An Evaluation of Universal Screening for MRSA at the Ottawa Hospital

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Abstract

Statement of the problem: Methicillin-resistant *Staphyloccocus aureus* (MRSA) is a pathogen of increasing concern and is associated with higher hospital readmission rates, poorer prognosis, and increased mortality resulting in increasing costs to the Canadian healthcare system.[1-13] Institutions have been challenged with developing effective infection control programs to prevent the spread of MRSA. The purpose of this thesis was to examine the clinical and cost-effectiveness of a universal MRSA screening intervention within a large tertiary care facility. **Methods of investigation:** The retrospective population-based observational study consisted of two periods. In the first period (24 months), patients admitted to the Ottawa Hospital underwent risk factor-based screening. In the second period (20 months), universal MRSA screening was implemented in which all patients were screened for MRSA upon admission. **Results:** The regression analysis demonstrated that the universal MRSA screening intervention was not effective in reducing the number of nosocomial MRSA cases. The economic analysis estimated that the universal MRSA screening intervention incurred an additional cost of $1.16 million/year with an estimated additional cost per patient screened of $17.76. **Conclusions:** The universal MRSA screening intervention was not clinically or economically effective. Further research is required to verify/dispute these findings in other settings.

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This thesis is dedicated to my son Cohen, who for the last 2 ½ years has spent a lot of 'quality' time with his Daddy and to my Dido, the one person who would have read this thesis from front to back, simply because I wrote it.

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1.0 Chapter 1 – Introduction and Study Objectives

1.1 Introduction

Methicillin-resistant *Staphyloccocus aureus* (MRSA) is a pathogen of increasing concern to healthcare facilities around the world.[1,2] MRSA has been associated with higher hospital readmission rates, poorer prognosis and increased mortality (21% -54%)[9,13] when compared to other infections.[3-13] Financially, MRSA costs the Canadian healthcare system an estimated $42-59 million per year.[14] Institutions have been challenged with developing effective infection control programs to prevent the spread of MRSA to vulnerable populations within their facilities. However, there are few well designed, large-scale studies evaluating the effectiveness of different MRSA infection control programs. This leaves each institution, region and/or country to develop MRSA control strategies which may or may not be the most clinically or cost effective practice. This thesis aims to address this gap in the research by examining the clinical and cost-effectiveness of a universal MRSA screening intervention within a large tertiary care facility.

1.2 Objectives

The primary objective of this project was to determine if a universal MRSA screening intervention reduced the incidence of nosocomial MRSA over time in a large tertiary care facility compared to regional rates. The secondary objective was to determine the cost effectiveness of implementing a universal MRSA screening intervention using both patient-based and population-based approaches

1.3 Background and Rationale

The incidence of MRSA in Ottawa, Ontario, Canada has more than doubled since 2000 with more than 500 new cases identified per year.[15] In recent years, the incidence of community MRSA strains is increasing, accounting for nearly one-quarter of all newly identified MRSA cases in 2007.[15] Due to the rising incidence of MRSA in our community, regions throughout Canada and around the world, this study has the opportunity to change clinical practice and hospital policies to potentially decrease the transmission MRSA within the hospital environment. A reduction in MRSA transmission would lead to improved clinical outcomes and reduced healthcare costs.

1.3.1 MRSA

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an antimicrobial resistant form of *S. aureus,* and a pathogen of increasing concern in North America.[1,2] *S. aureus* is found on the skin or in the nares of approximately 30% -50% of the population.[16, 17] Although most people are simply carriers (or colonized), *S. aureus* can cause serious disease including skin and soft tissue infections, bloodstream infections and pneumonia.[17] MRSA is a group of *S. aureus* strains which are resistant to several classes of antibiotics and all beta-lactam antibiotics.[16] MRSA has become the most prevalent antibiotic-resistant pathogen in many parts of the world,[1] and is one of the leading causes of health-care associated infections.[17] Infections due to MRSA are associated with a higher hospital readmission rate, poorer prognosis and increased mortality when compared to infections due to methicillin-susceptible *S. aureus*.[3-13] The mortality attributed to MRSA infections is estimated to be between 21% -54%.[9,13]

In recent years, MRSA control in hospitals has been increasingly challenged by the emergence of new, more virulent, community MRSA strains.[18] Community MRSA strains are primarily transmitted among close-contact community groups such as prisoners, sports team members, daycare children, military personnel and illicit drug users. However, once introduced into the healthcare setting, their potential for nosocomial transmission and outbreaks has been clearly demonstrated.[19]
Due to the high morbidity, mortality and costs associated with MRSA infections, it is especially important to protect vulnerable patients within the healthcare system from acquiring or transmitting an MRSA infection.

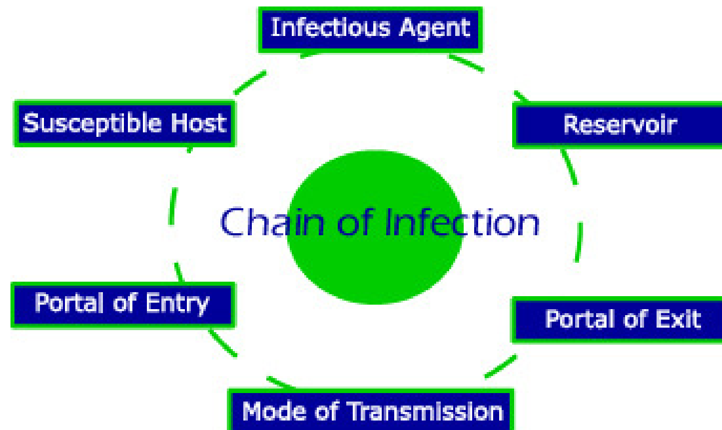
Most MRSA infections are nosocomial, that is, acquired in hospital,[20] where MRSA is spread through the unwashed hands of healthcare workers or via contaminated equipment or environmental surfaces.[21] Since the inception of the Canadian Nosocomial Infection Surveillance Program (CNISP) in 1995, it has been noted that the incidence of MRSA in hospitals has increased nearly 20-fold from 0.46 per 1,000 admissions in 1995 to 9.5 per 1,000 admissions in 2009.[22]

1.3.2 MRSA - Chain of Infection

Transmission of infection in a hospital requires at least three elements: a source of infecting microorganisms, a susceptible host and a means of transmission for bacteria and viruses.[109] As most MRSA carriers are asymptomatic, the chain of infection becomes especially important and challenging for healthcare institutions. The specific links in the chain of infection are: reservoir, infectious agent, susceptible host, portal of entry, mode

of transmission and portal of exit (Figure 1).[109,110] Each link must be present and in sequential order for an infection to occur.

FIGURE 1 CHAIN OF INFECTION[110]



While experts agree that following standard infection control precautions (i.e. isolation, proper hand hygiene) is essential to breaking the chain of infection, an example below by Pyrek (2002) illustrates how an organism, such as MRSA, can affect the chain of infection.[109] A healthcare worker caring for patients within a facility can break the chain in the following way:

- Infectious agent: MRSA
- Reservoir: patient with MRSA in an open wound
- Portal of exit: drainage from the open wound; *Break in the chain: HCW uses proper handwashing techniques, wears protective gloves and handles bed linens properly*

- Mode of transmission: MRSA transferred on to hands by indirect contact; *Break in the chain: HCW performs proper handwashing, gloving and linen handling*
- Portal of entry: *Break in the chain: Organisms isolated with use of medical asepsis and body-substance isolation*
- Susceptible host: protected due to chain of infection being broken

1.3.3 MRSA Control in Healthcare Facilities

Infection control interventions within hospitals are major contributing factors in reducing and preventing the transmission of nosocomial pathogens amongst vulnerable patients in a healthcare environment.[17,21,23-25] These interventions have potential economic benefits, as the costs saved due to decreased transmission often outweigh the costs associated with policy and program implementation,[17,23] and have been credited with saving countless lives as well.[26]

Since 85% - 90% of patients with MRSA are asymptomatic carriers who can serve as a silent reservoir for further transmission,[27] screening to detect MRSA and placing patients with MRSA on contact precautions have become the cornerstone of MRSA control within healthcare facilities. Muto et al. (2003) reported that countries with the lowest prevalence of MRSA are those which adopted strict transmission-based infection control policies which include screening cultures to identify those colonized/infected with MRSA and the use of contact precautions for patients identified as having MRSA.[28] Guidelines from the Centers for Disease Control and Prevention recommend contact precautions for patients colonized with antibiotic-resistant pathogens, including MRSA; these guidelines

have been implemented throughout the United States since 1983.[28, 47] In order to identify patients colonized with MRSA who require contact precautions, it is now recommended that facilities implement a screening program.[28,30,47]

1.3.4 Principles of Screening

Wilson & Jungner (1968) developed a framework for screening for disease over 50 years ago which was adopted by the World Health Organization (WHO) as the gold standard for disease screening.[111] While the focus is primarily on chronic conditions, the criteria have been used for infectious diseases as well. The classic Wilson and Jungner screening criteria is as follows;

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a "once and for all" project.

Based on the above criteria, MRSA can be considered a suitable condition for screening as it meets all of the pre-defined criteria. However, the method of screening for MRSA (i.e. universal versus risk-factor based) has yet to be determined and needs to be further discussed and evaluated.

