COST-EFFECTIVE SOLUTIONS TO HEALTHCARE-ASSOCIATED INFECTION
PREVENTION AT THE HOSPITAL AND NATIONAL LEVEL

by

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ABSTRACT

Statement of the Problem: Healthcare-associated infections (HAIs) are a leading preventable cause of death in the United States. Despite being preventable, these infections negatively affect one out of every 25 hospitalized patients and are associated with an economic burden of more than $40 billion each year. To combat these infections, hospitals are implementing prevention strategies including isolation and decolonization of patients. At the national level, federal funds have been provided to state health departments to support their efforts in preventing HAIs. These efforts are commendable, but before widespread implementation, it is important to understand if the implementation costs are justified by improved health outcomes.

Objective: The first objective of this dissertation was to determine if HAI surveillance and prevention strategies are a good use of resources and to recommend the most efficient practice to hospitals. Additionally, the health and economic impact of a national policy to fund state HAI prevention efforts was evaluated.

Approach: Decision analyses using cohort and patient-level models were used to evaluate the hospital surveillance and prevention strategies. A difference-in-differences study design was used to evaluate the reduction in HAIs due to the national policy. Infections averted were then monetized to determine the return on investment.
Results: Rapid screening tests reduce inappropriate costs for surveillance practices, with polymerase chain reaction reducing total costs for facilities that implement universal preemptive isolation and chromogenic agar 24-hour reducing total costs for facilities that implement targeted isolation. Decolonization prevention strategies dominate the current standard of care in intensive care units, screening and isolation, for all screening tests. When comparing universal decolonization to targeted decolonization, universal decolonization remains cost-effective, with cost-effectiveness increasing as the cost of the screening test increases. At the national level, providing public health funding for HAI prevention reduced bloodstream infections by 34% and was associated with a positive return of $5.88 for every $1 invested.

Conclusions and Significance: Rapid screening tests and decolonization prevention strategies are an efficient use of resources and are often cost saving when implemented. Providing funding to state health departments is also a good way to improve health and reduce costs.

The form and content of this abstract are approved. I recommend its publication.

Approved: Adam J. Atherly
DEDICATION

This dissertation is dedicated to my husband, Nick, who made me realize I can positively impact health through research and continues to remind me of the impact of my work. You have consistently been a source of encouragement and support, but most importantly, you make me excited for what I do and enthusiastic for our future. My deepest love and appreciation for the sacrifices you made during this graduate program. I am blessed to have you in my life.

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CHAPTER I
INTRODUCTION

Introduction

Healthcare-associated infections (HAIs) are infections patients contract while receiving medical care for an unrelated condition\(^1\) and become clinically evident at least 48 hours post-admission.\(^2\) These infections continue to be the most common complication associated with hospital care\(^3\) and are one of the leading causes of preventable death in the United States.\(^4\) At the patient level, HAIs lengthen hospital stays, increase resistance to antimicrobials, create long-term disability, and result in preventable death.\(^5\) At the economic level, these infections substantially increase health care costs and result in a financial burden of more than $40 billion annually.\(^6\) The goal of this dissertation was to provide evidence for efficient practices in HAI prevention at the hospital and national level to improve patient and economic outcomes.

To combat these infections, hospitals are implementing a variety of prevention strategies including isolation and decolonization of patients.\(^7\) At the national level, the federal government has provided funding to state health departments to support their efforts in preventing HAIs as part of the Prevention and Public Health Fund.\(^8\) These efforts are commendable, but before widespread and increased implementation, it is important to understand the impact these actions have on both cost and outcomes. The cost-effectiveness of most HAI prevention strategies is still unknown, as is the effectiveness of state-level funding in improving clinical outcomes at the hospital level. This dissertation fills these gaps in the literature and informs decision makers, both at the hospital and national level, on efficient practices in HAI prevention.
Background to the Problem

HAIs are one of the top ten preventable causes of death in the United States. These infections, acquired by an individual receiving medical care, occur when colonizing bacteria on the individual overcomes the body’s immune system. Despite being preventable, these infections negatively affect one out of every 25 hospitalized patients and are associated with an economic burden of more than $40 billion each year. For hospitalized patients, HAIs more than double a patient’s risk for morbidity and mortality and are associated with more than 20,000 deaths annually. Symptoms associated with HAIs vary by type, but can include inflammation, discharge, fever, abscesses, pain, and irritation. The most frequently occurring HAIs include central line-associated bloodstream infections (CLABSI), catheter-associated urinary tract infections (CAUTI), surgical site infections (SSI), and ventilator-associated pneumonias (VAP).

The majority of HAIs are caused by bacteria that colonized a patient before infection. Staphylococcus aureus, a bacterium found in 30% of individuals, commonly on the skin or in the nose, is a common cause of HAIs. Methicillin-resistant Staphylococcus aureus (MRSA) is a form of Staphylococcus aureus resistant to beta-lactam antibiotics, including methicillin. MRSA is of particular concern due to its multi-drug resistance, virulence, and disease spectrum. These infections can be transmitted in the healthcare setting through contact, either direct or indirect, with an infected individual or asymptomatic carrier. Symptoms commonly associated with an MRSA infection include: rash, headaches, chills, fever, shortness of breath, malaise, and chest pains. Severe problems, such as pneumonia, urinary tract infections, bloodstream infections, and bone infections can also result from an MRSA infection. Besides being detrimental to an individual’s health, these
infections are very costly. A MRSA infection nearly doubles the cost of a hospitalization, largely due to the increase in the length of stay that results from the infection. The average length of stay for a patient infected with MRSA (10 days) is double the mean length of stay for a patient without MRSA (5 days).

Patients in the intensive care unit (ICU) are at the greatest risk of contracting these infections because severe illness, immunosuppression, and length of stay are the most common patient-related risk factors associated with HAIs. In fact, more than 20% of patients admitted to the ICU will contract an HAI. The majority of HAIs that occur within the ICU (60%) are caused by bacteria that colonized the patient before he/she was admitted. Many fewer infections are due to a bacterium a patient acquired while in the ICU.

To mitigate these infections, ICUs conduct MRSA surveillance to detect and isolate the pathogen in the environment. Two common surveillance practices in the ICU are universal preemptive isolation and targeted isolation of only MRSA-positive patients. Under the universal preemptive isolation surveillance practice, all patients are screened upon admission and are immediately isolated until the absence of MRSA carriage has been shown. Preemptively isolating all patients is effective in reducing the transmission of MRSA; however, noncolonized patients are unnecessarily isolated, leading to unnecessary resource use (contact precautions, disinfectant, etc.) and thus excess cost. With targeted isolation, ICUs wait to isolate the patients until the screening test results come back and then only isolate those who test positive for MRSA. This targeted surveillance practice reduces the number of patients unnecessarily isolated, but delays the initiation of isolation for colonized individuals, potentially increasing the transmission of MRSA. These surveillance practices differ in when isolation precautions are implemented, but both include universal
screening upon admission to the ICU. Hospitals pay for the implementation of these surveillance practices with little evidence on the cost of each practice and the screening test that can minimize total costs.

Despite these surveillance practices, MRSA infections persist at high levels resulting in the implementation of novel techniques, such as decolonization, to mitigate the nosocomial transmission of MRSA. Prevention strategies are most common at the hospital level, but due to the importance of combating these infections, changes in policy are occurring at the national level as well.

At the hospital level, decolonization of patients has become an increasingly common prevention strategy. Decolonization consists of twice daily intranasal mupirocin ointment for five days and daily bathing with chlorhexidine-impregnated cloths for the entire length of stay. With targeted decolonization, all patients admitted are first screened for MRSA and those that test positive are decolonized. Conversely, no screening test is used with universal decolonization; instead, every patient is decolonized upon admission. Decolonization eliminates the colonization of MRSA, as well as other microbiota, on individuals’ skin and in their nose. Thus, decolonization should protect MRSA carriers and reduce the transmission of harmful bacteria to others. A randomized controlled trial found universal decolonization to be the most effective strategy in preventing MRSA infections, by reducing infection rates 37%. However, the cost-effectiveness of this prevention strategy is still unknown and research is needed to determine if the health improvements justify the implementation costs.

At the national level, the government and the Centers for Disease Control and Prevention (CDC) have dedicated funds to invest in HAI prevention. Section 4002 of the Patient Protection and Affordable Care Act created the Prevention and Public Health Fund
with the intent to improve the nation’s health and restrain the ever increasing health care costs.\textsuperscript{20} Initially, legislation allocated $15 billion to this fund over its first ten years with the intent to expand and sustain prevention and public health programs.\textsuperscript{8} Fiscal year 2010 marked the first year of funding allocation in the amount of $500 million.\textsuperscript{21} This money was allocated to states and local communities to support and expand their prevention and public health efforts to improve population health and the quality of care delivered.\textsuperscript{21} The fund increased to $750 million in 2011 and $1 billion in 2012 to enhance health department capacity, improve public health research, and increase infrastructure to track public health.\textsuperscript{21} In 2013, $1.25 billion was supposed to be appropriated to the Prevention and Public Health Fund; however, the amount was cut to $949 million due to sequestration and the Middle Class Tax Relief and Job Creation Act.\textsuperscript{21} Of this $949 million, nearly half was allocated to the CDC to aid in their disease prevention, surveillance, and tracking efforts.\textsuperscript{21} The CDC then allocated $11.75 million to state health departments to sustain and expand their HAI prevention efforts.\textsuperscript{19} Of this $11.75 million, nearly $7 million was awarded to 15 states for the Prevention of HAIs across the Spectrum of Healthcare, an activity designed to develop and implement evidence-based multi-facility prevention initiatives.\textsuperscript{19}

The Prevention and Public Health fund was set to increase to $2 billion each year in 2015 and each year thereafter; however, controversy has surrounded the effectiveness and necessity of this fund leading to legislation that cut portions of this budget and even bills that suggest elimination of this fund altogether.\textsuperscript{8} Due to this debate, it is essential to determine the effectiveness of public health spending on community health and clinical outcomes such as HAIs to provide evidence to decision makers on whether or not this fund should be cut or eliminated. Little research on the impact of this fund previously existed likely due to its
recent implementation; however, other public health research has shown that increases in public health spending are associated with improved health outcomes, such as a decrease in mortality.  

Despite implementation of MRSA surveillance and prevention strategies at the hospital and national level, evidence was lacking that showed these practices were an efficient use of resources. This dissertation fills these gaps in the literature by informing hospital decision makers and national policy makers on efficient practices in HAI surveillance and prevention to reduce the magnitude of these infections in a clinically-effective and cost-effective manner. 

**Statement of the Problem** 

In both commonly implemented surveillance practices, there is a screening component. MRSA screening has historically relied on the growth and identification of the bacterial species on culture. Culture methods are inexpensive but can take multiple days to detect MRSA.  

An increasingly common alternative is to use more rapid screening tests, such as chromogenic agars or polymerase chain reactions. Although costlier, these tests generate results in a few hours. Evidence is needed to determine if these rapid screening tests can actually reduce the overall costs of MRSA surveillance by reducing the number of isolation days, and thus the costs associated with isolation, or by reducing the number of days colonized patients are left unisolated, and thus the transmission of MRSA. 

The REDUCE MRSA trial assessed the comparative effectiveness of common MRSA prevention strategies and found universal decolonization to be the most effective strategy in preventing MRSA infections, by reducing infection rates 37%. Targeted decolonization and screening and isolation reduced infection rates by 25% and 8%, respectively. Despite this
knowledge in clinical effectiveness, little is known regarding the cost-effectiveness of these strategies. Research has started to assess the cost-effectiveness of these prevention strategies, but the strategies evaluated and populations included have been limited.\textsuperscript{26,27} More evidence is needed to inform hospital decision makers on whether or not the health improvements from these prevention strategies justify their implementation costs.

Analyzing the cost of common MRSA surveillance and prevention strategies can greatly inform hospital decision makers on efficient practices at the hospital level. However, prevention efforts have expanded beyond the hospital level to the national policy level as well. The federal government created the Prevention and Public Health Fund as part of the Patient Protection and Affordable Care Act.\textsuperscript{20} Part of this fund was allocated to the CDC who then funded state health departments in their HAI prevention efforts.\textsuperscript{19} This is an interesting funding mechanism in that money was provided to state health departments, not hospitals, with the intent to prevent infections at the hospital level. This funding mechanism needed to be evaluated to determine if public health funding can effectively reduce hospital infection rates. The return on this investment also needed to be calculated to determine if the cost savings due to infections averted offset the initial investment.

**Purpose of the Study**

The purpose of this dissertation was to calculate the cost of each MRSA surveillance practice and determine which MRSA screening test minimized total surveillance costs. Additionally, this dissertation conducted a cost-effectiveness analysis to determine which MRSA prevention strategy (screening and isolation, targeted decolonization, or universal decolonization) was most cost-effective in preventing MRSA infections. This dissertation also provides insight into the effectiveness of public health funding in preventing hospital
infections to determine if this funding mechanism generated a positive return on investment. Together, these objectives determined efficient practices in HAI prevention at the hospital and national level to better inform hospital decision makers and national policy makers.

**Specific Aims and Hypotheses**

**Aim 1**

Calculate the cost of two MRSA surveillance practices (universal preemptive isolation and targeted isolation) and recommend the MRSA screening test that minimizes costs for each surveillance practice.

**Hypothesis**

Rapid MRSA screening tests, although costlier, will reduce total costs because their added cost per test will be offset by the cost savings due to reduced isolation and transmission of MRSA.

**Approach**

A cost-minimization analysis from the hospital perspective was conducted to calculate the total cost for each surveillance practice. The screening test used as part of the surveillance practice was varied to determine which screening test minimized inappropriate and total costs. The following MRSA screening tests were assessed: conventional culture, chromogenic agar 48-hour, chromogenic agar 24-hour, and polymerase chain reaction. The screening test that minimized total costs was recommended as the most efficient screening test for each surveillance practice. The analysis was modeled using a decision tree that accounted for the diagnostic accuracy and turnaround time of the different MRSA screening tests. Clinical inputs were retrieved from published diagnostic accuracy literature and cost inputs were retrieved from published medical literature.
Rationale

Existing economic literature around MRSA surveillance has reported conflicting results. Some research has concluded that rapid screening tests reduced surveillance costs as well as unfavorable health outcomes and can be considered cost-saving. However, other research has contradicted this showing more conventional screening methods to be less costly than rapid screening tests. Due to these contradicting findings, decision makers are still left unknowing whether or not the incremental cost of rapid MRSA screening tests is offset by reductions in isolation costs and the transmission of MRSA.

Impact

Results from this aim can guide hospital decision makers on which screening test is most efficient for the surveillance practice implemented at their facility.

Aim 2

Calculate the cost-effectiveness of MRSA prevention strategies, including screening and isolation, targeted decolonization, and universal decolonization, to determine if their improvements in health outcomes justify their implementation costs.

Hypothesis

Universal decolonization will be a dominant, less costly and more effective, strategy in preventing MRSA infections as compared to the standard practice of screening and isolation.

Approach

A decision analysis from the hospital, payer, and societal perspective was conducted to determine which prevention strategy (screening and isolation, targeted decolonization, or universal decolonization) was most cost-effective in preventing MRSA infections and
improving quality-adjusted life years. The three prevention strategies were compared with one another and two different outcomes were assessed: incremental cost per MRSA infection averted and incremental cost per QALY gained. A separate analysis was conducted for each of the commonly used MRSA screening tests to determine the effect of the screening test on the overall cost-effectiveness of the prevention strategy. The primary model was a Markov model; however, a decision tree and agent-based transmission model were also modeled to determine the degree to which the results and conclusions varied by the method selected. Clinical effectiveness data was retrieved from the REDUCE MRSA trial, and cost data was taken from published medical literature.

Rationale

Comparative effectiveness data from the REDUCE MRSA trial found universal decolonization to be the most effective MRSA prevention strategy. After the publication of the REDUCE MRSA trial, the CDC and the Agency for Healthcare Research and Quality published protocols for universal decolonization implementation in ICUs.\textsuperscript{29} It is important to determine if the incremental effect of universal decolonization over other prevention strategies justifies the implementation costs to ensure hospitals are allocating their limited resources efficiently. Additionally, existing economic literature has failed to incorporate the variation in the cost and diagnostic accuracy of MRSA screening tests into the evaluation, and thus this aim explored this relationship to provide hospitals with tailored recommendations based on the screening test they use.

Impact

Results from this aim can guide hospital decision makers on which MRSA prevention strategy is most cost-effective for the screening test used at their facility.
Aim 3

Measure the impact of a Prevention and Public Health Fund activity (The Prevention of HAIs across the Spectrum of Health Care) on hospital-associated bloodstream infection rates to determine if public health funding can be effective in preventing infections at the hospital level and whether or not there was a positive return associated with the investment.

Hypothesis

Hospitals in states that received state health department funding for the Prevention of HAIs across the Spectrum of Health Care will have greater reductions in the standardized infection ratios for bloodstream infections than hospitals in states that did not receive funding.

Approach

A quasi-experimental design using a difference-in-differences model was designed to quantify the treatment effect of the funding. Regression to the mean was assessed to account for the potential for extreme measurements to be more near the mean upon repeated reporting. The dependent variable (CLABSI standardized infection ratio) was log transformed to better fit the data and adjust for the positive skew in the data. CLABSI standardized infection ratios were retrieved from the Centers for Medicare and Medicaid Services (CMS) Hospital Compare data. Control variables, including hospital type, ownership, teaching status, service offering, bed count, and staffing counts, were retrieved from CMS Hospital Compare and CMS Provider of Services data. A panel dataset was created for two years before funding allocation (2011 and 2012), the year the funding was allocated (2013), and one year after the funding was allocated (2014). The reductions in CLABSI were monetized to calculate the return on investment.
Rationale

Since the creation of the Prevention and Public Health Fund, controversy has surrounded its effectiveness and necessity. In 2012, President Barack Obama signed legislation that cut the fund by $5 billion over a ten year period. This fund was also targeted for complete elimination in the United States House of Representatives’ 2016 Budget Resolution as well as in other bills being considered in the House of Representatives. There is an urgent need for research around the effectiveness of this funding mechanism to determine if it is an effective approach to reduce these infections before this funding is further cut or eliminated altogether. This study evaluated the impact of this public health funding on hospital HAI rates to determine if these infections were reduced to a point that generated a positive return on investment.

Impact

The results from this aim can inform policy makers on the impact and return on investment of public health funding on health outcomes, specifically HAI rates.

Significance of the Study

This research provides hospital decision makers and national policy makers with efficient practices for HAI detection and prevention at the hospital and national level. The contributions of this research are significant as the results can inform hospital decision makers of the most efficient MRSA screening tests and prevention strategies for their facility based on the practices they implement and capacity they have. From this research, hospitals will now know if the incremental cost of one strategy over another is justified by a comparable incremental effect. This allows them to use their limited resources in the most beneficial way. By highlighting the cost-effectiveness of certain prevention strategies,
hospitals will hopefully see the feasibility of implementation, making this research pivotal in improving the quality of healthcare by increasing the use of prevention strategies and thus reducing HAIs. This research is timely because CMS started reducing hospital payments by 1% for all hospitals that rank among the lowest-performing 25% of hospitals for certain hospital-acquired conditions in 2015 as part of their Hospital-Acquired Conditions Reduction Program.\textsuperscript{32} MRSA rates will be included in this ranking starting in fiscal year 2017. This research thus provides hospital decision makers with knowledge on how to reduce their facility MRSA rate in the most efficient manner and thus reduce the likelihood of having their reimbursement reduced.

On top of interventions at the hospital level, the federal government began dedicating funds to the prevention of HAIs as part of the Prevention and Public Health Fund.\textsuperscript{19} Little research on the impact of this public health funding on clinical outcomes has occurred; however, other public health research has shown that increases in public health spending can be associated with improved health outcomes.\textsuperscript{22} This study contributes to this literature by evaluating if public health spending is an effective mechanism to reduce hospital infections and is associated with a positive return on investment. This research has the potential to drive national policy change in public health funding by showcasing the impact of these funds on health outcomes, specifically HAI rates. The need for this evaluative research was urgent as there have been recent cuts to the Prevention and Public Health Fund and legislation has suggested elimination of this fund altogether.

**Theoretical Framework**

The theory of extra-welfarism provided a framework in conducting the economic evaluations to achieve Aims 1 and 2 of this dissertation. Extra-welfarists believe that health
is maximized when treatments that are most efficient are implemented. These treatments are considered efficient if their incremental cost-effectiveness ratio is below an established threshold. In extra-welfarism, this threshold is often established by policy makers and is for the society as a whole; not necessarily an individual’s willingness to pay as this threshold likely varies from person-to-person. Unlike welfarism, extra-welfarism analyzes and weighs the costs and benefits to the society, not the individual. The primary objective is to enhance the well-being of society.

Extra-welfarism is unique in that it acknowledges that stakeholders outside of the immediately affected group may be impacted by an action. Additionally, extra-welfarism is a more pragmatic framework as the outcomes of interest can vary based on the problem on hand. Potential outcomes can extend beyond utility measures and into health measures; in this case health is the maximand. When outcomes are restricted to utility weights, like in welfarism, it becomes challenging to discern whether or not an unhealthy person has less utility than a healthy person. However, if health is used as the outcome, we are able to discern that an unhealthy person has less health than a healthy person. Furthermore, when the goal is to monitor policies designed to improve health, having a directly related health outcome more closely monitors and evaluates the impact of these policies. Extra-welfarism acknowledges that health likely leads to utility, but is able to measure the effects of an action on a specific health state. Lastly, extra-welfarism differs from a welfarist approach in how an outcome can be valued. The welfarist approach requires the benefits related to an action outweigh the costs with both expressed in monetary terms. The extra-welfarist approach broadens the evaluative space in that it allows for the benefits to be uncompensated in the form of social improvements.
This study determined which prevention strategy was most cost-effective by comparing each incremental cost-effectiveness ratio to a threshold. The perspective taken was that of an entire ICU, not an individual, because benefits that stem from prevention strategies such as decolonization go beyond the individual in preventing the transmission of these harmful infections to other patients. Hospital rates, not individual cases, were assessed in this study. The outcomes evaluated in this dissertation were health measures directly related to the screening test or prevention strategy, including the number of MRSA infections averted, the number of inappropriate isolation days, and the number of inappropriate open days. The goal of Aims 1 and 2 was to maximize health and resource use by determining the screening test that reduced total surveillance costs and the prevention strategy that produced the smallest incremental cost-effectiveness ratio.

