribed by clinicians that include virtually all non-experimental antibiotics (e.g. methicillin, oxacillin, amoxicillin, and penicillin). The MRSA microorganism is intrinsically resistant to ß-lactams by virtue of a genetic mutation that evolved from survival to failed antibiotic treatment. These mutations provide the MRSA organism with a newly-acquired, low-affinity penicillin-binding protein 2A (PBP2A) that can help it biosynthesize a cell wall when other penicillin-binding proteins are blocked by ß-lactam antibiotics (Guignard, Entenzan, & Moreillon, 2005). In this evolution of antimicrobial resistance, it is important to note that MRSA is not originated from the de novo development of methicillin resistance among susceptible strains; instead it comes from only a few ancestral clones (Hidron et al., 2008).

Methicillin and other semisynthetic penicillins were once represented as the universal treatment of *Staphylococcus aureus* infection, but within two years of their introduction the first clinical isolates of methicillin-resistant *S. aureus* appeared. These ancestral clones of MRSA led to the current manifestation of disease currently observed. Research shows that methicillin was introduced in 1959 to treat infections caused by penicillin-resistant *Staphylococcus aureus*, and MRSA isolates were first identified in 1961 (Enright, Robinson, Randle, Fell, Grundmann, & Spratt, 2002). Beyond that little is known epidemiologically with regard to initial origination. The evolutionary origin of MRSA remains a scientific mystery with no rational bacterial nomenclature. Consequently, there is no consensus on the number of major MRSA clones that exist or the relatedness of clones described from different countries (Enright et al., 2002).

Transmission and Pathogenesis of MRSA

Staphylococcus aureus has solidified its standing as the most virulent species of staphylococci affecting the human race. The bacterium is an enigma to the scientific community, as the ability of the organism to cause disease is based on several unique attributes which are not well understood at this time. The virulence of the microorganism is attributed to a variety of enzymes released into the tissue at the site of infection; toxicity from an opportunistic *S. aureus* infection can become rapidly life-threatening if not diagnosed and treated appropriately (Rohde, 2010). Although Staphylococcus is a ubiquitous bacterium that resides on skin and in nasal passages as normal flora, it can cause infections if it enters the body and/or bloodstream through an opening in the skin, and these infections can be very serious.

"Humans are a natural reservoir for *Staphylococcus aureus*, and asymptomatic colonization is far more common than infection" (Chambers, 2001, p. 178). Worldwide, an estimated two billion people carry some form of *S. aureus*; of these, up to 53 million are thought to carry MRSA. In the US, 95 million carry *S. aureus* in their noses and on their skin; of these, 2.5 million carry MRSA (Graham, Lin, & Larson, 2006). Nasal colonization of *S. aureus* has been identified as a major risk factor for subsequent invasive (life-threatening) infections and inter-patient transmission of strains, including MRSA (Rohde, 2010). "The emergence of MRSA infections adds to the overall number of *S. aureus* infections, thus increasing the total number of nosocomial (healthcare-associated) infections caused by this pathogen" (Rohde, 2010, p. 3). The overall nasal carriage rate of *S. aureus* within the general population is around 30-percent, and asymptomatic nasal colonization is the common etiology of surgical site infection, especially in orthopaedic patients (Price, et al., 2008; CDC, 2014). *S. aureus* is predominantly transmitted through person-to-person contact, usually from direct contact with an infected wound or from the contaminated hands of healthcare providers (CDC, 2014).

The global emergence of methicillin-resistant *Staphylococcus aureus* has caused substantial health and economic burdens on healthcare systems and their infected patients. Over the last few decades, this epidemic has occurred concurrently with institutional policies promoting fee-for-service optimization leading to higher patient throughput in hospitals with many services operating at full capacity. The net result has been limited ability to scale services according to fluctuations inpatient admissions and available staff, and hospital overcrowding and understaffing. Overcrowding and understaffing lead to failure of MRSA control programs via decreased healthcare worker hand hygiene compliance, increased movement of patients and staff between hospital wards, decreased levels of quarantining, and overburdening of screening and isolation facilities (Clements, et al., 2008.) In turn, a high MRSA incidence leads to increased inpatient length of stay and bed blocking, exacerbating overcrowding and leading to a vicious cycle characterized by further infection control failure.

In the case of high MRSA incidence leading to additional downstream infection control failures, it readily appears that the operational dynamics of fee-for-service medicine are contributing to the unintended consequences of iatrogenic injury. Preventable injuries in hospitals, in this case MRSA infection, are resulting from system failures in infection control – not individual inadequacy. "Human factors research in nonmedical settings (e.g. aviation) suggests that people tend to take the path of least effort; hence, demanding greater vigilance from providers of medical care may not result in meaningful safety improvement. Instead, redesigning faulty systems appears to be a more promising way to reduce human error" (Stelfox, Bates, & Redelmeir, 2003, p. 1899). To the extent that health information technology can help in this systems redesign in healthcare to streamline infection control protocols and improve antimicrobial stewardship, methicillin-resistant *Staphylococcus aureus* infections in the hospital can be prevented.

MRSA infections typically occur among hospitalized patients who undergo surgery or who have suppressed immunity (known as healthcare associated MRSA or HA-MRSA); however, they also increasingly occur among non-hospitalized patients who are otherwise healthy (known as community associated MRSA or CA-MRSA). HA-

MRSA infections are associated with a variety of risk factors, including: "use of indwelling medical devices such as bloodstream, endotracheal, and urinary catheters; surgical procedures; injections; contamination of the health care environment; transmission of communicable diseases between patients and healthcare workers; and overuse or improper use of antibiotics" (Department of Health and Human Services, 2012, para. 2). The typical patient with HA-MRSA is typically someone with one of these three characteristics: 1) recently admitted to a skilled nursing facility after a recent hospitalization; 2) recently admitted into an intensive care unit (ICU); or 3) a person with diabetes mellitus or renal disease receiving dialysis. Contrarily, those infected with CA-MRSA are athletes, prisoners, or college residents living in shared spaces (Wiener, 2008). The epidemiology of CA-MRSA has typically been identified to drug abusers in inner city areas or the previously hospitalized chronically ill; however, studies show that the disease is now affecting the community at large (Pate, Nolan, Bannermen, & Feldman, 1995). Although rates of severe infection with methicillin-resistant *Staphylococcus aureus* has been rising over recent years, there is encouraging news from the CDC indicating that this rise may be abating for healthcare-associated pathogens, though not for community-acquired ones as CA-MRSA now comprises 30-percent of all isolates (Kallen et al., 2010; Fish & Ohlinger, 2006).

Despite an overall decline in infection rates over the last few years, HA-MRSA is still one of the most deleterious types of healthcare-associated infections because of the relative high frequency of morbidity and mortality reported among patients receiving medical care. The Healthcare Cost and Utilization Project shows that there was an upward trend in MRSA infections over the 13 years from 1993 to 2005 (Elixhauser &

Steiner, 2006); however, more recent data shows that invasive MRSA infections in healthcare settings declined 54% (30,800 cases) between 2005 and 2011 (Dantes, et al., 2013). Moreover, there was a 13-percent decrease in MRSA bacteremia between 2011 and 2014 (CDC, 2016b).

Antimicrobial Stewardship and MRSA

Antimicrobial stewardship programs (ASPs) are an important approach that hospitals seek to optimize antimicrobial prescribing and efficacy in order to improve patient care outcomes, ensure cost-effective therapy, and reduce adverse sequelae of antimicrobial use (primarily antimicrobial resistance) to slow the spread of HAI-causing pathogens such as MRSA. The terms used to refer to ASPs may vary considerably: "antibiotic policies, antibiotic management programs, antibiotic control programs, and other terms may be used more or less interchangeably" (MacDougall & Polk, 2005, p. 639). These terms generally refer to a comprehensive program to facilitate appropriate antimicrobial use at a health care institution, which may include any number of strategies to guide clinical decision-making. In the first national assessment of hospital ASP adoption, only 39% of United States acute care hospitals were reported as having comprehensive stewardship programs that met all seven of the ASP definition criteria outlined by the CDC (Pollack et. al, 2016).

"The design of an effective antimicrobial management program should be based on the best current understanding of the relationship between antimicrobial use and resistance. Such programs should be administered by multidisciplinary teams composed of infectious diseases physicians, clinical pharmacists, clinical microbiologists, and infection control practitioners and should be actively supported by hospital administrators" (MacDougall & Polk, 2005, p. 638). Multidisciplinary collaboration is crucial to the success of an ASP to achieve sustainable reductions in healthcare-associated infections. For example, in a University of Washington Medical Center collaborative, systems-level ASP initiative that was sponsored by senior leadership, multidisciplinary teams were able to reduce HA-MRSA infections by 58% over a two-year period. "Critical project success factors were believed to include organizational alignment by declaring eliminating HAIs as an organizational breakthrough goal, having the organization's executive leadership highly engaged in the project, coordination by an experienced and effective project leader and manager, collaboration my multidisciplinary project teams, and promoting transparency of results across the organization" (Henderson et al., 2012, p. 39).

Improved use of antibiotics is of paramount concern in the healthcare industry. Recent estimates by the CDC indicate one in three antibiotics prescribed in the U.S. are medically unnecessary for the conditions they are meant to treat (Fleming-Dutra et al., 2016). Antimicrobial stewardship programs led by multidisciplinary teams have empirically been shown to limit the emergence and transmission of antimicrobial-resistant bacteria through enhanced efficacy in antibiotic selection. Of those hospitals without an effective ASP, approximately 33% of patients with MRSA infections do not receive antibiotics that are microbiologically active against their pathogens at the time of organism identification (Lodise & McKinnon, 2007). Dellit, et al. (2007) states that "the primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organism, and the emergence of resistance" (p. 159). However, a secondary goal of antimicrobial stewardship should always be to reduce health care costs without adversely impacting quality of care. Because antimicrobial stewardship has a beneficial impact on both clinical outcomes and healthcare expenditures, it is an important population health initiative.

Implementing antimicrobial stewardship programs can vastly improve antibiotic use in acute care hospitals which can, in turn, prevent HA-MRSA infection. Consequently, other targeted clinical outcomes associated with such programs include reductions in hospital length of stay and readmissions which are significant drivers of preventable cost within the healthcare industry. Hospital readmissions are particularly a key quality indicator and target for reducing healthcare spending, and there is a direct association between readmissions and HA-MRSA infection. Research shows that approximately 20% of Medicare beneficiaries are readmitted within 30 days after hospital discharge at an annual cost of approximately $17.4 billion (Jencks, Williams, & Coleman, 2009) and patients with MRSA site infections are more likely than other patients to be readmitted to the hospital within 30 days (Emerson et al., 2012).

Patient safety and healthcare cost containment are logically sound reasons for acute care hospitals to adopt antimicrobial stewardship programs in the fight against MRSA; these programs readily align with the Triple Aim goals of a hospital Accountable Care Organization (ACO). The Institute for Healthcare Improvement (IHI), a leading not-for-profit organization dedicated to using quality improvement strategies to achieve safe and effective health care, developed the Triple Aim initiative as a rubric for health care transformation towards a more value-based, patient-centered care delivery system like an ACO. The three linked goals of the Triple Aim include improving the experience of care, improving the health of populations, and reducing per capita costs of health care (Hacker & Walker, 2013). These Triple Aim goals all justify the rationale to implement antimicrobial stewardship programs; however, many hospital executives are still averse to investing in new patient safety programs that do not show an immediate return on investment.

When implementing an antimicrobial stewardship program, hospitals should formulate strategy in accordance to its needs and available resources, and debate still persists on the costs versus benefits of implementing MRSA control programs – even in hospitals in which MRSA is endemic. Fortunately, research is on the side of innovation and investment in MRSA control programs within a Triple Aim, value-based care model. Not only have these programs been shown to improve patient outcomes and the overall inpatient care experience, resource use for MRSA hospital stays is also much lower. "MRSA hospitalizations cost nearly double that for non-MRSA stays – $14,000 for MRSA stays compared with $7,600 for non-MRSA stays. The average length of stay in the hospital for a patient with MRSA infection is also more than double that for non-MRSA stays – 10.0 days versus 4.6 days" (Elixhauser & Steiner, 2007, p. 2). The high costs of treating MRSA does not quantify the effect on patients, which include "the emotional toll of having a drug-resistant infection requiring a hospital isolation room, lost time from work and family due to a prolonged hospitalization and recovery period, and the long-term consequences of having a MRSA infection" (Lodise & McKinnon, 2007, p. 1004). Given that an effective ASP will result in improved patient experience, health outcomes, and medical cost containment, it will be an important strategy for hospital ACOs in which gainsharing bonuses are awarded based on the quality of care provided.

Hospitals must always assess which capital-intensive strategies will improve population health and yield the best return on investment (ROI). A new clinical initiative, backed by evidence-based research and a robust health information technology framework, should always demonstrate both ROI and improved patient outcomes. In this respect, ASPs should always be given prioritization by hospitals – even in light of resource constraints. Research have validated that effective ASPs can be financially self-supporting thus warranting that higher prioritization. From the institutional perspective, antimicrobials account for upwards of 30% of hospital pharmacy budgets, and it has been shown that up to 50% of antimicrobial use is inappropriate which adds considerable cost to patient care (John and Fishman, 1997). Comprehensive stewardship programs have consistently demonstrated a decrease in antimicrobial use (22%–36%), with annual savings of $200,000–$900,000 in both larger academic hospitals and smaller community hospitals (Dellit et al., 2007).

Reduced MRSA morbidity and treatment costs can occur even if only a relatively small fraction of MRSA infections are averted. The mean cost attributable to MRSA infection is $9275 (median, $5885; interquartile range, $1400-$16,720) in the United States. Total costs of a MRSA control program range from $340 to $1480 per patient. A 14% reduction in MRSA infection rate resulted in the control program being beneficial (Chaix, Durand-Zaleski, Alberti, & Brun-Buisson, 1999). A more recent study shows even greater potential for ROI of antimicrobial stewardship programs, as researchers found the adjusted mean cost of medical services received by patients infected with MRSA was $51,252 (95% CI, $46,041–$56,464) thus requiring even smaller reductions in infection rates to achieve cost/benefit breakeven point (Filice et al., 2010). These studies, among many others, show that outcomes of an effective ASP are associated with a financial benefit that is sufficient to justify the capital resources apportioned to develop and maintain such programs.

Hospital ICUs are the main reservoir of methicillin-resistant *Staphylococcus aureus* and, thus, should be the main institutional focus of an effective ASP. Approximately 65% of all healthcare-associated infections are reported in the critical care setting (Hidron et al., 2008), and 60% of all reported MRSA infections come from intensive care patients (Griffin, 2007). Methicillin-resistant *Staphylococcus aureus* poses a particularly major threat in the ICU where 8% of patients are colonized at admission to the ICU, resulting in an eight-fold increase in the risk of an MRSA-associated infection (Ziakas, Zacharioudakis, Zervou, & Mylonakis, 2015). Increased antibiotic resistance is related to several variables associated with the higher severity of illness found among ICU patients, including the presence of invasive devices, such as endotracheal tubes and intravascular and urinary catheters; prolonged length of hospital stay; immunosuppression; malnutrition; and ease of cross-transmission of pathogens owing to poor adherence of hospital personnel to infection control techniques, contamination of equipment, and frequent overcrowding of patients (Fish & Ohlinger, 2006). Due to these endemic characteristics, a major aim of health services research on HAIs over the last decade is to estimate the costs and overall effectiveness of methicillin-resistant *Staphylococcus aureus* prevention policies within acute care hospital ICUs.