1.3.5 Approaches to Admission Screening for MRSA

In order to promptly initiate contact precautions, it is necessary to know a patient's MRSA status at the time of admission. Three major forms of admission screening have been identified in the literature (risk factor-based screening, search and destroy and universal MRSA screening) and will be further discussed in Chapter 2. Some facilities selectively screen patients based on certain high risk factors, such as previous hospitalizations or previous known infection with MRSA (i.e. risk factor-based screening),[29] whereas other facilities systematically screen all patients on admission to certain high risk wards or departments (i.e. universal MRSA screening).

Currently, the Ontario Provincial Infectious Diseases Advisory Committee (PIDAC) recommends admission screening of those patients which are at increased risk for MRSA. This risk factor-based screening includes patients who have;

- recently been transferred from another healthcare facility
- spent time in a healthcare facility outside of Canada in the past year
- spent more than 12 hours in a healthcare facility in the past 12 months

Within these guidelines, PIDAC allows for flexibility within each organization based on local epidemiology and risk factors.[30]

Recent modelling studies have suggested that a universal MRSA screening intervention should be effective in reducing the transmission of MRSA within a healthcare facility.[1,25,31-33,43] Nonetheless, for every study supporting the use of universal MRSA

screening, there are others which refute its use.[34-36] A systematic review conducted by McGinigle et al. concluded that the available studies examining MRSA screening were of poor quality and several publications have expressed the need to close the gap of information in regards to preventing healthcare associated infections (HAIs), including MRSA.[37-40] Furthermore, inconsistent implementation of preventative measures such as screening has been stated as a contributing factor to the growing number of HAIs.[38]

Infection control experts, policy makers, and consumer advocacy groups are weighing in on the debate around the optimal MRSA screening method, and many strongly support universal MRSA screening.[39,41,42] Universal MRSA screening has already been adopted by some institutions within the United States and Europe.[39,43] However, due to the lack of clear evidence supporting one form of screening over another, uncertainty remains regarding the best way to limit the transmission of organisms such as MRSA.[40] The literature demands more detailed and well designed studies to examine the clinical and cost-effectiveness of various approaches to MRSA screening using real life data and scenarios.[40]

This thesis focuses on comparing the previous screening practice (risk factor-based screening) at the Ottawa Hospital with the current practice of universal MRSA screening. Since 2000, The Ottawa Hospital has performed MRSA admission screening for patients at risk of MRSA colonization. Patients who test positive for MRSA are placed under contact precautions until hospital discharge or documented eradication of MRSA, as previously described.[24] However, admission screening compliance with risk factor-based

screening was moderate at approximately 60% (i.e. only 60% of those who should have been screened were, in fact, screened) , and was often delayed greater than the recommended 24 hours after admission.[15] Furthermore, patients with community MRSA strains often did not meet the criteria for risk factor-based screening and were not identified as having MRSA at the time of admission. In 2008, a universal MRSA screening intervention was implemented at The Ottawa Hospital.

This thesis will assess if the additional costs associated with a universal MRSA screening intervention for all patients admitted to hospital is effective in preventing the transmission of MRSA within the hospital, and if it is cost effective in both the short term and long term. Additionally, the project addresses the long term consequences of preventing the transmission of MRSA and the impact on associated hospital readmission rates and complications. Regardless of the outcome of the study, the results will represent an important contribution to the literature, and it will aid policy makers and infection control professionals in choosing appropriate and cost effective screening methods which are suitable for implementation in their institutions.

1.3.6 Economic impacts

Patients colonized or infected with MRSA place an enormous economic burden on the healthcare system due to prolonged hospitalization, increased treatment costs, and the need for costly control measures.[9] It is estimated that MRSA costs the Canadian healthcare system between $42-$59 million annually,[14] although one paper suggests direct costs may be as high as $82 million in 2005.[10] In addition to hospital associated

costs, societal costs are also accrued. MRSA has been associated with decreased productivity and household income, and increased social and non-hospital health service costs.[44,45]

Screening for MRSA upon admission to hospital will help the institution identify those patients who are colonized and/or infected with MRSA. However, screening programs incur additional financial costs as well. The costs of such a program can fluctuate based on the units screened and total number of patients admitted to the facility. Each institution is therefore challenged to balance the financial impact of a screening program with the benefits gained once positive patients are identified and placed on contact precautions.

Therefore there is considerable uncertainty regarding the effectiveness of efforts to control MRSA, the cost of implementing a universal MRSA screening program, and the cost of MRSA colonization. A desire to reduce this uncertainty justified this study.

1.3.7 Description of the Ottawa Hospital

The Ottawa Hospital is a large multi-centre tertiary care facility consisting of three main campuses. There are approximately 47,000 admissions per year filling nearly 1, 200 in-patients beds.[46]

Pilot Study

A universal screening intervention pilot project was conducted at the Ottawa Hospital in July and August of 2007 on four general medicine units. The pilot was conducted to address two barriers to nosocomial MRSA control at the Ottawa Hospital: (1) increasing numbers of patients admitted with community strains of MRSA that did not meet the criteria for risk-factor based screening, and (2) poor compliance with the risk-factor based screening approach due to its complexity. During the pilot project, 384 cultures/month were taken on four different units throughout two campuses of the Ottawa Hospital, compared with 209 cultures/month taken prior to the pilot project on those same units.[15] Of the 11 cases of MRSA detected during this pilot project, 2 (18%) were patients with community MRSA and would have been missed by the selective screening policy.[15] Furthermore, the overall compliance rate for admission screening during the pilot project was 86% compared to the 65% at baseline. These results suggested that a universal MRSA screening intervention will detect patients without the usual risk factors, including those with community strains of MRSA, and has the potential to reduce the nosocomial MRSA rates by improving case detection on admission and reducing subsequent transmission of MRSA to other patients.[15] However, implementing a universal MRSA screening intervention is associated with increased costs which were not thoroughly captured during the Pilot study.

1.3.8 Hypothesis

The apriori hypothesis to be tested in this thesis:

A universal MRSA screening intervention has been effective in reducing the nosocomial spread of MRSA within the Ottawa Hospital

In addition, the cost effectiveness of a universal MRSA screening intervention will be assessed.

1.3.9 Ethics Approval

Due to the nature of this study, no associated harms or risks were identified to the participants involved, as this was a quality assessment and evaluation of practice which was already underway at The Ottawa Hospital.

It was noted that due to the nature of the disease being studied, it may have been possible to identify patients based on their diagnosis. However, every effort was made to ensure privacy and confidentiality of patient data by de-identifying data sets, ensuring only those directly involved in the study had access to the study data, keeping data on password protected computers or in locked cabinets in locked offices and agreeing to destroy all associated study data by shredding hard copies, deleting files and erasing hard drives when the mandatory 15 years time frame has expired.

Ethics approval was obtained from the Ottawa Hospital Research Ethics Board.

1.4 Thesis overview

MRSA rates are increasing throughout the world, including Ottawa. A combination of increasing rates and increasing MRSA-associated costs can pose a challenge to any health care system. Appropriate and effective methods are needed to detect and control the spread of MRSA in a hospital setting. One such measure may include universal MRSA screening of all patients upon admission. This thesis will examine the clinical and cost effectiveness of a universal MRSA screening intervention in a large tertiary care centre. Chapter 1 presented the background and study objectives. Chapter 2 will present a review of the literature, synthesizing what is currently known about universal MRSA screening interventions and the economic impacts of these interventions on the healthcare system and society. Chapter 3 describes in detail the results of statistical analyses evaluating the effect of the universal MRSA screening intervention on the nosocomial transmission of MRSA. The economic analysis of the universal MRSA screening intervention is depicted in Chapter 4 and includes detailed probabilities and costs based on patient and population models. Chapter 5 summarizes the findings and draws conclusions on the effectiveness of this intervention.

2.0 Chapter 2 - Background – MRSA Screening

2.1 Chapter overview

Screening patients for MRSA carriage at the time of admission to hospital has the potential to identify MRSA positive patients early, thereby allowing the timely implementation of infection control measures (e.g. isolation precautions) and the subsequent reduction of transmission to others within the facility. There are several ways in which healthcare facilities choose to screen for MRSA at the time of admission. However, there is conflicting evidence in the literature regarding which screening method is most appropriate and most effective (clinically and economically) in reducing the number of nosocomial MRSA cases. This literature review will briefly describe the most common MRSA screening interventions with a focus on universal screening and, in addition, will address what is known with respect to the economic impacts of a universal MRSA screening intervention.

Based on the findings of the review, three main screening interventions were highlighted (risk factor-based, search and destroy, and universal). While it was not the original intent of the literature review to provide an in depth analysis on all three approaches, a brief description of the methods follows. It should be noted that a more in depth examination of MRSA universal screening methods was undertaken, as it is the primary focus of the thesis.