Additionally, the consequentialism philosophy provided a framework for Aim 3. With consequentialism, an action is considered right if the consequences are more favorable than unfavorable. This is determined by tallying up the good and bad consequences and then determining if the good consequences outweigh the bad. If the good outweigh the bad, the action is right; if the good do not outweigh the bad, the action is wrong. There are subdivisions of consequentialism that determine which consequences, and to whom, should be considered. One subdivision, utilitarianism, believes an action is right if the consequences are more favorable than unfavorable to everyone, not just the person(s) performing the action.

Using the consequentialist philosophy, this study analyzed the consequences of a Prevention and Public Health Fund activity awarded to 15 state health departments in 2013. This funding was evaluated under the framework that good consequences should outweigh
bad consequences. The primary consequences of interest were the monetary investment and the occurrence of hospital bloodstream infections. If the good consequences, reductions in bloodstream infections, outweighed the bad consequences, monetary investment, the funding mechanism was deemed right or effective. To weigh these consequences, the reductions in bloodstream infections were monetized to determine if the cost savings due to infections averted outweighed the initial investment. If a positive return on investment resulted, the funding mechanism was deemed effective and efficient. Taking a utilitarian approach, the consequences to every state involved were considered, not just the consequences experienced by the 15 states who received the funding.

**Assumptions and Limitations**

**Assumptions**

The following assumptions were made for the hospital evaluations (Aims 1 and 2):

- The clinical efficacy for all interventions was the same as observed in clinical trials.
- The diagnostic accuracy of the screening tests was the same as observed in diagnostic accuracy tests.
- The only screening site was the nose.
- There was 100% adherence to each intervention.
- There was continuous application of each intervention, regardless of clinical outcomes, for the entire duration of the hospitalization.
- Hospitals were willing to pay $100,000 per QALY gained.
- In the Markov model, patients could not move backwards. In other words, due to the short time horizon and long typical length of colonization and infection, patients could not improve their health status.
The following assumptions were made for the public health evaluation (Aim 3):

- All data retrieved from secondary sources was accurate and all-encompassing.

**Limitations**

This analysis was bounded by the following limitations:

- **Aim 1** does not compare surveillance practices (universal preemptive isolation versus targeted isolation).

- **The generalizability of Aim 2** was limited to patients in adult ICUs of Hospital Corporation of America (HCA) hospitals due to the sample used in the effectiveness data source.

- **The effectiveness inputs for Aim 2** came from a single randomized controlled trial and it is possible the effectiveness could vary beyond what was observed in this single study due to differences in compliance and adherence to the prevention strategy practices.

- **Potential adverse outcomes** due to decolonization such as rash and increased resistance to antimicrobials were not accounted for in the Aim 2 models due to lack of evidence.

- **Other potential health advantages** (horizontal effects) to decolonization besides a reduction in MRSA infections, such as a reduction in other HAIs, were not included in the Aim 2 models.

- **The decision tree analysis** in Aim 2 did not account for the increased risk of contracting HAIs as length of stay increases.
• Aim 3 only evaluated one type of HAI and thus the estimates may underestimate the impact of the Prevention and Public Health Fund by not considering other infections that could have been reduced.

• The return on investment calculated in Aim 3 is likely a conservative estimate as the only cost offset considered was the cost of a CLABSI to hospitals.

• It was unknown which hospitals were targeted by public health departments in Aim 3 and what type of prevention strategies were implemented.

**Delimitations**

The delimitations of the study include:

• Clinical effectiveness data around MRSA prevention strategies only included adult ICUs in HCA hospitals.

• Facilities included in the funding evaluation only included those that accept Medicare or Medicaid since the HAI rates for these facilities were publicly reported through CMS’ Hospital Compare data.

**Definition of Terms**

The following definitions are provided to ensure uniformity and understanding of these terms throughout the study. The researcher developed all definitions not accompanied by a citation.

*Abscess:* when pus accumulates in a part of the body and is surrounded by swelling

*Antibiotic stewardship:* program that endorses the appropriate use of antibiotics in order to reduce resistance and decrease the spread of resistant organisms

*Antibiotic resistance:* the incidence of not being affected by something, in this case when a bacterium is not affected by an antibiotic
**Antimicrobials:** a drug or some other substance that destroys or slows the growth of bacteria, fungi, or viruses\(^{40}\)

**Asymptomatic:** when an individual either has recovered from an infection and no longer displays symptoms or when an individual has an infection but does not display symptoms\(^{38}\)

**Bacteria:** free-living or parasitic organisms that can infect an individual and cause disease\(^{40}\)

**Beta-lactam antibiotics:** some of the most commonly prescribed drugs that have a beta-lactam ring in their structure including penicillins, cephalosporins, cephamycins, carbapenems, monobactams, and beta-lactamase inhibitors\(^{41}\)

**Bilateral screening (of nares):** both nostrils of the nose are swabbed and tested for the presence of bacteria, fungi, or virus\(^{40}\)

**Carrier:** a person that has contracted an infectious disease but is asymptomatic and can thus transmit the infection to others\(^{42}\)

**Catheter-associated urinary tract infection:** an infection in the urinary tract likely due to an indwelling catheter\(^{38}\)

**CAUTI:** abbreviation for catheter-associated urinary tract infection

**Centers for Medicare and Medicaid Services:** a federal agency that administers Medicare, Medicaid, and the State Children’s Health Insurance Program\(^{43}\)

**Central line-associated bloodstream infections:** an infection in the blood likely due to a catheter that goes into a vein\(^{38}\)

**Chlorhexidine:** an antibacterial that targets gram-negative and gram-positive organisms\(^{42}\)
Chromogenic agar: a medium to identify and differentiate gram-positive and gram-negative isolates from specimens

CLABSI: abbreviation for catheter-associated bloodstream infection

CMS: abbreviation for the Centers for Medicare and Medicaid Services

Colonization: when bacteria is present on an individual but the person does not have the disease

Colonizing bacteria: see colonization

Comparative effectiveness: research that compares the outcomes, including the risks and benefits, of at least two different treatments in order to determine which one is most effective

Consequentialism: the philosophy that the value of something is entirely based on the value of the consequences it produces

Contact precautions: protective equipment, such as gloves, makes, goggles, aprons, shoe covers, and aprons to prevent transmission and exposure to pathogens

Conventional agar: a medium to identify and differentiate gram-positive and gram-negative isolates from specimens

Cost-consequence analysis: a type of economic evaluation that presents the benefits in multiple different outcomes instead of presenting the costs and benefits in the same units; unlike other economic evaluations, the results are not presented in one summary measure

Cost-effectiveness analysis: a type of economic evaluation that compares two treatment options based on the costs (expressed in monetary terms) and the benefits (expressed in a health outcome measure)

Culture: a lab test to check for the presence of a bacteria, fungi, or virus
Decolonization: a strategy to reduce the transmission of *Staphylococcus aureus* and protect carriers using a regimen of twice daily nasal mupirocin for five days and daily baths with chlorhexidine-impregnated wipes\(^7\)

Diagnostic accuracy: how correct a screening test is at identifying a certain condition or pathogen often determined from the sensitivity and specificity of the test\(^{48}\)

Difference-in-differences: a method used in econometrics to evaluate the changes in health outcomes before and after the implementation of a treatment or policy\(^{49}\)

Dominant: a strategy that is both less costly and more effective than the comparator\(^{47}\)

Extra-welfarism: a theoretical framework that judges actions on the health that is attained by an individual\(^{34}\)

GeneOhm MRSA PCR: a screening test using PCR technology that rapidly identifies patients colonized with MRSA with results in less than 18 hours\(^{50}\)

Generalizability: the extent to which the research applies to individuals beyond those included in the study\(^{42}\)

HAIs: abbreviation for healthcare-associated infections

HCA: abbreviation for Healthcare Corporation of America hospitals

Healthcare-associated infections: infections that become clinically evident 48 hours post-admission that patients contract while receiving medical care for an unrelated condition\(^2\)

Inappropriate open days: days MRSA positive patients are not isolated and could thus easily transmit MRSA to their environment\(^{51}\)

ICU: abbreviation for intensive care unit

Immunosuppression: when the immune system has a reduced ability to fight infection\(^{40}\)
**Intensive care unit:** unit within the hospital that is dedicated to providing care to those patients who have the most severe illness\(^{40}\)

**Isolation:** precautions that help prevent the spread of germs by creating barriers between germs and people\(^{38}\)

**Malaise:** an overall feeling of tiredness, discomfort, or illness\(^{38}\)

**Markov model:** a model that describes a sequence of events with probabilities that are assigned to the transition from state-to-state; these models are best used with chronic diseases when an individual can progress and digress\(^{47}\)

**Maximand:** something that is to be maximized\(^{42}\)

**Methicillin-resistant Staphylococcus aureus:** a type of *Staphylococcus aureus* bacteria resistant to beta-lactam antibiotics such as Methicillin known for causing skin infections\(^{40}\)

**Morbidity:** related to disease or illness\(^{40}\)

**Mortality:** related to death\(^ {40}\)

**MRSA:** abbreviation for Methicillin-resistant *Staphylococcus aureus*

**Mupirocin:** an antibiotic ointment often applied inside the nostril to treat skin infections\(^{40}\)

**Nosocomial:** originating in a hospital\(^ {40}\)

**Pathogen:** an agent that causes a disease\(^ {40}\)

**Patient Protection and Affordable Care Act:** the health reform law often referred to as ObamaCare that provides US residents with health security as it expands coverage, lowers health care costs, improves the quality of care delivered, and enhances accountability of health insurance companies\(^ {20}\)
PCR: abbreviation for polymerase chain reaction

Pragmatic: in a realistic or practical manner

Preemptive Isolation: when all patients are isolated upon admission until absence of MRSA is confirmed through a negative screening test or discharge

Prevention and Public Health Fund: Section 4002 of the Affordable Care Act that is intended to invest in public health and disease prevention and to improve health care and reduce health care costs in the United States

Polymerase chain reaction: a method to analyze and reproduce a segment of DNA or RNA; highly efficient as results can be generated in a few hours

Quasi-experimental design: a pre-post intervention study design that does not include randomization

REDUCE MRSA trial: a randomized controlled trial published in the New England Journal of Medicine in 2013 that assessed the comparative effectiveness of common MRSA prevention strategies

Regression to the Mean: the phenomenon that if an observation is extreme on the first measurement, it is more likely to be more near the average on the following measurement

Resistance: see antibiotic resistance

Roche LightCycler MRSA advanced: a screening test that rapidly identifies patients colonized with MRSA with results in less than 2 hours

Screening and isolation: universal screening upon admission followed by contact precautions for those with a positive screening test
Sensitivity: percentage of patients/samples correctly identified as having a disease or condition according to a gold standard criterion\textsuperscript{54}

Specificity: the percentage of patients/samples correctly identified as not having a disease or condition according to a gold standard criterion\textsuperscript{54}

SSI: abbreviation for surgical site infection

Staphylococcus aureus: the most common type of Staphylococcus infection that can cause serious infection if the bacteria gains access into the body\textsuperscript{40}

Surgical site infection: an infection an individual contracts after receiving surgery at the body part where the surgery occurred\textsuperscript{9}

Surveillance: the systematic collection and analysis of disease rates in order to control an infectious disease\textsuperscript{40}

Targeted decolonization: universal screening upon admission followed by decolonization for those with a positive screening test or those with a positive history of MRSA infection\textsuperscript{7}

Universal decolonization: a prevention strategy that doesn’t include a screening test component, instead every patient receives a decolonization regimen upon admission\textsuperscript{7}

Utilitarianism: the philosophy that an action is right if the consequences of that action are more favorable than unfavorable to everyone\textsuperscript{37}

Ventilator-associated pneumonia: an infection in the lungs that a person contracts while they are on a ventilator\textsuperscript{9}

Virulence: ability of an agent, such as bacteria, fungi, or virus that has the ability to produce disease\textsuperscript{40}
Welfarism: a theoretical framework that judges actions solely on the utility levels that are attained by society\textsuperscript{34}

Xpert MRSA Assay: a screening test that rapidly identifies patients colonized with MRSA with results in less than 66 minutes\textsuperscript{55}

Summary

HAIs continue to be one of the most common complications associated with hospital care\textsuperscript{3} and are one of the leading causes of preventable death in the United States.\textsuperscript{4} These infections negatively affect one out of every 25 hospitalized patients\textsuperscript{9} and are associated with an economic burden of more than $40 billion each year.\textsuperscript{6} To combat these infections, hospitals are implementing surveillance and prevention strategies and the federal government has dedicated funds to improve the detection and prevention of these infections. Due to variation in the cost of MRSA screening tests and prevention strategies, as well as variation in the turnaround time of the screening tests and the effectiveness of the prevention strategies, research was needed to determine which screening test and prevention strategy was the most efficient use of resources. Additionally, the recent increase in public health funding dedicated to HAI prevention needed to be evaluated to ensure that funds were being allocated in a way that maximizes efficiency. Chapter One highlighted the problems associated with HAIs and stated the objectives of this dissertation. Chapter Two presents a review of the current literature to showcase what is already known and how the proposed research filled a void in the existing literature. Chapter Three provides details of the methodological rigor of this research and highlights the strategies used to complete this dissertation’s objectives. Chapter Four presents the results of the dissertation, and Chapter Five concludes with a discussion around the implications of this dissertation.
CHAPTER II

REVIEW OF RELATED LITERATURE

Introduction

HAIs continue to be one of the most common complications associated with hospital care\(^3\) and one of the leading causes of preventable death in the United States.\(^4\) These infections negatively affect four percent of all inpatients\(^9\) and cost more than $40 billion each year.\(^6\) This dissertation assessed the cost of MRSA surveillance and prevention strategies to determine if rapid screening tests reduce total surveillance costs by reducing the costs associated with isolation and MRSA transmission and to determine if prevention strategies are cost-effective by preventing enough HAIs to justify their implementation costs. This dissertation also evaluated the effectiveness of public health funding on reducing hospital HAI rates to determine if the investment generated a positive return. Together, these objectives suggest best practices in HAI prevention at the hospital and national level to better inform hospital decision makers and national policy makers.

This chapter presents existing research related to these three aims and includes a comprehensive review of literature related to the surveillance, prevention, and public health funding for HAIs. This chapter starts by explaining how articles were selected for inclusion into this literature review and then details the number of articles retrieved and included. The section “Review of Literature” contains the bulk of the content and presents existing literature relevant to this dissertation separated by aim. The chapter concludes with a summary of what is already known about each aim and identifies the gaps in the literature filled by this study.
**Literature Search Method**

A literature review was conducted to identify published research that analyzed the cost of MRSA surveillance and prevention strategies, as well as literature that evaluated the Prevention and Public Health Fund. Tufts Medical Center Cost-Effectiveness Analysis Registry and PubMed were used to gather existing literature. For Aim 1, the following key words were used: MRSA, surveillance, screening test, cost, effectiveness. For Aim 2, the following key words were used: cost-effectiveness, MRSA, prevention, decolonization, and for Aim 3, the following key words were used: public health spending, bloodstream infection prevention, prevention and public health fund, return on investment, and effectiveness. The retrieved articles were then evaluated using the defined exclusion criteria. If an article met at least one of the exclusion criteria, it was removed from the analysis. The following exclusion criteria were used for Aim 1:

- The article did not assess either the cost or the effect of MRSA surveillance practices.
- The article detailed a study’s protocol without reporting results.

The following exclusion criteria were used for Aim 2:

- The article did not assess either the cost or the effect of MRSA prevention strategies.
- The article did not include decolonization as one of the prevention strategies.

The following exclusion criterion was used for Aim 3:

- The article did not assess the effectiveness of a public health activity or investment.

Titles of articles and their abstracts were first evaluated according to the exclusion criteria. If an article was not discarded after the initial review, the entire article was read and assessed in accordance with the exclusion criteria. Due to the limited literature around Aim 3,
the reference lists of all retrieved articles for this aim were used as a source to identify additional relevant literature.

**Literature Search Results**

Twenty-three articles were retrieved using the search criteria for Aim 1, of which none were duplicates. However, 11 articles were removed after reading the titles and abstracts, which left 12 articles for full article review. After reading the articles, two more studies were removed which left ten articles in the review for Aim 1. Using the search criteria for Aim 2, 25 articles were retrieved. After removing duplicates, the titles and abstracts were read for the remaining 23 articles. None of the articles met any of the exclusion criteria after reading the titles and abstracts; however, seven articles were excluded from the review after reading the entire article. The remaining 16 articles for Aim 2 were included in the literature review. For Aim 3, three articles were retrieved from the initial searches, none of which were duplicates. Two of the articles were excluded due to meeting the exclusion criterion; however, seven additional articles were identified from the references of those three articles. Therefore, nine articles were included in the review for Aim 3.

**Review of Literature**

The following review of literature details commonly used methods to test and prevent MRSA as well as the impact of public health funding on health outcomes. The information is presented by first elaborating on the existing literature around the comparative and cost-effectiveness of MRSA surveillance and prevention strategies, and then focusing on the potential impacts of the Prevention and Public Health Fund.
Aim 1

MRSA is of particular concern due to its multi-drug resistance, virulence, and disease spectrum, and continues to be a common cause for many HAIs. Because of the negative health consequences associated with MRSA, it is important to detect these infections quickly so appropriate actions, such as antibiotic therapy or decolonization, can be initiated. There are multiple mechanisms to test for MRSA including conventional culture, chromogenic agar and PCR. The traditional method of MRSA testing is a culture-based method where a specimen is obtained from a patient, often by swabbing the nose or throat, and is then streaked on culture. The bacterial species that grow on the culture are then identified in a few days. This culture-based method often takes around three days before results are available, which delays the response and postpones the appropriate response. To reduce this time delay, there have been recent developments in rapid MRSA screening tests. Rapid MRSA screening tests come in two primary types: PCRs and rapid culturing techniques, both of which can detect MRSA within a day and with good diagnostic accuracy. The introduction of these rapid MRSA screening tests has changed the way facilities test for MRSA; however recommendations are still needed to determine if the added cost per test of these more rapid screening tests is offset by cost savings in reduced isolation and transmission of MRSA.

Conventional Culture vs. Rapid Screening Tests

Both the culture-based method and more rapid screening tests have their advantages and disadvantages. Primarily there is a tradeoff between cost and turnaround time. Tests using conventional cultures are inexpensive but there is a time delay of about three days for results to be generated. Chromogenic agars are slightly more expensive, but can provide
results in 24 to 48 hours, and PCRs are much more expensive per test and require expensive technology, yet produce a result in just a few hours.\textsuperscript{23,24} Conventional cultures have been the traditional method to test for MRSA; however, this method is time consuming as it requires incubating the samples for 24 to 72 hours after detecting bacterial growth to ensure resistance to methicillin.\textsuperscript{57} PCR technology is quicker in detecting MRSA because it amplifies specific \textit{Staphylococcal} DNA sequences and methicillin resistance and does not require waiting for bacterial growth.\textsuperscript{56}

Although more costly than traditional conventional culture methods, the quicker turnaround time associated with rapid MRSA screening tests allows for the rapid implementation of either decolonization or isolation, which can thus reduce the spread of this harmful pathogen to others by detecting carriers as soon as possible.\textsuperscript{59} It is important to determine if the benefits of detecting a carrier more quickly are worth the added cost per test.

\textbf{Importance of Patient Isolation}

To reduce the transmission of MRSA to other patients while waiting for the screening test results, many facilities preemptively isolate patients. In fact, in ICUs, it is common practice to screen all patients upon admission and then isolate them until the absence of MRSA carriage has been shown.\textsuperscript{15} Isolation often involves being nursed in a single patient room and the use of barrier precautions, including gloves, masks and gowns.\textsuperscript{15} Preemptively isolating all patients has been shown to be effective in reducing the transmission of MRSA; however, noncolonized patients are unnecessarily isolated which leads to unnecessary resource use and excess cost.\textsuperscript{15} Additional costs associated with isolation include the cost of the barrier precautions for each visit and disinfectant to clean the room.\textsuperscript{16} Screening tests that
produce results quicker could thus reduce the number of inappropriate isolation days, and thus the costs associated with isolation.

Not all ICUs preemptively isolate all patients, instead, some follow a targeted isolation surveillance practice and only isolate those who test positive for MRSA. Screening tests that produce results quicker could thus reduce the number of inappropriate open days, which are the days a MRSA positive patient is not isolated and could thus transmit the pathogen to others. By determining disease status quicker, hospitals could more quickly implement isolation precautions and potentially reduce the transmission of MRSA to other patients. Therefore, rapid screening tests, although costlier, may actually reduce overall costs by reducing the number of isolation and open days due to their quicker turnaround time. It is important to determine if the incremental costs of these rapid screening tests are offset by other cost savings.

**Effectiveness of Common MRSA Screening Tests**

Since the development of these rapid MRSA screening tests, there have been a few studies that compared the effectiveness of these rapid tests to culture methods. Schulz and colleagues compared the effectiveness of an active screening strategy using PCR with an active screening strategy using culture methods for trauma surgery and heart surgery patients in a German university hospital. The PCR test showed a sensitivity of 85% for nasal swabs and 42.11% for throat swabs. If both nasal and throat swabs were examined together and a minimum of one positive result showed MRSA carriage, the PCR had a sensitivity of 100%. Similarly, the PCR had a specificity of 99.39% for nasal swabs and 98.78% for throat swabs. The researchers concluded an active surveillance strategy with PCR can detect MRSA-positive patients with good diagnostic accuracy.
Geiger and Brown conducted a similar analysis comparing the effectiveness of current rapid MRSA screening tests.\textsuperscript{56} GeneOhm MRSA Assay, Xpert MRSA Assay, and LightCycler MRSA Advanced, all of which are PCRs, returned results in two hours with good sensitivity and specificity.\textsuperscript{56} Hyplex StaphyloResist, another form of PCR, took between two and four hours to retrieve results, with a sensitivity between 84\% and 90\% but with low specificity.\textsuperscript{56}

Polisena and colleagues compared the effectiveness of various PCR technologies with chromogenic agar.\textsuperscript{51} The mean turnaround time for Xpert MRSA Assay was 17.1 hours, which was 38.6 hours quicker than chromogenic agar.\textsuperscript{51} The mean turnaround time for BD GeneOhm MRSA Assay was between 13.2 and 21.6 hours, whereas chromogenic agar took on average between 46.2 and 79.2 hours.\textsuperscript{51} When the researchers considered the outcome of inappropriate isolation days, the PCR arm had many fewer inappropriate isolation days as compared to the agar arm, 277 and 399 respectively.\textsuperscript{51} The researchers concluded that PCR screening tests have a lower turnaround time and result in fewer isolation days than chromogenic agar.\textsuperscript{51}

This research has been pivotal in showing the diagnostic accuracy of these rapid MRSA screening tests, but there continues to be a gap in the economic literature to determine if the costs saved due to a quicker turnaround offset the more expensive cost per test.