There are three main MRSA prevention policies used in ICUs, namely, “1) nasal screening and contact precautions of methicillin-resistant *Staphylococcus aureus*–positive patients; 2) nasal screening, contact precautions, and decolonization (targeted decolonization) of methicillin-resistant *Staphylococcus aureus* carriers; and 3) universal decolonization without screening” (Ziakas et al., 2015, p. 382). Recent studies have documented the outcomes effectiveness of universal decolonization (with nasal mupirocin and chlorhexidine bathing at admission to the ICU). In the ICU setting, universal decolonization outperforms the other two strategies and is likely to be cost-effective even at low willingness-to-pay thresholds (Huang et al., 2013). Assuming 700 annual ICU admissions in an average 12-bed ICU, the projected annual savings reach $129,500 to $135,100 (Ziakas et al., 2015). “Although some evidence supports each of these approaches to reduce nosocomial MRSA infection, it remains unclear which is most effective. A cluster randomized trial is an efficient, relatively low-cost method to compare the effectiveness of these approaches” (Platt et al., 2010, p. S54).

Studies have shown that ineffective institutional ASP programs within the ICU setting will contribute to increased hospital and ICU lengths of stay, increased duration of mechanical ventilation, increased treatment costs, and an increase in avoidable patient deaths (Fish & Ohlinger, 2006). In a prospective cohort study of 492 critically ill patients admitted to the intensive care unit setting with a bloodstream infection, inadequate antimicrobial treatment proved to be the single most important risk-factor for in-hospital mortality (Ibrahim, Sherman, Ward, Fraser, & Kollef, 2000). In this study, the mortality rate for patients who initially received inappropriate antimicrobial treatment was significantly greater than the rate for patients who received appropriate antimicrobial treatment that matched the pathogen from the start.

Another aspect of antimicrobial stewardship specific to methicillin-resistant *Staphylococcus aureus* is the control of fluoroquinolone use in health care institutions. Patient exposure to fluoroquinolone – a synthetic broad-spectrum antibiotic – is epidemiologically linked with the isolation of methicillin-resistant *Staphylococcus aureus* (Weber, et al., 2003). This association is unfortunate since fluoroquinolones are among the most commonly prescribed classes of antimicrobial drugs in hospitals. Ciprofloxacin, one of the most common fluoroquinolones to treat bacterial infections, was originally heralded for its activity against a broad range of pathogens, including MRSA. However, MRSA isolates from clinical specimens started to show resistance to ciprofloxacin in the early 1990s (Weber et al., 2003). The magnitude of the association between fluoroquinolones and the presence of MRSA infection appears to exceed what would be expected through simple selection pressure since other agents that lack activity against MRSA do not show the same degree of association (Weber et al., 2003). Given these research findings, it appears that the control of fluoroquinolone use as part of an antimicrobial stewardship program will aid in reducing the growth of MRSA in health care institutions.

Electronic Health Records and Antimicrobial Stewardship

As antimicrobial stewardship programs are the main institutional strategy for preventing MRSA infection, hospital leaders must find ways to leverage their existing health information technology infrastructure to improve program effectiveness. The

Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA) has created guidelines for developing ASPs that recommend hospitals invest in health information technology that is capable of measuring key performance indicators from an antimicrobial stewardship implementation (Dellit et al., 2007). Electronic medical record systems, computerized provider order entry, and clinical decision support systems have a key role to play in the transformation of antimicrobial stewardship.

Strategies for modifying antimicrobial prescribing behavior include “education of prescribers regarding proper antimicrobial usage, creation of an antimicrobial formulary with restricted prescribing of targeted agents, and review of antimicrobial prescribing with feedback to prescribers” (MacDougall & Polk, 2005. P. 648). Electronic health record systems can aid in the implementation of each of these strategies, especially as expert systems able to provide patient-specific data and clinical decision support at the point of care. An electronic health record is “a longitudinal record of patient health information generated by one or more encounters in any care delivery setting” (HIMSS, 2016a, para. 1). The EHR adoption model survey developed by HIMSS Analytics is able to assess which hospitals have been able to implement an electronic health system with computerized provider order entry and clinical decision support; therefore, it can be used to evaluate the effectiveness of institutional ASPs in reducing the incidence of HA-MRSA.

The advanced use of electronic health records presents an innovative opportunity for programs to optimize antimicrobial utilization in hospitals. Most specifically, ASP effectiveness has been primarily associated with computerized physician order-entry

(CPOE) as part of an overall electronic health record system. The order-entry encounter can be designed to facilitate many antimicrobial stewardship strategies such as provider education on institutional guidelines for therapy and formulary management control. MacDougall & Polk (2005) state the example of how a sophisticated CPOE system can integrate patient-specific laboratory and microbiology data in formulating a therapeutic regimen: "If a prescriber enters an order for a restricted agent, a list of formulary alternatives could be suggested, along with the pager number needed to obtain authorization. When an agent targeted for review is ordered, the data can be forwarded in real time or entered into a queue for later review by antimicrobial stewardship personnel" (p. 650).

Medication errors and adverse drug events (ADEs) are the most common, costly, and clinical important issues to be addressed by CPOE (Wager, Lee, & Glaser, 2009). CPOE, as part of an overall advanced electronic medical records system, is a major strategic advancement for acute care hospitals to improve quality of care and lower HAIs since they can intercept errors when they most commonly occur at the time antimicrobials are ordered. Yu et al. (2009) found that CPOE hospitals outperformed comparison hospitals on "5 of 11 measures related to ordering medications and on 1 of 9 non-medication related quality measures" (p. 278). Using a large sample of hospitals, there was a significant positive association between specific objective quality measures and the use of computerized physician order entry.

In response to the alarming statistics cited by the IOM report on medical errors and patient deaths (*To Err is Human*), CPOE systems are now considered a key technology for improving patient safety. Given that CPOE allow providers to electronically write orders, maintain an online medication administration record, and review changes made to an order by support personnel, there are clear technological advantages to adoption. CPOE systems also offer patient safety alerts that are activated when a potentially harmful order (such as for a duplicate drug therapy) is entered, as well as clinical decision support to guide clinicians to less expensive alternatives or to choices that better fit established hospital protocols.

A clinical decision support system (CDSS), as part of a CPOE system integrated with an electronic medical record, is an important functionality to enhance antimicrobial stewardship. Computerized evidence-based guidelines and decision support systems are key to improving the effectiveness and efficiency of an ASP because they can reduce error and variation in antibiotic prescribing. Sintchenko, Coiera, & Gilbert (2008) outline a task-specific decision support heuristic for antibiotic prescribing that shows subtasks such as infection risk assessment, antibiotic prescribing algorithms tied to evidence-based guidelines, interdisciplinary ASP team communication, provider education on institutional guidelines for therapy, formulary management control, antimicrobial resistance surveillance, microbiology test result integration, and therapy monitoring of culture susceptibility results.

The implementation of CDSS within an electronic health record may create long-lasting improvement in clinical decision-making when prescribing antibiotic therapy. EHRs and CDSSs are a key technology solution to enable clinicians to more proficiently review the pharmacy, microbiology, and clinical data required of an effective ASP. Decision support for prescribing are most effective in preventing HAIs when the CDSS is sufficiently integrated with laboratory and clinical information and pharmacy systems.

Computerized physician order-entry and clinical decision support systems capitalize on the interface with laboratory and pharmacy information systems in many ways. For example, advanced EHR systems with CDSS can "take into account the patient's pathophysiological state, medical condition and pathological test results in order to present the physician with a prescribing recommendation" (Sintchenko, Coiera, & Gilbert, 2008, p. 576). CPOE enhancement with a clinical decision support system can actually present the physician with a prescribing recommendation, as opposed to just merely warning of a potential ADE like the most basic of computerized ordering systems.

Electronic health records with integrated clinical decision support have been shown to improve clinical and economic outcomes through their support of institutional ASP strategies. Despite these many practical advantages, however, "their impact on improving antimicrobial use and infectious disease–specific patient outcomes has been limited, primarily owing to the paucity of included CDSS capability" (Forrest, et al., 2014, p. S123). Since CDSSs assist clinicians in selecting appropriate antimicrobial therapy and avoiding medical errors, it is well accepted that they do improve the overall quality of care (Blumenthal, 2010). The most effective CDSSs within an antibiotic stewardship program will provide clinicians with secure and immediate access from bedside computers and handheld personal digital assistants through the local healthcare network (Sintchenko, Coiera, & Gilbert, 2008).

The greatest benefit of a fully-optimized CPOE system with clinical decision support is critical care in which prescribing decisions are innumerable and costly. Recent studies indicate that the use of CDSS in critical care can contribute to the reduction of patient length of stay by leading to changes in prescribing patterns that decreases the frequency of ß-lactamase resistant infections of *Staphylococcus aureus* (Sintchenko, Coiera, & Gilbert, 2008). When correctly configured and implemented, research has shown that CPOE with clinical decision support can result in markedly increased efficiency and improved patient safety and patient care. CPOE can reduce medication error rates by 55% -- from 10.7 to 4.9 per 1000 patient-days (Bates et al., 1998). There is also a strong statistical correlation between increased rates of CPOE and lower lengths of stay in the hospital; approximately 63 percent of the reduction in length of stay for a community hospital was directly correlated with the rise in CPOE utilization (Schreiber, Peters, & Shaha, 2014). Another study has found that there are higher rates of adoption of key EHR functions such as CPOE among high quality hospitals (as determined by the Hospital Quality Alliance program), suggesting that high quality and advanced EHR adoption may be linked (Elnahal, Joynt, Bristol, & Jha, 2011).

Given the potential benefits of CPOE, The Leapfrog Group -- a nonprofit organization aimed at mobilizing employer purchasing power to improve patient safety – has selected CPOE as one of its hospital performance standards. The Leapfrog Hospital Survey is a widely-reviewed reporting system for comparing hospitals' performance on the national standards of safety, quality, and efficiency that is most relevant to consumers and purchasers of care. Leapfrog's standard for CPOE requires that at least 75 percent of medication orders across all inpatient units are ordered through a CPOE system and that the hospital has tested the system to make sure physicians are alerted to common and serious medication errors. In 2013, 43 percent of hospitals responding to the 2013 Leapfrog Hospital Survey met Leapfrog's safety standard for computerized physician order entry, an all-time high (The Leapfrog Group, 2013).

Other important functionalities of advanced electronic health records to improve MRSA treatment outcomes are interoperable data sharing and the secondary analysis of standardized EHR data elements. Algorithmic analysis of electronic health data from disparate EHR instances in a community is an encouraging alternative to conventional, centrally-planned surveillance systems without refined connectivity. Algorithms designed to analyze EHR data can query combinations of diagnosis codes, microbiology results, and/or antimicrobial dispensing to identify HAIs with sensitivities and positive predictive values that surpass those found through conventional surveillance means (Klompas, Yokoe, & Weinstein, 2009). More accurate surveillance through these advanced EHR features will be critical to improve the quality of patient care and measure the impact of infection prevention initiatives. Although still in the early stages, electronic surveillance for HAIs is clearly here to stay and CMS is looking to capitalize on advanced EHRs by enhancing the current NHSN LabID surveillance of MRSA bacteremia (Woeltje et al., 2014).

Industry research has shown that the widespread adoption of advanced electronic health records has helped hospitals reduce costs and patient deaths stemming from healthcare-acquired conditions, including HA-MRSA. A recent report from the Agency for Healthcare Research and Quality (AHRQ) compared the rates of avoidable healthcare-acquired conditions between 2010 and 2014, using a baseline estimate of consequent deaths and healthcare costs developed when HHS launched the Partnership for Patients initiative in 2011. According to the report, the number of healthcare-acquired conditions among patients fell by 2.1 million -- or 17% -- between 2010 and 2014. As a result, fewer patients died and health care costs were lowered by almost $20 billion. AHRQ primarily attributed to decrease to the advanced implementation and improved use of electronic health records (Carter, 2016).

ASP Capability Review of Commonly Used EHR Platforms

In the hospital marketplace for health information technology, there are only a few software vendors that attempt to provide integration for institutional EHR and ASP efforts and these advancements are typically in the nascent stage (Kullar, Goff, Schulz, Fox, & Rose, 2013). Although it would seem that the most commonly used EHR platforms should naturally work to enhance antimicrobial stewardship programs through physician education, enterprise data sharing, and proactive alert notifications during a planned intervention, "the initial design and implementation of EMR systems were not built around the strategies of current needs of ASPs" (Kullar et al., 2013, p. 1006). With the increased adoption and ongoing development of electronic health records, there is a need to integrate ASPs into these systems to provide enhanced decision-making support. An advanced implementation of both CPOE and CDSS will typically "utilize individual patient data coupled with population statistics and computerized clinical guidance to provide patient-specific management recommendations either on clinician request or at the point of care" (Forrest et al., 2014, p. S123). Given the growing national impetus to implement ASPs within an overall population health management model to improve patient outcomes, Epic Systems Corporation (Verona, Wisconsin) and Cerner Corporation (North Kansas City, Missouri) are developing software with enhanced stewardship functionality. These two EHR vendors have the largest US market share of electronic health records in the acute care hospital setting.

Epic Systems Corporation is the foremost provider of hospital EHRs and has been especially favored by large hospitals and clinically integrated networks. According to a 2012 report of EHR market share, “Epic captured 65% (53 of 82) and 25% (75 of 300) of new-vendor contracts for hospitals with ≥200 and <200 beds, respectively” (Forrest et al., 2014, p. S123). The primary Epic software tool created to enhance ASP functionality is iVents, which can “record and communicate ASP recommendations and interventions; antibiotic order forms; dose-checking decision support; a navigator that presents information needed to make an educated decision about patient therapy in one location; “best practice advisories”; 96-hour stop-date notifications; patient prioritization and monitoring forms; intravenous-to-oral algorithms; and order sets” (Forrest et al., 2014, p. S123). A retrospective analysis showed that iVents use was associated with more ASP recommendations, decreased antimicrobial utilization, and a significant reduction in nosocomial methicillin-resistant *Staphylococcus aureus* infections (Forrest et al., 2014, p. S123).

Cerner Corporation in a secondary position in the EMR market and has been gaining market share. While Epic has historically been overwhelmingly favored by large hospitals, Epic's 5:1 advantage over Cerner in new installations in 2010 has shrunk to 2:1 in 2012 (Buckley, 2014). The Cerner PowerChart EHR provides little “out of the box” entry-level functionality to optimize stewardship efforts; however, the ability to locally customize the software has provided the opportunity for hospital with in-house software development resources to develop their own proprietary enhancements to assist their local ASP. To harness the stewardship potential of the Cerner EHR system, significant hospital information technology resources are needed (Pogue et al., 2014). Cerner still does not currently employ dedicated stewardship personnel, although the company has described an interest in focusing more toward antimicrobial stewardship in the future. From a stewardship prospective, the biggest drawback of the Cerner functionality is that it "fails to effectively identify appropriate patients for antimicrobial-related follow-up and interventions" (Pogue et al., 2014, p. 424).