(1) Risk factor-based Screening

Risk factor-based screening involves selectively screening only those patients who possess certain high risk factors for MRSA at the time of admission to hospital. The most common factors utilized when determining which patients to screen for MRSA are;

- hospitalization within the past 12 months
- hospitalization outside of the patient's residing country
- transfer from another health care facility[29,48,49]

The literature suggests that risk factor-based screening is effective in reducing the transmission of MRSA within the hospital setting and is a cost effective strategy for the institution.[21,29,34, 48-55] Based on this evidence, the current Ontario Provincial Infectious Diseases Advisory Committee guidelines recommend facilities within the province adopt a risk factor-based approach.[30]

(2) The Search & Destroy Method

Certain countries, including the Netherlands, have implemented national search and destroy policies to counteract the effects of the rising MRSA prevalence.[56,57] The method can be described as one which facilitates the detection of MRSA by actively searching for it and once found, implementing isolation and control measures. A patient is classified into one of four risk categories (proven MRSA carrier, high risk of being a carrier, moderately elevated risk of being a carrier, no elevated risk of being a carrier). This classification also applies to staff members within the facility. If classified as a proven or high risk carrier, strict isolation measures are implemented immediately upon admission,

without waiting for the screening results to confirm MRSA carriage (i.e. pre-emptive isolation). It is also recommended that only a small and consistent team of staff care for the patient and contact with other disciplines minimized. In addition, any staff member who is colonized with MRSA may not return to work until all three sets of cultures (day 7, 15 and 20) are negative. This national strategy is consistently utilized by every institution throughout the country.[58]

The search and destroy method has been successful in maintaining the prevalence of MRSA in areas to < 1%.[50,57] However, despite its reported accomplishments, this method is associated with additional costs, reduced quality of patient care and a reduction in hospital admission capacity.[50]

<u>(3) Universal Screening</u>

Universal screening involves screening all patients for MRSA upon admission, regardless of their level of risk for MRSA carriage. Screening swab specimens are obtained upon admission from the nares and rectum of each patient, as well as any open skin lesions (up to a maximum of two sites) and catheter exit sites, where applicable. Swabs are then processed overnight in selective broth, followed by real-time Polymerase Chain Reaction (PCR) testing of the overnight broth culture. The test has a negative predictive value of 98%, however, with a lower positive predictive value of 65%, PCR-positive broth samples undergo culture confirmation.[24] Results are generally available within 24 hours of specimen collection.

The review of the literature demonstrates the limitations of available evidence and clearly underscores the need for well designed, large scale studies to evaluate the real life effectiveness of a universal MRSA screening intervention.

2.2 Methods

2.2.1 Search strategy

The review searched published and unpublished research and relevant literature in OVID. Electronic searches were conducted to explore medical, nursing and allied health databases. These searches included; MEDLINE, EMBASE, CINAHL, and CENTRAL from 1950 until January 2011 (Table 2.0 & 2.1). All literature identified during the initial database search were assessed for relevance based on the information provided in the title, abstract and descriptor/MeSH terms, a full report was retrieved for all literature that met the criteria of interest. For the initial screen all available abstracts were considered for relevance or, in instances when the abstract was not available, the original article was obtained. Studies identified from reference list searches and 'related article' searches were also assessed for relevance based on the study title. The search was limited to literature which had a human focus.

TABLE 2.0 DETAILED SEARCH STRATEGY FOR UNIVERSAL MRSA SCREENING

DATABASE	DATE RANGE	STRATEGY
OVID: Medline Embase	1950 -2011	1 Methicillin/ or exp Staphylococcus aureus/ or methicillin resistant staph aureus.mp. or exp Methicillin Resistance/ MRSA.mp./ or exp Staphylococcal Infections/ or exp Methicillin/ or exp Resistance/
		2 Mass Screening/ or universal screening.mp.
		3 1 and 2
		4 limit 3 to humans

Content experts (key researchers and clinicians) in the area of Infection Control, Infectious Diseases, and Health Economics were consulted for guidance and suggestions throughout the literature review process. Articles that were identified as relevant according to the search strategies were imported into RefWorks.

2.2.1.1 Acceptance criteria: Universal screening literature review

For the literature search focusing on MRSA screening methods, the search strategy included medical subject headings and keywords related to MRSA, surveillance and screening. The full text of an article was retrieved for review if the title or abstract suggested there was a focus on an MRSA surveillance method. Upon further in depth review, articles were included if they examined a universal MRSA screening method/program and were an original study, regardless of study setting or design.

2.2.1.2 Economic literature review

The search strategy for the economic component of the literature review included medical subject headings and keywords related to MRSA, surveillance and screening, and cost. The full text of an article was retrieved for review if the title or abstract suggested there was a focus on an MRSA surveillance method with a financial component included or addressed. Upon a further in depth review, articles were included if they examined a universal MRSA screening method/program, were an original study (regardless of study setting or design) and included an appropriate economic analysis component. This was described as a study which included detailed costs of the intervention.

TABLE 2.1 DETAILED SEARCH STRATEGY FOR ECONOMIC ANALYSIS OF UNIVERSAL MRSA SCREENING

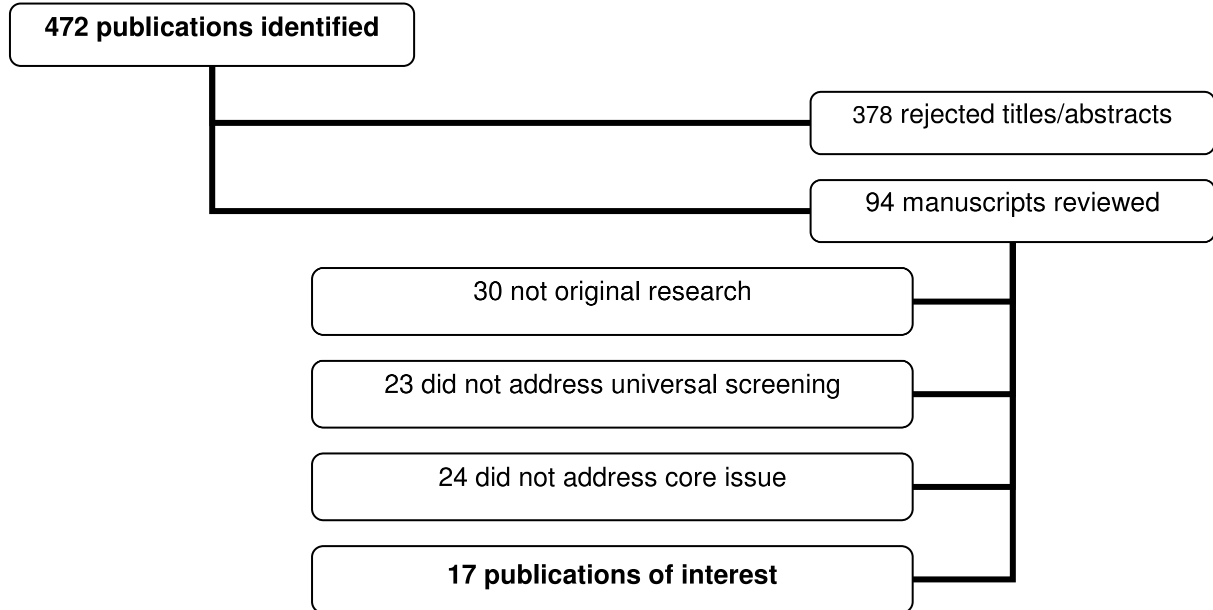
DATABASE	DATE RANGE	STRATEGY
OVID: Medline Embase	1950-2011	1 exp "Cost of Illness"/ or exp "Costs and Cost Analysis"/ or exp Health Care Costs/ or exp Economics/ or economic impact.mp.
		2 Methicillin/ or exp Staphylococcus aureus/ or methicillin resistant staph aureus.mp. or exp Methicillin Resistance/ MRSA.mp./ or Mass Screening/ or universal screening.mp./ or exp Staphylococcal Infections/ or exp Methicillin/ or exp Resistance/
		3 1 and 2
		4 limit 3 to humans

2.3 Results

2.3.1 Part 1: Universal MRSA screening

The literature review identified a total of 472 studies which matched the search criteria (Figure 2.0). Of those, 378 were excluded as they did not address our topic of interest. Upon review of the remaining 94 articles, 30 were not original research, 23 did not have a universal screening component, and 24 did not address core issue. The literature review identified 17 published studies examining a form of universal MRSA screening intervention. The majority of studies conducted universal screening on particular in-patient populations, with 47 % (8/17) of the studies focusing their interventions on surgical units.[1,31,32,35,60,62,63,64] Forty one percent (7/17) of the studies were conducted within the United States.[1,33,59,62,65,71,72] The prevalence of MRSA within these areas ranged from 0.03%[36] – 8.3%.[33]

Figure 2.0 Literature Review Results: MRSA Universal Screening Intervention



Sixty five percent (11/17) of the identified studies suggested that universal screening is an effective way to reduce the number of MRSA cases within a facility.[1,25,31-33,59-64] However, of the eleven studies which suggested universal screening was effective, only two were conducted on a hospital wide population, and only one of these used a real patient population.[33,65] Robiseck et al. observed a substantial reduction in the burden of nosocomial MRSA infections following the introduction of a universal MRSA screening intervention.[33] This study documented a 69.6% reduction in the aggregate hospital-associated MRSA disease prevalence density from the baseline of no screening.[33] Lee et al. utilized a computer simulated model of all hospital admissions and reported that universal screening was an effective intervention at various prevalence and reproductive rates.[65] A more detailed description of these studies is summarized in Table 2.3.