Cost-Effectiveness of Common MRSA Screening Tests

Li and colleagues estimated the cost-effectiveness of a strategy that combined the Xpert MRSA Assay PCR test and a broth-enriched culture test to a culture-based strategy alone.\textsuperscript{16} Two Xpert MRSA Assays were compared, the daytime assay and the 24-hour assay.\textsuperscript{16} The researchers found that PCR reduced the length of preemptive isolation per
patient (by 44 hours for the daytime strategy and 57 hours for the 24-hour strategy) and the 24-hour Xpert MRSA Assay was superior in that it reduced costs and unfavorable outcomes. An opposite conclusion was reached by Lee and colleagues. They evaluated the economic value of an agar-based screening test as compared to a PCR screening test for different MRSA prevalence rates, decolonization success rates, and costs of decolonization for hemodialysis patients. They found routine surveillance using an agar-based screening test had a lower incremental cost-effectiveness ratio than routine surveillance using PCR methods. This suggests the marginal gains in diagnostic accuracy associated with the rapid screening test did not outweigh the increased cost per test, and thus agar-based screening tests are more cost-effective.

Wassenberg and colleagues conducted a similar analysis that compared two PCR technologies (BD GeneOhm MRSA PCR and Xpert MRSA Assay) to conventional culture and chromogenic agar. Using the hospital perspective, the researchers calculated the costs associated with isolation and the cost per test for each screening test. For the PCR technologies, the duration of isolation ranged from 16.1 to 19.7 hours. The duration of isolation for chromogenic and conventional agar was 30.0 and 76.2 hours respectively. Using a Markov computer simulation model, the researchers discovered that rapid MRSA screening tests can reduce the number of inappropriate isolation days, but only chromogenic agar was cost-saving. Information was limited as to if PCRs could be considered cost-effective.

Robotham and colleagues assessed the cost-effectiveness of three different screening tests (conventional agar, chromogenic agar and PCR) combined with a decolonization
prevention strategy in England and Wales ICUs. From the hospital perspective, universally screening all patients using PCR combined with decolonization had a 30% chance of being cost-effective. However, without decolonization, universal PCR screening was not likely to be cost-effective. More research is needed to determine the generalizability of these results outside of England and Wales and to determine the cost-effectiveness of these screening tests alone (not coupled with a prevention strategy).

Research has started to assess the cost of these rapid MRSA screening tests and conflicting results have been reported. After reviewing the literature, more research was needed to explore the conflicting reports and understand if the costs saved due to the quicker turnaround time justify the added cost per test associated with these rapid screening tests.

Aim 2

*Staphylococcus aureus* is a common cause of HAIs, with many of these infections caused by methicillin-resistant strains. *Staphylococcus aureus* is of particular concern for patients in the ICU. Patients in the ICU are at the greatest risk of acquiring an HAI as 65% of all HAIs are reported in the critical care setting. Because of this, adult ICUs are the primary focus for this aim. Gidengil and colleagues estimated a model to determine the economic impact of MRSA infections if no prevention strategies were implemented. Assuming four million ICU visits each year in the United States, there would be approximately 218,000 MRSA infections resulting in an economic burden of $3.3 billion.

To reduce the burden of these infections, both in monetary terms and lives impacted, prevention strategies have been developed. Before discussing potential MRSA prevention strategies, it is important to differentiate between MRSA colonization and MRSA infection. When a patient carries MRSA bacteria but displays no signs of clinical infection, they are
considered to be colonized. Infection occurs when a patient develops an invasive infection and shows clinical symptoms. Some patients admitted to the hospital are colonized with MRSA upon admission, which poses a constant risk to other patients of acquiring an MRSA infection. This risk of acquiring an MRSA infection is largely related to the facility’s MRSA prevalence rate. MRSA colonized patients not only pose a risk to other patients, but pose a risk to themselves since colonization is a risk factor for subsequent infection. To protect both parties, prevention strategies should target both the removal of bacteria on colonized individuals to further protect the individual from developing an invasive infection and reducing the existence of the pathogen in the environment to reduce the transmission to other patients.

One of the most common prevention strategies, screening and isolation, involves universal screening upon admission followed by contact precautions for patients with a positive screening test or positive history for MRSA. Screening and isolation is considered standard practice in the ICU but it primarily protects other patients by reducing the transmission of the pathogen through the use of contact precautions and involves fewer safeguards in protecting the colonized individual.

A more recent prevention strategy, decolonization, strives to protect both the carrier and other patients by removing the bacteria altogether on the colonized individual which would thus reduce the spread to others by removing the pathogen from the environment and protect the individual from subsequently developing an infection. A typical decolonization regimen consists of twice daily intranasal mupirocin ointment for five days and daily baths with chlorhexidine-soaked cloths. With a targeted decolonization approach, all patients admitted are first screened for MRSA and those that test positive for MRSA are
decolonized. Conversely, no screening test is used with a universal decolonization approach; instead, every patient is decolonized upon admission.

Effectiveness of Common MRSA Prevention Strategies

As these novel prevention strategies, such as decolonization, are developed, it is important to compare their effectiveness in preventing MRSA infections with traditional strategies. In 2013, a randomized controlled trial was published in the *New England Journal of Medicine* that assessed the comparative effectiveness of screening and isolation, targeted decolonization, and universal decolonization. Researchers found universal decolonization to be the most effective strategy in reducing MRSA infection by reducing infection rates 37%. Targeted decolonization and screening and isolation reduced infection rates by 25% and 8%, respectively. From these results, the Agency for Healthcare Research and Quality and the CDC published recommendations and a protocol for the implementation of universal decolonization in the ICU. To ensure these recommendations are best practices and to better guide hospital decision makers, the cost-effectiveness of these prevention strategies should be assessed to determine if the incremental effect outweighs the potential incremental cost.

Cost-Effectiveness of MRSA Prevention Strategies

Every prevention strategy has implementation costs, which may be offset by their effects on health outcomes such as decreased infection risk or improved patient outcomes. Before widespread implementation or adoption of a novel prevention strategy, it is important to determine if their improved effect on health outcomes justifies their implementation costs. Farbman and colleagues conducted a systematic review to assess the clinical and cost-effectiveness of common MRSA prevention strategies. They found a large economic
benefit from MRSA prevention strategies with cost savings nearly seven times higher than associated implementation costs.\textsuperscript{65} This review provided justification for the implementation of MRSA prevention strategies.

Existing literature assessing the cost-effectiveness of MRSA prevention strategies is largely focused on preoperative prevention activities for surgery patients. Clancy and colleagues modeled the cost-effectiveness of routine preoperative \textit{Staphylococcus aureus} screening and decolonization for heart and lung transplant patients from the hospital and third party payer perspective.\textsuperscript{66} They found the cost savings per case averted were $240,602 from the hospital perspective and around $15,000 in cost savings from the payer perspective.\textsuperscript{66} The researchers concluded that targeted decolonization was economically dominant and therefore they recommended routine screening and decolonization of heart and lung transplant patients.\textsuperscript{66} Besides the limited patient population, this study was also limited in that it screened for all \textit{Staphylococcus aureus} infections, and not specifically MRSA. Additionally, each prevention strategy was compared to a no treatment strategy; this comparator may not be the best choice for the ICU population since screening and isolation is often considered standard practice.\textsuperscript{66}

Similarly, Slover and colleagues assessed the cost savings that result from a preoperative \textit{Staphylococcus aureus} screening and decolonization prevention strategy for hip and knee arthroplasties and spine fusions using a Markov model.\textsuperscript{67} They found a screening program would need to result in a 35\% reduction in the revision rate for hip and knee arthroplasties and a 10\% reduction in the revision rate for spine fusions to be cost saving.\textsuperscript{67} They concluded a screening and decolonization program would only need to modestly reduce the revision rate to be considered cost-saving and therefore they would recommend such a
policy. Besides the external validity concerns by only including hip and knee arthroplasties and spinal fusions, this study only looked at when these prevention strategies would be cost-saving, and thus did not determine the cost-effectiveness of these interventions.

Courville and colleagues also performed a cost-effectiveness analysis from the societal perspective to evaluate the preoperative use of mupirocin in an outpatient total joint arthroplasty clinic. They found both a universal and targeted decolonization strategy dominated a strategy of no treatment, making both strategies cost-effective interventions. However, due to the similarity in effect, they recommended a universal approach to avoid missing potential carriers due to false-negative tests in a targeted approach. This study was limited in that the researchers only used the least expensive screening test and only assessed the results in a total joint arthroplasty outpatient clinic. Similar to the study conducted by Clancy and colleagues, this study also compared the decolonization regimen to a no treatment option, which is likely not the most appropriate comparator for ICUs.

Lee and colleagues conducted three similar analyses to determine the economic value of an MRSA screening and decolonization strategy for vascular surgery patients, cardiac surgery patients, and orthopedic surgery patients. Within each analysis, the researchers varied the MRSA prevalence rate and decolonization success rates and found preoperative targeted decolonization to likely be cost-effective over a range of MRSA prevalence and decolonization success rates. For cardiac surgery patients, even when MRSA prevalence was as low as 1% and the decolonization success rate was as low as 25%, the incremental cost-effectiveness ratio of implementing routine screening and decolonization was less than $15,000/QALY. For orthopedic surgery patients, the researchers found that preoperative
MRSA screening and decolonization was typically less than $6,000/QALY for payers and likely a dominant strategy for hospitals.\textsuperscript{71}

Lastly, Chen and colleagues conducted a systematic review to determine if \textit{Staphylococcus aureus} screening and decolonization was cost-effective in orthopedic and trauma patients.\textsuperscript{62} Out of the 19 studies they included in their review, all of them showed a reduction in SSIs or other wound complications.\textsuperscript{62} The reduction of \textit{Staphylococcus aureus} SSIs ranged from 40-200\% and the reduction of SSIs specifically related to MRSA ranged from 29-200\%.\textsuperscript{62} They concluded that preoperative screening and decolonization of \textit{Staphylococcus aureus} in orthopedic patients is cost-effective due to the reduction in SSIs.\textsuperscript{62} From their review, preoperative MRSA screening was conducted with PCR in four studies, culture methods in 13 studies, mixed methods in one study, and was unknown for another study.\textsuperscript{62} This review shows the potential health benefits of targeted decolonization as well as the utilization of different screening tests by different facilities. Due to this variation in screening test utilization, tailored recommendations for facilities based on the screening test they employ was needed.

This body of literature is largely focused on the cost-effectiveness of MRSA prevention strategies for surgery patients preoperatively. Although valuable, this research has a limited patient population. Furthermore, the recommendations following the REDUCE MRSA trial recommended ICU-wide implementation of universal decolonization, and due to the limited population for each of these studies, the generalizability of these results to the ICU is limited. There is little existing research on the use of decolonization for all inpatient admissions.
The researchers engaged in the REDUCE MRSA trial also conducted a cost analysis to assess the impact that screening and isolation, universal decolonization, and targeted decolonization have on healthcare costs.\textsuperscript{72} They found universal decolonization to be a dominant strategy that would have lower implementation costs and lower ICU costs as compared to targeted decolonization or screening and isolation.\textsuperscript{72} They further estimated that universal decolonization would save $171,000 and prevent nine additional bloodstream infections for every 1,000 ICU admissions. This analysis was limited in that an incremental analysis was not conducted, which is essential in determining if the incremental cost of one strategy over another is justified by the incremental effect in improved health outcomes.

You and colleagues examined the clinical outcomes and cost of active MRSA surveillance with and without decolonization in neonatal ICUs in Japan.\textsuperscript{27} Using a decision tree approach, they took the perspective of healthcare providers in Japan and found that active surveillance plus decolonization resulted in a lower MRSA infection rate, lower MRSA mortality rate, and lower total cost per patient.\textsuperscript{27} They concluded that active surveillance plus decolonization was cost saving and thus dominated a strategy of active surveillance alone.\textsuperscript{27} This study was limited, however, in its population to Japan neonatal ICUs and only assessed screening with PCR, thus ignoring other commonly used screening tests such as conventional culture or chromogenic agar. Furthermore, this study did not include universal decolonization as an intervention of interest.

Similarly, Nelson and colleagues assessed the cost-effectiveness of active surveillance plus decolonization as compared to a strategy of active surveillance alone and to a no treatment strategy in Veteran’s Affairs hospitals.\textsuperscript{26} They found active surveillance plus decolonization dominated both comparators and thus showed a strong economic justification
for adding a decolonization protocol to their current active surveillance strategy.\textsuperscript{61} This study was also limited in their select population and did not include universal decolonization as an intervention of interest.

Ziakas and colleagues estimated the cost-effectiveness of screening and isolation, targeted decolonization, and universal decolonization and found that universal decolonization increased QALYs by 1.06\% over targeted decolonization and by 1.29\% over screening and isolation.\textsuperscript{63} This resulted in an average cost savings of $172 compared to targeted decolonization and $189 compared to screening and isolation.\textsuperscript{63} The researchers concluded that universal decolonization was likely to be cost-effective even at low willingness to pay thresholds.\textsuperscript{63} Although this analysis included universal decolonization as an intervention of interest, it only looked at screening with chromogenic agar and did not consider the use of more expensive tests like PCRs.

After reviewing the literature around the cost-effectiveness of MRSA prevention strategies, further cost-effectiveness research around MRSA prevention strategies was needed to expand the population beyond surgery patients to the entire ICU and include universal decolonization as an intervention of interest. Furthermore, the variation in the diagnostic accuracy and cost of the screening test needed to be accounted for to determine the influence of the screening test selection on the incremental cost-effectiveness ratio for the prevention strategy.

\textbf{Aim 3}

In 2010, the Prevention and Public Health Fund was created as part of the Patient Protection and Affordable Care Act.\textsuperscript{20} This fund is intended to improve the nation’s health and restrain the ever increasing health care costs. Legislation allocated $15 billion dollars to
this fund over its first ten years with the intent to expand and sustain prevention and public health programs. Fiscal year 2010 marked the first year of funding allocation in the amount of $500 million. The funds increased to $750 million in 2011 and $1 billion in 2012. In 2013, $949 million was dedicated to the Prevention and Public Health Fund, of which nearly half was allocated to the CDC to aid in their disease prevention, surveillance, and tracking efforts. The CDC awarded nearly $7 million of the fund to 15 states for the Prevention of HAIs across the Spectrum of Healthcare, an activity designed to develop and implement evidence-based multi-facility prevention initiatives. The Prevention and Public Health fund was set to increase to $2 billion each year starting in 2015 and each year thereafter; however, much controversy has surrounded the effectiveness and necessity of this fund leading to legislation that cut portions of this budget and even bills that suggest elimination of this fund altogether. Due to this debate, it is essential to determine the effectiveness of public health spending on community health and clinical outcomes, such as HAIs, to provide evidence to decision makers on whether or not this fund should be further cut or eliminated altogether.

Rationale for Implementation

Despite large investments and expenditures in health care, the United States has consistently ranked poorly on quality outcome measures. It has been a long-standing need for the United States to improve the quality of health care as well as reduce health care costs. Investing in public health and prevention is one proposed way to achieve these goals. Many public health advocates believe investments in public health by the federal government are insufficient. Of the trillions of dollars spent on health care in the United States, less than five percent is dedicated to public health. The Trust for America’s Health identified an annual deficit of $20 billion in public health investments. This shortfall is large enough in magnitude
Many believe that investments in public health should be increased as they can be associated with large payoffs, both in monetary terms and in health outcomes. The Trust for America’s Health also discovered that investments in effective public health actions are associated with a positive return on investment. This association between higher levels of public health spending and improved population health has been explored by other researchers as well. To improve community health, reduce the deficit in public health dedicated funds, and to hamper the growth in private and public health care costs, the Patient Protection and Affordable Care Act created the Prevention and Public Health Fund.

Value of Public Health Spending Debate

There has been an ongoing debate on whether or not public health spending and efforts are effective in improving health and reducing health care costs. Many researchers have evaluated the impact of public health funding on mortality rates, and differences in conclusions have been reached. Some studies claim that increases in public health spending are associated with decreases in mortality rates; others conclude there is no association between public health spending and mortality rates; while others claim that increases in public health spending leads to increases in mortality.

Mays and Smith analyzed the impact of public health spending on mortality rates for nearly 3,000 local public health agencies over a thirteen-year period. They found increases in public health spending were associated with statistically significant reductions in mortality rates for infant mortality, cardiovascular disease mortality, diabetes mortality, and cancer mortality. These rates fell by 1.1-6.9% for every 10% increase in spending. Conversely, Marton, Sung, and Honore claimed that increases in public health spending were associated
with increases in mortality.\textsuperscript{75} These researchers used a 12-year panel dataset for county public health agencies in Georgia to determine how differences in spending contributed to differences in health outcomes.\textsuperscript{75} Unlike Mays and Smith,\textsuperscript{22} they found increases in public health spending leads to worse health outcomes.\textsuperscript{75}

Dr. Timothy Brown estimated the causal impact of California county public health expenditures on mortality rates.\textsuperscript{76} Using a dynamic panel model to assess the cumulative impact of expenditures on all-cause mortality rates, Brown found public health spending significantly reduced mortality rates in the long-term; however, the short-term effects were minimal.\textsuperscript{76} Investing an additional $10 per person in public health reduced the all-cause mortality rate by 9.1 deaths per 100,000.\textsuperscript{76} In the long-term, 27,000 California lives were saved due to local public health funding.\textsuperscript{76} Using the value of a statistical life, the annual value of these lives saved equated to more than $200 billion.\textsuperscript{76}

Schenck and colleagues also examined the impact of local public health spending, staffing, and service delivery with health outcomes in North Carolina.\textsuperscript{77} These researchers did not find any significant associations between the changes in public health spending and mortality rates in North Carolina.\textsuperscript{77} However, increases in staffing were significantly associated with decreases in infant mortality.\textsuperscript{77} Milstein and colleagues used a simulation model to determine which strategy was best at reducing deaths and health care costs.\textsuperscript{78} One proposed strategy was referred to as protection, which enabled healthier behavior and created safer environments.\textsuperscript{78} Ten years post-implementation, the protection intervention would prevent 721,000 deaths in the United States but would require a cost increase of $179 billion.\textsuperscript{78} This cost increase was the lowest of all other included strategies including expanding health insurance coverage and delivering better clinical care.\textsuperscript{78} Twenty-five years
post-implementation, the protection intervention prevented 4.5 million deaths and saved $596 billion.\textsuperscript{78} Therefore, in the long-run, a protection strategy is most likely the most cost-effective intervention by improving health outcomes and reducing health care costs.\textsuperscript{78} The protection strategy is closely related to the functions of public health. These researchers believe that investments of this type could greatly improve the performance of the United States’ health care system.\textsuperscript{78}

This study focused on one Prevention and Public Health Fund activity that provided funding to 15 state health departments. This activity, The Prevention of HAIs across the Spectrum of Healthcare, is interesting in that money was provided to state health departments who then developed and implemented HAI prevention initiatives at hospitals. Little evidence exists to show the effectiveness of this kind of practice, where a health department relays information to a facility but relies on the facility to implement the information and guidelines. However, the CDC often follows a similar practice and effectiveness has been shown. From the early 1960s, the CDC have been advocates in preventing CLABSIs by developing guidelines related to their prevention.\textsuperscript{79} The CDC then relies on providers and administrators to take that knowledge and implement the prevention strategies in their facilities. To assess the impact of their efforts, the CDC conducted a study to calculate the costs and benefits associated with their federal investments in preventing CLABSIs.\textsuperscript{79} Researchers estimated between 40,556 and 75,067 CLABSIs were prevented in the Medicare and Medicaid population in critical care units between 1990 and 2008 due to CDC’s efforts.\textsuperscript{79} The costs required to achieve these benefits was approximately $33 million.\textsuperscript{79} The net benefits ranged between $640 million to $1.8 billion.\textsuperscript{79} This equated to a return on investment between $3.88 and $23.85 per dollar invested.\textsuperscript{79} This positive return on
investment led researchers to conclude that investing in prevention efforts through the CDC was just as effective as if the funds were invested directly into the hospitals.\textsuperscript{79} 

When examining whether public health spending is an effective mechanism to improve health outcomes and restrain health care costs, some studies suggest that public health is a good investment, and thus health improves when governments devote funds to public health.\textsuperscript{22,76–79} These findings would support the creation of the Prevention and Public Health Fund. However, other studies have shown that public health spending does not always lead to health improvements.\textsuperscript{75} After reviewing this literature, additional research was needed that evaluated the effectiveness of specific public health interventions to determine the value associated with public health spending and whether or not public health is a good buy.

**Controversy Surrounding the Fund**

Likely due to the uncertainty in the value of public health spending, many people question the impact of public health investments. Since the inception of the Prevention and Public Health Fund, controversy has surrounded it leading to uncertainties in the continuation of the fund. Republicans advocated for cuts and complete elimination of the fund because they thought investing this money would be wasteful and would achieve little in addition to the already federally funded programs working toward health promotion.\textsuperscript{8} Although $15 billion was initially allocated to the Prevention and Public Health Fund in its first decade, President Barack Obama passed legislation in 2012 that reduced the fund by $5 billion over a ten year period, starting in fiscal year 2013.\textsuperscript{8} Most recently, this fund was targeted for complete elimination in the United States House of Representatives’ 2016 Budget Resolution as well as in other bills being considered in the House of Representatives.\textsuperscript{30,31} Research was needed to show the effectiveness of public health spending on improving health outcomes to
guide policy-makers and politicians on the impact of this fund before the program is further cut or eliminated.