Key Strategies and Lessons Learned in Implementing EHR Systems

If implemented successfully, electronic health record systems can provide safer, more effective care than is possible through paper-based charting. EHRs can also help hospitals monitor, improve, and report data on quality performance measures related to care processes and patient outcomes. However, poor implementation of EHRs within a hospital can also lead to catastrophic results, including poor antimicrobial stewardship program support which compromises patient safety. A recent study that performed an examination of nine hospitals that recently implemented a comprehensive EHR system found that successful implementation depended on: "strong leadership, full involvement of clinical staff in design and implementation, mandatory staff training, and strict adherence to timeline and budget" (Silow-Carroll, Edwards, & Rodin, 2012, p. 1). The attributes of leadership and multidisciplinary teamwork required within an EHR implementation framework is not mutually exclusive with an institutional stewardship effort; both require collaboration amongst all key stakeholders to realize sustainable reductions in healthcare-associated infections.

Health care quality improvement organizations such as the Leapfrog Group and AHRQ are actively encouraging the advanced implementation of electronic health records in hospitals and health care systems. Notwithstanding the favorable impact on patient outcomes that would be experienced by a hospital that successfully implement an EHR system; there are still many barriers and challenges that inhibit systems proliferation in the industry. Among hospitals without electronic-records systems, the most common barriers outlined in a survey of chief information officers, other hospital leaders were "inadequate capital for purchase (74%), concerns about maintenance costs (44%), resistance on the part of physicians (36%), unclear return on investment (32%), and lack of availability of staff with adequate expertise in information technology (30%)" (Jha et al., 2009, p. 1632). Given that the federal government views the absence of an electronic health record in a hospital as a public health concern, financial barriers to adoption are being addressed with the provision of monetary incentives through the 'meaningful use' EHR adoption program.

With the meaningful use program, electronic health records are becoming more prevalent in acute care hospitals, and with that, there are increased opportunities for computer-assisted antimicrobial stewardship strategies to prevent HA-MRSA infection. Consequently, one could hypothesize that lower rates of HAIs could be a very important patient outcome improvement linked to successful adoption of an advanced electronic health record with CPOE functionality. Simply adding computerized physician order entry to an EHR system, however, does not guarantee that it will add value to an antimicrobial stewardship program. A robust and effective EHR system "must be designed with functionalities that can be leveraged by the antimicrobial stewardship team or must be flexible enough to allow reprogramming (usually at significant effort)" to support ASPs (MacDougall & Polk, 2005, p. 651).

Despite the compelling data-driven argument to support the advanced implementation of CPOE to support patient safety initiatives, the experience with computerized systems has not always been favorable. Poorly planned CPOE implementations can be blamed system failures that compromise patient safety. There is not a more infamous example of a botched CPOE implementation that that of Cedars-Sinai Medical Center in early 2003. Medical staff there rebelled after a house-wide "big bang" rollout, realizing that the poorly planned system increased their workloads and encouraged cutting corners. It took another eight years before Cedars successfully implemented CPOE. Cedars-Sinai ultimately failed despite having a very strong track record and deep experience in informatics, strong leadership, and substantial resources. According to Bates (2006), there were several reasons for this failure: "many decision-support mechanisms were introduced at the outset, especially for drug-drug interactions; with the way the application was set up, alerts could not be overridden; and it was hard to achieve buy-in from the very large number of providers using the system" (p. 311). Since integration of an antimicrobial stewardship program into a CPOE system would likely add steps to the ordering process (e.g. pop-up screens with guidelines and notifications of restricted antimicrobials), ASP enhancements should be carefully designed and user-tested by an interdisciplinary team before implementation (MacDougall & Polk, 2005).

Implementing EHRs, CPOE, and CDSSs is a formidable challenge for project stakeholders on all sides – from the vendors offering the software to the hospitals and clinicians actually using the system. The major barriers to implementing advanced electronic health records "include system costs; administrative, ethical, and legal issues;

and ineffective implementation because of alert fatigue" (Forrest et al., 2014, p. S128). Excessive warnings resulting in alert fatigue are of particular concern because when a provider unintentionally disregards clinically relevant alerts, the efficacy of the entire system is undermined. This could potentially lead to missed opportunities for appropriate interventions, whereby propagating the spread of MRSA within the hospital and local community.

Given the well-publicized CPOE implementation failure of Cedars-Sinai and other healthcare organizations, there is a growing fear that the exponential growth of EHR adoption may compromise patient safety and quality of care due to irresponsible and unplanned technology implementation. When healthcare organizations rush to install health information technologies, they overlook the attendant risks of implementing, using and storing these complex information systems. There is particular concern that small- and medium-size hospitals may not completely understand the risks of EHR software because they lack technical expertise, management sophistication and economies of scale that larger hospitals have to implement EHRs in meaningful and financially viable ways (Weaver, 2011).

The most significant barrier to implementation of a CDSS both within and external to an EHR is a lack of IT personnel available for development. "Creation of decision support within an existing EHR requires many hours to develop, build, and test so that it is both functional and efficient. Many facilities lack the personnel or are unable or unwilling to prioritize the creation of CDSSs to improve antimicrobial use" (Forrest et al., 2014, p. S129). As hospitals with limited resources begin to use EHRs, the chance of

EHR-associated harm increases significantly, according to researchers (Walker et al., 2008).

Healthcare delivery involves such information-intensive processes; therefore, the success of information technology in its supporting role to improve operations does depend upon how well it is aligned with the strategic goals and objectives of the organization (Glandon, et al., 2008). Successful implementation of an advanced EHR system necessitates an organizational commitment from the top-down, a shared vision for the intended effect on patient care, flawless execution and effective change management, and ample human and financial resources. Antimicrobial stewardship program leaders (infectious disease physicians, hospital pharmacists, clinical microbiologists, infection control staff and hospital epidemiologists) should position themselves as high-priority end-users and pledge their time and expertise to develop the software system to support the ASP, particularly in deriving the rules and algorithms used in decision support (MacDougall & Polk, 2005). During any health information technology implementation project plan, there are common areas of focus (e.g. plans to manage costs and timelines, collection of requirements, policies for change management, user training and support, etc.) that are important to success, but without the right people and the right team in place the project is likely to fail (Amatayakul and Hodges, 2006).

Although computerized expert systems may allow for automation of some stewardship processes pertaining to clinical decision support, they are not a replacement for the hospital's stewardship personnel taking an active role in the implementation. As with implementation of any information technology that automates a workflow process, organization readiness for advanced EHR adoption is imperative for success. Lack of organization-wide readiness is a major contributor to the overwhelmingly high failure rate of EHR adoptions within healthcare organizations (Weaver, 2011). Failed implementations of health information technology can have profound consequences on the delivery of care and potentially create risks of harming patients.

Meaningful Use Adoption of Electronic Health Records

Health information technology has grown exponentially over the last decade, as electronic health records and computerized provider order entry systems have become omnipresent in the healthcare landscape. EHR adoption has accelerated primarily because of incentives provided by the federal government. In February 2009 the United States Congress passed the American Recovery and Reinvestment Act which included a provision for the Health Information Technology for Economic and Clinical Health Act to encourage US physicians and hospitals to adopt EHR systems. HITECH, through the meaningful use program, has provided up to $27 billion to serve as an economic catalyst to spur adoption of electronic medical records (Glaser, 2010).

Financial incentives provided through the passage of HITECH are available to "qualified institutions as they adopt, implement, upgrade, or show meaningful use of certified EHR technology by meeting several predefined objectives established by CMS" (Forrest et al., 2014, p. S122). The HITECH Act is most widely known as the health policy promulgated to invest in electronic health records, but the government intention was to leverage these technology investments to improve the health and wellbeing of Americans who will all eventually become patients in healthcare system. The former head of the ONC, David Blumenthal, stated during the implementation of the HITECH Act that, "The installation of EHRs is an important first step. But EHRs will accomplish little unless providers use them to their full potential; unless health data can flow freely, privately, and securely to the places where they are needed; and unless HIT becomes increasingly capable and easy to use" (Blumenthal, 2010, p. 382).

The Office of the National Coordinator is the principal federal entity in charge of coordinating the nationwide effort to implement the meaningful use program. The ONC created meaningful use goals that were designed to occur in three progressive stages of EHR implementation. Stage 1 focused on data capture and sharing. Stage 2 includes advanced clinical processes and clinical decision support, and focuses on demonstrating health system improvement through wider adoption and process improvement. Stage 3 focuses on transforming healthcare outcomes through health IT (Hessels, Flynn, Cimiotti, Bakken, & Gershon, 2015). CMS plans to add electronic reporting of antibiotic use and resistance data to Stage 3 in order to better address healthcare-acquired infections such as MRSA (The White House, 2015).

Several studies have attempted to measure the extent to which HITECH incentive payments caused mass proliferation of electronic health records in acute care hospitals. A study by the National Bureau of Economic Research (NBER) determined that adoption rates for all independent hospitals grew from 48 percent in 2008 to 77 percent by 2011. (Absent HITECH incentives, they estimated that the adoption rate would have instead been 67 percent in 2011.) They also estimated that in the absence of HITECH incentives, the 77 percent adoption rate would have been realized by 2013, just 2 years after the date achieved due to HITECH (Dranove, Garthwaite, Li, & Ody, 2014). The results from the NBER study tell a slightly different story than that of the federal government. According to the Office of the National Coordinator, while only 72% of hospitals possessed a certified EHR technology in 2011 during the first year of HITECH incentive payments, hospital adoption of certified EHR has since grown to 96% in 2015 (Henry, Pylypchuk, Searcy, & Patel, 2016).

Of those hospitals that have participated in the meaningful use program, findings from the 2016 HIMSS Value of Health IT Survey paint a generally positive picture surrounding the perceived value derived from employing an electronic health record system. By leveraging the HIMSS STEPS model to categorize respondent HIT value experiences into one of five generalized areas (Satisfaction, Treatment/Clinical, Electronic Information/Data, Patient Engagement and Population Management, Savings), the findings of this study uncovered that approximately 88 percent of the executives reported at least one positive outcome of their EHR. The majority of EHR value examples offered by respondents fell under the Treatment/Clinical heading of the STEPS model (HIMSS, 2016b).

A CPOE system is characteristically an integral part of a comprehensive electronic health record system and not a standalone application; therefore, the meaningful use program for EHR adoption does require the use of CPOE. In order to meet Stage 2 objectives, the measure for CPOE is as follows: More than 60% of medication, 30% of laboratory, and 30% of radiology orders are recorded using CPOE (Department of Health and Human Services, 2016). (The Stage 1 requirement for CPOE was more than 30% of unique patients for medication orders only.) Despite the substantial growth in EHR adoption as a result of the meaningful use program, advanced implementation (as defined as EHR with CPOE functionality) is not as common as one would think. As of the Q1 2015, 29.7 percent of acute hospitals lacked with EHRs lacked CPOE capabilities (HIMSS Analytics, 2015).

To qualify for an incentive payment through the CMS Medicare EHR Incentive Program, eligible hospitals must adopt certified EHR technology and use it to achieve specific objectives outlined in the specific stage being measured for a given performance year. Of the identified hospitals achieving meaningful use criteria, using data from the 2011 American Hospital Association Annual Survey, it has been determined that 38 percent of eligible hospitals achieved incentive thresholds by the end of 2012 (Diana, Harle, Huerta, Ford, & Menachemi, 2014). Of these hospitals, Diana et al. (2014) identified characteristics associated with these hospitals: "having a larger bed size, having a single health information technology vendor, obtaining Joint Commission accreditation, operating under for-profit status, having Medicare share of inpatient days in the middle two quartiles, being eligible for Medicaid incentives, and being located in the Middle Atlantic or South Atlantic census region" (p, 272), Diana et al. (2014) concluded that little evidence suggests that the HITECH incentive program has enticed hospitals without an EHR system to adopt meaningful use criteria. Policy makers should consider modifying the incentive program to accelerate the adoption of and meaningful use in hospitals without EHRs in order to improve societal outcomes with regard to MRSA infection.

Summary

There has been little research on the association of advanced EHR implementation and MRSA infection. The CMS Meaningful Use program is attempting to incentivize technology adoption of EHR systems in order to improve healthcare outcomes. Overall, the review of the available literature illustrates the importance of EHRs and how this technology can be leveraged to enhance patient safety practices within an antimicrobial stewardship program to prevent healthcare- associated MRSA infection. Our study attempts to add to the knowledge base in the area of patient safety.

CHAPTER THREE

METHODOLOGY

Study Objective

The purpose of this study is to determine the association between advanced use of electronic health records in acute care hospitals and rates of Methicillin-resistant *Staphylococcus aureus* infections acquired by patients during a recent hospitalization. Prior to this study, there has been no known research on the relationship between advanced EHRs and rate of HA-MRSA infection using the HIMSS Analytics participating hospitals as the sample population.

Study Design

We conducted a retrospective cross sectional patient-level study using the data from HIMSS Analytics for each hospital's advanced EHR adoption scores and National Inpatient Sample data from the Hospital Cost and Utilization Project (HCUP) for MRSA infection identification on the inpatient level. The data was analyzed to determine to what extent MRSA healthcare-acquired infection rates are associated with the advanced implementation of EHRs. We identified the principal independent variable as advanced EHR usage, and its effects on MRSA diagnosis rates (percentage of MRSA diagnosis among all patient hospitalizations) were measured for hospitals included in the dataset. Parameters were established in the coding of data to distinguish between healthcare-associated MRSA and community-associated MRSA. Propensity score matching was utilized in order to estimate the effect of confounding variables. Covariates considered included various demographic and clinical characteristics.

Practice Implications

Given that EHR adoption rates have increased significantly over the past few years as a result of the HITECH Act, this study is important because it investigates the relationship between advanced EHRs and healthcare-associated infection. The implications of such a query have a far-reaching impact and can contribute to development of strategies that can significantly improve the quality of patient care. In this study, we analyzed HIMSS Analytics and NIS data to evaluate the impact of advanced EHRs on HA-MRSA infection, specifically comparing coded MRSA diagnoses between hospitals using advanced EHRs (Stage 3) and hospitals not using an advanced EHR. For the purposes of this study, an advanced EHR necessarily included Computerized Provider Order Entry (CPOE) and a Clinical Decision Support System (CDSS), which corresponds to Stage 3 EHR adoption. Logistic regression was used to analyze and identify if a statistically significant relationship exists where patients hospitalized in an acute care facility with an advanced EHR system have a lower odds of contracting HA-MRSA. It will serve as a foundation for future study in the prediction of quality outcomes improvement facilitated by health information technology.

Research Question

Is there a significant relationship between the adoption level of electronic health records in acute care hospitals and the risk of Methicillin-resistant *Staphylococcus aureus* infections acquired by patients during a recent hospitalization?

Research Hypothesis

Null hypothesis: there is no difference in risk of MRSA infection by advanced and non-advanced levels of EHR adoption.

Alternate hypothesis: Higher level of EHR adoption (HIMSS Analytics, 2015) will result in a lower odds of MRSA infection.

Ethics Approval

The Institutional Review Board for Human Research at the Medical University of South Carolina approved this study (Approval # Pro00048571).