2.3.2 Part 2: Economic impacts of MRSA

The economic impact of MRSA on the healthcare system is, for the most part, poorly studied. In general, the majority of the research focused on the broader condition of *Staphylococcus aureus* and does not address MRSA specifically. This is problematic as MRSA is associated with an increased length of stay (LOS) and increased mortality when compared to the other well known *Staphylococcus aureus* strain, methicillin-susceptible *Staphylococcus aureus* (MSSA). Translating the results from the MSSA to the MRSA population is probably not appropriate.[3,5, 67,68] In addition, most economic papers involving MRSA dealt with either pharmacotherapy (e.g. treatments such as decolonization) and/or difference in costs associated with treatment of MRSA vs. MSSA infections. Often these papers utilized costs from other literature sources instead of utilizing real time data or Canadian-based costs.

TABLE 2.3
RESULTS OF LITERATURE REVIEW – EFFECTIVENESS OF A UNIVERSAL MRSA SCREENING INTERVENTION

REFERENCE	REF. #	YEAR	SAMPLE SIZE	SCREENING METHODS	COUNTRY / DEPARTMENT	RESULTS
Clancy et al. Active screening in high-risk units is an effective and cost-avoidant method to reduce the rate of Methicillin-Resistant *Staphylococcus aureus* infection in the hospital *Infection Control and Hospital Epidemiology*. 2006; 27(10): 1009-17.	1	2003	2 740	During a 15 month period, all patients admitted to the adult medical and surgical intensive care units were screened for MRSA on admission and weekly thereafter.	USA / Medical & Surgical ICUs	Active screening targeted to high-risk units may be an effective and cost-avoidant strategy for deceasing MRSA infections throughout the hospital Prevalence 3.7%
Cordova et al. Preoperative Methicillin-Resistant Staphylococcus aureus screening in Mohs surgery appears to decrease postoperative infections. *Dermatol Surg*. 2010 Oct;36(10):1537-40.	59	NA	963	During the 11-month screening period, all new patients except patients from the Veterans Affairs Medical Center (VAMC) were screened for nasal MRSA colonization during the preoperative consultation appointment using a rapid nasal swab screen.	USA / All preop hospital admissions	Preoperative MRSA screening and implementation of a decontamination protocol appears to decrease postoperative MRSA wound infections after Mohs surgery. Prevalence 2.4%
Diller et al. Evidence for cost reduction based on pre-admission MRSA screening in general surgery. *International Journal of Hygiene and Environmental Health.* 2008; 211:205-12.	31	2004	2 299	Every patient who was admitted to the surgical department received an MRSA screen on the day their admission was prepared (8-14 days prior to admission). If transferred, patients were screened on the day of admission. (12 months)	Germany / Surgical department	Pre-admission screening of all surgical patients is an effective method to reduce the hospital burden of MRSA-colonized patients. Prevalence 4.1%
Girou et al. Comparison of systematic versus selective screening for Methicillin-Resistant	34	1996-1997	729	During a 16 month period, two screening strategies were implemented: (1) only high-risk	France	Selective screening has similar sensitivity and is more cost-effective than systematic

REFERENCE	REF. #	YEAR	SAMPLE SIZE	SCREENING METHODS	COUNTRY / DEPARTMENT	RESULTS
Staphylococcus aureus carriage in a high-risk dermatology ward *Infection Control and Hospital Epidemiology.* 2000; 21(9):583-7.				patients screened (8.5 months); (2) all patients admitted to the dermatology ward were screened (7.5 months).	Dermatology Ward	screening Prevalence 6.5-7.2%
Gopal Rao et al. Prevalence and risk factors for Methicillin-Resistant *Staphylococcus aureus* in adult emergency admissions – a case for screening all patients? *Journal of Hospital Infection.* 2007; 66:15-21.	25	2004-2005	6 469	All adult emergency admissions were screened for MRSA (12 months).	UK / Emergency Dept.	Screening of all emergency admissions to detect MRSA colonization is preferable to selective screening, relatively inexpensive, and might reduce the MRSA colonization rates among emergency admissions. Prevalence 6.7%
Harbarth et al. Universal screening for Methicillin-Resistant *Staphylococcus aureus* at hospital admission and nosocomial infection in surgical patients. *JAMA.* 2008; 299(10):1149-57.	64	2004-2006	21 754	A crossover design was used to compare two control strategies: (1) rapid screening on admission plus standard infection control measures (9 months); (2) standard infection control measures alone (9 months).	Switzerland / Surgical departments	A universal, rapid MRSA admission screening strategy did not reduce nosocomial MRSA infection in a surgical department with endemic MRSA prevalence but relatively low rates of MRSA infection Prevalence 5.1%
Hardy et al. Reduction in the rate of methicillin-resistant Staphylococcus aureus acquisition in surgical wards by rapid screening for colonization: a prospective, cross-over study. *Clin Microbiol Infect.* 2010; 16:333–339.	60	2005-2007	10 934	Seven surgical wards at a large hospital were allocated to two groups, and for the first 8 months four wards used rapid MRSA screening and three wards used a standard culture method. The groups were reversed for the second 8 months. Regardless of the method of detection, all patients were screened for nasal carriage on admission and then	UK / Surgical wards	Screening of surgical patients using rapid testing resulted in a statistically significant reduction in MRSA acquisition. Prevalence 3.6%

Reference	Ref. #	Year	Sample Size	Screening Methods	Country / Department	Results
				every 4 days		
Hassan et al. Methicillin-Resistant *Staphylococcus aureus* in orthopaedics in a non-selective screening policy. *Surgeon.* 2008: 201-3.	61	2005	690	All patients underwent nasal and perineal swabs taken within 24 hours of admission	UK / Two orthopaedic wards	MRSA screening for all orthopaedic patients is needed when admitted to hospital. Selectively screening may miss MRSA colonized/infected cases. Prevalence 3.9%
Lee et al. Universal methicillin-resistant Staphylococcus aureus (MRSA) surveillance for adults at hospital admission: an economic model and analysis. *Infection Control and Hospital Epidemiology.* 2010; 31(6):598-606.	65	2008	Computer simulation model N/A	A computer simulation model was used to determine the potential impact of universal screening for all hospital admissions at various prevalence and transmission rates.	USA / Adults	Universal screening was the dominant strategy (more effective) for the following prevalence and basic reproductive rate combinations: when the basic reproductive rate was ≥ 1.5 and the prevalence was ≥ 15%, when the basic reproductive rate was ≥ 2.0 and the prevalence was ≥ 10%, and when the basic reproductive rate was ≥ 2.5 and the prevalence was ≥ 5%.
Lucet et al. Prevalence and risk factors for carriage of Methicillin-Resistant *Staphylococcus aureus* at admission to the intensive care unit. *Arch Intern Med.* 2003; 163:181-8.	32	1997	2 399	A prospective multicenter study screened all patients admitted to 14 French ICUs. A cost-benefit analysis was preformed.	France	Only universal screening detected MRSA carriage with acceptable sensitivity. A cost-benefit analysis confirmed that universal screening and protective isolation were

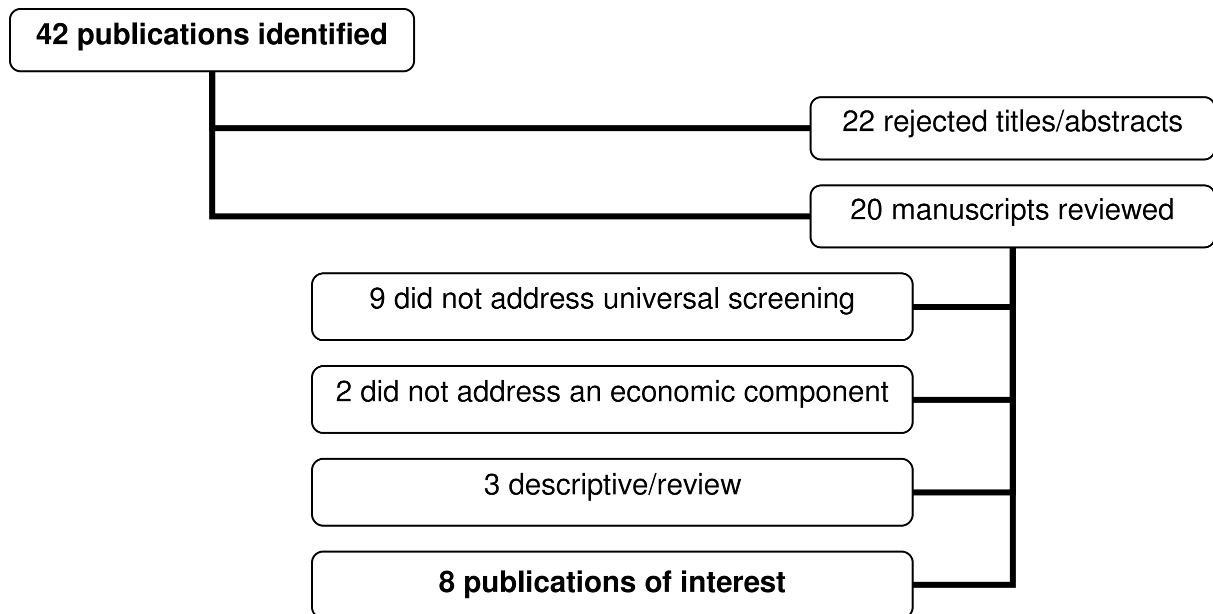
REFERENCE	REF. #	YEAR	SAMPLE SIZE	SCREENING METHODS	COUNTRY / DEPARTMENT	RESULTS
					Medical & Surgical ICUs	beneficial. Prevalence 6.9%
Murthy et al. Cost-effectiveness of universal MRSA screening on admission to surgery. *Clinical Microbiology and Infection.* 2010; 16(12):1747-53.	35	2004-2006	21 754	The economic analysis used data from a large, prospective cohort study conducted at the surgical department of the University of Geneva Hospital.	Switzerland / Surgical department	Reducing the risk of MRSA infection with universal PCR screening was not strongly cost effective. Local epidemiology may play a critical role, settings with a higher prevalence of MRSA colonization may find universal screening cost-effective and, in some cases, cost-saving. Prevalence 5.1%
Pofahl et al. Active surveillance screening of MRSA and eradication of the carrier state decreases surgical-site infections caused by MRSA. *Coll Surg* 2009; 208:981–988.	62	2007	5 094	All surgical admissions to a tertiary care hospital were screened for MRSA by nasal swab using polymerase chain reaction-based testing.	US / All surgical hosp. admissions	Surveillance for MRSA and eradication of the carrier state reduces the rate of MRSA SSI. Prevalence 6.8%
Robicsek et al. Universal screening for Methicillin-Resistant *Staphylococcus aureus* in 3 affiliated hospitals. *Annals of Internal Medicine.* 2008; 148(6):409-18.	33	2003-2007	Period 1 39 521 Period 2 40 392 Period 3 73 427	Examined the effect of expanded surveillance for MRSA using a 3-period before-and-after design. Period 1 (no active surveillance) was baseline. Period 2 introduced ICU-based admission surveillance and Period 3 universal admission surveillance.	US / Period 2 – ICU / Period 3 – all hosp. admissions	The universal screening program was associated with a reduction by more than half of health care-associated MRSA bloodstream, respiratory, urinary tract, and surgical site disease occurring during admission and in the 30 days after discharge. Prevalence 6.3-8.3%