Future Directions

Due to the conflicting and limited research around the value of public health spending, it was important to expand research in this area. Controversy surrounds public health spending due to the little evaluative research that has been conducted to show its effectiveness. Because of this, policy makers are left wondering if the funds dedicated to public health could be better spent elsewhere.\(^\text{22}\) In 2012, the National Research Agenda for Public Health Services and Systems Research acknowledged the need for research that identified which public health investments and actions had the greatest impact on health outcomes.\(^\text{80}\) On top of this effectiveness research, original research was needed to identify the downstream consequences and health impacts of public health spending to assess its value.\(^\text{22}\) Due to the differences in conclusions reached by different researchers assessing the value of public health spending, rigorous research on the association between public health spending and health outcomes was needed.\(^\text{75}\) Furthermore, with the recent cuts and proposed elimination of the Prevention and Public Health Fund, it was essential to determine the effectiveness of this type of spending on improving community health and reducing health care costs. The Prevention and Public Health Fund requires a monetary investment; however, this investment may be cost saving in the long run if it prevents illnesses and improves health outcomes. This study evaluated the effectiveness of public health spending on hospital HAI rates to determine if this investment in public health was associated with improved health outcomes and a positive return on investment.
Summary

Research has shown preemptively isolating all patients is effective in reducing the transmission of MRSA; however, noncolonized patients are unnecessarily isolated which leads to unnecessary resource use and excess cost.\textsuperscript{15} Similarly, for facilities that only isolate patients following a positive screening test, there is a delay in implementing isolation precautions while waiting for the results of the screening test. Thus, MRSA positive patients can transmit this pathogen to other patients while they are waiting for their results. Rapid MRSA screening tests have a shorter turnaround time and result in fewer isolation days and open days than conventional cultures.\textsuperscript{51} Thus, rapid screening tests, although costlier, may actually reduce overall costs by reducing the costs associated with isolation and MRSA transmission. Existing economic literature around MRSA surveillance have reported conflicting results. Some research has concluded that rapid screening tests reduced costs as well as unfavorable health outcomes\textsuperscript{16} and can be considered cost-saving.\textsuperscript{15} However, other research has contradicted this showing more conventional screening methods to be less costly than rapid screening tests.\textsuperscript{28} Aim 1 of this dissertation added to this literature to provide clarification to the contradicting conclusions.

Comparative effectiveness literature around MRSA prevention strategies has shown universal decolonization to be the most effective strategy in preventing infection, by reducing infection rates 37\textsuperscript{\%}.\textsuperscript{7} Targeted decolonization and screening and isolation reduces infection rates by 25\textsuperscript{\%} and 8\textsuperscript{\%}, respectively.\textsuperscript{7} To guide hospital decision makers, the cost-effectiveness of these prevention strategies needed to be assessed to determine if the incremental effect offsets the implementation costs. There was some previous evidence around the cost-effectiveness of these strategies; however, this body of literature was largely
focused on the cost-effectiveness of MRSA prevention strategies for surgery patients preoperatively. Although valuable, this research had a limited patient population and the generalizability of these results to the ICU is limited. Also, these studies rarely included universal decolonization as an intervention of interest. This dissertation filled these gaps in the literature by including universal decolonization as an intervention of interest and expanding the population to the entire ICU. Furthermore, the screening test used in each of the existing studies varied and it was uncommon for a study to assess the impact of multiple different screening tests, although a variety of screening tests are used in practice that range in cost, turnaround time and diagnostic accuracy. In Aim 2, multiple screening tests were evaluated, including culture and rapid screening tests, to determine the influence of the screening test selection on the incremental cost-effectiveness ratio for the prevention strategy.

Lastly, there has been controversy around the Prevention and Public Health Fund as well as the value of public health spending, and thus there was a need for original research around the impact of the Prevention and Public Health Fund to determine if investing in public health is an effective strategy to improve health and reduce health care costs. The effect of public health spending on health outcomes has been mixed. Some studies claim that increases in public health spending are associated with decreases in mortality rates; others conclude there is no association; while others claim that increases in public health spending actually leads to increases in mortality. This study conducted research on the impact of an activity of the Prevention and Public Health Fund to determine if providing funding to state health departments was an effective way to reduce hospital bloodstream infections and if this funding was associated with a positive return. The next chapter, Chapter Three, provides
details on the approach used to conduct this research in order to fill these gaps in the literature. Chapter Four presents the results of each aim and Chapter Five discusses the implications of this research for clinical practice and policy change.
CHAPTER III

METHODODOLOGY

Introduction

MRSA surveillance is standard practice in hospital ICUs. There is variation in the screening tests used as part of these surveillance practices, including cultures, chromogenic agars, and PCR technologies. These tests range from low-cost, slow turnaround to high-cost, quick turnaround. Literature has compared the diagnostic accuracy of these screening tests; however, these evaluations did not incorporate cost. Thus, evidence was needed to determine if rapid screening tests, although costlier, actually reduce total surveillance costs by reducing the number of isolation days or number of open days. Similarly, the comparative effectiveness of common MRSA prevention strategies was known; however, little was known regarding the cost-effectiveness of these interventions. Existing economic evaluations were limited in that they rarely included universal decolonization, largely pertained to special populations such as preoperative surgical patients, and did not vary the screening test used in the analysis. Aims 1 and 2 of this dissertation were designed to fill these gaps in the literature and provide hospital decision makers with evidence-based recommendations for screening test and prevention strategy selection for their facility.

The results from Aims 1 and 2 can greatly inform hospital decision makers on efficient practices at the hospital level. However, prevention efforts have expanded beyond the hospital to federal policies. Section 4002 of the Patient Protection and Affordable Care Act created the Prevention and Public Health Fund with the intent to improve the nation’s health and restrain the ever increasing health care costs. Legislation allocated $15 billion to this fund over its first ten years with the intent to expand and sustain prevention and public
In 2013, $949 million was dedicated to the Prevention and Public Health Fund, of which nearly half was allocated to the CDC to aid in their disease prevention, surveillance, and tracking efforts. The CDC then awarded nearly $7 million to 15 states for the Prevention of HAIs across the Spectrum of Healthcare, an activity designed to develop and implement evidence-based multi-facility prevention initiatives. Little research on the impact of this fund had occurred likely due to its recent implementation; however, previous research showed that increases in public health spending can be associated with improved health outcomes, such as a decrease in mortality rates. Aim 3 of this study evaluated the effectiveness of public health funding on reducing hospital HAI rates to determine if this investment generated a positive return. Together, these objectives suggest efficient practices in HAI prevention at the hospital and national level to better inform hospital decision makers and policy makers.

**Study Designs**

**Aim 1**

Calculate the cost of two MRSA surveillance practices (universal preemptive isolation and targeted isolation) and recommend the MRSA screening test that minimizes costs for each surveillance practice.

**Hypothesis**

Rapid MRSA screening tests, although costlier, will reduce total costs because their added cost per test will be offset by the cost savings due to reduced isolation and transmission of MRSA.
Background

A variety of screening tests are used to detect MRSA that range from expensive tests capable of producing results in a few hours to cheaper tests that produce results in a few days. Both universal and targeted surveillance practices could be enhanced if coupled with screening tests that produce results quicker. With universal preemptive isolation, a quicker result would allow noncolonized patients to be removed from isolation sooner and thus reduce the total isolation costs. Similarly, with targeted isolation, a quicker result would allow the earlier implementation of isolation precautions and thus reduce the number of open days, or the days a MRSA-positive patient is not isolated and could transmit the pathogen to other patients. Therefore, although these rapid screening tests are more costly, they could result in cost offsets.

Rationale

The first objective of this aim was to determine the cost of MRSA surveillance practices for each commonly used screening test. The second objective was to identify the screening test that minimized total costs for each MRSA surveillance practice. To achieve these objectives, we tested the hypothesis that the added cost per test associated with the rapid screening tests would be offset by the cost savings due to reduced isolation and transmission of MRSA, making surveillance with rapid screening tests less costly. We tested our hypothesis using the approach of a decision tree to examine the differences in cost, outcomes, and diagnostic accuracy between MRSA screening under two different ICU surveillance practices, universal preemptive isolation and targeted isolation.
**Justification**

Existing economic literature around MRSA surveillance has reported conflicting results. Some research has concluded that rapid screening tests reduced surveillance costs as well as unfavorable health outcomes\(^\text{16}\) and can be considered cost-saving.\(^\text{15}\) However, other research has contradicted this showing more conventional screening methods to be less costly than rapid screening tests.\(^\text{28}\) Due to these contradicting findings, decision makers are still left unknowing whether or not the incremental cost of rapid MRSA screening tests is offset by reductions in isolation costs and the transmission of MRSA.

**Impact**

The results from this aim can inform decision makers if the incremental cost of more rapid screening tests is offset by cost savings in isolation and MRSA transmission. Results can guide hospital decision makers on which screening test minimizes costs for the surveillance practice used at their facility.

**Approach**

The approach for Aim 1 was divided into three primary tasks. First, a cost-consequence analysis was conducted to determine the diagnostic accuracy and associated outcomes for each MRSA screening test category, including conventional culture, chromogenic agar, and PCR. Second, a cost-minimization analysis was conducted to determine which MRSA screening test minimized total costs for a universal preemptive isolation surveillance practice. Third, a cost-minimization analysis was conducted to determine which MRSA screening test minimized total costs for a targeted isolation surveillance practice.
**Activity 1. Conduct a cost-consequence analysis for commonly used MRSA screening tests.** The following costs were included in the total cost of each screening test category: the cost of each test and the laboratory personnel time required to conduct each test. The following consequences related to the diagnostic accuracy of each screening test were evaluated: the true positive rate or the sensitivity of the test, the true negative rate or the specificity of the test, the false negative rate, and the false positive rate. The average turnaround time, the number of appropriate and inappropriate isolation days, and the number of appropriate and inappropriate open days were also compared. This cost-consequence analysis presented the costs associated with each test, as well as their consequences. This was important to highlight the differences, both in cost and diagnostic accuracy, for MRSA screening tests and to provide the inputs for the modeling used in activities 2 and 3.

**Activity 2. Conduct a cost-minimization analysis to determine which MRSA screening test minimized total costs for a universal preemptive isolation surveillance practice.** A cost-minimization analysis from the hospital perspective was conducted to calculate the total cost of universal preemptive isolation for a hypothetical cohort of patients admitted to the ICU. Cost categories included costs associated with the screening test, including the cost per test and personnel time to administer and read the test, and costs associated with isolation, including the cost of contact precautions and disinfectant. Isolation costs were separated into appropriate and inappropriate. Appropriate isolation costs were those isolation costs spent on patients who were colonized with MRSA. Inappropriate isolation costs were those isolation costs spent on patients who were unnecessarily isolated because they were not colonized with MRSA. The screening test used as part of the surveillance practice was varied to determine which screening test minimized inappropriate isolation costs.
and total costs. The following MRSA screening tests were assessed: conventional culture, chromogenic agar 48-hour, chromogenic agar 24-hour, and polymerase chain reaction. The screening test that minimized total costs was recommended as the most efficient screening test for each surveillance practice.

The analysis was modeled using a decision tree that accounted for the diagnostic accuracy and turnaround time of the different MRSA screening tests (Figure 3.1). The decision tree modeled pathways to represent patients that were appropriately and inappropriately preemptively isolated. Because this analysis modeled preemptive isolation of all ICU admissions, a hypothetical patient was screened and isolated upon admission. The patient was removed from isolation if his/her screening test came back negative.

**Figure 3.1. Decision Tree Structure for Aim 1, Activity 2.**

![Decision Tree](image)

The payoff is denoted by a 1 or 0 at the end of the terminal node. Pathways ending in a 1 were appropriately preemptively isolated. Pathways ending in a 0 were inappropriately preemptively isolated.

To assess the impact of variation in the inputs on the results and conclusions, sensitivity analyses were conducted. A univariate sensitivity analysis using the lower and upper bounds of the input range in Table 3.1 determined parameters with influence over the
incremental cost-effectiveness ratio. Additionally, a probabilistic sensitivity analysis of 1,000
Monte Carlo simulations varied all of the inputs over their plausible range simultaneously to
create a distribution of each cost component and the total cost of the surveillance practice.
Input ranges represented the 95% confidence interval where available. When 95% confidence
intervals were unavailable for an input, the range was estimated by adding and subtracting
25% to the base-case value.

The inputs and source for each input are depicted in Table 3.1. All cost inputs were
inflated to 2015 US dollars using the medical-cost inflation rate.81

Table 3.1. Inputs and Source of Each Input for Aim 1, Activity 2.

<table>
<thead>
<tr>
<th></th>
<th>Base-Case</th>
<th>Range</th>
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<tbody>
<tr>
<td>Colonization Rate</td>
<td>8%82</td>
<td>6-10%</td>
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<tr>
<td>Conventional Culture Sensitivity</td>
<td>86.9%23</td>
<td>74.7%-93.7%</td>
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<tr>
<td>Conventional Culture Specificity</td>
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<td>77.7%-95.6%</td>
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<tr>
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<td>82.1%-91.6%</td>
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<td>$3.47-$5.79</td>
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<td>Chromogenic Agar 24-Hour Sensitivity</td>
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<td>71.0%-84.1%</td>
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<tr>
<td>Chromogenic Agar 24-Hour Specificity</td>
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<td>Polymerase Chain Reaction Specificity</td>
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<tr>
<td>Cost per Inappropriate Open Day†</td>
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<tr>
<td>Cost per Appropriate Open Day‡</td>
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<td>$0</td>
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</table>

*The cost of an isolation day includes costs associated with contact precautions and disinfectant.83
†The cost of an open day was calculated by multiplying the daily risk of contracting an MRSA infection if
susceptible (0.006)17 by the incremental cost of an MRSA infection ($8,147).13
‡An appropriate open day used no additional resources as these patients are not colonized and cannot transmit
the MRSA infection to other patients.
Activity 3. Conduct a cost-minimization analysis to determine which MRSA screening test minimized total costs for a targeted isolation surveillance practice. A cost-minimization analysis from the hospital perspective was conducted to calculate the total cost of targeted isolation for a hypothetical cohort of patients admitted to the ICU. Cost categories included costs associated with the screening test, including the cost per test and personnel time, and costs associated with leaving a person open (not isolated). Open costs were separated into appropriate and inappropriate. Appropriate open costs were the resources associated with not isolating a noncolonized patient. Inappropriate open costs were assigned to those patients who were colonized with MRSA and not isolated. The screening test used as part of the surveillance practice was varied to determine which screening test minimized inappropriate and total costs. The following MRSA screening tests were assessed: conventional culture, chromogenic agar 48-hour, chromogenic agar 24-hour, and polymerase chain reaction. The screening test that minimized total costs was recommended as the most efficient screening test.

The analysis was modeled using a decision tree that accounted for the diagnostic accuracy and turnaround time of the different MRSA screening tests (Figure 3.2). The decision tree modeled pathways to represent patients that were appropriately and inappropriately left open. Because this analysis modeled preemptive isolation of all ICU admissions, a hypothetical patient was screened upon admission, but only isolated if he/she tested positive for MRSA.
Figure 3.2. Decision Tree Structure for Aim 1, Activity 3.

The payoff is denoted by a 1 or 0 at the end of the terminal node. Pathways ending in a 1 denoted patients who were appropriately left open (without isolation precautions) upon admission. Pathways ending in a 0 denoted patients who were inappropriately left open (without isolation precautions) upon admission.

To assess the impact of variation in the inputs on the results and conclusions, sensitivity analyses were conducted. A univariate sensitivity analysis using the lower and upper bounds of the input range in Table 3.2 determined parameters with influence over the incremental cost-effectiveness ratio. Additionally, a probabilistic sensitivity analysis of 1,000 Monte Carlo simulations varied all of the inputs over their plausible range simultaneously to create a distribution of each cost component and the total cost of the surveillance practice. Input ranges represented the 95% confidence interval where available. When 95% confidence intervals were unavailable for an input, the range was estimated by adding and subtracting 25% to the base-case value.

The needed inputs and source for each input are depicted in Table 3.2. All cost inputs were inflated to 2015 US dollars using the medical-cost inflation rate.81
Table 3.2. Inputs and Source of Each Input for Aim 1, Activity 3.

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</table>

*The cost of an isolation day includes costs associated with contact precautions and disinfectant.[^83]
†The cost of an open day was calculated by multiplying the daily risk of contracting an MRSA infection if susceptible (0.006)[^17] by the incremental cost of an MRSA infection ($8,147).[^[13]
ǂAn appropriate open day used no additional resources as these patients are not colonized and cannot transmit the MRSA infection to other patients.

**Aim 2**

Calculate the cost-effectiveness of MRSA prevention strategies, including screening and isolation, targeted decolonization, and universal decolonization, to determine if their improvements in health outcomes justify their implementation costs.

**Hypothesis**

Universal decolonization will be a dominant, less costly and more effective, strategy in preventing MRSA infections as compared to the standard practice of screening and
isolation. When considering the implementation of rapid, more expensive screening tests, universal decolonization will be more cost-effective when expensive screening tests are used.

**Background**

The REDUCE MRSA trial was a randomized controlled trial that assessed the comparative effectiveness of screening and isolation, targeted decolonization, and universal decolonization in preventing MRSA infections. The trial found universal decolonization to be the most effective strategy in reducing MRSA infections, by reducing infection rates 37%, whereas targeted decolonization and screening and isolation reduced infection rates 25% and 8% respectively. Following the publication of these results, the CDC and the Agency for Healthcare Research and Quality advocated for the implementation of universal decolonization in ICUs and updated their prevention policy to reflect universal decolonization. However, before widespread implementation, the cost-effectiveness of these prevention strategies should have been evaluated to ensure hospitals are allocating their limited resources in the most efficient way.

**Rationale**

The first objective of this aim was to determine if the added effect of universal and targeted decolonization justified the potential added costs. The second objective of this aim was to evaluate the effect of the screening test on the cost-effectiveness of each prevention strategy to determine which prevention strategy is most cost-effective given a specific screening test. To fulfill the first objective, we tested the hypothesis that universal decolonization would be a dominant strategy in preventing MRSA infections due to the large incremental effect over screening and isolation and targeted decolonization. For the second objective, we tested the hypothesis that universal decolonization would be more cost-
effective for facilities that use more expensive tests. These findings would provide tailored recommendations to facilities based on their available resources and capacity.

**Justification**

Despite the comparative effectiveness of these prevention strategies, there is little literature on the cost-effectiveness of these interventions. Existing cost literature rarely included universal decolonization as an intervention of interest, often had limited generalizability by only including special populations (neonatal ICUs or specific surgery patients), and did not account for the differences in cost and diagnostic accuracy of the screening tests used and how these differences could impact the overall cost-effectiveness. Because screening and isolation and targeted decolonization contain a screening component, and universal decolonization does not, the cost-effectiveness of these prevention strategies is dependent on the cost of the screening test used. Therefore, the cost-effectiveness of universal decolonization, the applicability of the results outside the sub-populations studied, and the influence of the screening test selection on the cost-effectiveness remained unknown. Due to these gaps in the literature, it was important to determine the cost-effectiveness of each prevention strategy, including universal decolonization, for the entire ICU patient population as they are at the greatest risk of contracting these infections. Additionally, it was important to evaluate the impact of the screening test selection on the overall cost-effectiveness of the prevention strategy.

**Impact**

Completion of this aim will inform hospital decision makers on which prevention strategy is most cost-effective and whether or not their implementation costs are justified by an improvement in health outcomes. Results from this aim can guide hospital decision
makers on which prevention strategy is most cost-effective for the screening test used at their facility.

**Approach**

Aim 2 was divided into three primary activities. Activity 1 calculated the cost-effectiveness of each prevention strategy using a decision tree model. Activities 2 and 3 repeated Activity 1 using a Markov model and agent-based transmission model instead of a decision tree.

**Activity 1. Assess the cost-effectiveness of each prevention strategy varying the screening test using a decision tree.** This analysis determined the cost-effectiveness of screening and isolation, targeted decolonization, and universal decolonization for each commonly used MRSA screening test. Prevention strategies were compared to one another. The cost-effectiveness of these strategies was determined by evaluating the incremental cost per MRSA infection averted and incremental cost per QALY gained for each prevention strategy. A prevention strategy was cost-effective if the incremental cost per MRSA infection averted was less than the average cost of an MRSA infection or if the incremental cost per QALY gained was less than $100,000 per QALY gained. This analysis was modeled using a decision tree from the hospital, payer, and societal perspective and had a time horizon of a hospitalization. The hospital perspective included all direct medical costs (screening, isolation, decolonization, hospitalization) plus the economic value of lost bed days due to the prolonged length of stay associated with a MRSA hospitalization. The payer perspective only included the reimbursement for the hospitalization, as payers rarely pay for patient screens, prevention strategies, or MRSA infections. The societal perspective included all costs above plus the costs to the patient, including productivity losses such as additional time off work.
Two decision trees were evaluated; one for each outcome. Decision Tree 2.1A was used to calculate the incremental cost per MRSA infection averted for each MRSA prevention strategy, whereas Decision Tree 2.1B was used to calculate the incremental cost per QALY gained for each MRSA prevention strategy. The structures of each tree are presented in Figures 3.3 and 3.4. Each model was conducted for each screening test separately; therefore, since there are four screening test categories of interest, there were four decision analyses for outcome one (incremental cost per MRSA infection averted) and four decision analyses for outcome two (incremental cost per QALY gained). Each tree assessed the cost-effectiveness of the three prevention strategies.

Figure 3.3. Decision Tree Structure 2.1A for Aim 2, Activity 1.
To assess the robustness of the results, sensitivity analyses were conducted. A univariate sensitivity analysis was used to determine parameters with influence over the incremental cost-effectiveness ratio. Additionally, a probabilistic sensitivity analysis using 1,000 Monte Carlo simulations varied all of the parameters at once. The results from the probabilistic sensitivity analysis were graphed as a cloud on the cost-effectiveness plane to visualize and evaluate the range of possible cost-effectiveness estimates under different input values.

The needed inputs and source for each input are depicted in Table 3.3. All cost inputs were inflated to 2015 US dollars using the medical-cost inflation rate.81
### Table 3.3. Inputs and Source of Each Input for Aim 2, Activity 1.