Data Source

The data for this cross-sectional patient-level analysis were obtained from the National Inpatient Sample and the Health Information Management Systems Society databases. The 2009 National Inpatient Sample (NIS) Database is part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality. It includes "discharge data from more than 1000 hospitals in 45 states, which encompass 96% of the United States population", and represents over 8 million hospital stays (Kazley, Simpson, A.N., Simpson, K.N., & Teufel, 2014, p. e184). The HIMSS data were used to measure the sophistication of hospital EHR use; this data was derived from the 2009 HIMSS Analytics Database (also known as the Dorenfest IHDS+ Database).

HIMSS Analytics is a global, cause-based, not-for-profit organization focused on better health through information technology. The HIMSS data "represent a broad canvassing of acute care hospitals, chronic care facilities, ambulatory practices on their adoption and plans to adopt various HIT components" and have been widely used in studies pertaining to technology diffusion and health services research (Jha et al., 2011; Kazley et al., 2014, p. e184). It contains data from 3989 hospitals, excluding Veterans Administration hospitals, and includes detailed descriptions of hospital information system implementation, such as hardware and software installations as well as other organizational and strategic information technology information. In discussing advantages of HIMSS Analytics, McCullough (2008) noted, it "is the most comprehensive database of hospital IT adoption decisions" in the USA and has been available since the late 1980s (p. 654). HIMSS follows an annual process to update the database, which involves initial data gathering conducted by phone followed by an IT inventory survey completed by hospital administrators. HIMSS provides benchmarking reports to respondents as an incentive for participation. In any given year, the HIMSS Analytics Database represents nearly all of the 100+ bed non-federal hospitals and >90% of all US hospitals (McCullough, 2008

The study sample included all hospitals with data available on EHR use and HA-MRSA diagnosis. Hospital Medicare ID codes were used to link the HCUP and HIMSS data sets. Patients were included in the analysis if they were 18 years of older. In the NIS, some states do not release the American Hospital Association identifiers, and thus the individual patient cases cannot be included because EHR use cannot be determined. The presence of healthcare-acquired MRSA infection is theorized to have been coded by hospital personnel if a clinical culture from blood, sputum, urine, or a wound obtained during the hospitalization was positive for *S. aureus*, the isolate was resistant to oxacillin by screen agar test, and there was no prior history of MRSA infection. (In microbiological testing of antibiotic resistance, oxacillin is used as a proxy for testing of susceptibility to all ß-lactam antimicrobials, including methicillin) (Kuehnert et al., 2005).

A MRSA-positive clinical culture of a healthcare-acquired infection was determined by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis coding captured during hospitalization. Our research confirmed the clinical finding of healthcare-acquired MRSA infection cases through identification of the appropriate ICD-9-CM code(s) and ruled out CA-MRSA cases through exclusionary ICD-9-CM codes. In order to identify patients with healthcare-associated MRSA infection, as opposed to a community associated MRSA infection, the patients in this study would have had no history of MRSA colonization or infection prior to the hospital admission. CA-MRSA patient exclusions were determined by the presence of ICD-9-CM codes signifying either MRSA carrier status or personal history of MRSA.

ICD-9-CM discharge diagnosis codes have attributes that make them suitable for detecting HAIs; therefore, this code set was utilized in the study. Diagnosis coding for HAIs is commonly used to "facilitate automated surveillance, freeing up infection control personnel to perform other important tasks, such as staff education and outbreak investigation" (Jhung & Bannerjee, 2009, p. 950). There are known limitations associated with the use of ICD-9-CM data in detecting HAIs since medical coding data may lack elements necessary for surveillance (Jhung & Bannerjee, 2009). Speed and accuracy of the data collection is the most common obstacle faced by hospitals when surveillance is conducted using manual review of microbiology culture, laboratory and other patient information. According to Evans et al. (2009), “while computer surveillance using ICD-9-CM codes as triggers for possible HAIs was found to provide a retrospective role, the time lag rendered the data of low utility for infection prevention” (p. 178).

The ICD-9-CM coding accuracy for healthcare-associated methicillin-resistant *S. aureus* infections has not been specifically evaluated, but the accuracy of coding for sepsis from all causes has been researched and has demonstrated a “sensitivity of >75% for any septicemia or bacteremia code and positive and negative predictive values >80% for the code specific for *Staphylococcus* spp. septicemia” (Kuehnert et al., 2005, p. 871). Although the relationship between *S. aureus* infections and ICD-9-CM discharge coding has not been formally validated, this coding method was chosen for this study as it the only way to currently identify facility-specific MRSA diagnoses in publically available datasets. Administrative coding data are inappropriate as the sole means of HAI surveillance but do have value to the healthcare researcher, as the only feasible approach to study HAIs. Currently, only facilities in 19 states mandate use of the National Healthcare Safety Network system for active surveillance of HAIs, and a number of states either do not specify a data source or explicitly identify administrative data as the source for HAI rates (Edmond & Bearmon, 2007). Since NHSN participation is voluntary and diagnosis coding is a requirement that hospitals must fulfill in order to get reimbursed for services provided, administrative coding is most commonly utilized in HAI-related research. Traditional methods of surveillance are too time-consuming and resource-intensive for many hospitals so diagnosis coding of HAIs is the best way to aggregate data at a substantive level to be considered generalizable for health services research.

Prior to October 1st, 2008, MRSA infection was identified by the presence of the V09.0 secondary ICD-9-CM code. The infection was reported using one of three primary codes: 041.11 (Staphylococcus aureus infection, unspecified site), 038.11 (Staphylococcus aureus septicemia), or 482.41 (Staphylococcus aureus pneumonia) with V09.0 (methicillin- resistant Staphylococcus aureus) to capture the nature of a MRSA infection. Hospital diagnosis coding for MRSA has since been changed by the Centers for Medicare and Medicaid Services, as it was desirable to have standalone ICD-9 codes to identify MRSA infections. The following updated codes were created to identify and track MRSA infection: 038.12 Methicillin resistant Staphylococcus aureus septicemia; 041.12 Methicillin resistant Staphylococcus aureus in conditions classified elsewhere and of unspecified site; and 482.42 Pneumonia due to methicillin resistant Staphylococcus aureus. There are also two codes for MRSA colonization and history (V02.54 Carrier or suspected carrier of methicillin resistant Staphylococcus aureus; and V12.04 Personal history of methicillin resistant Staphylococcus aureus). Even though V02.54 and V12.04 can be coded concurrently with 038.12, 041.12, or 482.42 to signify an active infection, these patients were excluded from the analysis since they could potentially represent CA-MRSA instead of HA-MRSA.

Since the NIS 2009 was used for this study, only the standalone ICD-9 MRSA codes (post- October 1st, 2008) were used to identify healthcare-associated infections so as to ensure that episodes were detected at the highest specificity. Records that contained multiple *S. aureus*–related discharge codes were counted once, with septicemia preferentially included, followed by *S. aureus*–related pneumonia. Only patients with a hospital length of stay of greater than three days was included in this study to further enhance the identification of MRSA cases that were acquired in a healthcare setting.

Electronic Health Records Classification

The level of sophistication and advancement with regard to electronic health record adoption was based on criteria adopted from the technology adoption model reported in the HIMSS Analytics database. The Electronic Medical Record Adoption Method (EMRAM) is an eight-step model of advancing EHR use created by HIMSS Analytics that allows healthcare organizations to analyze their level of EHR adoption, chart their accomplishments and track their progress against other healthcare organizations across the country. Each of the EMRAM stages are measured by cumulative capabilities within each stage that must be reached before moving to the next stage. All lower-level stages must be completed before a higher level will be considered completed (Garets and Davis 2006).

Based on the HIMSS EMR Adoption Model, EHR applications were grouped into three categories representing stage of EHR implementation as reported by hospitals. This classification was based on previous research (Furukawa, Raghu, & Shao, 2010; Teufel, Kazley, Ebeling, & Basco, 2012; Kazley, et al., 2014). These classifications include "stage 0 (no automation), stage 1 (automation of ancillary services including a clinical data repository, and pharmacy, laboratory, and radiology information systems), stage 2 (stage 1 + automation of nursing workflow with electronic nursing documentation, and medication administration records), and stage 3 (advanced EHR including: stages 1 and 2 + CPOE and clinical decision support)" (Kazley, et al., 2014, p. e185). For a hospital to advance to a higher stage, they must have achieved all of the criteria for the lower stage.

Therefore, a hospital at stage 3 has reported success at automating all of the aforementioned processes and listed applications in stages 1, 2, and 3. Many of the functions present in advanced EMRAM Stage 3 would be considered minimal functions required to meet Meaningful Use objectives (Teufel et al., 2012). Since Stage 3 consists of more advanced automated features, it is expected that Stage 3 hospitals have enhanced capabilities to support the provision of higher quality care and patient safety.

This model for staging of EHR was adopted for two primary reasons according to Teufel et al. (2012). The first is it accounts for the EHR environment and not simply the presence of an individual application. The second reason is that this model for staging EHR is similar to the one used by other researchers that have associated EHR use with measures of cost, utilization, and outcomes. In addition, it should be noted that many of the functions present in advanced stage 3 would be considered minimal functions to successfully compete for meaningful use objectives (DesRoches & Rosenbaum, 2010). Since meaningful use EHR implementation criteria are consistent with stage 3 adoption of EHR, it was determined that hospitals that have advanced EHRs be compared with all others; this staging comparison has been used in previous research (Kazley, et al., 2014). HIMSS describes various levels of implementation of an EHR application including: not automated, contracted/not yet installed, installation in progress, and live and operational. For the purpose of this study, only hospitals with "live" and "operational" status as users of an application were included because this would be the most likely level to improve operations, resource utilization, and ultimately lower rates of healthcare-acquired infection through an effective antimicrobial stewardship program. Previous research demonstrates that non-respondents to EHR surveys have characteristics more similar to nonusers of EHR than to users of EHR; therefore, during analyses it was assumed that if a hospital had not reported information to HIMSS it has not adopted the application (Yu et al., 2009; Jha et al., 2009).

Data Analysis

A multivariable logistic regression model was used to model the association between advanced EHR adoption and MRSA infection controlling for covariates. Covariates included in the model were those that have been shown to have the potential for confounding this association. Hospital-level covariates were nurse staffing levels (RN FTEs per 1000 adjusted inpatient days), hospital size, teaching status, rural/urban location, bed size, and geographic region. Patient-level covariates were age, gender, race/ethnicity, marital status, ADL functional status, All Patient Refined Diagnosis Related Groups (APDRGs) mortality and severity, neonatal or maternal status, private insurance coverage, Medicare or Medicaid coverage, Diagnosis Related Group (DRG) case mix group, and whether the patient arrived as a transfer. The independent variable (EHR Group) was dichotomized as advanced EHR and non-advanced EHR use with coding of 1 for advanced EHR and 0 for non-advanced EHR. Those with stage 3 advanced EHR including stages 1 and 2 + CPOE and clinical decision support were classified as having non-advanced EHR. Stage 0, 1, and 2 were classified as non-advanced EHR. The dependent variable (MRSA infection) was dichotomized as those with and without incident MRSA infection using a similar 0/1 coding assignment.

There were multiple ICD-9-CM codes that define antimicrobial resistant organisms in greater detail, including the standalone MRSA codes of 038.12, 041.12, and 482.42 that were implemented in the year this NIS data was generated. The narrow definitions used in the analysis were chosen to maximize the specificity and positive predictive value for identifying MRSA infections. The end result of binning the different types of MRSA infection was a binomially–distributed outcome (i.e., an outcome with exactly two mutually exclusive outcomes).

The primary analysis performed was a logistic regression to model a binomial outcome with one explanatory variable, i.e. assessing whether the proportion of HA-MRSA patient cases differs from hospitals with and without advanced EHRs. The dependent variable in the logistic regression equation was MRSA infection, while the independent variable of interest was advanced EHR. Our binomial logistic regression consisted of a generalized linear model with a logit linking function. The logit linking function was the natural log of the odds of the outcome of interest (MRSA infection). Odds were determined from probabilities and range between 0 and infinity, and computed as the probability of an outcome divided by 1 – the probability of the outcome. Chi-square testing was applied to the results of the logistic regression to determine that the variables included in the study were in fact significant predictors of the dependent variable (Mertler & Vannatta, 2002). Analysis was conducted using SAS 9.2 statistical software.

Several features of logistic regression methodology make it desirable for predicting the rate of MRSA healthcare-acquired infection within institutions that have varying levels of EHR adoption. To begin, the outcome for the prediction of lower infection rate is binary (no MRSA infection = 0, MRSA infection = 1). Logistic regression allows for the prediction of collective group outcomes from variables that are continuous, discrete, dichotomous, or a combination of all (Tabachnick, Fidell, &

Osterlind, 2001). Additionally, logistic regression can form predictive functions, yet the predictor variables used in the equation are not required to be normally distributed, linearly related, or of equal variance (homoscedasticity) within each group (Tabachnick, Fidell, & Osterlind, 2001). This is particularly important in this a priori exploratory study, consisting of an EHR survey that may produce data that do not conform to these assumptions and would otherwise compromise the integrity of any other inferential methodology. Finally, logistic regression can be useful when nonlinear associations exist within the data (Tabachnick, Fidell, & Osterlind, 2001). With regard to this study, this means that the dependent variable (MRSA infection) may turn out to have a nonlinear relationship with the independent variable in the study (EHR implementation). Such nonlinearities in relationships between variables do not present any issues with logistic regression analysis.

Propensity Scoring for Bias Reduction

In this observational study, the investigator had no control over the treatment assignment. Potential confounding variables hypothesized to affect patient outcomes include nurse staffing levels, nurse education, hospital size, teaching status, high technology status (defined as facilities with open-heart surgery, major organ transplant services, or both), and geographic categories (Hessels, Flynn, Cimiotti, Bakken, & Gershon, 2015). Patient risk-adjusted covariates were extracted from the State Inpatient Databases (SIDS) as part of the family of databases and software tools developed for the Healthcare Cost and Utilization Project. These include age, sex, race, insurance type, and ICD-9-CM primary and secondary diagnosis codes.

Significant differences on covariates in the two observed groups may exist, and these differences could produce biased estimates of treatment effects. In simulation of a comparable study using the same dataset, we controlled for possible selection bias of advanced EHR use in hospitals by recognizing "potential differences in patient demographics, severity, and hospital case mix through the use of a propensity score stratification" (Kazley, et al., 2014, p. e185). To calculate the propensity score, a logistic regression analysis was performed to determine the propensity of each patient to be seen in a hospital with an advanced electronic health record. Use of a propensity score approach can remove upward of 95% of bias from estimates (Teufel et al., 2012).

As propensity score matching was deemed to be the best method to control for possible variables that could affect diagnosis status, the propensity score model was designed to include patient and hospital attributes. More specifically, the generalized linear model and propensity models controlled for patient-level variables: age, gender, race/ethnicity, marital status, ADL functional status, All Patient Refined Diagnosis Related Groups (APDRGs) mortality and severity, neonatal or maternal status, private insurance coverage, Medicare or Medicaid coverage, Diagnosis Related Group (DRG) case mix group, and whether the patient arrived as a transfer. Both models also controlled for the following hospital-level variables: hospital type, teaching status, rural/urban location, bed size, and geographical region. The main outcome measure was MRSA infection diagnosis per patient-billed hospitalization.

The propensity score was calculated by logistic regression analysis; each estimate represented the propensity of each patient to be seen in a hospital with advanced EHRs. The propensity score for a patient, defined as the conditional probability of being treated given the individual's covariates, was used to balance the covariates in groups, and thus reduce selection bias. Traditional methods of adjustment (matching, stratification and covariance adjustment) are often limited since they can only use a limited number of covariates for adjustment. However, propensity scores, which provide a scalar summary of the covariate information, do not have this limitation (d'Agostino, 1998).