Reference	Ref. #	Year	Sample Size	Screening Methods	Country Department	Results
Robotham et al. Screening strategies in surveillance and control of methicillin- resistant Staphylococcus aureus (MRSA). *Epidemiol. Infect*. 2007; 135: 328–342.	71	NA	Mathematical model	A closed population consisting of both a fixed-size hospital and the community it serves was modelled. Individuals in both the hospital and community populations are categorized as either MRSA-positive and infectious or MRSA-negative and susceptible to infection. Random and universal screening interventions were compared.	USA All	Random screening is more efficient in an epidemic situation, in that more infectious individuals are detected and the pattern of timing of detection with random screening closely follows the pattern of the overall hospital prevalence, whereas detection with screening on admission follows the community prevalence pattern, which is slower with a pronounced lag of about half a year. On-admission screening cannot control MRSA within a facility even at 100% screening. On-admission screening alone cannot be used to manage any epidemic which is driven by in-patient transmission. Random screening is more efficient, in that, less detection effort is required for successful control. Prevalence (0.1-0.4%)
Sankar et al. The role of MRSA screening in joint-replacement surgery. *International Orthopaedics*. 2005; 29: 160–163.	63	2000-2001	395	Patients admitted to the orthopaedic ward for total hip or knee replacement prior to Oct. 2000 – Apr. 2001 were not	UK	There was a significant reduction in the incidence of hospital-acquired infections following

REFERENCE	REF. #	YEAR	SAMPLE SIZE	SCREENING METHODS	COUNTRY / DEPARTMENT	RESULTS
				universally screened for MRSA. All patients admitted from Apr. 2001 – Oct. 2001 were pre-screened for MRSA	Orthopedic patients undergoing total hip and knee replacement	the introduction of pre-admission screening. Prevalence (NS)
Wertheim et al. Low prevalence of Methicillin-Resistant *Staphylococcus aureus* at hospital admission in Netherlands: the value of search and destroy and restrictive antibiotic use. *Journal of Hospital Infection.* 2004; 56:321-5.	36	1999-2000	9 859	All patients admitted to non-surgical departments were screened for MRSA nasal carriage.	Netherlands / Non-surgical Dept.	Extending the screening procedure to patients without risk factors does not appear to be indicated. Prevalence (0.03%)
Wibbenmeyer et al. Effectiveness of Universal Screening for Vancomycin- Resistant enterococcus and Methicillin-Resistant Staphylococcus aureus on Admission to a Burn-Trauma Step-Down Unit. *Journal of Burn Care & Research.* 2009; 30(4):648-56.	72	2002-2005	484	All patients admitted to the burn trauma unit (BTU) were screened for MRSA and placed in contact precautions until the results of their admission screening tests were available. A patient remained in isolation precautions if the nares culture is positive for MRSA.	US / Burn trauma unit	Without typing, it could not be proven that pre-emptive isolation and universal screening decreased the risk of MRSA transmission in the study population. Prevalence 3.7%

The literature review identified a total of 42 studies which matched the search criteria (Figure 2.1). Of those, 22 were excluded as they did not address our topic of interest, 9 did not have a universal screening component, 3 were not studies and 2 articles did not have an economic component. Eight studies assessed the economic impacts of MRSA in hospitals. Of these, four conducted a quality economic analysis which included an economic model, probability assignment and explanation of detailed costs.[35,65,66,69] Three of the studies were computer-simulated models [65,66,69] and only one of the studies examined the impacts of MRSA on society.[69]

Figure 2.1 Literature Review Results: Economic Impacts of MRSA



It is difficult to draw conclusions from the economic literature review as the studies utilized different populations, included varied costs in varying currencies and measured various cost outcomes (Table 2.4). In terms of cost per case prevented or avoided, existing studies suggest a very wide range of costs for universal screening between

$5,086.02 (£3200)[70] and $33,601.94 (CHF 30 784)[35] in Canadian currency. The rough estimated total costs (CAD) of the program per month was between $2177.58 (18 971€ = $26,130.95 / 12 months)[31] and 3,444.68 (USD $3 475).[1]

2.4 Discussion

2.4.1 MRSA screening methods

There are three major forms of admission screening for MRSA, all of which have their own limitations. To date, the effectiveness of different screening interventions have not been compared by means of a properly conducted large scale study.

The literature search identified seventeen studies which examined a universal MRSA screening intervention, but only three of these studies applied the policy to the entire adult hospital population.[33,65,71] As the remaining studies only examined universal screening on a select population/ward within the hospital they were not universal from a hospital perspective, and as such were not an accurate representation of the impact that such a screening method might have on an entire hospital population.

Two of the three studies which examined universal screening on the entire hospital population identified that it was an effective method in reducing MRSA infections.[33,65] Robiscek et al. was the only study from the literature review to evaluate universal screening on all hospital admissions for 21 months in a real life scenario. The study consisted of three periods, the first in which no active surveillance was conducted (baseline period), the second in which universal screening was conducted on all ICU admissions, and the final period in which all hospital admissions were screened for

MRSA. The prevalence of MRSA within this location was reported as 6.3-8.3%. The authors concluded that a universal MRSA screening intervention was associated with a large reduction, by more than half, the number MRSA infections.[33] However, there are some limitations to this study. First, the authors did not account for any threats to the validity of the study by utilizing internal and external control groups. It is therefore unclear whether any other factors, such as, decreasing community MRSA rates or changes to other infection control practices (i.e. hand hygiene, decolonization etc.) might have impacted the results. Second, the authors did not address the economic impacts of the universal MRSA screening intervention. This is an important limitation of the study as administrators and decision-makers base policy recommendations on both clinical and economic effectiveness. Third, this study did not look at overall MRSA transmission as indicated by the number of patients who acquired MRSA, but focused only on clinical infections.

Lee et al. used a stochastic computer model to determine the impact of performing universal screening on an entire hospital population. The authors determined that universal screening was effective at a variety of prevalence and reproductive rates.[65] While the report did include a well conducted economic analysis, it was a computer simulation model which is a simplistic portrayal of real life scenarios and may not accurately represent true hospital scenarios. For example, the computer model did not account for the fact that transmission of MRSA may occur between patients before positive results are known and perhaps, most importantly, the model compared no screening at all to universal screening. This particular fact is an unrealistic portrayal of

TABLE 2.4

RESULTS OF LITERATURE REVIEW - ECONOMIC IMPACT OF A UNIVERSAL MRSA SCREENING INTERVENTION

REFERENCE	YEAR	SAMPLE SIZE	METHODS	LOCATION / DEPARTMENT	RESULTS
Beigi et al. Epidemiologic and economic effect of Methicillin-Resistant *Staphylococcus aureus* in obstetrics. *Obstet Gynecol* 2009;113:983–91.	2007	Computer simulated N/A	A year of pregnancies and live Births was simulated. Using the number of live births in the United States and the seasonal distribution, simulated pregnant women were sent one-by-one through the model.	USA / Obstetrics	From a societal perspective, economic modeling estimates that on a national scale MRSA-associated infectious morbidity currently generates $8,747,009 ± 267,867 of costs. From a payer perspective, the total economic burden of MRSA is $8,037,789 ± 237,346 per year. The average additional cost per case of MRSA infection is $611.68. Universal screening and decolonization efforts do not currently seem to be cost-effective. None of the incremental cost-effectiveness ratios approximate the benchmark of $50,000.00 per quality adjusted life year gained, regardless of the assumed success of surveillance and decolonization.
Clancy et al. Active screening in high-risk units is an effective and cost-avoidant method to reduce the rate of Methicillin-Resistant *Staphylococcus aureus* infection in the hospital *Infection Control and Hospital Epidemiology*. 2006; 27(10): 1009-17.	2003	2 740	During a 15 month period, costs were calculated retrospectively and included the cost of screening plus the cost of placing patients in isolation.	USA / Medical & Surgical ICUs	Total cost of the program was approximately $3 475/month. Using the lowest published literature cost associated with an MRSA infection ($9 275), the authors estimated a cost avoidance of $19 714/month (averting a mean of 2.5 MRSA infections per month).