<table>
<thead>
<tr>
<th></th>
<th>Base-Case</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colonization Rate</strong></td>
<td>8%82</td>
<td>6-10%</td>
</tr>
<tr>
<td><strong>Probability of MRSA Infection over Hospitalization</strong></td>
<td>0.01482</td>
<td>0.010-0.018</td>
</tr>
<tr>
<td><strong>Screening and Isolation Hazard Ratio</strong></td>
<td>0.927</td>
<td>0.77-1.1</td>
</tr>
<tr>
<td><strong>Targeted Decolonization Hazard Ratio</strong></td>
<td>0.757</td>
<td>0.62-0.88</td>
</tr>
<tr>
<td><strong>Universal Decolonization Hazard Ratio</strong></td>
<td>0.637</td>
<td>0.53-0.77</td>
</tr>
<tr>
<td><strong>Conventional Culture Sensitivity</strong></td>
<td>86.9%23</td>
<td>74.7%-93.7%</td>
</tr>
<tr>
<td><strong>Conventional Culture Specificity</strong></td>
<td>89.7%23</td>
<td>77.7%-95.6%</td>
</tr>
<tr>
<td><strong>Conventional Culture Turnaround Time</strong></td>
<td>3.2 days15</td>
<td>2.1-4.0 days</td>
</tr>
<tr>
<td><strong>Conventional Culture Cost</strong></td>
<td>$2.11</td>
<td>$1.58-$2.64</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Sensitivity</strong></td>
<td>87.6%23</td>
<td>82.1%-91.6%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Specificity</strong></td>
<td>94.7%23</td>
<td>91.6%-96.8%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Turnaround Time</strong></td>
<td>2 days23</td>
<td>1.9-2.1 days</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Cost</strong></td>
<td>$4.6325</td>
<td>$3.47-$5.79</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Sensitivity</strong></td>
<td>78.3%23</td>
<td>71.0%-84.1%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Specificity</strong></td>
<td>98.6%23</td>
<td>97.7%-99.1%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Turnaround Time</strong></td>
<td>1 day23</td>
<td>0.8-1.1 days</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Cost</strong></td>
<td>$4.6325</td>
<td>$3.47-$5.79</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Sensitivity</strong></td>
<td>92.5%23</td>
<td>87.4%-95.9%</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Specificity</strong></td>
<td>97.0%23</td>
<td>94.5%-98.4%</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Turnaround Time</strong></td>
<td>0.6 days24</td>
<td>0.1-0.8 days</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Cost</strong></td>
<td>$28.5125</td>
<td>$21.38-$35.64</td>
</tr>
<tr>
<td><strong>Daily Cost of Contact Precautions</strong></td>
<td>$9083</td>
<td>$68-$113</td>
</tr>
<tr>
<td><strong>Daily Cost of Chlorhexidine Baths</strong></td>
<td>$5.5226</td>
<td>$4-$7</td>
</tr>
<tr>
<td><strong>Cost of Mupirocin for Five Days</strong></td>
<td>$7.5568</td>
<td>$7.05-$68.2</td>
</tr>
<tr>
<td><strong>Cost per Hospitalization (no MRSA)</strong></td>
<td>$9.67313</td>
<td>$7.255-$12,091</td>
</tr>
<tr>
<td><strong>Cost per Hospitalization (with MRSA)</strong></td>
<td>$17.82013</td>
<td>$13,365-$22,275</td>
</tr>
<tr>
<td><strong>Length of Hospitalization (no MRSA)</strong></td>
<td>4.6 days13</td>
<td>3.45-5.75 days</td>
</tr>
<tr>
<td><strong>Length of Hospitalization (with MRSA)</strong></td>
<td>10 days13</td>
<td>7.5-12.5 days</td>
</tr>
<tr>
<td><strong>ICU-Specific Mortality without MRSA</strong></td>
<td>14%82</td>
<td>10.5%-17.5%</td>
</tr>
<tr>
<td><strong>ICU-Specific Mortality with MRSA</strong></td>
<td>21%82</td>
<td>15.8%-26.3%</td>
</tr>
<tr>
<td><strong>Utility during and after ICU admission</strong></td>
<td>0.6882</td>
<td>0.51-0.85</td>
</tr>
</tbody>
</table>

Activity 2. Assess the cost-effectiveness of each prevention strategy varying the screening test using a Markov model. The objective of Aim 2, Activity 1 was also assessed using a Markov model instead of a decision tree to determine the influence of model selection on the results and conclusions. A limitation of a decision tree is its inability to account for time in its assumption that everything happens at the same time point. With the...
transmission of MRSA, as length of stay (time) increases, an individual is at an increased risk of becoming MRSA colonized or infected.\(^2\) By varying the modeling technique from a decision tree to a Markov model, this limitation can be overcome as the Markov model will increase the risk of MRSA acquisition as the length of stay (number of cycles) increases. The cost-effectiveness of screening and isolation, targeted decolonization, and universal decolonization was still assessed and a separate model was conducted for each commonly used MRSA screening test. Again, two outcomes were evaluated: incremental cost per MRSA infection averted and incremental cost per QALY gained. The analysis was conducted from the hospital, payer, and societal perspective and followed the hypothetical ICU patient for one year.

Similar to the analysis using decision trees, the model was run for each screening test to determine the effect of the screening test selection on the cost-effectiveness of each prevention strategy. Because there are four screening test categories of interest, four Markov models were evaluated, each of which assessed the cost-effectiveness of the three MRSA prevention strategies. The Markov model was considered superior to the decision tree approach as it modeled the increased risk of colonization and infection as length of stay increased. The Markov model (Figure 3.5) was used to calculate the incremental cost per MRSA infection averted and incremental cost per QALY gained for each MRSA prevention strategy. The model included the following health states: susceptible (a patient is neither colonized nor infected with MRSA), colonized (a patient is colonized with MRSA, but not infected), infected (a patient has signs of a MRSA clinical infection), discharged (a patient is discharged alive), and dead (a patient dies either due to a MRSA infection or some other cause). A daily cycle was applied to account for the increased risk of MRSA acquisition as
the length of stay (number of cycles) increases. At the start of the model, 92% of the cohort was in the susceptible state and 8% were colonized. A key assumption of the Markov model was that patients could not move backward. In other words, a colonized patient could not move to the susceptible state and an infected patient could not move to the colonized or susceptible state. This assumption is in line with clinical practice due to the lengthy carriage times of MRSA and the short average length of an ICU admission.

Figure 3.5. Markov Model Structure for Aim 2, Activity 2.

The inputs used in this analysis included the data inputs used in Aim 2, Activity 1; however, additional transition probabilities were needed for the Markov modeling approach. The transition probabilities for each health state are presented in Table 3.4. Transition probabilities were updated to reflect the effectiveness of the prevention strategy by multiplying the susceptible to colonized, susceptible to infected, colonized to colonized, and colonized to infected transition probabilities by the hazard ratios for each prevention strategy found in Table 3.3.
Table 3.4. Additional Data Inputs Needed for Aim 2, Activity 2.

<table>
<thead>
<tr>
<th>Transition From:</th>
<th>Susceptible</th>
<th>Colonized</th>
<th>Infected</th>
<th>Discharged</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible</td>
<td>.8934</td>
<td>.0037</td>
<td>.0006</td>
<td>.0807</td>
<td>.0216</td>
</tr>
<tr>
<td>Colonized</td>
<td>0.00</td>
<td>.8507</td>
<td>.0470</td>
<td>.0807</td>
<td>.0216</td>
</tr>
<tr>
<td>Infected</td>
<td>0.00</td>
<td>0.00</td>
<td>.9238</td>
<td>.0499</td>
<td>.0263</td>
</tr>
<tr>
<td>Discharged</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>1.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Dead</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Activity 3. Assess the cost-effectiveness of each prevention strategy varying the screening test using an agent-based transmission model. The objective of Aim 2, Activity 1 was also assessed using an agent-based transmission model instead of a decision tree or Markov model to determine the influence of model selection on the results and conclusions. A limitation of cohort models (decision trees and Markov models) is their inability to account for patient-level characteristics, such as prior history of disease or disease severity, in the risk of acquiring an infection. By varying the modeling technique from a cohort model to a patient-level model, this limitation could be overcome as the interplay of patient-level characteristics on the probability of an outcome could be modeled. The cost-effectiveness of screening and isolation, targeted decolonization, and universal decolonization were still assessed and a separate simulation was conducted for each commonly used MRSA screening test category. Again, two outcomes were assessed: incremental cost per MRSA infection averted and incremental cost per QALY gained. The analysis was conducted from the hospital, payer, and societal perspective and followed a cohort for one year after ICU admission.

The agent-based transmission model schematic is pictured in Figure 3.6. Similar to the methods used in Activities 1 and 2, the simulation was run for each screening test.
Therefore, since there are four screening test categories of interest, four simulations were evaluated, each of which assessed the cost-effectiveness of the three prevention strategies. The simulation clock was set for one day. The model was stochastic as the number colonized/infected depended on the number colonized/infected from the previous day. As MRSA prevalence increased, the risk of colonization/infection increased. The model assumed 100% bed occupancy in the ICU.

**Figure 3.6. Agent Based Transmission Model Schematic for Aim 2, Activity 3.**

**Aim 3**

Measure the impact of a Prevention and Public Health Fund activity (The Prevention of HAIs across the Spectrum of Health Care) on hospital-associated CLABSI rates to determine if public health funding is effective in preventing infections at the hospital level and whether or not there was a positive return associated with the investment.
Hypothesis

Hospitals in states that received state health department funding for the Prevention of HAIs across the Spectrum of Health Care will have greater reductions in the standardized infection ratios for bloodstream infections than hospitals in states that did not receive funding.

Background

Section 4002 of the Patient Protection and Affordable Care Act created the Prevention and Public Health Fund with the intent to improve the nation’s health and restrain the ever increasing health care costs. Initially, legislation allocated $15 billion dollars to this fund over its first ten years with the intent to expand and sustain prevention and public health programs. In 2013, $949 million was dedicated to the Prevention and Public Health Fund, of which nearly half was allocated to the CDC to aid in their disease prevention, surveillance, and tracking efforts. The CDC then awarded nearly $7 million to 15 states for the Prevention of HAIs across the Spectrum of Healthcare, an activity designed to develop and implement evidence-based multi-facility prevention initiatives. Little research on the impact of this fund exists likely due to its recent implementation; however, previous research has shown that increases in public health spending can be associated with improved health outcomes, such as a decrease in mortality. Public health spending is most effective when allocated to activities that are proven to be effective; therefore, the goal of this aim was to determine if this funding was effective in reducing hospital HAI rates to the extent the cost savings due to infections averted outweighed the initial investment.
**Rationale**

The objective of this analysis was to evaluate public health funding from the Prevention and Public Health Fund to determine its effect on health outcomes, specifically HAIs. To reach this objective, we tested the hypothesis that hospitals in states that received state health department funding specific to the prevention of HAIs would have greater reductions in the standardized infection ratios for CLABSI than hospitals in states that did not receive funding. To test this hypothesis, a quasi-experimental study using a difference-in-differences design was used to assess the treatment effect of the program. The treatment effect (reductions in CLABSI) was then monetized to determine the cost savings associated with the funding.

**Justification**

The Prevention and Public Health Fund was set to increase to $2 billion each year starting in 2015 and each year thereafter; however, controversy has surrounded the effectiveness and necessity of this fund leading to legislation that cut portions of this budget and even bills that suggest elimination of this fund altogether. In 2012, President Barack Obama signed legislation that cut the fund by $5 billion over a ten year period. This fund has also been targeted for complete elimination in the United States House of Representatives’ 2016 Budget Resolution as well as in other bills being considered in the House of Representatives. Thus, there was an urgent need for original research around the effectiveness of this funding to determine if this funding mechanism is an effective approach to reduce these infections before this funding is further cut or eliminated. This study conducted original research on the impact of this public health funding on hospital HAI
rates to determine if these infections were reduced to a point that generated a positive return on investment.

**Impact**

The results from this aim can inform policy makers on the impact and return on investment of public health spending on health outcomes, specifically HAI rates.

**Approach**

Aim 3 consisted of a quasi-experimental design. A true experiment includes a pre-period and a post period, a treatment group and a control group, and random assignment of participants to the groups. This study was not a true experiment as it lacked random assignment. This study evaluated the changes in bloodstream infection rates over time for hospitals in states that received the funding as compared to hospitals in states that did not receive the funding. However, because the funding was not randomly allocated, instead the CDC selected states to receive the funding, this study was not a true experiment. To control for the fact that the funding was not randomized, control variables were used to adjust for the potential differences between the two groups.

A difference-in-differences design was used to assess the treatment effect of the funding to evaluate the changes in the bloodstream infection rates before and after the allocation of the funds.49 By using a difference-in-differences model, trends were able to be observed before and after an intervention, as well as have a group to compare the trends in the treated group to. To test the validity of the difference-in-differences specification, pre-period trends were evaluated to determine if they were parallel between the states that received the funding and the states that did not. The parallel trends assumption was met. The effect of the payment reform on the hospital bloodstream infection rates was calculated by
comparing the average change over time in the states that received the funding to the average change over time in the states that did not receive the funding. A hospital fixed and random effect were used to control for all observed and unobserved time-invariant factors. Random effects were rejected in favor of fixed effects based on the results of a significant Hausman specification test.87

The following model was evaluated:

\[ \text{Log}_{-} \text{CLABSI}_{-} \text{SIR}_{it} = \beta_0 + \beta_1 \text{Funding} \text{*Year}2013_{it} + \beta_2 \text{Funding} \text{*Year}2014_{it} + \beta_3 \text{Funding}_{it} + \beta_4 \text{Year}2013_{it} + \beta_5 \text{Year}2014_{it} + \beta_6 \text{Hospital} \text{-Characteristics}_{it} + \beta_7 \text{Staffing}_{it} + \beta_8 \text{Service} \text{-Offerings}_{it} + \beta_9 \text{Observed} \text{-Cases}_{it} + \beta_{10} \text{Reporting} \text{-Mandate}_{it} + \alpha_i + \epsilon_{it} \]

The unit of analysis was the hospital. The outcome of interest was CLABSI standardized infection ratios. Thousands of deaths each year are attributed to CLABSIs and billions of dollars in excess health care costs result from these infections.9 These rates are defined as a standardized infection ratio calculated by dividing the number of observed CLABSI cases by the number of expected CLABSI cases for each hospital.88 The number of expected CLABSI cases is adjusted for factors that may influence the number of infections including location, affiliation with a medical school, and bed count.88 Hospital CLABSI standardized infection ratios were modeled as a function of the control variables.49 The following hospital-level covariates were added to control for hospital differences that may be correlated with hospital infection rates: location in an urban or rural location, affiliation with a medical school, bed count, ownership, provision of inpatient surgeries, provision of emergency services, presence of a clinical laboratory on site, presence of an intensive care unit on site, and percent of total nurses that were registered. In addition to the hospital-level covariates, a state reporting mandate was controlled for because a reporting mandate can
influence reported standardized infection ratios independent of the receipt of funding. Hospitals in states that received the funding in 2013 were the “treated” hospitals and hospitals in states that did not receive funding in 2013 were the “control” hospitals. The log of CLABSI standardized infection ratios was estimated as a function of a dichotomous variable indicating whether the hospital was in a state that received funding (Funding), a year fixed effect for 2013 (Year2013) and 2014 (Year2014), and interactions between Funding and Year2013 and Funding and Year2014 to calculate the treatment effect in 2013 and 2014, respectively.

To assess the stability of the results, the parameter estimates were bootstrapped. Bootstrapping is a process that involves resampling the sample data multiple times to increase the accuracy of the parameter estimates and standard errors and to gain a better and more accurate understanding of the variation in the parameter estimates. The dependent variable, CLABSI standardized infection ratio, was positively skewed, and thus it was log–transformed. Because approximately 40% of hospitals had no observed CLABIs (i.e. numerator of standardized infection ratio=0 and thus standardized infection ratio=0), 0.0001 was added to the standardized infection ratio before log transforming to prevent the omission of those observations. This number is small enough in magnitude that it should not impact the results; however, it ensured a larger and more complete sample as the observations with a “0” for the standardized infection ratio would not be dropped. Lastly, the model also accounted for regression to the mean to control for the facilities that had extreme standardized infection ratios before funding allocation moving closer to the mean through random chance.52 Funding is allocated to public health departments in a variety of ways, often to those in the greatest need (based on the prevalence of health problems) or to
departments that can develop the best proposals (usually those communities with more resources and greater capacity). Because the parallel trends assumption was met and the model accounted for regression to the mean, this potential bias was less of a concern.

Multiple sensitivity analyses were conducted to assess the robustness of the results. For the first sensitivity analysis, the results were stratified by whether or not the states had a reporting mandate, hospital ownership, hospital affiliation with a medical school, and urban/rural designation to determine differences in treatment effect for these subgroups. Also, the model was fit using generalized linear models (GLM) with a gamma family and log link specification. Because the dependent variable was skewed, GLM might have been a better fit for the data. The favored specification for the GLM family (gamma) was selected based on which family had a nonsignificant p value for the chi square estimate. The following families were tested: Gaussian, Poisson, Negative Binomial, and Gamma. Pregibon’s link test was used to determine if the model was a good fit for the data and if there were any variables omitted or if the link (log) was not correctly specified. For a sensitivity analysis, GLM was used in lieu of log transforming the dependent variable but should produce similar results. Furthermore, due to the dependent variable being a ratio, the error variance depends on the numerator and denominator of the ratio (the number of observed and expected cases). The standard error for the standardized infection ratio is equivalent to the square root of the number of observed cases divided by the number of expected cases. To normalize the error variance, an analytic weight of the mean of the inverse of the standard error was applied to the model. Weighting by the frequency of the denominator (expected cases) could determine if the decline was dominated by large changes in smaller facilities.
Lastly, the return in health outcomes in monetary units was calculated. In 2013, nearly $7 million was awarded to fifteen state health departments to prevent HAIs across the spectrum of healthcare.\textsuperscript{19} Although this program required a monetary investment, the program could have actually saved costs to society by decreasing HAIs. The reductions in CLABSIs were monetized to determine if the cost savings due to infections averted outweighed the initial investment. The cost offsets associated with the reduction in infections were calculated to determine if they outweighed the initial investment. To calculate the cost offsets, the reductions in CLABSIs were monetized by multiplying the number of infections averted by the hospital cost per CLABSI ($24,145).\textsuperscript{79} The return on investment was then calculated by dividing the cost offsets due to infections averted by the funding amount provided to the 15 states.\textsuperscript{90} Each of the bootstrapped treatment effect parameter estimates from the regression to the mean adjusted, fixed effect model were used to calculate the infections averted, cost offsets due to infections averted, and return on investment. This allowed for the determination of the expected value and a 95\% interval for each of these parameters. To account for the potential price variation and uncertainty in the cost of each CLABSI case, the break-even price per CLABSI was calculated by dividing the initial investment by the number of infections averted.

Data Sources

Data were collected from three sources. The study period spanned four years including two years before funding allocation (2011 and 2012), the year the funding was allocated (2013), and a year when the activity was no longer funded (2014). Information on which states received the funding and had a reporting mandate were gathered from the CDC’s website.\textsuperscript{19} Centers for Medicare and Medicaid Services (CMS) Hospital Compare
data from 2011-2014 were the sources for hospital infection rates. Additional hospital control variables were taken from 2011-2014 CMS Point of Service (POS) data.

**Population and Sample**

The population for Aims 1 and 2 consisted of all adult ICUs in the United States. Because a modeling structure was used with a hypothetical cohort and hypothetical patients, no direct sampling technique was used. However, the effectiveness data was taken from the REDUCE MRSA trial which was a clinical trial that included 74 ICUs from 43 HCA hospitals. Because the effectiveness of each strategy may vary outside of HCA hospitals, the effectiveness inputs were varied in the sensitivity analyses to ensure the generalizability of the results. The population for Aim 3 included all acute care hospitals. However, since the CLABSI standardized infection ratio data was only available through CMS, the sample only included acute care facilities that accept Medicare or Medicaid. Facilities in Arizona were excluded because the Arizona state health department also received funding in 2013 to improve the detection of HAIs for antimicrobial-resistant pathogens. To prevent any detection bias, all hospitals in this state were excluded from the analysis. Due to this, the sample for Aim 3 included those acute care facilities that accept Medicare or Medicaid patients in 49 United States and Washington, D.C.

**Summary**

This chapter explained the methodology used to achieve the three aims of this dissertation. The primary method used to achieve Aims 1 and 2 was decision tree analysis, however, the modeling technique was varied to include Markov modeling and agent-based transmission modeling to determine the degree to which the results differ based on the modeling technique used. Aim 3 was addressed through regression analysis using a
difference-in-differences model to determine the effect of the Public Health and Prevention Fund on HAI rates. Chapter Four presents the results of each aim as three publishable papers, and Chapter Five provides a summary and interpretation of the work and explores the implications for clinical practice and policy with a discussion on future research needed.
CHAPTER IV
RESULTS

Introduction

This dissertation follows the three paper dissertation structure. As such, this chapter presents the results of each aim as three separate, publishable papers of normal journal length. The results of Aim 1 are presented in a manuscript written for the *Journal of Infection Control and Epidemiology*. The title of this manuscript is, “Screening Test Recommendations for Methicillin-Resistant *Staphylococcus aureus* Surveillance Practices: A Cost-Minimization Analysis”. The results of Aim 2 are presented in a manuscript written for *Critical Care Medicine* and is titled, “Recommendations for Methicillin-Resistant *Staphylococcus aureus* Prevention in the ICU: A Cost-Effectiveness Analysis”. The results of Aim 3 are presented in a manuscript titled “Value of the Prevention and Public Health Fund in Preventing Hospital Infections” and is written for the *American Journal of Public Health*.