Propensity score adjustment allowed for the creation of 5 equal strata of propensity to receive care with advanced EHR. These strata were included in the model to control for nonrandom assignment to advanced EHR. The use of a propensity score adjustment to group observations into 5 equal strata is believed to remove 90% or more of the treatment bias present in observational data (Rubin, 1997). The primary logistic regression model was performed with and without the propensity score adjustment to ensure the results persisted and the model was adequate.

Sensitivity Analyses

Generalized estimating equation (GEE) methods were used to confirm results persisted after accounting for correlated outcomes across patients treated within the same hospital. Potential for selection bias was examined due to case mix, patient characteristics, and hospital characteristics in a sensitivity analysis using a 5% random sample of the data. This sensitivity analysis used a portion of the data in a propensity score–matching methodology, allowing for an estimation of the potential selection bias of known confounders that might have remained after using propensity score stratification methods. The data were prohibitively large, this was the rationale to limiting propensity score–matching sensitivity analyses to a 5% sample.

Limitations

One set of limitations pertaining to this research study would be with the dataset itself. The dataset utilized for analysis is not recent; therefore, EHR functionality related to antimicrobial stewardship may have changed significantly since the data was collected. Another limitation would be that the data were not randomized and thus selection bias may remain.

MRSA healthcare-acquired infection was determined by the International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis coding captured during hospitalization, and ICD-9-CM coding may still need to be validated against medical chart review. There are many reasons why codes may not be assigned consistently across hospitals such as differing versions of medical billing software used by hospitals that may or may not have prompts asking whether the patient had MRSA, overcoding in cases of prior history of MRSA, or coding for an MRSA test even though the test result was negative (Schweizer & Rubin, 2012). HA-MRSA infections may also not have been recorded in administrative billing data if culture results were not available at the time of hospital discharge, if only a limited number of diagnosis codes were available for each hospitalization, or if there were coding errors. Even though HA-MRSA infections are typically thought of as being exclusively originated from hospitals, patients may have obtained the infection from another health care facility, such as long term care facilities and nursing homes prior to being readmitted to the hospital. This scenario was not able to be controlled for given limitations with coding due to incident outbreak of disease.

ARTICLE MANUSCRIPT

Association of Electronic Health Records with Methicillin-Resistant Staphylococcus Aureus Infection in a National Sample

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Abstract

Objective

To determine whether advanced electronic health record (EHR) use in hospitals is associated with lower rates of Methicillin-resistant *Staphylococcus aureus* (MRSA) infection rates in an inpatient setting.

Study Design

National Inpatient Sample (NIS) and Health Information Management Systems Society (HIMSS) Annual Survey are combined in the retrospective, cross-sectional analysis. We study patients 18 years or older and admitted to an acute care hospital for greater than three days.

Methods

Using 2009 data and a cross-sectional design with a gamma-distributed generalized linear model, a patient-level analysis is conducted with propensity scores to control for selection bias. Patient- and organizational-level variables are included as controls.

Results

A twenty percent simple random sample of the combined 2009 NIS and HIMSS datasets included a total of 1,032,905 patient cases of MRSA in 550 hospitals. Results of the propensity-adjusted logistic regression model revealed a statistically significant association between advanced EHR and MRSA, with patient cases from an advanced EHR being less likely to report a MRSA diagnosis code.

Conclusions

Hospitals with advanced EHRs are less likely to report patients with a healthcare-associated MRSA infection, thus advanced EHR use may contribute to higher quality care.

Association of Electronic Health Records with Methicillin-Resistant Staphylococcus Aureus Infection in a National Sample

The Health Information Technology for Economic and Clinical Health Act (HITECH), as part of the American Reinvestment & Recovery Act of 2009, was created to accelerate the pace of technology diffusion in the American healthcare system. The promulgation of this health policy led to the Meaningful Use incentive program – a $30 billion initiative to transform healthcare delivery in hospitals through the advanced implementation of electronic health records system technology. The potential of health information technology to transform healthcare delivery and patient outcomes has been demonstrated in innumerable studies; however, there has been limited research on its effect on antimicrobial stewardship in association with healthcare-associated infections (HAIs).

The development and widespread use of antimicrobial agents to combat bacterial infection has been one of the most important public health interventions in the history of mankind (CDC, 1999). In the milieu of a modern-day hospital, however, antibiotic resistance is likely to develop when there is a convergent coupling of extensive antimicrobial use with a high concentration of acutely ill patients at risk of infection. Both the Centers for Disease Control and Prevention and the World Health Organization have identified antimicrobial resistance as a "major public health issue" and "one of the three greatest threats to human health" (So et al., 2010). Multidrug-resistant organisms account for more than 70% of all hospital-associated infections, with limited antimicrobial treatment options and consequently higher mortality rates in comparison to "normal" strains of bacteria (APIC, 2010).

The Centers for Disease Control estimates there are over 2.7 million HAIs per year in acute care hospitals within the United States, resulting in 99,000 deaths and an estimated $28-33 billion in preventable healthcare expenditures annually (Henderson, et al., 2012). At any given time, approximately 1 in 20 admitted patients will contract a HAI during their stay in an American hospital, with HAIs being the most common type of complication for patients who are hospitalized (Jeeva & Wright, 2014). Methicillin-resistant *Staphylococcus aureus* (MRSA) is one the 'superbugs' that are among the most deadly antibiotic-resistant bacteria. Of all the antibiotic-resistant bacterial microorganisms that cause infection, MRSA is considered to be one of the most virulent and prevalent, as it is the most commonly identified multidrug-resistant pathogen in Europe, the Middle East, and Africa, Asia-Pacific, and the Americas (APIC, 2010). The global emergence of methicillin-resistant *Staphylococcus aureus* has caused substantial health and economic burdens on healthcare systems and their infected patients.

Clinicians and epidemiologists now see MRSA as a major public health threat because of its "rising rate of occurrence in both hospital and community settings and the dearth of proven treatment options available" (Lodise & McKinnon, 2007, p. 1002). The MRSA epidemic is a national health crisis where more people in the U.S. now actually die from MRSA infections than from AIDS, Parkinson's disease, emphysema, and homicide combined (IDSA et al., 2011). The prevalence of MRSA in the US community is now at over 25%; with rates that are alarmingly triple that in hospitals (Chambers, 2001). The reasons for the emergence of MRSA are multifactorial; attributed causes of the epidemic are infection control practices and various host factors that can lead to insusceptibility from antimicrobial pressures (Graffunder & Venezia, 2002). Despite its complex and poorly-understood etiology, the main reason methicillin-resistant *S. aureus* has become such a massive public health problem is due to ineffective institutional programs to combat antimicrobial resistance.

Research indicates that antimicrobial stewardship in U.S. hospitals is poor, as one in three antibiotics prescribed are medically unnecessary for the conditions they are meant to treat (Fleming-Dutra et al., 2016). Antimicrobial stewardship programs (ASPs) enabled by health information technology offer a possible solution to improve patient outcomes. ASPs are an important approach that hospitals seek to optimize antimicrobial prescribing and efficacy in order to improve patient care outcomes, ensure cost-effective therapy, and reduce adverse sequelae of antimicrobial use (primarily antimicrobial resistance) to slow the spread of healthcare-associated infections.

Electronic health records (EHRs) and clinical decision support systems (CDSSs) are the main technologies used to enhance existing antimicrobial stewardship programs within hospitals (Forrest et al., 2014). A clinical decision support system, as part of a computerized physician order-entry (CPOE) system, provides evidence-based guidelines and decision support to improve the effectiveness and efficiency of an ASP. Sintchenko, Coiera, & Gilbert (2008) specifically outline a task-specific decision support heuristic for an automated ASP application that can reduce error and variation in antibiotic prescribing when programmed into EHR software. Advanced EHR use will not singularly eradicate the epidemic of healthcare-associated MRSA, but it can be a foundational component of an effective institutional antimicrobial resistance program to combat this deadly pathogen.

Research evaluating the impact of EHRs on antimicrobial stewardship program effectiveness is lacking (Forrest et al., 2014). This study attempts to evaluate the relationship between advanced EHR use and MRSA infection in order to meet a critical need for additional research in this area. Our research question attempts to illuminate whether there is there a significant relationship between the adoption level of electronic health records in acute care hospitals and the risk of Methicillin-resistant *Staphylococcus aureus* infections acquired by patients during a recent hospitalization. Given that EHR adoption rates have increased significantly over the past few years as a result of the HITECH Act, this study is important because it investigates the relationship between advanced EHRs and healthcare-associated infection. The implications of such a query have a far-reaching impact and can contribute to development of strategies that can significantly improve the quality of patient care.

Methods

We conducted a retrospective cross sectional patient-level study using the data from the Health Information Management Systems Society (HIMSS) Survey and the National Inpatient Sample (NIS) 2009 datasets to determine the relationship between advanced EHR use and MRSA rates in hospitals. The HIMSS 2009 dataset consists of data related to health information technology components. The NIS is a cross-sectional sample containing patient-level hospital discharge data from over 1,000 hospitals in 45 states.

The data was analyzed to determine to what extent healthcare-acquired MRSA infection rates are associated with the advanced implementation of EHRs. For the purposes of this study, an advanced EHR necessarily included CPOE and a CDSS. Logistic regression was used to analyze and identify if a statistically significant relationship exists where patients hospitalized in an acute care facility with an advanced EHR system have a lower odds of contracting healthcare-associated MRSA.

A MRSA-positive clinical culture of a healthcare-associated infection was determined by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis coding captured during hospitalization. A hospital admission was classified as being positive for MRSA if any of the following ICD-9 codes was listed as diagnosis codes on the admission: 038.12 (Methicillin resistant Staphylococcus aureus septicemia), 041.12 (Methicillin resistant Staphylococcus aureus in conditions classified elsewhere and of unspecified site), and 482.42 (Pneumonia due to methicillin resistant Staphylococcus aureus).

The four stages of EHR use in hospitals were measured based on surveys reported by hospitals using advanced EHR classification methodology developed by Kazley, et al. (2014). The stages included stage 0 (no automation), stage 1 (automation of ancillary services including a clinical data repository, and pharmacy, laboratory, and radiology information systems), stage 2 (stage 1 + automation of nursing work flow with electronic nursing documentation, and medication administration records), and stage 3 (advanced EHR including: stages 1 and 2 + CPOE and CDSS). Stage 3 adoption of EHR is consistent with meaningful use criteria, and therefore was categorized as advanced EHR.

Overall means (continuous variables) and proportions (categorical variables) were computed. Unadjusted analyses of patient and hospital-level characteristics were compared by advanced EHR status. MRSA was also compared descriptively by age, race, insurance, hospital bed size, and hospital region.

The logistic regression model predicting the probability of healthcare-associated MRSA infection as well as the logistic regression predicting probability of an admission originating from hospital with advanced electronic health records (i.e. propensity model) were controlled for the following patient level variables: patient age, gender, race, All Patient Diagnosis Related Groups (APDRGs) mortality and severity, insurance type (Medicaid, Medicare, Private, Other), neonatal or maternal status, Diagnosis Related Group (DRG) case mix group, and whether the patient arrived as a transfer. The following hospital-level variables were also controlled for in each model: teaching status, hospital location (urban vs. rural), bed size, and hospital geographical region and number of RN FTEs per 1000 adjusted patient days. Models were also weighted by hospital.

A logistic regression was used to assess patient cases reporting at least one MRSA diagnosis from hospitals with advanced EHRs. Two different methods were used to control for selection bias.

First, potential selection bias of advanced EHR use in hospitals and potential differences in patient demographics, case severity, and hospital case mix were controlled by using propensity score stratification. The propensity score was generated by modeling advanced EHR use by fitting a logistic regression model and estimating the probability of advanced EHR for each patient case. These probabilities were stratified into quintiles, and the stratified variable was added to the final model associating advanced EHR with the outcomes of interest, MRSA. Use of a propensity score approach has been shown to remove upward of 95% of bias from estimates (Teufel, et al., 2012). Data were analyzed using SAS version 9.3, and the model was run using the GENMOD procedure.

Second, potential selection bias due to case mix, patient and hospital characteristics were examined using propensity score matching techniques. A random sample of one third of the data was used to develop propensity matched sample based on the nearest neighbor-matching greedy algorithm approach. The matched sample was comprised of a total of 43,130 randomly selected observations from each group (hospitals with and without advanced EHR).

Results

A twenty percent simple random sample of the combined 2009 NIS and HIMSS datasets were utilized for this analysis in order to reduce computation resources. A total of 1,032,905 patient cases were selected. Of these, the sample was further restricted to patient cases aged >=18 years and with admissions greater than 3 days. This left a remaining sample size of 527,593 patients.

A total of 147,956 (28.0%) patient cases originated from hospitals with an advanced EHR. A total of 550 hospitals were included in the analysis, with 104 (18.9%) reporting use of advanced EHR. The total number of patients with at least one MRSA diagnosis was 9,664 (1.8%), with a total of 6,742 (1.3%) reporting at least one ICD-9 code for methicillin resistant staphylococcus aureus in conditions classified elsewhere and of unspecified site in conditions classified elsewhere and of unspecified site (041.12), 1,438 (0.3%) reporting at least one code for methicillin resistant staphylococcus aureus septicemia (038.12), and 1,726 (0.3%) reporting at least one code for pneumonia due to methicillin resistant Staphylococcus aureus (048.42).

Table 1 displays unadjusted differences in patient and hospital characteristics by advanced EHR status. All differences were statistically significant. With the exception of small hospital size and geographic differences in advanced EHR, the majority of covariate differences were small. Compared with patient cases from hospitals without advanced EHR, those with advanced EHR included a lower proportion of MRSA cases (2.0% vs. 1.5%, $p<0.0001$), were slightly younger in age, had a higher proportion of teaching hospitals and hospitals in an urban location. Other differences are displayed in the Table 1.

Overall, initial unadjusted results demonstrated lower rates of MRSA in advanced EHR hospitals compared with non-advanced EHR hospitals. These differences decreased slightly but remained statistically significant after adjustments for confounding. Patient cases from hospitals with advanced EHRs were ultimately less likely to have indicated a MRSA diagnosis code. Note that since the focus of this study was to quantify differences in MRSA between advanced and non-advanced EHR, overall rate calculations may not be comparable to other sources since we excluded admissions <3 days, are restricted to only adults (>=18 years) and have not adjusted for or excluded cases for which MRSA transmission may be more frequent (i.e. chronic dialysis patients).

Results of the propensity-adjusted logistic regression model revealed a statistically significant association between advanced EHR and MRSA, with patient cases from an advanced EHR being less likely to report a MRSA diagnosis code. After controlling for all potential confounders (listed in Table 2), the odds of healthcare-associated MRSA among patients seen in hospitals with advanced EHRs were 15% lower (OR=0.85, 95% CI 0.83-0.88) compared with patients treated in hospitals without advanced EHRs. The model also revealed statistically significant differences in the infection rates of MRSA among advanced and non-advanced EHR hospitals (1.05% vs. 1.23%, $p<0.0001$, respectively). With the exception of hospital location, all covariates in the model were associated with MRSA (Table 2).