Reference	Year	Sample Size	Methods	Location Department	Results
Diller et al. Evidence for cost reduction based on pre-admission MRSA screening in general surgery. *International Journal of Hygiene and Environmental Health.* 2008; 211:205-12.	2004	2 299	Not stated	Germany Surgical department	The total costs for the screening program was 18 971€/year
Gopal Rao et al. Prevalence and risk factors for Methicillin-Resistant *Staphylococcus aureus* in adult emergency admissions – a case for screening all patients? *Journal of Hospital Infection.* 2007; 66:15-21.	2004-2005	6 469	The cost of the screening program was calculated by including labour, equipment and institutional overheads. The average cost of the screening procedure was calculated by direct observation.	UK Emergency Dept.	The total cost of the screening program was £24 417.13/year
Lee et al. Screening cardiac surgery patients for MRSA: An economic computer model. *Am J Manag Care.* 2010;16(7):e163-e173.	N/A	Computer simulation model (1000 hypothetical patients)	A computer simulation model representing the decision of whether to perform preoperative MRSA screening and decolonizing those patients with a positive MRSA culture.	USA Cardiac patients	Even when MRSA colonization prevalence and decolonization success rate were as low as 1% and 25%, respectively, the ICER of implementing routine surveillance was well under $15,000 per quality-adjusted life-year from both the third-party payer and hospital perspectives. The results suggest that routine preoperative screening of cardiac surgery patients may be a cost-effective strategy for a wide range of MRSA colonization prevalence levels, decolonization success rates, and screening/decolonization costs.
Lee et al. Universal methicillin-resistant Staphylococcus aureus (MRSA) surveillance for adults at hospital admission: an economic model and analysis. *Infection*	2008	Computer simulation model N/A	A computer simulation model was used to determine the potential impact of universal screening for all hospital admissions at various prevalence and transmission rates from the societal and third party-payor	US	Universal MRSA surveillance was cost-effective (defined as an incremental cost-effectiveness ratio of less than $50,000 per quality-adjusted life-year) when the basic reproductive

Reference	Year	Sample Size	Methods	Location / Department	Results
Control and Hospital Epidemiology. 2010; 31(6):598-606.			perspectives.	All adults	rate was 0.25 or greater and the prevalence was 1% or greater. Universal MRSA surveillance appears to be cost-effective at a wide range of prevalence and transmission rates.
Murthy et al. Cost-effectiveness of universal MRSA screening on admission to surgery. *Clinical Microbiology and Infection.* 2010; 16(12):1747-53.	2004-2006	21 754	Costs were extracted from the hospital's cost accounting systems. Actual costs were used instead of charges to obtain a more accurate estimate of financial burden. The costs of PCR and agar screening included test materials, laboratory staff and overheads. Staff costs for testing were estimated by allocating the salary costs of the full-time equivalent laboratory technicians required during the study period across the number of tests conducted to determine the unit cost per test. The costs of infection control measures included protection materials, decolonization therapy and staff time. Costs associated with MRSA infection were estimated as a function of excess length of hospital stay (LOS) attributable to infection and the cost per bed-day.	Switzerland Surgical department	Reducing the risk of MRSA infection with universal PCR screening was not strongly cost effective. Compared to no screening, the PCR strategy resulted in higher costs (CHF 10 503 vs. 10 358) but a lower infection probability (0.0041 vs. 0.0088), producing a base-case incremental cost-effectiveness ratio of CHF 30 784 per MRSA infection avoided.
Nixon et al. Methicillin-Resistant *Staphylococcus aureus* on orthopaedic wards. *Journal of Bone and Joint Surgery*. 2006; 88(6):812-7.	2003-2004	5 594	All orthopaedic admissions were screened for MRSA upon admission.	UK Orthopaedic wards	The cost of preventing one MRSA infection was £3200.

hospital function as the majority of institutions incorporate some form of selective screening for MRSA. These factors make comparisons with our study challenging.

Finally, Robotham et al. examined random and universal MRSA screening methods. The authors determined that random screening was more efficient than universal screening for hospital surveillance and allowed for effective nosocomial control.[71] The authors used a stochastic computer model to analyse the two interventions which makes application to real life patient scenarios challenging.

2.4.2 Economic impacts of MRSA

The literature search uncovered five research studies and three mathematical modelling studies which evaluated the economic impacts of a universal MRSA screening intervention.[1,31,25,35,65,66,69,70] Four articles conducted a quality economic analysis similar to ours (including an economic model, probability assignment and explanation of detailed costs in report);[35,65,66,69] three of these were computer-simulated models [65,66,69] and only one examined the impacts of MRSA on society.[66] Murthy et al. was the only identified study which conducted its research based on actual hospital patients. The authors included an economic analysis, complete with associated probabilities and detailed costs, however, the intervention was only applied to a surgical population and was not truly universal from a hospital standpoint. Overall, the authors concluded that the program was not cost effective, likely due to a low prevalence of MRSA and successful infection control practices.[66]

As mentioned, three mathematical modelling studies were included in our literature review. Lee et al. evaluated the cost effectiveness of a universal MRSA surveillance program at various prevalence and reproductive rates. They concluded that a universal MRSA screening intervention is cost effective at a variety of prevalence and reproductive rates.[65] The project, however, compared universal screening to no screening at all. This factor makes the results of the project less generalizable, as most hospitals have some form of risk factor-based screening program in place for MRSA.

In a second study, Lee et al. reported that universal screening of perioperative cardiac patients was a cost-effective strategy for a wide range of MRSA colonization prevalence levels, decolonization success rates, and screening/decolonization costs. Once again, these authors chose to compare the universal screening intervention to no screening. This fact, combined with the limited population (perioperative cardiac cases) make the results even less generalizable to real life hospital scenarios.[66]

Beigi et al. also utilized computer simulation models to demonstrate the effects of an MRSA universal screening intervention on a virtual hospital population. Unlike the Lee et al. studies, however, they concluded that a universal screening intervention is not cost effective.[69] However, the three computer simulation studies cannot be compared to one another as they involve different virtual populations (cardiac vs. obstetric vs. general adult patients). In addition, it should be kept in mind that these studies were based on results from a mathematical modelling program, which may not be a realistic portrayal of true hospital function; therefore, they cannot be compared to real patient data studies.

Finally, the models included routine decolonization methods; therefore, the results may not be applicable to centers where decolonization is not routinely performed.

2.5 Conclusions

The literature search indicated a need for studies which provide proper assessment of the clinical and economic values associated with universally screening all patients admitted to a healthcare facility.[25,32,33,35,65] The reviewed studies were not adequately designed to evaluate the clinical and financial effectiveness of a large-scale, hospital-wide, universal MRSA screening intervention. In addition, there was a lack of pertinent Canadian studies. This thesis project will address the gap in the current knowledge with regards to universal MRSA screening as it will apply the intervention to all hospital admissions and include a formal economic analysis component to evaluate the intervention from clinical and financial perspectives.

This thesis incorporates the positive elements of the aforementioned studies, and, in addition, to enhance the body of knowledge associated with MRSA universal screening interventions by:

1. improving the generalizabilty and reliability of the results by increasing the size of the study to include an entire hospital population;
2. improving the validity of the study by adding an internal/external comparison/control group to account for any threats to the validity of the project;
3. strengthening the results by including an economic analysis of the intervention from both a hospital and societal perspective;

4. including both infected and colonized patients for a more complete assessment of MRSA transmission.

These results will inform the research, clinical and administrative communities about the effectiveness and cost-effectiveness of screening all patients for MRSA upon admission to hospital. Our aim is to clearly demonstrate whether such a screening program would alter the rates of nosocomial (hospital-acquired) MRSA colonization and/or infection among those inpatients at the Ottawa Hospital, compared to the current standard of risk-factor based screening.

3.0 Chapter 3 - Universal Screening for MRSA at the Ottawa Hospital

3.1 Chapter overview

This chapter of the thesis aims to statistically analyze the effectiveness of the universal MRSA screening intervention in reducing the nosocomial transmission of MRSA at the Ottawa Hospital. A description of the intervention, data collection and statistical analysis are included in this section, along with a discussion of the findings. Overall, the analysis concludes that the universal MRSA screening intervention did not decrease the nosocomial rates of MRSA within the institution. The presence of threats to the internal validity were evaluated by means of internal and external control groups.

3.2 Study design

Our study aimed to assess the effectiveness and cost effectiveness of a universal MRSA screening intervention compared with the previous policy of selectively screening patients for MRSA (i.e. risk factor-based screening). To measure the effectiveness of this intervention, we examined monthly nosocomial MRSA incidence rates per 100,000 patient days prior to, and during the intervention period as our main outcome of interest.