Results of Dissertation

**Aim 1**

**Introduction**

Healthcare-associated infections (HAIs) are one of the most common complications associated with hospital care\(^3\) and are one of the leading causes of preventable death in the United States.\(^4\) Despite being largely preventable, these infections negatively affect one out of every 25 hospitalized patients\(^9^1\) and are associated with an economic burden of more than $40 billion each year.\(^6\) Methicillin-resistant *Staphylococcus aureus* (MRSA) is a well-established cause of HAIs that includes the extra designation of being a drug-resistant
In addition to causing increased morbidity and mortality, MRSA infections are associated with a large economic burden, as they nearly double the cost of a hospitalization.\textsuperscript{13} Patients in the intensive care unit (ICU) are at the greatest risk of contracting these infections because severe illness, immunosuppression, and extended lengths of stay are common patient-related risk factors associated with HAIs like MRSA.\textsuperscript{14} To mitigate MRSA infections, ICUs conduct MRSA surveillance through screening of the nares upon patient admission followed by isolation precautions.\textsuperscript{7} Two approaches to MRSA surveillance in the ICU are universal preemptive isolation and targeted isolation of only MRSA-positive patients.\textsuperscript{15}

Under the universal preemptive isolation surveillance practice, all patients are screened upon admission and are immediately isolated until the absence of MRSA carriage has been shown.\textsuperscript{15} Preemptively isolating all patients is effective in reducing the transmission of MRSA; however, noncolonized patients are unnecessarily isolated, leading to unnecessary resource use (contact precautions, disinfectant, etc.)\textsuperscript{16} and thus excess cost.\textsuperscript{15} Therefore, some ICUs wait to isolate patients until the screening test results come back and then only isolate those who test positive for MRSA. This strategy of targeted isolation reduces the number of patients unnecessarily isolated, but delays the initiation of isolation for colonized individuals which could lead to the transmission of MRSA between patients. When colonized patients are not isolated, susceptible patients are at risk of acquiring MRSA at a rate of approximately 1\% per day.\textsuperscript{17}

Universal preemptive isolation and targeted isolation differ in when isolation precautions are implemented, but both include universal screening upon admission to the ICU. MRSA screening has historically relied on the growth and identification of the bacterial
species on culture. Culture methods are inexpensive but can take multiple days to detect MRSA.\textsuperscript{15,23} An increasingly common alternative is to use more rapid screening tests, such as chromogenic agars or polymerase chain reactions.\textsuperscript{23,24} Although costlier, these tests generate results in a few hours.\textsuperscript{23–25} These more rapid and expensive screening tests also tend to have a higher sensitivity in detecting the bacterial species.\textsuperscript{23}

Both universal and targeted surveillance practices could be enhanced if coupled with screening tests that produce results quicker. With universal preemptive isolation, a quicker result would allow noncolonized patients to be removed from isolation sooner and thus reduce the total isolation costs. Similarly, with targeted isolation, a quicker result allows earlier implementation of isolation precautions and thus reduces the number of open days, or the days a MRSA-positive patient is not isolated and could transmit the pathogen to other patients.\textsuperscript{51} Therefore, although these rapid screening tests are more costly, they could result in cost offsets. The objective of this study was to calculate the cost of universal preemptive isolation and targeted isolation and identify the MRSA screening test that minimizes costs for each surveillance practice.

\textbf{Methods}

\textbf{Study design.} A cost-minimization analysis from the hospital perspective was conducted to calculate the total cost of MRSA surveillance practices for a hypothetical cohort of patients admitted to the ICU. Two surveillance practices were assessed: 1) universal preemptive isolation upon admission and 2) targeted isolation of only MRSA-positive patients. For the universal preemptive isolation surveillance practice, cost categories included costs associated with the screening test, including the cost per test and personnel time to administer and read the test, and costs associated with isolation, including the cost of contact
precautions and disinfectant. Isolation costs were separated into appropriate and inappropriate. Appropriate isolation costs were those isolation costs spent on patients who were colonized with MRSA. Inappropriate isolation costs were those isolation costs spent on patients who were unnecessarily isolated because they were not colonized with MRSA. For the targeted isolation surveillance practice, cost categories included costs associated with the screening test, including the cost per test and personnel time, and costs associated with leaving a person open (not isolated). Open costs were separated into appropriate and inappropriate. Appropriate open costs were the resources associated with not isolating a noncolonized patient. Inappropriate open costs were assigned to those patients who were colonized with MRSA and not isolated.

This analysis is from the hospital perspective because hospitals are responsible for covering the cost of surveillance. Although hospitals are currently paying for the implementation of these surveillance practices, resources could be used more efficiently if inappropriate and total costs were minimized. The screening test used as part of the surveillance practice was varied to determine which screening test minimized inappropriate and total costs. The following MRSA screening tests were assessed: conventional culture, chromogenic agar 48-hour, chromogenic agar 24-hour, and polymerase chain reaction. This analysis calculated the cost of universal preemptive isolation under these four different screening test selections. The results of each of the four universal preemptive isolation scenarios were compared. This analysis also calculated the cost of targeted isolation under the four different screening test selections, and the results of each of the four targeted isolation scenarios were compared. Because the comparisons were within the same intervention, the outcomes were equivalent and thus a cost-minimization analysis was used to
determine which screening test minimized total costs. The screening test that minimized total costs was recommended as the most efficient screening test for each surveillance practice.

**Model design.** The analysis was modeled using a decision tree that accounted for the diagnostic accuracy and turnaround time of the different MRSA screening tests. The decision tree modeled pathways to represent patients that were appropriately and inappropriately preemptively isolated for the universal preemptive isolation surveillance practice and pathways to stratify patients that were appropriately and inappropriately left open (unisolated) for the targeted isolation surveillance practice. For the universal preemptive isolation model (Figure 4.1), a hypothetical patient was screened and isolated upon admission. The patient was removed from isolation if his/her screening test came back negative. For the targeted isolation model (Figure 4.2), a hypothetical patient was screened upon admission, but only isolated if he/she tested positive for MRSA.

**Figure 4.1. Decision Tree Structure for Universal Preemptive Isolation**

A ‘1’ at the end of the pathway represents a patient that was appropriately isolated. A ‘0’ at the end of the pathway represents a patient that was inappropriately isolated.
Figure 4.2. Decision Tree Structure for Targeted Isolation

A ‘1’ at the end of the pathway represents a patient that was appropriately left open. A ‘0’ at the end of the pathway represents a patient that was inappropriately left open.

Model inputs. Published infection control literature was reviewed to retrieve clinical and cost inputs. Clinical inputs included the colonization rate, sensitivity and specificity for each screening test, and the turnaround time for each screening test. Cost inputs included the cost of each screening test (including the cost of materials and laboratory personnel time), the cost per isolation day, and the cost per open day. All cost inputs were inflated to 2015 US dollars using the medical-cost inflation rate. Model inputs are detailed in Table 4.1.
Table 4.1. Model Inputs for Base-Case and Sensitivity Analyses

<table>
<thead>
<tr>
<th></th>
<th>Base-Case</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colonization Rate</strong></td>
<td>8%(^{82})</td>
<td>6-10%</td>
</tr>
<tr>
<td><strong>Conventional Culture Sensitivity</strong></td>
<td>86.9%(^{23})</td>
<td>74.7%-93.7%</td>
</tr>
<tr>
<td><strong>Conventional Culture Specificity</strong></td>
<td>89.7%(^{23})</td>
<td>77.7%-95.6%</td>
</tr>
<tr>
<td><strong>Conventional Culture Turnaround Time</strong></td>
<td>3.2 days(^{15})</td>
<td>2.1-4.0 days</td>
</tr>
<tr>
<td><strong>Conventional Culture Cost</strong></td>
<td>$2.11</td>
<td>$1.58-$2.64</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Sensitivity</strong></td>
<td>87.6%(^{23})</td>
<td>82.1%-91.6%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Specificity</strong></td>
<td>94.7%(^{23})</td>
<td>91.6%-96.8%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Turnaround Time</strong></td>
<td>2 days(^{23})</td>
<td>1.9-2.1 days</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Cost</strong></td>
<td>$4.63(^{25})</td>
<td>$3.47-$5.79</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Sensitivity</strong></td>
<td>78.3%(^{23})</td>
<td>71.0%-84.1%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Specificity</strong></td>
<td>98.6%(^{23})</td>
<td>97.7%-99.1%</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Turnaround Time</strong></td>
<td>1 day(^{23})</td>
<td>0.8-1.1 days</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Cost</strong></td>
<td>$4.63(^{25})</td>
<td>$3.47-$5.79</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Sensitivity</strong></td>
<td>92.5%(^{23})</td>
<td>87.4%-95.9%</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Specificity</strong></td>
<td>97.0%(^{23})</td>
<td>94.5%-98.4%</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Turnaround Time</strong></td>
<td>0.6 days(^{24})</td>
<td>0.1-0.8 days</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Cost</strong></td>
<td>$28.51(^{25})</td>
<td>$21.38-$35.64</td>
</tr>
<tr>
<td><strong>Cost per Isolation Day</strong>(^{83})</td>
<td>$90 (^{83})</td>
<td>$68-113</td>
</tr>
<tr>
<td><strong>Cost per Inappropriate Open Day</strong>(^{13,17})</td>
<td>$48.88 (^{13,17})</td>
<td>$36.66-$61.10</td>
</tr>
<tr>
<td><strong>Cost per Appropriate Open Day</strong>(^{1})</td>
<td>$0</td>
<td>$0</td>
</tr>
</tbody>
</table>

*Sensitivity analyses.* To assess the impact of variation in the inputs on the results and conclusions, sensitivity analyses were conducted. A univariate sensitivity analysis using the lower and upper bounds of the input range in Table 4.1 determined parameters with influence over the incremental cost-effectiveness ratio. Additionally, a probabilistic sensitivity analysis of 1,000 Monte Carlo simulations varied all of the inputs over their plausible range simultaneously to create a distribution of each cost component and the total cost of the surveillance practice. Input ranges in Table 4.1 represent the 95% confidence interval where...
available. When 95% confidence intervals were unavailable for an input, the range was estimated by adding and subtracting 25% to the base-case value.

This study was exempt from human subjects’ review by the Colorado Multiple Institutional Review Board.

Results

**Base-case analysis.** Under the universal preemptive isolation surveillance practice, rapid screening tests like chromogenic agar and polymerase chain reaction were less costly and avoided more inappropriate isolation days compared to conventional culture (Table 4.2). Therefore, the savings in isolation costs due to more quickly removing noncolonized patients from isolation precautions were greater than the added cost per test. Total and inappropriate costs were reduced as the turnaround time of the test increased, with costs being minimized for both inappropriate and total costs with the use of a polymerase chain reaction screening test.

**Table 4.2. Cost of Universal Preemptive Isolation for Different MRSA Screening Tests**

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Appropriate Isolation Costs per Patient</th>
<th>Inappropriate Isolation Costs per Patient</th>
<th>Total Costs per Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional Culture</td>
<td>$2.11</td>
<td>$25.20</td>
<td>$262.80</td>
</tr>
<tr>
<td>Chromogenic Agar 48-Hour</td>
<td>$4.63</td>
<td>$14.4</td>
<td>$165.60</td>
</tr>
<tr>
<td>Chromogenic Agar 24-Hour</td>
<td>$4.63</td>
<td>$7.20</td>
<td>$82.80</td>
</tr>
<tr>
<td>Polymerase Chain Reaction</td>
<td>$28.51</td>
<td>$4.50</td>
<td>$49.50</td>
</tr>
</tbody>
</table>

Under the targeted isolation surveillance practice, the use of chromogenic agar 24-hour resulted in the smallest total costs (Table 4.3). Although the polymerase chain reaction screening test resulted in fewer inappropriate costs, the much higher cost of the screening test resulted in the use of polymerase chain reaction having the highest total costs. Inappropriate
costs were reduced as the turnaround time of the test increased, but total costs were minimized with the use of chromogenic agar 24-hour.

**Table 4.3. Cost of Targeted Isolation for Different MRSA Screening Tests**

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Screening Costs per Patient</th>
<th>Appropriate Isolation Costs per Patient</th>
<th>Inappropriate Isolation Costs per Patient</th>
<th>Total Costs per Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional Culture</td>
<td>$2.11</td>
<td>$0</td>
<td>$12.22</td>
<td>$14.33</td>
</tr>
<tr>
<td>Chromogenic Agar 48-Hour</td>
<td>$4.63</td>
<td>$0</td>
<td>$7.82</td>
<td>$12.45</td>
</tr>
<tr>
<td>Chromogenic Agar 24-Hour</td>
<td>$4.63</td>
<td>$0</td>
<td>$3.91</td>
<td>$8.54</td>
</tr>
<tr>
<td>Polymerase Chain Reaction</td>
<td>$28.51</td>
<td>$0</td>
<td>$2.44</td>
<td>$30.95</td>
</tr>
</tbody>
</table>

**Sensitivity analysis.** A univariate sensitivity analysis was conducted to determine inputs with the most influence over the cost of each surveillance practice. Parameters with the most influence included the screening test price and screening test turnaround time. However, the variation in these inputs did not change the conclusions from the base-case analysis.

A similar trend resulted from the probabilistic sensitivity analysis. The total cost of each surveillance practice was calculated after varying all model inputs simultaneously for 1,000 Monte Carlo simulations. The distribution of the total costs was plotted to determine which screening test minimized total costs. Figure 4.3 presents the distribution of total costs for each screening test assuming the use of a universal preemptive isolation surveillance practice. Similar to what was observed in the base-case analysis, the use of conventional culture produced the highest distribution of total costs, and the use of polymerase chain reaction minimized total costs.
Figure 4.3. Distribution of Total Costs for Universal Preemptive Isolation

Figure 4.4 presents the distribution of total costs for each screening test assuming the use of a targeted isolation surveillance practice. Similar to what was observed in the base-case analysis, the use of polymerase chain reaction produced the highest distribution of total costs, and the use of chromogenic agar 24-hour minimized total costs.
Discussion

For ICUs that preemptively isolate all patients, rapid MRSA screening tests minimize total costs because the inappropriate isolation costs saved from the quicker turnaround time are greater than the added cost per test. The more rapid the screening test is, the smaller the total cost due to the isolation cost savings. These results were robust through sensitivity analyses. There would need to be implausible increases in either the screening test price or turnaround time for rapid screening tests to no longer be less costly than conventional culture. Rapid screening tests, like polymerase chain reactions, are therefore recommended for ICUs with a universal preemptive isolation surveillance policy to minimize inappropriate isolation costs and reduce total implementation costs.

For ICUs that only isolate MRSA-positive patients, the added cost for chromogenic agar is offset by the reductions in costs associated with inappropriate open days and therefore
chromogenic agar minimizes total cost. Although the inappropriate costs were minimized with the polymerase chain reaction screening test, the added cost for the test was not offset by these reductions in inappropriate open costs. There would need to be dramatic reductions in the polymerase chain reaction screening test price or increases in the daily risk of MRSA acquisition to make these screening tests the cheapest method. Chromogenic agar 24-hour is therefore recommended for ICUs with a targeted isolation surveillance policy.

This research calculates the cost of two common MRSA surveillance practices and provides recommendations on screening test selection for ICUs based on their surveillance practice. Existing cost-effectiveness literature around rapid MRSA screening tests have reported conflicting results. Some research has concluded that rapid screening tests reduced costs as well as unfavorable health outcomes\(^{16}\) and can be considered cost-saving.\(^{15}\) However, other research has contradicted this showing more conventional screening methods to be less costly than rapid screening tests.\(^{28}\) This study adds to this literature to provide clarification to the contradicting conclusions by suggesting the most efficient screening test is dependent on the surveillance practice implemented.

Similar to other economic evaluations, this study is limited by potential variations in prices between facilities. However, this limitation was addressed in multiple sensitivity analyses. Even when cost inputs were varied across a large range, the conclusions remained the same. Additionally, this study does not evaluate which surveillance practice (universal preemptive isolation versus targeted isolation) is the best use of resources due to the limited comparative effectiveness evidence between the two surveillance practices. However, this study adds to the literature by providing hospitals with information on how to most efficiently use their resources given implementation of both of these surveillance practices is
common. Hospitals are currently paying for these surveillance practices and this study provides evidence on the cost of each practice and the screening test that can minimize the total cost. The implications of this analysis extend beyond MRSA surveillance and can be adjusted in future work to analyze the costs and help in the decision making related to other drug-resistant organisms for which screening and isolation of colonized patients is common.

Preventable HAIs like MRSA remain a health and economic burden in hospitals, especially in ICUs. With knowledge on the screening test that minimizes inappropriate and total costs, hospitals can maximize the efficiency of their resource use and improve the health of their patients.

Aim 2

Introduction

Healthcare-associated infections (HAIs) affect one out of every 25 hospitalizations and result in excess healthcare costs of more than $40 billion each year. Patients in the ICU are at the greatest risk of acquiring an HAI as 65% of all HAIs are reported in the critical care setting. Methicillin-resistant *Staphylococcus aureus* (MRSA), a resistant strain of *Staphylococcus aureus*, is a common cause of HAIs that increases morbidity and mortality for the infected patient and nearly doubles the cost of a hospitalization. If ICUs do not take action to mitigate these infections, there would be approximately 218,000 MRSA infections a year resulting in an annual economic burden of $3.3 billion for the United States alone.

Many HAIs are preventable, which creates opportunities for interventions at decreasing their incidence. To prevent MRSA infections, common practice in the ICU involves bilateral screening of the nares upon patient admission followed by the
implementation of isolation precautions.\(^7\) Despite this practice, the rate of MRSA infection persists at high levels resulting in the implementation of novel prevention strategies, such as decolonization, to mitigate the nosocomial transmission of MRSA. Decolonization eliminates the colonization of MRSA and other microbiota on individuals’ skin and in their nose and thus should protect MRSA carriers from subsequent infection and reduce the transmission of bacteria to others.\(^7\)

After a randomized controlled trial found universal decolonization to be the most effective strategy in reducing MRSA infections,\(^7\) the Centers for Disease Control and Prevention and the Agency for Healthcare Research and Quality published protocols for universal decolonization implementation in ICUs.\(^9\) However, before widespread implementation, it is important to determine if the implementation costs are justified by improvements in health outcomes to ensure hospitals are allocating their limited resources efficiently. The objective of this analysis is to calculate the cost-effectiveness of MRSA prevention strategies and recommend specific strategies to ICUs based on the screening test they use.

**Materials and Methods**

A clinical decision analysis from the hospital perspective was conducted to determine the cost-effectiveness of MRSA prevention strategies for a hypothetical cohort of adult patients admitted to the ICU. The cohort was followed for one year. Cost-effectiveness was determined by calculating the incremental cost per MRSA infection averted and the incremental cost per quality-adjusted life year (QALY) gained. Decolonization strategies were compared to the standard practice of screening and isolation to determine if their implementation costs were justified by their reduction in MRSA infections and
improvements in overall QALYs. Additionally, decolonization strategies were compared to each other.

A Markov model (Figure 4.5) with a daily cycle was used to model the risk of MRSA infection. Health states included: susceptible (a patient is neither colonized nor infected with MRSA), colonized (a patient is colonized with MRSA, but does not exhibit symptoms of a MRSA clinical infection), infected (a patient exhibits symptoms of a MRSA clinical infection), discharged (a patient is discharged alive), and dead (a patient dies either due to a MRSA infection or some other cause). A daily cycle was applied to account for the increased risk of MRSA acquisition as the length of stay (number of cycles) increases. At the start of the model, 92% of the cohort was in the susceptible state and 8% were colonized.

Figure 4.5. Markov Model Structure

The model compared the costs and health outcomes for an adult patient in the ICU following screening and isolation, targeted decolonization, and universal decolonization. The model accounted for the costs associated with implementing each prevention strategy and the cost of a hospitalization with and without MRSA. The health outcomes observed were the
number of MRSA infections and QALYs gained. A separate model was evaluated for each screening test commonly used with these prevention strategies.

**Description of interventions.** Three prevention strategies were evaluated, including screening and isolation, targeted decolonization, and universal decolonization. Screening and isolation consists of universal nasal screening upon admission and contact precautions for patients that test positive for MRSA. Targeted decolonization also involves universal nasal screening upon admission, but includes both contact precautions and decolonization for patients that test positive for MRSA. A typical decolonization regimen consists of twice daily intranasal mupirocin ointment for five days and daily bathing with chlorhexidine-impregnated cloths for the entire length of stay. Unlike screening and isolation and targeted decolonization, universal decolonization does not include a screening component. Instead, all patients are decolonized upon admission. These interventions are consistent with a published randomized controlled trial designed by the Centers for Disease Control and Prevention. In this trial, universal decolonization was the most effective strategy at reducing MRSA infections by 37%, whereas targeted decolonization and screening and isolation reduced infections by 25% and 8% respectively.