Use of propensity score matching in the sensitivity analyses reduced the heterogeneity in the advanced EHR and non-advanced EHR groups as evidenced by the decrease in absolute standardized differences between covariates in the original sample and the matched sample (Figure 1). Using the propensity matched sample, a slightly higher proportion of MRSA was detected among the non-advanced EHR group. The infection rates of MRSA among those with advanced EHR and non-advanced EHR was 1.05% vs. 1.26%, and this difference was statistically significant ($p<0.0001$). This indicates that the difference observed in MRSA between groups remained present even after additional adjustments for selection bias (Table 3).

Discussion

Health information technology has grown exponentially over the last decade as electronic health records have become omnipresent in the healthcare landscape. EHR adoption has accelerated primarily because of incentives provided by the federal government. As antimicrobial stewardship programs are the main institutional strategy for preventing MRSA infection, hospital leaders must find ways to leverage their existing health information technology infrastructure to improve program effectiveness. The Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA) has created guidelines for developing ASPs that recommend hospitals invest in health information technology that is capable of measuring key performance indicators from an antimicrobial stewardship implementation (Dellit et al., 2007). Advanced electronic health records with CPOE and CDSS have a role to play in the transformation of antimicrobial stewardship through infection risk assessment, antibiotic prescribing algorithms tied to evidence-based guidelines, interdisciplinary ASP team communication, provider education on institutional guidelines for therapy, formulary management control, antimicrobial resistance surveillance, microbiology test result integration, and therapy monitoring of culture susceptibility results (Sintchenko, Coiera, & Gilbert, 2008).

Advanced electronic health records have been postulated to improve clinical and economic outcomes through their support of institutional ASP strategies. This study validates that EHRs affect clinical outcomes by showing that there is an association between advanced use of electronic health records in acute care hospitals and rates of Methicillin-resistant *Staphylococcus aureus* infections acquired by patients during a recent hospitalization. Prior to this study, there has been no known research on the relationship between advanced EHRs and rate of MRSA infection using the HIMSS Analytics participating hospitals as the sample population.

This study has several strengths. First, the use of a large, national dataset including detailed information on advanced EHR stage and MRSA diagnosis provides a rich data source to answer the question of interest. Secondly, few studies have explored the relationship between MRSA and advanced EHR, thus this analysis adds to the existing evidence base on the subject. Third, restriction of patient cases positive for MRSA who were also positive for carrier codes indicative of community-associated MRSA infection aided in ensuring that these data detected only healthcare-associated MRSA. Similarly, excluding patient cases in which the hospital was less than 3 days further ensured that healthcare-associated MRSA data were captured.

Although this study has strengths, there are some limitations to the dataset used, and thus the analysis. First, unlike pre-post interventions, these data are cross-sectional and cannot indicate cause and effect. Second, it is possible that confounding factors may have played a role in results. While we are able to control for several hospital-level factors, it is possible that unmeasured confounding variables could have contributed to results. The dataset utilized for analysis is also not recent; therefore, EHR functionality related to antimicrobial stewardship may have changed significantly since the data was collected. Another limitation would be that advanced EHR use was not randomized and thus selection bias or endogeneity may remain. Additionally, MRSA healthcare-associated infection was determined ICD-9-CM coding captured during hospitalization, and may still need to be validated against medical chart review. Finally, even though MRSA healthcare-associated infection are typically thought of as being exclusively originated from hospitals, patients may have obtained the infection from another health care facility, such as long term care facilities and nursing homes prior to being readmitted to the hospital. This scenario was not able to be controlled for given limitations with coding due to incident outbreak of disease.

Conclusions

With the meaningful use program, electronic health records are becoming more prevalent in acute care hospitals, and with that, there are increased opportunities for computer-assisted antimicrobial stewardship strategies to prevent healthcare-associated MRSA infection. MRSA is a serious infection that can have dire consequences and costs for patients and hospitals. In the hospital marketplace for health information technology, there are currently only a few software vendors that attempt to provide integration for institutional EHR and ASP efforts and these advancements are in the nascent stage (Kullar, Goff, Schulz, Fox, & Rose, 2013). There has been little research on the association of advanced EHR implementation and MRSA infection. This study confirms the importance of EHRs and how this technology can be leveraged to enhance patient safety practices within an antimicrobial stewardship program to prevent healthcare-associated MRSA infection. The results provide support for the continued adoption and use of EHRs to improve healthcare quality and patient safety.

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Figures and Tables

Figure 1: Standardized Mean Difference Plot

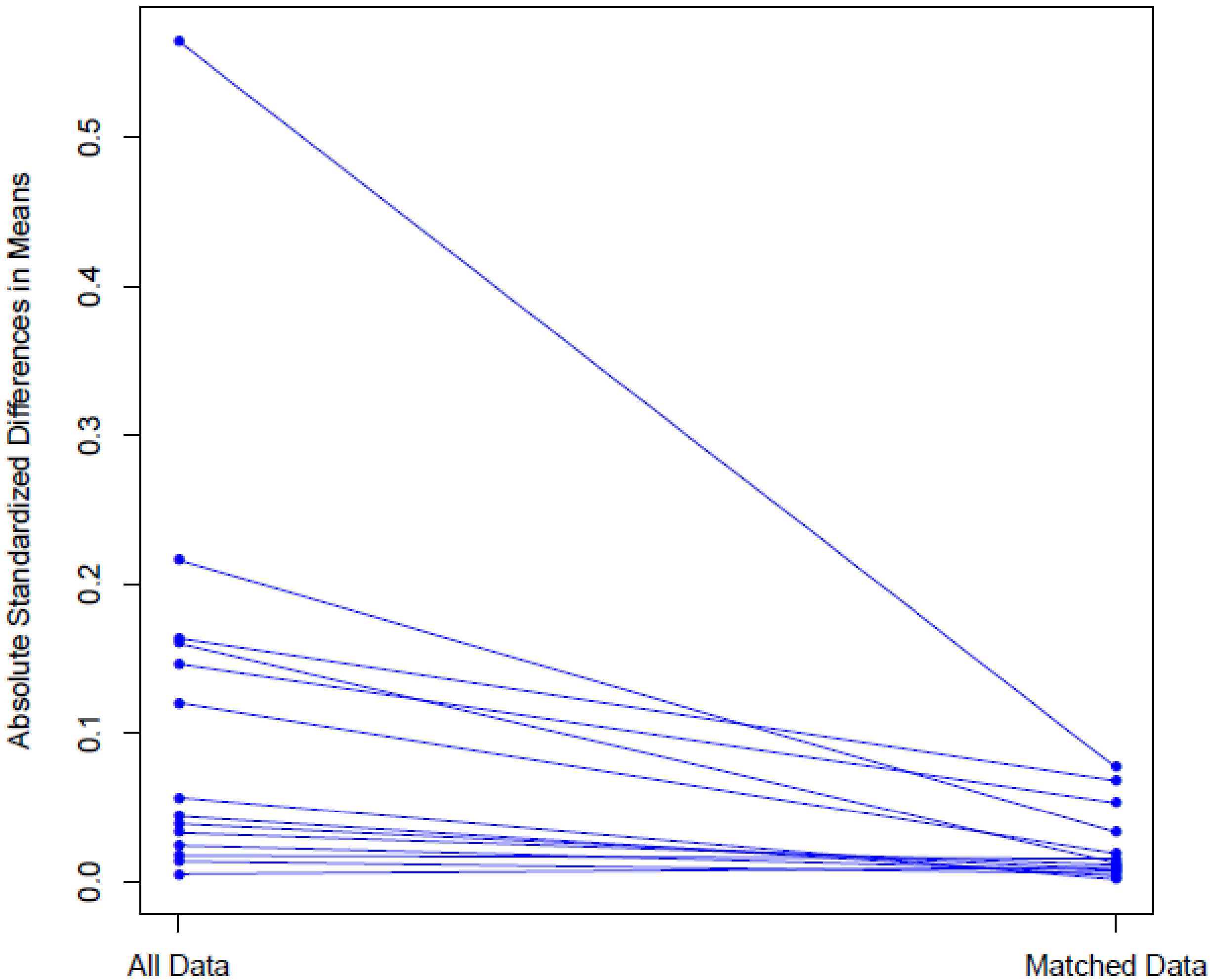

Table 1: Hospital and Patient Characteristics by Advanced EHR Status

	Total (n=527,593) Mean (SD)	No Advanced EHR (n=379,537) Mean (SD)	Advanced EHR (n=147,956) Mean (SD)	p-value
Age in years	60.4 (20.4)	61.1 (20.2)	58.4 (20.6)	p<0.0001
Risk mortality	1.9 (0.97)	1.9 (1.0)	1.9 (1.0)	p<0.0001
Risk severity	2.3 (0.91)	2.3 (0.9)	2.3 (0.9)	p<0.0001
RN FTEs per 1000 adjusted patient days	4.1 (1.4)	4.1 (1.4)	4.2 (1.4)	p<0.0001
	N (%)	**N (%)**	**N (%)**	
MRSA	9664 (1.8)	7454 (2.0)	2210 (1.5)	p<0.0001
Female	307246 (58.3)	221664 (58.5)	85582 (57.9)	p<0.0002
Insurance				
Medicaid	77271 (14.7)	53350 (14.1)	23921 (16.2)	p<0.0001
Medicare	267321 (50.7)	198707 (52.4)	68614 (46.5)	
Private insurance	140819 (26.7)	98174 (25.9)	12404 (8.4)	
Other ins/self pay/no charge	41205 (7.8)	28801 (7.6)	42645 (28.9)	
Neonatal/maternal admit	50267 (9.5)	33859 (8.9)	16408 (11.1)	p<0.0001
Transfer into hospital	37318 (7.1)	24114 (6.4)	13204 (8.9)	p<0.0001
Race/Ethnicity				
White	323119 (61.2)	238532 (62.8)	84587 (57.2)	p<0.0001
Black	62727 (11.9)	41909 (11.0)	20818 (14.1)	
Hispanic	49656 (9.4)	37496 (9.9)	12160 (8.2)	
Other/Missing	93088 (17.5)	61697 (16.3)	30391 (20.5)	
Teaching Hospital	252617 (47.9)	157302 (41.4)	95315 (64.4)	p<0.0001
Urban Hospital	474707 (90.0)	331527 (87.3)	143170 (96.8)	p<0.0001
Bed Size				
Small Hospital	58484 (11.1)	46610 (12.3)	11874 (8.0)	p<0.0001
Medium Hospital	125830 (23.9)	88365 (23.3)	37465 (25.3)	
Large Hospital	343279 (65.1)	244662 (64.5)	98617 (66.7)	
Region				
Northeastern US	155050 (29.4)	93633 (24.7)	61417 (41.5)	p<0.0001
Midwestern US	68031 (12.9)	38137 (10.1)	29894 (20.2)	
Western US	133797 (25.4)	106843 (28.1)	26954 (18.2)	
Southern US	170715 (32.4)	141024 (37.2)	29691 (20.1)	

Table 2: Propensity-adjusted Logistic Regression Model

	MRSA Diagnosis vs. No MRSA Diagnosis		
Variable	OR	95% Confidence Interval	P
Advanced EHRs	0.85	0.83-0.88	<0.0001
Age	0.99	0.985-0.987	<0.0001
Female	0.77	0.76-0.79	<0.0001
Race			
Black	1.02	0.99-1.05	0.1663
Hispanic	0.88	0.85-0.91	<0.0001
Other/unknown	0.78	0.76-0.81	<0.0001
White (ref)	ref	---	---
Risk mortality	1.06	1.04-1.08	<0.0001
Risk severity	1.92	1.88-1.95	<0.0001
Neonatal or maternal admit	0.07	0.06-0.08	<0.0001
Teaching hospital	0.89	0.86-0.91	<0.0001
Hospital bed size			
Medium	0.97	0.93-1.01	0.1514
Large	0.87	0.83-0.91	<0.0001
Small	Ref	--	--
Urban vs. Rural location	0.95	0.91-1.00	0.0302
Insurance			
Medicaid	1.34	1.29-1.38	<0.0001
Medicare	1.38	1.35-1.42	<0.0001
Other insurance/self-pay/no charge	1.41	1.36-1.47	<0.0001
Private	ref	--	--
Geographic Region			
Midwest	0.71	0.68-0.75	<0.0001
Northeast	0.61	0.58-0.64	
South	0.92	0.90-0.95	
West	ref	--	--
Transferred into hospital	1.25	1.21-1.29	<0.0001
Case Mix	1.04	1.04-1.05	<0.0001
Propensity strata	1.02	1.00-1.04	0.1187
Number of RN FTEs per 1000 admissions	0.92	0.92-0.93	<0.0001

*Hosmer-Lemeshow p=0.2899

Table 3: Base Estimate Propensity Strata and Matched Sample Proportions of MRSA among Hospitals with and without Advanced EHR (Logistic Regression Model)

	Base Estimate Propensity Strata (n=527,593)	Base Estimate Propensity Matched Sample (n=86,260)
Advance EHR	0.0105	0.0105
No Advanced EHR	0.0123	0.0126
Difference	-0.0018*	-0.0021*

*p<0.05

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APPENDICES

ICD-9 Codes Used in Data Analysis

HA-MRSA Coding Post-October 1st, 2008

Standalone ICD-9 Code	Code Definition
038.12	Methicillin resistant Staphylococcus aureus septicemia
041.12	Methicillin resistant Staphylococcus aureus in conditions classified elsewhere and of unspecified site
482.42	Pneumonia due to methicillin resistant Staphylococcus aureus

Historical MRSA Coding (Used for CA-MRSA Exclusion)