The study design was a retrospective population-based observational study conducted at the Ottawa Hospital between January 1, 2006 and August 31, 2009. The Ottawa Hospital is a 1,200 bed, multi-campus adult tertiary care hospital with approximately 46,000 admissions per year.[46] The study consisted of two periods. In the first period (January 2006 – December 31, 2007), patients admitted to the Ottawa Hospital underwent risk factor-based screening. These patients were screened for MRSA based on certain pre-

defined risk factors. These factors were: previous hospitalization in past 6 months, direct transfer from another healthcare facility, or history of MRSA colonization or infection.

In the second period (January 2008 to August 2009), all patients admitted to the Ottawa Hospital were screened for MRSA upon admission. Universal MRSA screening was implemented on January 14, 2008 at the General campus and January 28, 2008 at the Civic campus and the Heart Institute.

3.2.1 Study population

The study population consisted of all patients admitted to any campus of the Ottawa Hospital during the study period (excluding newborns). All patients admitted to hospital during the specified study period were considered eligible for enrolment in the study. Eligible patients were identified from the Ottawa Hospital Data Warehouse and there was no direct patient contact.

3.2.1.1 Intervention Criteria

<u>Pre-Intervention Period</u>: January 1, 2006 – December 31, 2007. During this period, risk factor-based screening was in effect, as described previously (section 1.3.3). Only those patients meeting these certain criteria were screened for MRSA.

<u>Intervention Period</u>: January 14, 2008 – August 31, 2009 (General campus) and January 28, 2008 – August 31, 2009 (Civic campus/Heart Institute). During this period, universal screening for MRSA was implemented, as previously described.

3.2.1.2 Exclusion criteria

Patients admitted to the Ottawa Hospital prior to January 2006 and newborns were excluded from the study.

3.2.2 Study Periods

The study consisted of two study periods. In the first, a period of 24 months (January 2006 until December 2007), patients underwent risk factor-based screening. The Ottawa Hospital has been using risk factor-based screening since 2000. The Ottawa Hospital's policy of screening those patients identified as high-risk and placing them under contact precautions in private rooms (following positive results) is in line with the best practice guidelines and is supported by the literature.[30,42]

The second study period consisted of 20 months (January 2008 until August 31, 2009). During this period the universal MRSA screening intervention was initiated and all inpatients were screened for MRSA colonization or infection upon admission.

3.2.3 Definitions

- A **nosocomial** MRSA case was defined as any patient in whom MRSA was detected from a screening swab or clinical specimen (taken due to signs and symptoms of infection and may include blood, wound and urine cultures) obtained more than 48 hours after admission.[20] This definition was chosen as it is the gold standard within infection control guidelines and is utilized throughout the literature. The patient could be colonized or infected with MRSA. Patients were counted only once at the time of their first MRSA-

positive culture; patients known to be colonized or infected with MRSA in the past were not counted.

- An **infected** MRSA case was defined as a patient with a positive MRSA culture with manifestation of clinical symptoms of infection (e.g. bloodstream, urinary, wound, or respiratory infection).[73]
- A **colonized** MRSA case was defined as a patient with a positive MRSA nasal/rectal screening culture who does not meet the definition of an infected case.[73]
- MRSA **bacteremia** was defined as a blood culture confirmed positive for MRSA.
- ***A Clostridium difficile*-associated diarrhea (CDAD)** case was defined as a patient with a positive stool culture for *C. difficile*. Furthermore, *C. difficile* is the most common cause of infectious diarrhea in hospitals and is one of the many types of bacteria that can be found in the environment and the bowel. Damage to the bowel causing diarrhea occurs when toxins are released as the *C. difficile* bacteria grow within the bowel.[74]
- **Risk factor-based screening** was defined as the process of screening patients for MRSA based on certain pre-defined high-risk factors. These factors included; previous hospitalization in past 6 months, direct transfer from another healthcare facility, or history of MRSA colonization or infection.
- **Universal MRSA screening** was defined as the intent to screen all hospital in-patients for MRSA upon admission.

3.2.4 Outcomes

3.2.4.1 Primary Outcome

Our outcomes were defined a priori in consultation with Infection Control experts and members of the thesis committee. Our primary outcome of interest was the nosocomial MRSA rate in both study periods. This was calculated by summing the number of nosocomial MRSA cases (those patients with a positive MRSA test who have been admitted to hospital $\geq$ 48 hrs) and dividing by the number of patient days.

3.2.4.2 Secondary Outcomes

To improve the strength and validity of the study, the following secondary outcomes were addressed in the statistical analysis: the regional rates of MRSA, mupirocin usage, nosocomial *Clostridium difficile*-associated diarrhea (CDAD) rates for both the pre- and post-intervention periods.

The analysis compared changes in nosocomial MRSA rates with both internal and external control groups to account for any potential threats to the validity of the study, including but limited to, any unplanned events or exposures, changes to the instrumentation or collection of information that may have occurred before or during the intervention period, therefore potentially biasing our results. Nosocomial CDAD rates were utilized as an internal control to assess whether any unanticipated factors may have influenced our results. CDAD rates were expected to remain constant despite our MRSA screening intervention and thus, would allow us to investigate unanticipated influences over time, as both groups are expected to be exposed to the same non-intervention

influences. Regional MRSA rates were utilized as an external control group to account for external factors (such as increasing rates of community MRSA).

The incidence of MRSA bloodstream infections were recorded monthly per 100, 000 patient days throughout both study periods. Finally, the short and long-term cost impacts of the intervention were calculated as discussed in Chapter 4.

3.3 Methods

3.3.1 Infection control practices and Laboratory methods

All eligible patients were expected to be screened for MRSA within 24 hours of admission during both study periods. Compliance with admission screening improved throughout the intervention study period (from 54% to 84%) and was explored further in the sensitivity analysis. Screening swab specimens were obtained from the anterior nares and rectum of each patient, as well as open skin lesions (up to a maximum of two sites) and catheter exit sites, where applicable. This method of screening has been well documented in the literature.[30] Swabs were processed in our clinical microbiology laboratory, as previously described, and involved overnight incubation in selective broth, followed by real-time Polymerase Chain Reaction (PCR) testing of the overnight broth culture using the IDI-MRSA assay kit (GenOhm) and a SmartCycler II device (Cepheid).[24] This assay has a negative predictive value of 98%, but a positive predictive value of only 65%. Therefore, all PCR-positive broth samples underwent culture confirmation.[24] Results were available within 24 hours of specimen collection.

Throughout both study periods, once screening swab specimens were obtained (as previously described) [24], patients who tested PCR positive for MRSA were placed on contact precautions until culture confirmation. Those patients confirmed MRSA positive by culture remained under contact precautions for the duration of their hospital stay or until eradication had been proven (three consecutive negative cultures, at least one week apart). Those patients who tested PCR positive but whose culture results were negative, were considered to be false-positives and had their contact precautions discontinued. Patients colonized or infected with MRSA who were in multiple-bed rooms were moved to private rooms, and use of the other beds was blocked until the roommates' screening results were available.

3.3.2 Data Collection

The data required for this analysis was obtained from the Ottawa Hospital Data Warehouse (OHDW), including nosocomial and non-nosocomial MRSA rates, confirmed MRSA bloodstream infections, admission rates, length of stay, nosocomial CDAD rates, and patient demographics and characteristics.

The majority of the patient data was collected using the OHDW. The data of interest extracted from the OHDW for each patient was;

Demograhics

- o Age
- o Sex
- o Admission date
- o Discharge date

o Campus of admission

o Number of patients in hospital per day (pt days)

o Admitting service

Outcomes

o Laboratory interventions (including dates) and associated results

o Pharmacological interventions (Mupirocin usage)

o Mortality

Potential Risk Factors

o Charlson score

o Total ICU days

o Length of hospital stay

o Number of acute care in-patient days

3.3.2.1 The Ottawa Hospital Data Warehouse

The OHDW is a relational database which links clinical, laboratory, and administrative data using common identification keys. [75] The OHDW has been backdated from 1996 and once weekly the OHDW administrators abstract data from the many operational data systems of the Ottawa Hospital. The data are maintained in a separate and secure electronic archive, in a series of tables linked by common identifying variables (for example patient number, or admission/encounter number). It incorporates a privacy framework which ensures secure and appropriate access to patient data in a manner which facilitates analysis with statistical software packages, such as SAS.

A series of complex SAS coding was used to extract and compile the information from the data warehouse to obtain a base set of data which included those patients who had been admitted to TOH during our study period. All MRSA positive patients were identified by either a positive screen or clinical specimen. After the study cohort was obtained, all lab reports were reviewed for these patients so that each could be classified as either a nosocomial or community acquired MRSA case. A nosocomial case was defined as one in which the positive MRSA swab was obtained greater than 48 hours after the patient was admitted to hospital. Alternatively, if the specimen was positive less than 48 hours after admission, it was deemed a community acquired MRSA case. Once the primary database was compiled, each MRSA positive patient was counted once by taking the first positive MRSA test. To avoid an overestimation of the pre-intervention period rate, all MRSA positive patients attributed to this time period were examined to ensure that they were not confirmed MRSA positive prior to this study period; if so, the patient was attributed to the year in which he/she was first deemed MRSA positive, according to the information backdated in the OHDW until 1996.

A detailed description of the tables and variables used from the OHDW for the purposes of this project can be found in Appendix A along with a diagrammatic representation of the organization of the tables within the OHDW (Appendix B).