Because screening and isolation and targeted decolonization have a screening component, the screening test in the model was varied to reflect commonly used screening test categories, including conventional culture, chromogenic agar 48-hour, chromogenic agar 24-hour, and polymerase chain reaction. These screening tests differ in their diagnostic accuracy, cost and turnaround time, all of which could affect the cost-effectiveness of the prevention strategy (Table 4.4).
Table 4.4. Diagnostic Accuracy, Turnaround Time, and Cost for MRSA Screening Tests

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Turnaround Time</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conventional Culture</strong></td>
<td>86.9%</td>
<td>89.7%</td>
<td>3.2 days</td>
<td>$2.11</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour</strong></td>
<td>87.6%</td>
<td>94.7%</td>
<td>2 days</td>
<td>$4.63</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour</strong></td>
<td>78.3%</td>
<td>98.6%</td>
<td>1 day</td>
<td>$4.63</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction</strong></td>
<td>92.5%</td>
<td>97.0%</td>
<td>0.6 days</td>
<td>$28.51</td>
</tr>
</tbody>
</table>

**Model inputs.** Published infection control literature was reviewed to retrieve clinical, cost, and utility inputs. Clinical inputs included the colonization rate, daily probability of transitioning to each health state with no prevention strategy, hazard ratio for each prevention strategy and the turnaround time for each screening test. Cost inputs included the cost of each screening test (including the cost of materials and laboratory personnel time), the cost for contact precautions, the cost per hospitalization with MRSA, the cost per hospitalization without MRSA, and the cost of decolonization. All cost inputs were inflated to 2015 US dollars using the medical-cost inflation rate. Utility inputs to adjust life years gained for quality included the utility during and after ICU admission. Model inputs are reported in Table 4.5.
Table 4.5. Model Inputs and Sources

<table>
<thead>
<tr>
<th>Model Inputs and Sources</th>
<th>Base-Case</th>
<th>Range*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colonization Rate</strong></td>
<td>8%³²</td>
<td>6-10%</td>
</tr>
<tr>
<td><strong>Susceptible to Susceptible</strong></td>
<td>89.34%</td>
<td>89.3%†</td>
</tr>
<tr>
<td><strong>Susceptible to Colonized</strong></td>
<td>0.37%¹⁷</td>
<td>0.28%-0.46%</td>
</tr>
<tr>
<td><strong>Susceptible to Infected</strong></td>
<td>0.06%¹⁷</td>
<td>0.04%-0.08%</td>
</tr>
<tr>
<td><strong>Susceptible to Discharged</strong></td>
<td>8.07%¹⁷</td>
<td>4.42%-13.3%</td>
</tr>
<tr>
<td><strong>Susceptible to Dead</strong></td>
<td>2.16%¹⁷</td>
<td>1.25%-3.37%</td>
</tr>
<tr>
<td><strong>Colonized to Colonized</strong></td>
<td>85.07%</td>
<td>85.07%†</td>
</tr>
<tr>
<td><strong>Colonized to Discharged</strong></td>
<td>4.70%¹⁷</td>
<td>3.53%-5.88%</td>
</tr>
<tr>
<td><strong>Colonized to Dead</strong></td>
<td>2.16%¹⁷</td>
<td>1.25%-3.37%</td>
</tr>
<tr>
<td><strong>Infected to Infected</strong></td>
<td>92.38%</td>
<td>92.37%†</td>
</tr>
<tr>
<td><strong>Infected to Discharged</strong></td>
<td>4.99%¹⁷</td>
<td>2.71%-8.35%</td>
</tr>
<tr>
<td><strong>Infected to Dead</strong></td>
<td>2.63%¹⁷</td>
<td>1.55%-4.16%</td>
</tr>
<tr>
<td><strong>Screening and Isolation Hazard Ratio</strong></td>
<td>0.92⁷</td>
<td>0.77-1.1</td>
</tr>
<tr>
<td><strong>Targeted Decolonization Hazard Ratio</strong></td>
<td>0.75⁷</td>
<td>0.62-0.88</td>
</tr>
<tr>
<td><strong>Universal Decolonization Hazard Ratio</strong></td>
<td>0.63⁷</td>
<td>0.53-0.77</td>
</tr>
<tr>
<td><strong>Conventional Culture Turnaround Time</strong></td>
<td>3.2 days¹⁵</td>
<td>2.1-4.0 days</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Turnaround Time</strong></td>
<td>2 days¹⁴</td>
<td>1.9-2.1 days</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 48-Hour Cost</strong></td>
<td>$4.63²⁵</td>
<td>$3.47-$5.79</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Turnaround Time</strong></td>
<td>1 day²³</td>
<td>0.8-1.1 days</td>
</tr>
<tr>
<td><strong>Chromogenic Agar 24-Hour Cost</strong></td>
<td>$4.63²⁵</td>
<td>$3.47-$5.79</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Turnaround Time</strong></td>
<td>0.6 days²⁴</td>
<td>0.1-0.8 days</td>
</tr>
<tr>
<td><strong>Polymerase Chain Reaction Cost</strong></td>
<td>$28.51²⁵</td>
<td>$21.38-$35.64</td>
</tr>
<tr>
<td><strong>Daily Cost of Contact Precautions</strong></td>
<td>$90³⁸</td>
<td>$68-$113</td>
</tr>
<tr>
<td><strong>Daily Cost of Chlorhexidine Baths</strong></td>
<td>$5.52²⁶</td>
<td>$4-$7</td>
</tr>
<tr>
<td><strong>Cost of Mupirocin for Five Days</strong></td>
<td>$7.55²⁸</td>
<td>$7.05-$68.2</td>
</tr>
<tr>
<td><strong>Cost per Hospitalization (no MRSA)</strong></td>
<td>$9,673¹³</td>
<td>$7,255-$12,091</td>
</tr>
<tr>
<td><strong>Cost per Hospitalization (with MRSA)</strong></td>
<td>$17,820¹³</td>
<td>$13,365-$22,275</td>
</tr>
<tr>
<td><strong>Utility during and after ICU Admission</strong></td>
<td>0.68³⁸</td>
<td>0.51-0.85</td>
</tr>
</tbody>
</table>

All cost inputs were inflated to 2015 US dollars.

*Lower and upper values of range were used in the one-way sensitivity analysis.
†Certain inputs are not varied as they are dependent upon another input (hazard ratio) that was varied.

**Analysis.** The Markov model evaluated competing prevention strategies and calculated the cost and effect (MRSA infections averted and QALYs gained) for each strategy using the base-case values detailed in Table 4.5. Costs were computed by calculating the cost of the prevention strategy (screening, contact precautions, and decolonization) and resulting hospitalizations (with or without MRSA). The incremental cost (difference in total
cost between strategies) and incremental effect (difference in MRSA infections and QALYs between strategies) was then calculated for each comparison. The incremental cost was divided by the incremental effect to calculate the incremental cost-effectiveness ratio. A prevention strategy was considered cost-effective if the incremental cost per MRSA infection averted was less than the incremental cost of an MRSA infection hospitalization ($8,147$) and if the incremental cost per QALY gained was less than a commonly cited value threshold of $100,000 per QALY gained.\textsuperscript{84}

To assess variation in model inputs, univariate and probabilistic sensitivity analyses were conducted. A univariate sensitivity analysis varied each input using the lower and upper bounds of the input range in Table 4.5 to determine parameters with the most influence on the incremental cost-effectiveness ratio. A probabilistic sensitivity analysis consisting of 1,000 Monte Carlo simulations varied all inputs over their plausible range. Input ranges listed in Table 4.5 represent the 95% confidence interval where available. When 95% confidence intervals were unavailable, the range was computed by adding and subtracting 25% to the base-case value.

This study was exempt from human subjects’ review by the Colorado Multiple Institutional Review Board.

Results

**Base-case analysis.** Decolonization strategies dominate (are less costly and more effective) the current standard practice in ICUs of screening and isolation for both outcomes of interest. Therefore, not only are decolonization strategies more effective in preventing MRSA infections and improving QALYs, but they are less costly to implement than screening and isolation. Although there are added costs to decolonization, including the cost
of chlorhexidine and mupirocin, the cost offsets due to fewer people needing contact precautions and fewer hospitalizations affected by MRSA are greater. This trend holds for all commonly used screening tests.

The cost of targeted decolonization is very similar to the cost of universal decolonization. The screening test selection influences which decolonization strategy is cheapest because targeted decolonization includes a screening component, whereas universal decolonization does not. Universal decolonization is cheaper than targeted decolonization when chromogenic agar and polymerase chain reaction screening tests are used, and therefore universal decolonization dominates targeted decolonization when implemented with these screening tests. Only when a very inexpensive screening test is used, such as conventional culture, targeted decolonization is cheaper than universal decolonization and thus universal decolonization no longer dominates targeted decolonization. However, even when universal decolonization is more expensive than targeted decolonization, the incremental cost-effectiveness ratio ($586 per MRSA infection averted or $7,471 per QALY gained) remains cost-effective. Therefore, the incremental costs are justified by the incremental improvements in health outcomes.

Table 4.6 presents the base-case results assuming the use of conventional culture. For the other screening tests (chromogenic agar 48-hour, chromogenic agar 24-hour, and polymerase chain reaction), all incremental comparisons were dominant because universal decolonization became the cheapest strategy.
Table 4.6. Base-Case Incremental Cost-Effectiveness Ratios

<table>
<thead>
<tr>
<th>Prevention Strategy Outcomes</th>
<th>SI</th>
<th>TD</th>
<th>UD</th>
<th>TD vs. SI</th>
<th>UD vs. SI</th>
<th>UD vs. TD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Costs ($)</td>
<td>$10,019</td>
<td>$9,799</td>
<td>$9,801</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effect (MRSA Infections)</td>
<td>0.0392</td>
<td>0.0141</td>
<td>0.0104</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effect (QALYs)</td>
<td>0.4571</td>
<td>0.4591</td>
<td>0.4594</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Incremental Comparisons

| Incremental Costs ($)        | -$219.85| -$217.69| $2.16   |
| Incremental Effect (Infections Averted) | 0.0252 | 0.0288 | 0.0037 |
| ICER ($/MRSA Infection Averted) | Dominant | Dominant | $586.02 |
| Incremental Effect (QALYs Gained) | 0.002 | 0.0023 | 0.0003 |
| ICER ($/QALY Gained)         | Dominant | Dominant | $7,471.48 |

Costs and effects reported are per person. Total costs include the cost of the intervention and the resulting hospitalization. Dominant means the prevention strategy was less costly and more effective than the comparator.

ICER=Incremental Cost-Effectiveness Ratio
MRSA=Methicillin-resistant *Staphylococcus aureus*
QALY=Quality-adjusted life year
SI=Screening and Isolation
TD=Targeted Decolonization
UD=Universal Decolonization

**Sensitivity analysis.** The base-case results were robust to sensitivity analyses. The univariate sensitivity analysis identified the effectiveness of each prevention strategy as the most influential input. Even when varying each input to the lower and upper bound of the plausible range for effectiveness, decolonization strategies continued to dominate a screening and isolation approach. Variation in other inputs, including the cost per isolation day and colonized prevalence, had a minimal impact on the cost-effectiveness of each prevention strategy.

A probabilistic sensitivity analysis was conducted to assess variation in all inputs. When comparing targeted decolonization and universal decolonization to screening and isolation, 100% of the iterations were dominant for all screening tests considered. The only comparison that was not dominant 100% of the time was when comparing universal
decolonization to targeted decolonization. However, the majority of iterations remain beneath the willingness-to-pay line of $8,147 per MRSA infection averted or $100,000 per QALY gained. Figure 4.6 presents each iteration of the probabilistic sensitivity analysis on the cost-effectiveness plane for the cost per QALY gained outcome. The results presented assume the use of conventional culture, but results were consistent for all other screening tests and for the cost per MRSA infection averted outcome. The variation in the incremental cost between universal decolonization and targeted decolonization is much smaller than the variation in incremental cost between targeted decolonization and screening and isolation and between universal decolonization and screening and isolation. This is because both are decolonization strategies and have similar cost inputs, therefore, variation in cost inputs affect each decolonization strategy and therefore cancel out.

**Figure 4.6. Probabilistic Sensitivity Analysis Results Comparing Universal Decolonization to Targeted Decolonization**

The solid line denotes a willingness-to-pay of $100,000 per QALY gained.
Discussion

Screening and isolation is considered standard practice in ICUs. 
When comparing decolonization prevention strategies to screening and isolation, targeted decolonization and universal decolonization are both less costly and more effective in preventing MRSA infections, which translates to more QALYs. This suggests updating the standard practice from screening and isolation to a decolonization strategy to use resources more efficiently and improve health by preventing more HAIs. When determining which decolonization strategy is best for a facility, universal decolonization is likely the most efficient strategy regardless of the screening test used. When inexpensive screening tests are used (less than $4 per test), targeted decolonization is cheaper than universal decolonization. However, even when targeted decolonization is cheaper than universal decolonization, the incremental cost-effectiveness ratio is considered cost-effective (considerably less than $100,000 per QALY gained), and thus the incremental improvements in health outcomes of universal decolonization over targeted decolonization justify the added cost. Furthermore, by implementing a universal approach over a targeted approach, the issue of missing potential carriers due to false-negative tests is avoided. 

Therefore, universal decolonization is recommended over screening and isolation and targeted decolonization in ICUs.

The results of this analysis are significant and timely because the Centers for Medicare and Medicaid Services recently started reducing hospital payments by 1% for all hospitals that rank among the lowest-performing 25% of hospitals for certain hospital-acquired conditions as part of their Hospital-Acquired Conditions Reduction Program. 

MRSA rates will be included in this ranking starting in fiscal year 2017. The results of this study can provide hospital decision makers with evidence on how to reduce their facility
MRSA rate in the most cost-effective manner and thus decrease the likelihood of having their reimbursement reduced.

This study fills a gap in the literature as the majority of the cost-effectiveness analyses around MRSA prevention strategies are for populations outside of the United States,\textsuperscript{17,27} are not specific to the ICU population and mostly focus on preoperative strategies for surgery patients,\textsuperscript{67–69,71,83,93} or do not include universal decolonization as an intervention of interest.\textsuperscript{26,27} This research is in line with a recently published cost-effectiveness analysis of MRSA prevention strategies conducted by Ziakas and colleagues. These researchers also found universal decolonization to be dominant over targeted decolonization and screening and isolation.\textsuperscript{82} They used a decision tree and assumed the use of chromogenic agar in their analysis.\textsuperscript{82} Our cost-effectiveness analysis expands their results and implications by using a Markov model instead of a decision tree which allowed for the increased risk of MRSA acquisition as length of stay increases to be modeled. Additionally, the screening test used was varied in our model to account for potential differences in cost-effectiveness for different screening test prices and to make the results applicable to facilities that use a screening test other than chromogenic agar.

This study is limited by the evidence that was available to inform the model. The univariate sensitivity analysis showed the effectiveness of the prevention strategy was a key input in determining the cost-effectiveness. The effectiveness inputs came from a single randomized controlled trial and it is possible the effectiveness could vary beyond what was observed in this single study due to differences in compliance and adherence to the prevention strategy. This limitation was addressed in the sensitivity analyses by varying the effectiveness parameters across a range. Secondly, potential adverse outcomes due to
decolonization such as rash and increased resistance to antimicrobials were not accounted for in the model due to lack of evidence. Similarly, other potential health advantages to decolonization besides a reduction in MRSA infections were not included despite some evidence suggesting that decolonization with chlorhexidine bathing could also prevent vancomycin-resistant enterococci, bloodstream infections, and ventilator-associated pneumonia.\textsuperscript{94–96} Lastly, this analysis is primarily concerned with the costs and health outcomes of these prevention strategies and does not incorporate patient preferences and attitudes toward being decolonized or isolated. Hospitals may not be motivated only by costs and health outcomes if a prevention strategy is unpopular among patients.

\textbf{Conclusions}

As compared to screening and isolation, the current standard practice in ICUs, targeted decolonization and universal decolonization are less costly and more effective. This finding is insensitive to the screening test used. Therefore, this study provides evidence that supports updating the standard practice in ICUs to a decolonization approach.

\textbf{Aim 3}

\textbf{Introduction}

Despite large investments and expenditures in health care, the United States has consistently ranked poorly on quality outcome measures.\textsuperscript{73} There has been a long-standing need for the United States to improve the quality of health care as well as reduce health care costs. Investing in public health is one proposed way to achieve these goals. Of the three trillion dollars spent on health care in the United States in 2014, less than five percent was allocated to public health.\textsuperscript{97} Public health advocates believe that investments should be increased as they potentially yield large returns, both in monetary terms and in health
outcomes. The Patient Protection and Affordable Care Act (ACA) created the Prevention and Public Health Fund with exactly that goal—to improve the nation’s health and restrain the growth in health care costs by increasing public health spending.

Initially, the ACA allocated $15 billion to this fund to be dispersed over ten years starting in fiscal year 2010. However, controversy has surrounded the effectiveness and need for this fund, which resulted in legislation passed in 2012 that reduced the fund by $5 billion. More recently, the Prevention and Public Health Fund was targeted for complete elimination in the House of Representatives’ 2016 Budget Resolution and in a separate bill under consideration in the House of Representatives. The impact of this fund on health outcomes needs to be evaluated to guide policy makers before the fund is further cut or eliminated altogether.

Among the areas targeted for health improvement by the Prevention and Public Health Fund is the prevention of healthcare-associated infections (HAIs). HAIs are infections patients contract while receiving inpatient medical care for an unrelated condition. These infections are one of the most common complications associated with hospital care and are a leading cause of preventable death in the United States. Despite being preventable, these infections negatively affect one out of every 25 hospitalized patients and are associated with an economic burden of more than $40 billion annually. In 2013, $949 million was dedicated to the Prevention and Public Health Fund, of which nearly half was allocated to the Centers for Disease Control and Prevention (CDC). The CDC then awarded nearly $7 million to 15 state health departments for the Prevention of HAIs across the Spectrum of Healthcare (Figure 4.7). This activity was unique in that the money was provided to state health departments with action and outcomes expected in hospitals. State health departments that
received the funding implemented evidence-based, multi-facility HAI prevention initiatives at healthcare facilities within their state.\textsuperscript{19} Initiatives could range from educational programs that provided information to patients, families, and medical professionals on the risk factors and routes of MRSA transmission to the implementation of monitoring and prevention strategies such as the use of a laboratory-based alert system to notify medical professionals of a patient colonized or infected with MRSA or initiating the use of contact precautions for MRSA colonized individuals.\textsuperscript{99}

**Figure 4.7. States that Received Funding for the Prevention of HAIs across the Spectrum of Healthcare in 2013**

![Map of the United States with shaded states indicating those that received funding for HAI prevention initiatives in 2013.](image)

Shaded states received funding for the Prevention of HAIs across the Spectrum of Healthcare in 2013. Fifteen states were awarded the funding.

The objective of this study was to evaluate the impact of this Prevention and Public Health Fund activity—Prevention of HAIs across the Spectrum of Healthcare—on preventing bloodstream infections and calculate the return on investment to inform policy makers of the value of this type of fund.

**Methods**

**Population.** HAIs are a health and economic burden to acute care hospitals.\textsuperscript{100} Nearly 750,000 HAIs occur each year in patients admitted to US acute care hospitals.\textsuperscript{100} On top of
being negative for patient health outcomes, hospitals are responsible for covering the incremental costs due to these infections. To reduce the health and economic burden of these infections, infection control boards have recommended practices for the monitoring and prevention of MRSA transmission for all acute care hospitals. Due to the prevalence of HAIs and existence of evidence-based prevention guidelines, the population for this analysis was all US acute care hospitals that accept Medicare or Medicaid. The unit of analysis was the hospital. All hospitals in Arizona were excluded because Arizona received funding in 2013 to improve the detection of HAIs, making it difficult to disentangle the effect of more accurate detection from health care delivery improvements related to the Prevention and Public Health Fund.

**Data sources.** This study exploits a natural experiment to compare infection rates before and after funding in states that received the funding to control states that did not. The study period spanned four years including two years before funding allocation (2011 and 2012), the year the funding was allocated (2013), and a year when the activity was no longer funded (2014). Data were collected from three sources. Information on which states received the funding and have a reporting mandate were gathered from the CDC’s website. Centers for Medicare and Medicaid Services (CMS) Hospital Compare data from 2011-2014 were the sources for hospital infection rates. Additional hospital control variables were taken from 2011-2014 CMS Point of Service (POS) data.

**Variables.** The outcome of interest was central line-associated bloodstream infection (CLABSI) rates. CLABSI rates were selected as the outcome for the evaluation because the CDC has a standardized measure for the detection of CLABSIs that has been considered valid by clinicians and there are mature guidelines around the prevention of CLABSIs that
health departments could use to disseminate and implement in hospitals. Data on other types of HAIs are not as standardized which could lead to discrepancies between facilities and between years. The primary outcome was defined as a standardized infection ratio (SIR) calculated by dividing the number of observed CLABSI cases by the number of expected CLABSI cases for each hospital. The number of expected CLABSI cases was adjusted for factors that may influence the number of infections including hospital location, affiliation with a medical school, and bed count.

The following hospital-level covariates were added to control for hospital differences that may be correlated with hospital infection rates: location in an urban or rural location, affiliation with a medical school, bed count, ownership, provision of inpatient surgeries, provision of emergency services, presence of a clinical laboratory on site, presence of an intensive care unit on site, and percent of nurses that are registered nurses. In addition to the hospital-level covariates, a state reporting mandate was controlled for because a reporting mandate can influence reported SIRs independent of the receipt of funding.

Statistical analysis. Hospital CLABSI SIRs were modeled as a function of the control variables using a difference-in-differences specification. Hospitals in states that received the funding in 2013 were defined as the “funded” hospitals and hospitals in states that did not receive the funding in 2013 were the “control” hospitals. CLABSI SIRs were modeled as a function of a dichotomous variable indicating whether the hospital was in a state that received funding (Funding), a year fixed effect for 2013 (Year2013) and 2014 (Year2014), and interactions between Funding and Year2013 and Funding and Year2014 to measure the association of the public health funding with the CLABSI SIRs in 2013 and 2014, respectively. A hospital fixed effect was used to control for all observed and
unobserved time-invariant factors. Random effects were rejected in favor of fixed effects based on the results of a Hausman specification test ($p=0.0003$). The dependent variable, CLABSI SIR, was positively skewed, and thus it was log–transformed. Because approximately 40% of hospitals had no observed CLABIs (i.e. numerator of SIR=0 and thus SIR=0), 0.0001 was added to the SIR before log transforming to prevent the omission of those observations.

We tested and confirmed that pre-period trends were parallel between the states that received the funding and the states that did not. Parallel pre-period trends imply that the funded and control hospitals were evolving in a similar manner prior to disbursement of the funding. This is a necessary condition for a difference-in-differences specification. We account for regression to the mean attributable to facilities with extreme SIRs before funding allocation moving closer to the mean through random chance using a two-stage approach. The first stage predicts the outcome residual and the second stage runs the entire model adding the residual as a covariate. Lastly, the parameter estimates were adjusted for heteroskedastic smearing and the standard errors were calculated using a bootstrap with state clustering.

The cost offsets associated with the reduction in infections were calculated to determine if they outweighed the initial investment. Reductions in CLABSIs were calculated using the parameter estimates from each specification of the difference-in-differences model. The parameter estimate was multiplied by the number of infections averted to yield the cost offsets. The hospital cost per CLABSI used to compute the cost offsets was $24,145. The return on investment (ROI) was then estimated by dividing the cost offsets by the funding amount provided to the 15 states. The infections averted and cost offsets were recomputed
within each bootstrap iteration. This allowed for the determination of the expected value and a 95\% interval for each of these parameters. To account for the potential price variation and uncertainty in the cost of each case, the break-even price per CLABSI was calculated by dividing the initial investment by the number of infections averted.

Robustness and specification checks were conducted. The model was re-fitted using a generalized linear model with a log-link function and gamma distribution to assess the influence of the fixed effect specification. Additionally, to normalize the error variance and determine whether the decline in infections was dominated by large changes in smaller facilities, an analytic weight of the SIR denominator (expected number of cases) was applied. The normalized error variance specification is considered a more conservative estimate.

Statistical analysis was completed in Stata 13.1.\textsuperscript{103}

Results

**Impact on infection rate.** States that received funding experienced sharper unadjusted declines in their CLABSI SIR as compared to states that did not receive funding (Table 4.7). Additionally, changes over time in funded hospitals did not significantly differ from changes over time in control hospitals over the sample period as evidenced by the far right column of Table 4.7. Table 4.8 reports the estimates of the association between the public health funding and CLABSI SIRs in 2013 and 2014. In 2013, states that received the funding experienced a 34.8\% reduction in infections. In 2014, after the funding for this activity stopped, the estimate was no longer significant (p=0.72). After accounting for regression to the mean and adjusting the estimates for heteroskedastic smearing and bootstrapping, the estimate in 2013 decreased to -0.337 (p=0.01), or a reduction in infections of 33.7\% in the funded states. These results were robust to the sensitivity analyses. The
estimate from the generalized linear model specification was in line with the estimates from the fixed effect model. The estimate weighted by the frequency of the SIR denominator was reduced to -0.098 (p=0.01), suggesting that the unweighted estimates may be influenced by large reductions at smaller facilities. Therefore, we treat this estimate as the lower bound.