V02.54	Carrier or suspected carrier of MRSA
V12.04	Personal history of MRSA

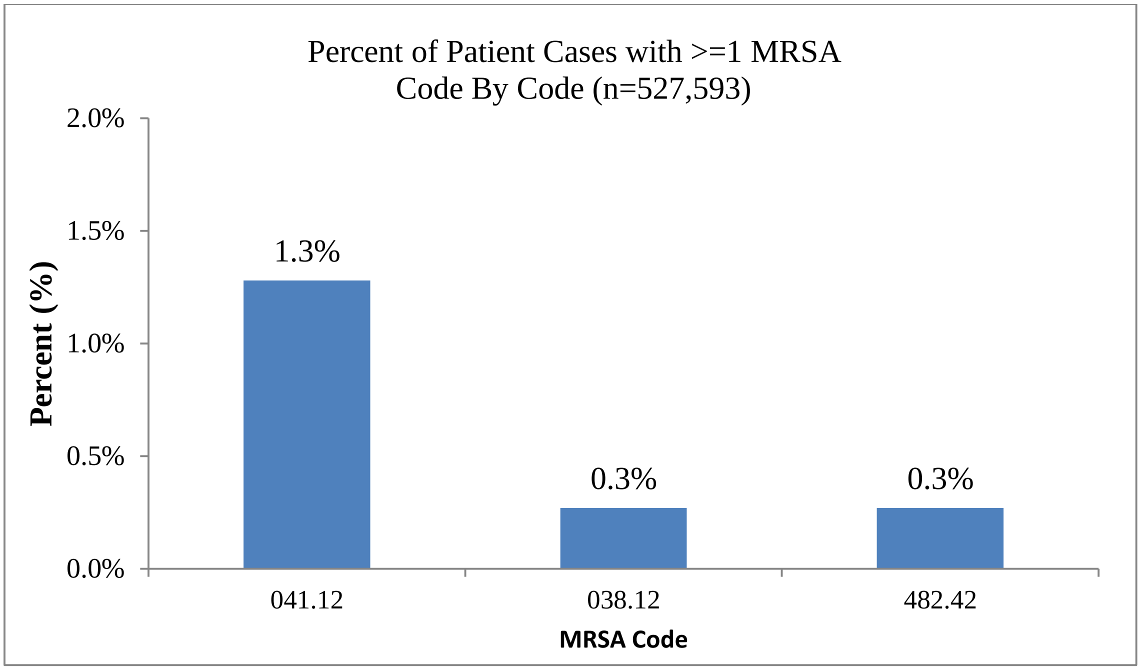
EHR Adoption Model

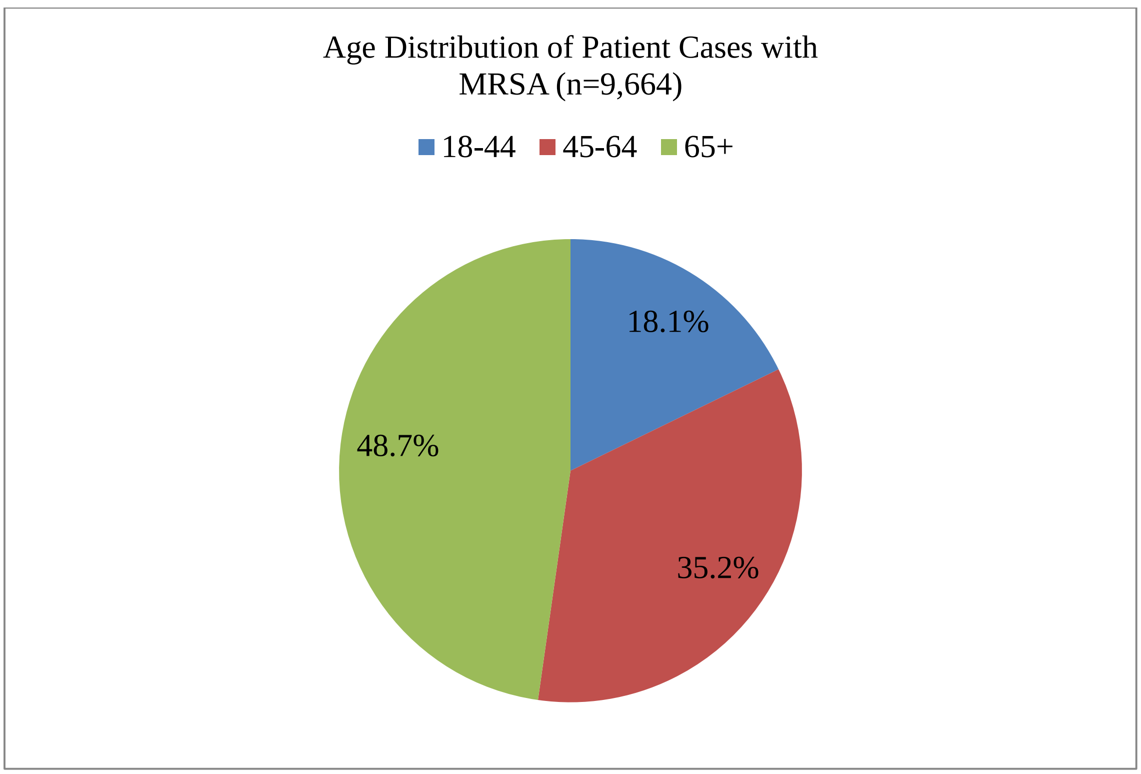
Stage	Descriptor
Stage 0	No EHR applications installed
Stage 1	EHR with ancillary services including a clinical data repository, pharmacy, laboratory, and radiology information systems
Stage 2	Stage 1 plus EHR with nursing workflow including electronic nursing documentation and medication administration records
Stage 3 (Advanced EHR)	EHR with Stage 1 and 2 components, plus CPOE and clinical decision support

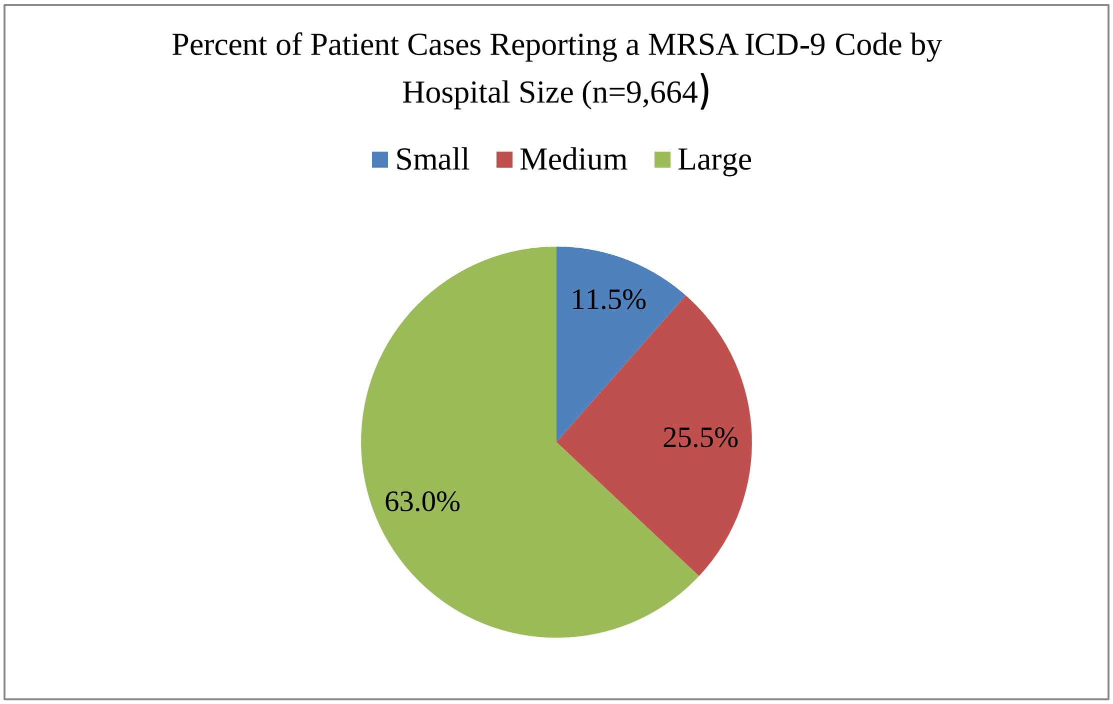
(Kazley et. al, 2014)

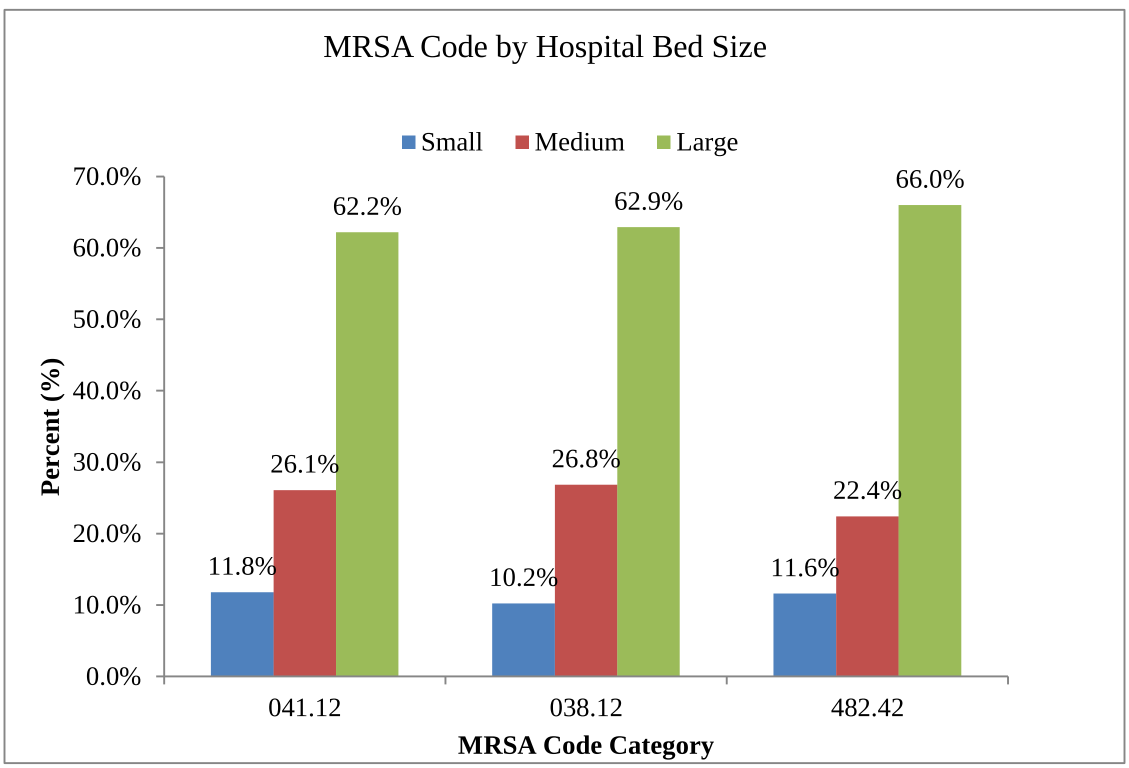
Crude Prevalence of MRSA in Non-Advanced and Advanced EHR Hospitals

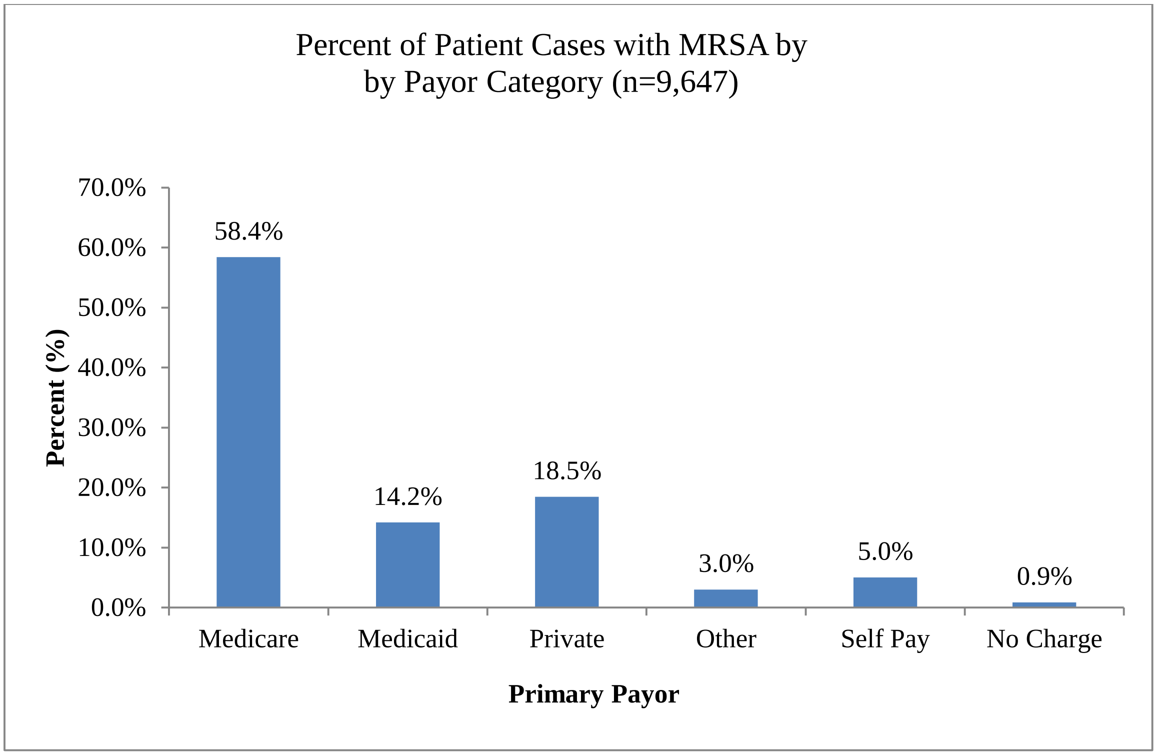
Total Number of Patient Cases with MRSA: 9,664 Crude Prevalence of MRSA: 9,664/527,593 = 1.83% Crude Prevalence of MRSA by 1000 patient cases: Approximately 18 per 1000 patient cases
Total Number Patient Cases with MRSA among non-advanced EHR hospitals: 7,454 Crude Prevalence of MRSA among non-advanced EHR hospitals: 7,454/379,637 = 1.96% Crude Prevalence of MRSA among non-advanced EHR hospital per 1000 patient cases: Approximately 20 per 1000 patient cases
Total Number Patient Cases with MRSA among advanced EHR hospitals: 2,210 Crude Prevalence of MRSA among advanced EHR hospitals: 2,210/147,956 = 1.49% Crude Prevalence of MRSA among advanced EHR hospital per 1000 patient cases: Approximately 15 per 1000 patient cases
Crude difference between cases in non-advanced and advanced EHR hospitals was statistically significant (1.96% vs. 1.49%, $p<0.0001$)

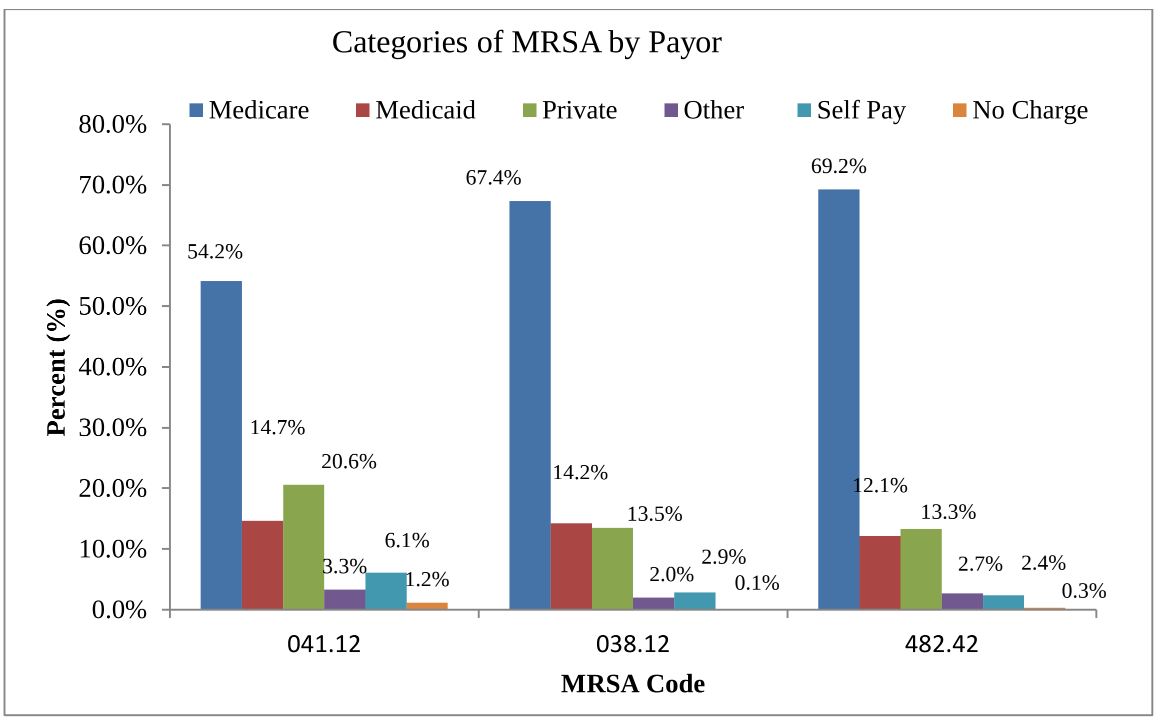

Percent of Patient Cases with >=1 MRSA Code By Code (n=527,593)
Percent (%)
2.0%
1.5%
1.0%
0.5%
0.0%
1.3%
0.3%
0.3%
041.12
038.12
482.42
MRSA Code

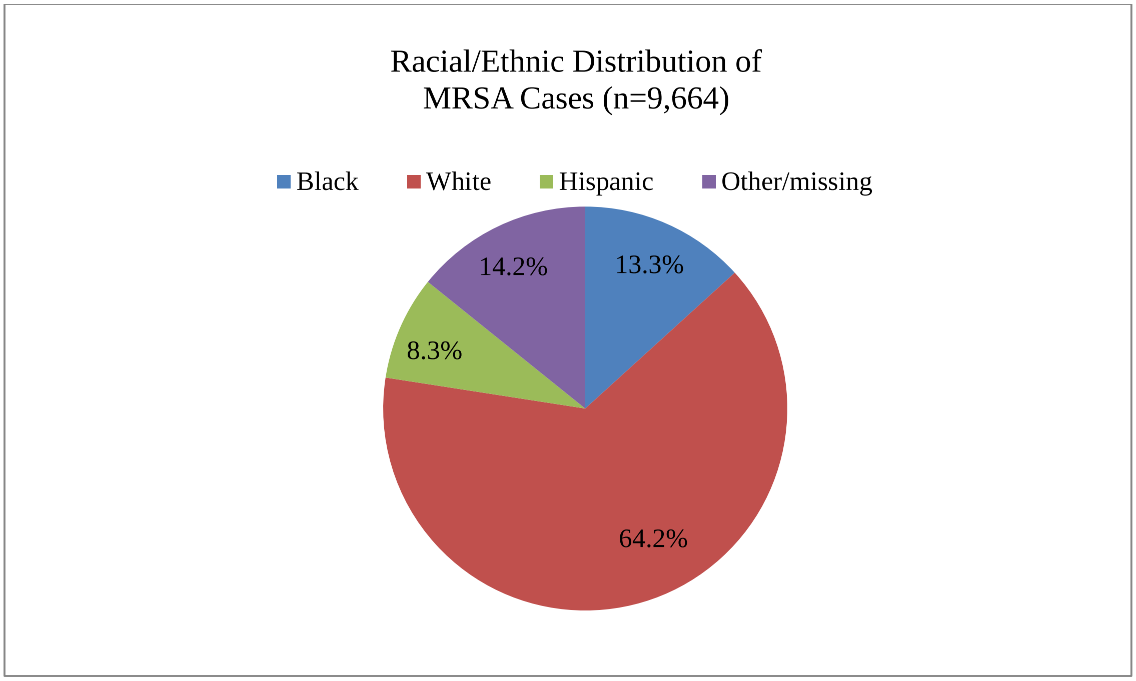

Age Distribution of Patient Cases with MRSA (n=9,664)
18-44
45-64
65+
18.1%
35.2%
48.7%

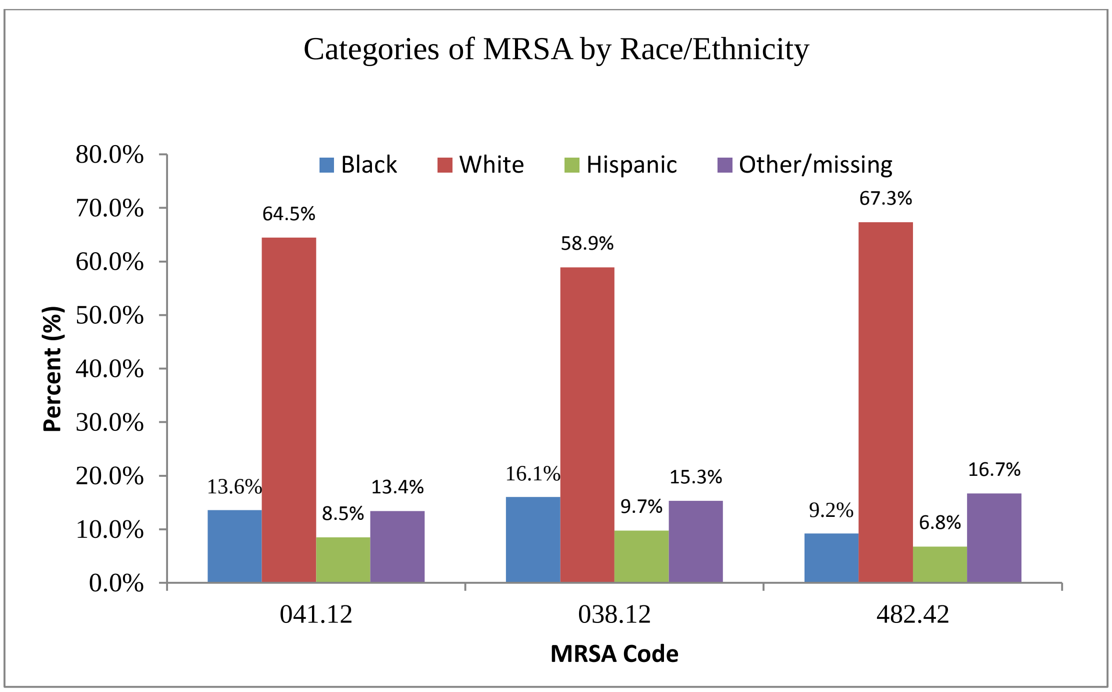

Percent of Patient Cases Reporting a MRSA ICD-9 Code by Hospital Size (n=9,664)
Small
Medium
Large
11.5%
25.5%
63.0%

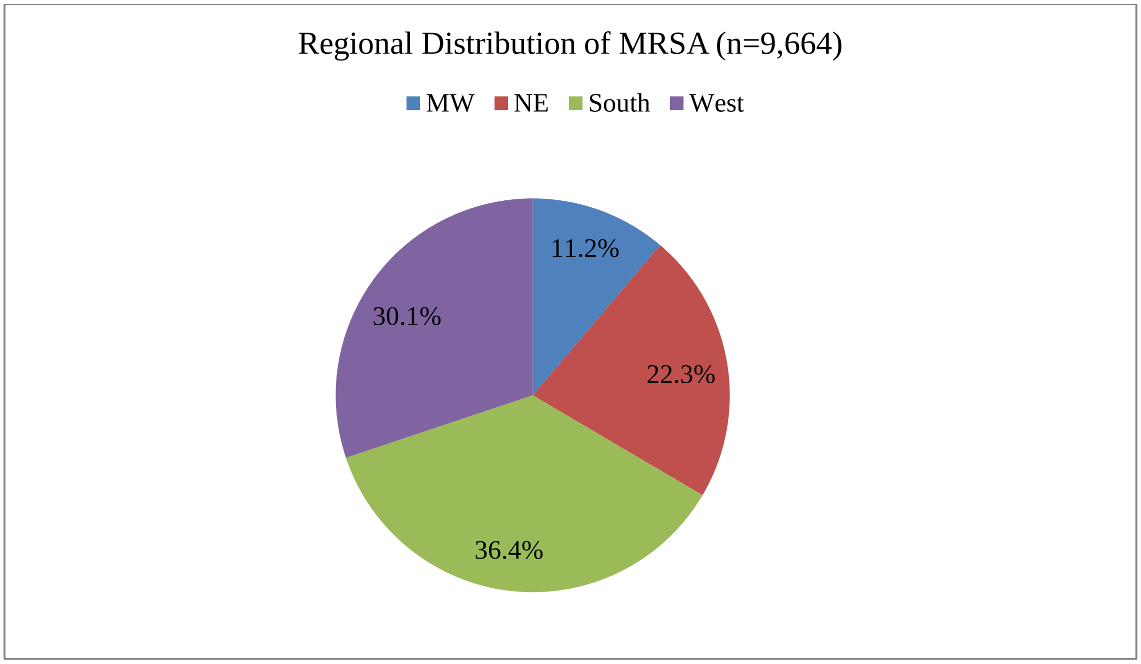

MRSA Code by Hospital Bed Size
Small
Medium
Large
Percent (%)
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
11.8%
26.1%
62.2%
10.2%
26.8%
62.9%
11.6%
22.4%
66.0%
041.12
038.12
482.42
MRSA Code Category


Percent of Patient Cases with MRSA by
by Payor Category (n=9,647)
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
Percent (%)
58.4%
14.2%
18.5%
3.0%
5.0%
0.9%
Medicare
Medicaid
Private
Other
Self Pay
No Charge
Primary Payor

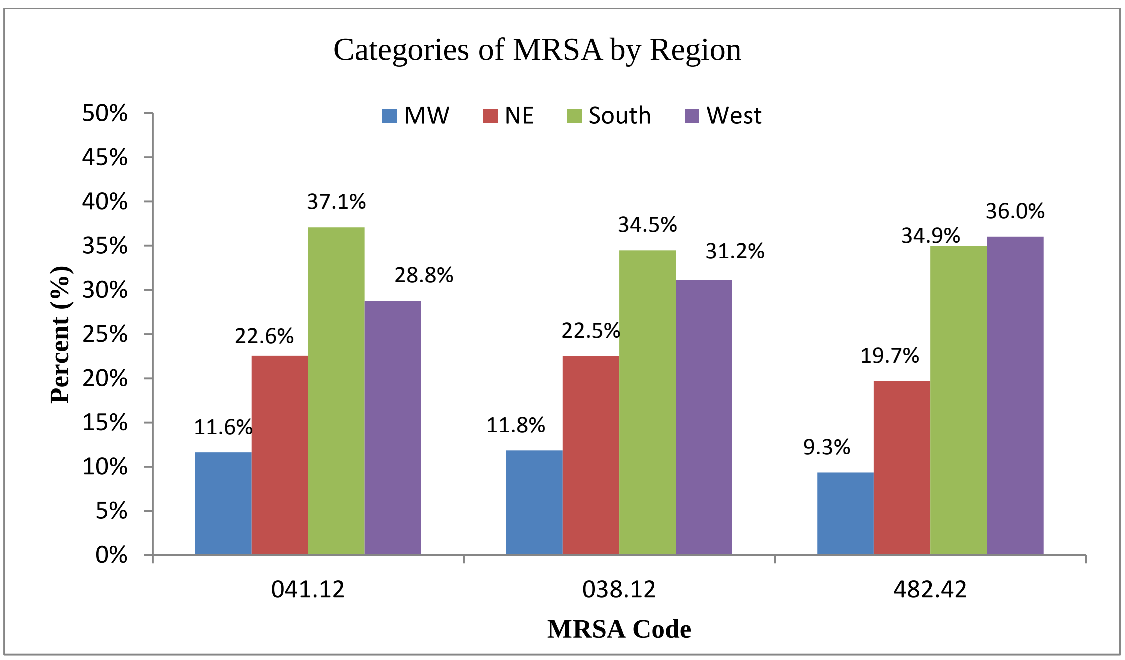

Categories of MRSA by Payor
Medicare
Medicaid
Private
Other
Self Pay
No Charge
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
Percent (%)
54.2%
14.7%
20.6%
3.3%
6.1%
1.2%
67.4%
14.2%
13.5%
2.0%
2.9%
0.1%
69.2%
12.1%
13.3%
2.7%
2.4%
0.3%
041.12
038.12
482.42
MRSA Code


Racial/Ethnic Distribution of
MRSA Cases (n=9,664)
Black
White
Hispanic
Other/missing
13.3%
64.2%
8.3%
14.2%

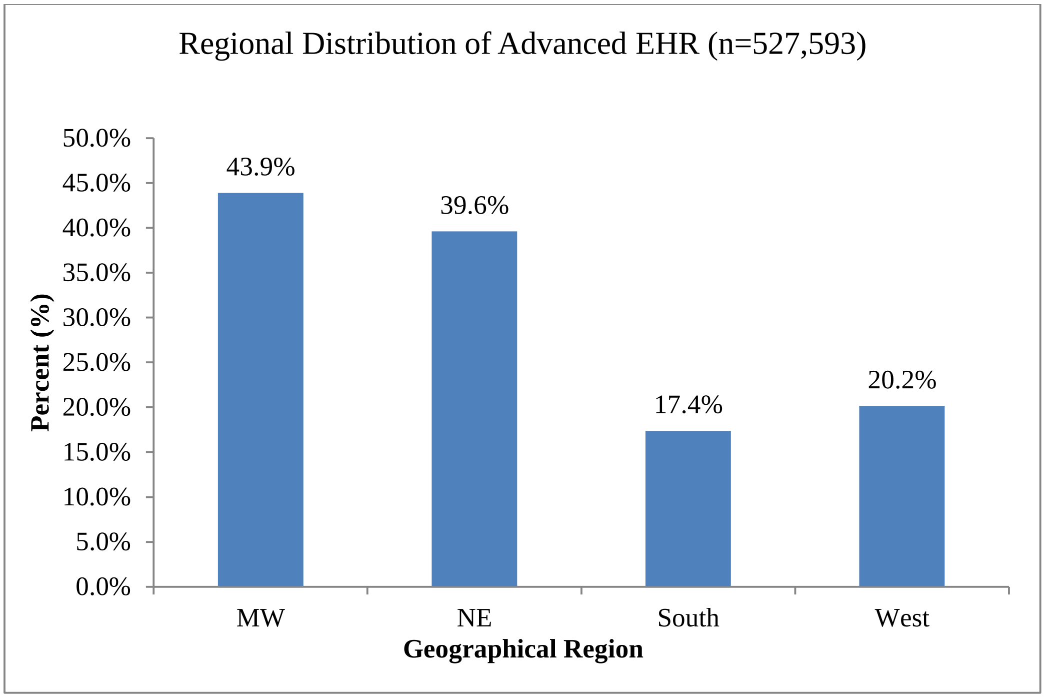

Categories of MRSA by Race/Ethnicity
Black
White
Hispanic
Other/missing
Percent (%)
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
13.6%
64.5%
8.5%
13.4%
16.1%
58.9%
9.7%
15.3%
9.2%
67.3%
6.8%
16.7%
041.12
038.12
482.42
MRSA Code



Regional Distribution of MRSA (n=9,664)
MW
NE
South
West
11.2%
22.3%
36.4%
30.1%



Categories of MRSA by Region
MW
NE
South
West
Percent (%)
50%
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
11.6%
22.6%
37.1%
28.8%
11.8%
22.5%
34.5%
31.2%
9.3%
19.7%
34.9%
36.0%
041.12
038.12
482.42
MRSA Code



Regional Distribution of Advanced EHR (n=527,593)
50.0%
45.0%
40.0%
35.0%
30.0%
25.0%
20.0%
15.0%
10.0%
5.0%
0.0%
Percent (%)
43.9%
39.6%
17.4%
20.2%
MW
NE
South
West
Geographical Region