**Table 4.7. Sample Characteristics Pre and Post Funding Allocation Stratified by Funding Status**

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Pre</th>
<th>Post</th>
<th>Difference</th>
<th>Pre</th>
<th>Post</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>SIR</em></td>
<td>0.55</td>
<td>0.54</td>
<td>0.01</td>
<td>0.45</td>
<td>0.50</td>
<td>-0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Control Variables</th>
<th>Pre (n=3,694)</th>
<th>Post (n=2,608)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td>80%</td>
<td>66%</td>
<td>14%</td>
</tr>
<tr>
<td>Teaching</td>
<td>19%</td>
<td>16%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Profit</td>
<td>67%</td>
<td>55%</td>
<td>12%</td>
</tr>
<tr>
<td>Public</td>
<td>15%</td>
<td>20%</td>
<td>-5%</td>
</tr>
<tr>
<td>For-Profit</td>
<td>18%</td>
<td>25%</td>
<td>-7%</td>
</tr>
<tr>
<td>Bed Count</td>
<td>261</td>
<td>215</td>
<td>46</td>
</tr>
<tr>
<td>Inpatient Surgeries</td>
<td>95%</td>
<td>95%</td>
<td>0%</td>
</tr>
<tr>
<td>Nurses with RN</td>
<td>88%</td>
<td>85%</td>
<td>3%</td>
</tr>
<tr>
<td>Clinical Lab on Site</td>
<td>99%</td>
<td>99%</td>
<td>0%</td>
</tr>
<tr>
<td>ICU on Site</td>
<td>31%</td>
<td>29%</td>
<td>2%</td>
</tr>
<tr>
<td>ED on Site</td>
<td>95%</td>
<td>94%</td>
<td>1%</td>
</tr>
</tbody>
</table>

*p<0.05
CLABSI=Central Line-Associated Bloodstream Infection; ED=Emergency Department; ICU=Intensive Care Unit, SIR=Standardized Infection Ratio
Table 4.8. Impact of State Health Department Funding on Hospital CLABSI Rates

<table>
<thead>
<tr>
<th>Reduction in CLABSI Rates</th>
<th>Fixed Effect</th>
<th>Regression to the Mean</th>
<th>Generalized Linear Model</th>
<th>Normalized Error Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Percent Change in 2013</strong></td>
<td>-34.8%*</td>
<td>-33.7%*</td>
<td>-36.7%*</td>
<td>-9.8%*</td>
</tr>
<tr>
<td></td>
<td>(16.6%)</td>
<td>(13.3%)</td>
<td>(14.5%)</td>
<td>(3.9%)</td>
</tr>
<tr>
<td><strong>Percent Change in 2014</strong></td>
<td>-6.1%</td>
<td>0.8%</td>
<td>13.8%</td>
<td>0.7%</td>
</tr>
<tr>
<td></td>
<td>(16.8%)</td>
<td>(18.0%)</td>
<td>(9.3%)</td>
<td>(4.0%)</td>
</tr>
<tr>
<td><strong>Model Specifications</strong>^\1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Error Component</strong></td>
<td>Fixed</td>
<td>Fixed</td>
<td>None</td>
<td>Fixed</td>
</tr>
<tr>
<td><strong>Regression to the Mean Adjusted</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Weight Applied</strong></td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Expected Cases</td>
</tr>
</tbody>
</table>

\*p<0.05. Robust standard errors with state clustering are reported in parentheses.
\^All models were adjusted for hospital characteristics reported in Table 4.7. Fixed hospital characteristics were subsumed in hospital fixed effect. N=8,092

CLABSI=Central Line-Associated Bloodstream Infection
GLM=Generalized Linear Model

**Return on investment.** Table 4.9 reports the expected value and 95% intervals for infections averted, cost offsets, and ROI. Using the parameter estimate from the regression to the mean specification, adjusted for smearing and bootstrapping (-0.337, p=0.01), public health funding is estimated to have prevented approximately 1,600 CLABSI\s in 2013. This resulted in cost savings due to infections averted of greater than $33 million and a positive ROI that ranged from 1.19 to 10.57, or a return of $1.19 to $10.57 for every $1 invested in this activity of the Prevention and Public Health Fund. The ROI using the estimates from other model specifications fall within this range. The cost of a CLABSI case would need to be $4,275 to break even, which is much less than the average cost per CLABSI of $24,145 (95\% interval of $22,031, $28,235).\(^79\) Although the reduction in infections was not sustained after the funding ended, the impact was enough in the first year to recoup the investment.
Table 4.9. Return on Investment due to Cost Offsets Associated with Infections Averted

<table>
<thead>
<tr>
<th></th>
<th>Mean (95% Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infections Averted</strong></td>
<td></td>
</tr>
<tr>
<td><em>(Percent Change x Number of Cases)</em></td>
<td>1,600*</td>
</tr>
<tr>
<td></td>
<td>(324, 2,876)</td>
</tr>
<tr>
<td><strong>Cost Offsets</strong></td>
<td></td>
</tr>
<tr>
<td><em>(Infections Averted x Cost per Case)</em></td>
<td>$40,216,000*</td>
</tr>
<tr>
<td></td>
<td>($8,143,740, $72,288,260)</td>
</tr>
<tr>
<td><strong>Cost Savings</strong></td>
<td></td>
</tr>
<tr>
<td><em>(Cost Offsets - Investment)</em></td>
<td>$33,376,265*</td>
</tr>
<tr>
<td></td>
<td>($1,304,005, $65,448,525)</td>
</tr>
<tr>
<td><strong>Return on Investment</strong></td>
<td></td>
</tr>
<tr>
<td><em>(Cost Offsets / Investment)</em></td>
<td>5.88*</td>
</tr>
<tr>
<td></td>
<td>(1.19, 10.57)</td>
</tr>
</tbody>
</table>

*p<0.05

Discussion

The Prevention and Public Health Fund activity—Prevention of HAIs across the Spectrum of Healthcare—was significantly associated with a 33.7% reduction in CLABSI SIRs at hospitals in states that received the funding. This estimate is robust through sensitivity analyses with a range of 9.8% to 36.7% for the year of the funding (2013). Statistically significant declines were no longer evident when funding ended in 2014. These findings are consistent with a study that evaluated the effectiveness of funding from the American Recovery and Reinvestment Act specifically devoted to building capacity for HAI prevention at the state-level. Researchers found that targeted funding to state health departments for HAI prevention was associated with significant reductions in CLABSI. Even though significant declines in infections were not evident when the activity was no longer funded, the number of infections averted in 2013 alone produced cost savings greater than the initial monetary investment, resulting in a positive ROI of 5.88 (range of 1.19 to 10.57). This ROI is in line with other federal investments such as the Clean Air Act and investments in public transportation which have an ROI of around four. Our calculated ROI also overlaps with a study that evaluated the economic benefits of the CDC’s CLABSI.
prevention efforts over an 18-year period, from 1990 to 2008.\textsuperscript{79} That study calculated a range in ROI of 3.88 to 23.85.\textsuperscript{79}

This study is limited primarily because it only evaluates one type of HAI and thus the estimates may underestimate the impact of this funding on other infections that could have been reduced. The ROI is likely also a conservative estimate as the only cost offset considered is the cost of a CLABSI to hospitals. Additionally, the model did not control for surgical volume or patient case-mix as covariates. Inclusion of these parameters was less of a concern because the outcome variable was risk-adjusted. A limitation common to many public health value evaluations is that funding is allocated to public health departments often based on the greatest need (e.g. prevalence of health problems) or to departments that can develop the best proposals (e.g. those communities with more resources and greater capacity).\textsuperscript{105} This source of potential bias is mitigated by taking into account regression to the mean. Lastly, this study only evaluates one public health funding source as part of the Prevention and Public Health Fund.

The perspective of this analysis was from the societal level. In taking that perspective, we were evaluating whether the returns in the funded states were greater than the total investment. Future research should limit the perspective to individual states and hospitals to determine what actions were most effective at yielding the largest returns. To be able to do this, data on which hospitals the state health departments targeted and how the state health departments used their funding would be needed. This would allow us to attribute the results to those hospitals that did and did not receive funding and determine which activities were most effective and sustainable.
Public Health Implications

Public health spending is most effective when allocated to activities with well-defined needs that can be addressed with evidence-based interventions proven to yield a positive health and economic impact. However, little evaluative research on public health activities exists. Thus, there are ongoing debates about whether public health investments generate a positive return. Similar to recommendations for other financed health interventions, such as the impact of health information technology on health outcomes, large investments into health should be complemented with evaluation on its effectiveness. This study provides one evaluation of the impact of a public health activity on health outcomes and cost savings to demonstrate the potential value of public health spending. However, public health researchers should continue to expand the evidence base around the value of public health investments and the type of investments made to better inform policy makers of its effectiveness.

This study reported that providing funding to state health departments was associated with a significant reduction in hospital bloodstream infections and yielded a positive return on investment within a one-year period. This funding allocation was cost saving as the improvement in health outcomes outweighed the initial investment. These savings provide important information that informs the debate regarding the effectiveness of the Prevention and Public Health Fund. However, although the funding reduced hospital infections enough to generate a positive return on investment, the reduction was not sustained after the activity was no longer funded. This suggests that ongoing investments may be necessary. Funding public health activities of this type should be encouraged, along with close evaluation of benefits and return on investment, as they potentially provide a mechanism to improve
population health and reduce health care costs. Additionally, continued and ongoing development of public health support and funding for HAI prevention is encouraged. These results provide information on the health and financial gains of one source of public health funding that was directed toward a large scale public health problem that occurs in the clinical setting.

Summary

This chapter detailed the results of the three aims of this dissertation. Aim 1 showed that rapid screening tests minimize total surveillance costs for facilities that implement universal preemptive isolation. For facilities that implement targeted isolation, rapid culturing methods like chromogenic agar minimize total costs. For Aim 2, decolonization prevention strategies dominated the current standard practice of screening and isolation. This was consistent for all screening tests considered. Aim 3 found public health funding significantly reduced bloodstream infections. Although reductions were not sustained after funding stopped, the number of infections prevented in the first year alone was enough to recoup the investment. The final chapter of this dissertation, Chapter Five, discusses the implications of this research for clinical practice and policy and explores future research that can build off this work.
CHAPTER V

DISCUSSION

Introduction

HAIs are one of the most common complications associated with hospital care and are one of the leading causes of preventable death in the United States. Despite being preventable, these infections negatively affect 4% of all hospitalizations and result in an annual economic burden of more than $40 billion each year. Because these infections are detrimental to patient health and are costly to treat, hospitals implement surveillance practices to detect these infections and prevention strategies to reduce the health and economic burden associated with them. Despite efforts at the hospital level, these infections continue to persist at high levels, which has led to federal funding provided to public health departments to assist hospitals in their efforts to combat these infections. These efforts at the hospital and national level are commendable, but they need to be evaluated to ensure the resources spent are justified by improvements in health outcomes.

The purpose of this dissertation was to evaluate these hospital and national practices to inform decision makers of the value of these types of activities. Aim 1 calculated the cost of MRSA surveillance practices using different screening tests to recommend the screening test that minimized total costs for each practice. Aim 2 estimated the cost-effectiveness of MRSA prevention strategies to determine if their implementation costs were offset by comparable improvements in health outcomes, and Aim 3 evaluated the national funding provided to public health departments to ascertain its impact on hospital infection rates and whether or not it produced a positive return. This chapter begins with a summary of the findings presented in Chapter Four and then discusses the implications this research has on
changes in clinical practice and at the policy level. The chapter concludes with a discussion around future research that is possible given the information from this dissertation.

**Summary of Findings**

**Aim 1**

The objective of Aim 1 was to calculate the cost of MRSA surveillance practices and identify the MRSA screening test that minimized total costs for each surveillance practice. Published research in this area largely focused on the diagnostic accuracy of the screening test and there was limited economic evidence as to their potential cost offsets due to the quicker turnaround time. Of the limited economic literature, conflicting findings were reported.

This dissertation found that for ICUs that preemptively isolate all patients, rapid MRSA screening tests minimize total costs because the inappropriate isolation costs saved from the quicker turnaround time are greater than the added cost per test. The more rapid the screening test, the smaller the total cost due to the isolation cost savings. There would need to be implausible increases in either the screening test price or turnaround time for rapid screening tests to no longer be less costly than conventional culture. Rapid screening tests, like polymerase chain reactions, are therefore recommended for ICUs with a universal preemptive isolation surveillance policy to minimize inappropriate isolation costs and reduce total implementation costs.

For ICUs that only isolate MRSA-positive patients, the added cost for chromogenic agar is offset by the reductions in costs associated with inappropriate open days and therefore chromogenic agar minimizes total cost. Although the inappropriate costs were minimized with the polymerase chain reaction screening test, the added cost for the test was not offset.
by comparable reductions in inappropriate open costs. There would need to be dramatic reductions in the polymerase chain reaction screening test price or increases in the risk of MRSA transmission to make these screening tests the cheapest method. Chromogenic agar 24-hour is therefore recommended for ICUs with a targeted isolation surveillance policy.

Completing this aim filled a gap in the literature and provided clarification to the contradicting conclusions previously published. These results suggest the most efficient screening test is dependent on the surveillance practice implemented.

Aim 2

The objective of Aim 2 was to calculate the cost-effectiveness of MRSA prevention strategies to determine if their improvements in health outcomes due to MRSA infections averted justified their implementation costs. Published research in this area was limited in that studies only included pre-operative surgical patients, failed to include universal decolonization as an intervention of interest, or did not vary the screening test used in the analysis.

This dissertation found that targeted and universal decolonization are not only more effective, but also less costly, than the current standard practice of screening and isolation. When selecting among universal and targeted decolonization, universal decolonization is the more cost-effective strategy. These findings are consistent across all screening tests. From this analysis, universal decolonization is recommended over screening and isolation and targeted decolonization in ICUs.

The results from this aim filled a gap in the literature by examining the entire ICU population, including universal decolonization as an intervention of interest, and conducting
a separate analysis for each commonly used screening test. These findings provide evidence to hospital decision makers of the most efficient MRSA prevention strategy for their facility.

Aim 3

The objective of Aim 3 was to determine the impact of public health funding on preventing hospital bloodstream infections and to calculate the return on this investment. Due to the lack of knowledge around the value of public health funding, the necessity of this type of funding is continually debated which often leads to budget cuts.

This dissertation found public health funding dedicated to the Prevention of HAIs across the Spectrum of Healthcare to be significantly associated with a 33.7% reduction in hospital bloodstream infection rates. Even though significant declines in infections were not observed when the activity was no longer funded, the number of infections averted in 2013 alone produced cost savings significantly greater than the initial monetary investment, resulting in a positive ROI of 5.88. This equates to a return of $5.88 for every $1 invested.

The results from this aim provide evidence to the value of public health funding to better inform the debate on the value of public health spending. Not only can public health activities have a positive impact at the clinical level, but funding these activities can generate a positive return due to the cost savings associated with the health improvements.

Implications for Practice and Policy

Aim 1

The results from Aim 1 provide recommendations on screening test selection for ICUs based on the surveillance practice they implement. The results from this aim found the added cost of rapid screening tests to be offset by cost savings due to reduced isolation when facilities are preemptively paying for isolation costs in a universal preemptive isolation
surveillance practice. However, if facilities are not preemptively isolating patients, polymerase chain reaction screening tests become very costly and the number of open days avoided by the rapid results does not offset the added cost per test. For facilities that implement a targeted isolation surveillance practice, chromogenic agar minimizes total surveillance costs.

These results are important because they provide infection control practitioners and hospital decision makers with screening test recommendations that are tailored to the surveillance practice they use. With knowledge on efficient screening test selection for their facility, infection control practitioners and hospital decision makers can update the screening test used in their facility to one that maximizes the use of their limited resources. Preventable HAIs like MRSA remain a health and economic burden in hospitals, especially in ICUs. Therefore, standard practice in ICUs involves screening and isolation. Currently, hospitals are paying for these surveillance practices with little guidance on how to use their resources most efficiently. With knowledge on the screening test that minimizes costs, hospitals can maximize the efficiency of their resource use and improve the health of their patients.

Aim 2

The results from Aim 2 provide recommendations for which MRSA prevention strategy an ICU should adopt given the screening test they use. The results of this aim found universal decolonization to be the most efficient strategy and was actually cost saving as compared to the current standard practice in ICUs. The results of this aim suggest that the current standard practice in ICUs of screening and isolation should be changed to a strategy of universal decolonization. This change in clinical practice would be cost saving as the costs
of universal decolonization are less than the costs of screening and isolation, and universal
decolonization is more effective in preventing MRSA infections.

The results of this analysis are significant and timely because the Centers for
Medicare and Medicaid Services recently started reducing hospital payments by 1% for all
hospitals that rank among the lowest-performing 25% of hospitals for certain hospital-
acquired conditions as part of their Hospital-Acquired Conditions Reduction Program.\textsuperscript{32} MRSA rates will be included in this ranking starting in fiscal year 2017. The results of this
study can provide hospital decision makers with evidence on how to reduce their facility
MRSA rate in the most cost-effective manner and thus decrease the likelihood of having their
reimbursement reduced.

**Aim 3**

This results of Aim 3 showed that providing funding to state health departments was
associated with a significant reduction in hospital bloodstream infections and yielded a
positive return on investment within the first year. Although this public health activity
required an initial monetary investment, it was cost saving as the improvement in health
outcomes outweighed the initial investment. These results are timely and important as the
necessity and effectiveness of the Prevention and Public Health Fund is debated. Results
from this analysis can thus inform policy makers of the value of this type of funding and
serve as justification for why this activity should be continually funded as it provided a
mechanism to improve population health and reduce health care costs.

Due to the little evaluative research on public health activities, it is still debated
whether allocating money to public health generates a positive return on investment. Because
of this debate, it was important to evaluate the effectiveness of this large investment in public
health. The results of this aim expand the evidence base around the value of public health funding to better inform policy makers of its effectiveness and necessity. By evaluating a public health activity funded by the Prevention and Public Health Fund, this study provides evidence of the positive impact one source of public health funding had on health outcomes and the cost savings associated with these health impacts. These results offer needed information on the health and financial gains of public health funding to inform policy makers of the value of these funds and give justification for the allocation of these funds to public health.

**Recommendations for Research**

**Aim 1**

Aim 1 provided evidence for which screening test is the most financially beneficial by reducing total costs given the surveillance practice implemented at a hospital. From this analysis, recommendations were provided on which screening test should be used with each surveillance practice. However, this aim did not recommend a certain surveillance practice for a hospital. Future research should examine the comparative effectiveness of different surveillance practices to determine which practice is most effective at reducing MRSA transmission. Results from the comparative effectiveness evaluation could then be incorporated into a cost-effectiveness analysis that evaluated the efficiency of the surveillance practice. From that research, hospitals would become aware of which surveillance practice is the best use of resources. The results from this aim would inform that future research by showing which screening test is most financially beneficial given the identified surveillance practice. Additionally, this population for Aim 1 included ICU patients, as these patients are at the greatest risk for contracting HAIs and surveillance is
standard practice in ICUs. However, future research should explore the cost of these surveillance practices for other wards outside of the ICU to determine if it would be beneficial to have hospital-wide surveillance for MRSA.

**Aim 2**

Aim 2 provided evidence for which MRSA prevention strategies are cost-effective. From this analysis, universal decolonization was cost saving as compared to the current standard practice of screening and isolation. Due to lack of evidence, adverse events due to decolonization, such as rash or increased resistance, were not accounted for in the model. Similarly, other potential health advantages to decolonization besides MRSA infection prevention, for example the prevention of other HAIs, were not incorporated into the model. Future research is needed to evaluate the adverse events due to decolonization and the impact of decolonization on other health outcomes besides MRSA. Once these data exist, they should be integrated into the cost-effectiveness modeling. Additionally, the population for Aim 2 included ICU patients as these patients are at the greatest risk for MRSA infections and there are standard practices in place to surveil and prevent these infections. However, MRSA infections occur outside of the ICU as well and these prevention strategies may also be efficient for other inpatient populations. Future research should explore the comparative effectiveness, and then the cost-effectiveness, of these prevention strategies outside of the ICU.

**Aim 3**

Aim 3 provided evidence for the impact of one source of public health funding on reducing hospital infection rates and calculated the return on the investment. This aim was primarily limited because it only evaluated one type of HAI and thus the treatment effect and
return on investment may actually be underestimates by not including other HAIs that could have been reduced. Future research should examine the impact of this funding on other HAIs, such as CAUTIs, SSIs, and VAPs, to determine if a similar impact was observed. Moreover, this study did not control for what types of activities public health implemented in the hospitals. Future research should identify and control for the different prevention activities (educational vs. program implementation) conducted by the state public health departments to determine if certain activities were associated with a greater treatment effect than others or were more sustainable than others. Similarly, this study did not control for which hospitals received the public health action. This study assumed all hospitals within a state that received funding received action. Future research should discover which hospitals the funded state health departments targeted to be able to attribute the results to those hospitals that did and did not receive the funding.

**Conclusion**

The goal of this dissertation was to identify the value of hospital and national HAI prevention strategies to guide hospital decision makers and national policy makers on the use of their limited resources. To inform hospital decision makers of the most efficient use of resources, Aim 1 discovered that polymerase chain reaction screening tests minimized total surveillance costs for hospitals that preemptively isolate all patients upon admission. For hospitals that implement a targeted isolation surveillance practice, chromogenic agar 24-hour is the best use of resources. Aim 2 found universal decolonization to be the most efficient MRSA prevention strategy and recommended it to eventually replace the current standard practice of screening and isolation. Aim 3 informed policy makers of the value of one source of public health spending and showed a positive impact of the spending on reducing hospital
bloodstream infections. The reduction in infections was large enough to recoup the investment within the first year.

HAIs, although largely preventable, negatively impact the health of individuals and result in a large economic burden. The results of this dissertation provide ways for hospitals to maximize their resource use to detect and prevent these infections. Similarly, HAIs have extended beyond a hospital problem to become a public health problem and the continued development of public health support and funding for HAI prevention is encouraged as this research showed public health activities can effectively and efficiently reduce these infections. To reduce the health and economic burden of these preventable infections, interventions should continue at both the hospital and national level. This dissertation informs hospital decision makers and national policy makers of interventions at both the hospital and national level that use resources efficiently.
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