3.3.2.2 Factors studied to investigate potential threats to validity introduced by study design

Throughout both study periods, to the best of our knowledge, infection control measures, with the exception of screening, remained constant. However, other events besides our intervention could have potentially impacted the nosocomial MRSA rates, such as hand hygiene compliance among healthcare workers, environmental cleaning practices, compliance with isolation protocols, MRSA decolonization therapy, and the prevalence of MRSA in the community. To control for these potential threats to internal validity, both internal and external control groups were used. Nosocomial CDAD rates were utilized as the internal control group, as all but two of the above mentioned factors were expected to impact nosocomial CDAD and MRSA rates to the same extent. Thus, any decrease in nosocomial MRSA incidence, in the face of constant or increased nosocomial CDAD incidence, was more likely attributable to the intervention. The data obtained for the internal comparison group was obtained from the OHDW in a similar fashion to the MRSA data, as mentioned above, and had the same quality assurance methods applied.

Two additional factors could impact nosocomial MRSA but not CDAD rates, MRSA decolonization therapy and prevalence of MRSA in the community. Decolonization therapy may theoretically reduce the reservoir of MRSA in hospital but is rarely performed due to lack of evidence to support this approach. Data was collected on the number of patients who received MRSA decolonization therapy. To assess this, the number of mupirocin orders were counted and accounted for in the adjusted analysis.

Mupirocin, a topical antibiotic, is standard therapy for MRSA decolonization. In the in-patient setting, MRSA decolonization is the predominate indication for mupirocin use.

To account for the prevalence of MRSA in the community, regional MRSA incidence rates were utilized as our external control (i.e. the incidence of MRSA in the region per 100,000 population). Regional rates were accrued through the Microbiology Department at the Ottawa Hospital, where the data is stored in a database created and maintained by a lead microbiologist at the Ottawa Hospital. Both hospital and private laboratories in the Champlain region (see Appendix C for map of region) submit MRSA isolates and basic epidemiologic data on a voluntary basis. The data were entered manually into Microsoft Access by the microbiologist, students, or myself. Each patient was only attributed to one positive MRSA test (always the first one detected). The regional rates were calculated by using all newly identified MRSA positive cases throughout the Champlain region (numerator) and the estimated population of the region, based on Champlain Local Health Integration Network (LHIN) demographics (denominator). The rates were converted to a per 100,000 population rate. A decrease in nosocomial MRSA incidence at the Ottawa Hospital while regional MRSA incidence remained constant or increased would be more likely attributable to the intervention than external factors. A major strength of this study compared to many published studies of interventions to reduce MRSA incidence was the availability of regional MRSA data.

3.3.2.3 Quality Assurance measures

Periodic checks to ensure data accuracy were performed throughout the data collection process by several means. Data obtained through the OHDW were cleaned by removing duplicate data, checking and correcting for missing values and running frequency distributions and summary statistics using SAS. Once raw case numbers were obtained through the OHDW, they were compared with the case numbers obtained independently by members of the Infection Control Department. A slight discrepancy in monthly numbers was expected and noted (≤ 5%), as data collected from the OHDW was more rigid in regards to case definitions and dates, whereas the Infection Control Department's data was softer and more dependent upon notification and investigation (i.e. reviews of patient medical records).

Every effort was made to ensure the highest quality data were obtained with regards to the external comparison group of regional MRSA rates. However, as the data was submitted from several third party sources, it can only be assumed that the data was collected, delivered and entered in an appropriate manner. It should be noted that the Montfort Hospital abruptly stopped contributing information to the database due to staffing shortages in July of 2009, thus leaving no records for the last two months of the study period. It is believed that all other institutions contributed consistently to the database as they have over the past several years. It should also be noted that the data are utilized by the region to determine future funding and policy decisions.

3.3.3 Statistical analysis

As the data in this study arose from a non-randomized design, the effectiveness of a MRSA admission screening intervention and isolation policy on nosocomial MRSA incidence over time was analyzed using segmented Poisson regression analysis. Segmented regression analysis, described as a model which can be fit to estimate changes in levels and trends throughout the study period,[76] has been utilized in the literature in various comparable studies.[13,33,76,77] The nonrandom assignment of the intervention requires strict control of the potential confounders.[76] Regression analysis quantifies the relationship between an outcome and an intervention, allowing for statistical control of known confounders.[76] Poisson regression is preferred over linear regression for estimating an association between an intervention and monthly rates while controlling for time, as the counts are not normally distributed.[76] A segmented Poisson regression differs from a non-segmented regression as it allows the slope (i.e. change in time trend) to differ before and after the intervention.[76] This is important to note, as forcing equal slopes before and after the intervention when they are not equal, can lead to incorrect conclusions about the effectiveness of the intervention.[76]

When building the model for analysis, overdispersion, autocorrelation and seasonality were considered.[78] Overdispersion, described as extra-variability arising from events that may not be considered independent, is most often a result of uncontrolled experimental conditions.[79] Various versions of the statistical model were fitted to account for possible overdispersion. A dispersion parameter was introduced into the relationship between the variance and the mean to account for any overdispersion in the model.[79] In the SAS

model, for example, SCALE = was introduced into the proc genmod statement. Versions of the model were run using SCALE=DEVIANCE and PEARSON to determine the most appropriate fit.

Autocorrelation, the fact that outcomes at two time points that are closer together may be more similar than outcomes at two time points which are further apart, can be adjusted for in segmented regression analysis.[78,80] Failing to correct for this can lead to an overestimated significance of the effects of the intervention.[78,80] Autocorrelation can be visually detected by plotting the residuals over time. If the residuals are randomly scattered, it supports the absence of autocorrelation; however if a pattern exists where consecutive residuals lie on one side of the line, it indicates the presence of positive autocorrelation. If they lie on either side of the regression line, negative autocorrelation may exist.[78,80] Additionally, a Durbin-Watson statistic was utilized to further examine the presence of autocorrelation.[78] Values close to 2.00 indicate no serious autocorrelation.[80] In order to err on the side of caution, proc autoreg was used for the analysis as it allows one to account and adjust for any autocorrelation.

Seasonality, a pattern in the data that may be due to seasonal trends or fluctuations, is important to adjust and control for to ensure the true intervention effects can be evaluated.[78] Segmented regression analysis requires data collected at equally spaced intervals over time and requires at least 12 data points before and 12 data points after the intervention to examine seasonal effects.[78,80] Seasonality was tested for using the Dickey-Fuller unit root test as demonstrated by Carroll et al.[78]

An appealing feature of segmented regression analysis is the graphical representation of the results, which allows for a visual inspection of the data - usually the first step in the analysis process.[76,78] A visual inspection allows the analyst to look for patterns in the data, although basing conclusions on the graphical data alone is not sufficient; further analysis is usually required to determine whether effects were due to the intervention, chance or other influential factors.[78,80]

Segmented regression allows the analyst to control for pre-intervention trends, estimate the size of the intervention effect at different time points and evaluate changes in trends over time.[78] In addition, it allows visual inspection for the presence of outliers. Segmented regression analysis can avoid some of the internal threats to validity that other observational studies might be subjected to, however, a potential threat to internal validity is the presence of factors which are related to the outcome of interest and that may have changed at the time of the intervention, such as; co-interventions, seasonal changes, changes in the study population, or changes in the measurement of the outcome of interest.[80] For this reason, we chose to examine internal and external control groups to investigate the presence of such potential threats to the validity of the study.

3.3.3.1 Pilot Project

During the pre-intervention period, a universal MRSA screening pilot was conducted on 2 units over a two-month period (July and August of 2007). Thus, some degree of contamination during the pre-intervention period was likely and we may therefore, as a result, underestimate the true effect of the intervention. We anticipated this effect would

be small given the short duration of the pilot and the involvement of only 4% of all in-patient units. If an effect was noted, it would bias the results towards the null, therefore maintaining the Pilot data in the analysis was a prudent approach.

3.3.3.2 Building our Model

For each day within the study period, the numbers of patients residing within the hospital was identified, as was the number of patients experiencing an incident case of nosocomial MRSA (i.e. the number of new nosocomial MRSA patients). The daily rates were then summed to calculate the monthly incidence of nosocomial MRSA.

A sufficient number of time points before and after the intervention were required to conduct a segmented regression analysis.[80] Whereas at least 12 data points before and after the intervention are recommended, we included 24 data points before the intervention to allow evaluation of a seasonal component and 20 data points during the intervention. Furthermore, based on inspection of historical data at the Ottawa Hospital, we chose monthly intervals in order to ensure acceptable stability of rates at each data point.

In our model, we estimated the pre-and post-intervention changes in MRSA levels and trends as our primary outcome of interest. A visual inspection of the data over time was used to determine any noticeable changes or patterns within the data, including the presence of any seasonal variation. A preliminary review of the MRSA rates over the past 3 years at the Ottawa Hospital did not identify any seasonal variation and we did not

expect that seasonal variation would influence our results. Assumptions underlying the regression model were checked by means of a residual analysis. Autocorrelation of the data was assessed by the Durbin-Watson statistic, seasonality was assessed using the Dickey-Fuller unit root test and goodness of fit statistics were utilized to assess overdispersion.

The following model was adapted from a similar model used by Carroll et al. and estimates nosocomial MRSA rates (nosocomial CDAD rates, regional MRSA rates and mupirocin usage) in the pre and post intervention periods during our study.[78]

$$Rate_t = \beta_0 + \beta_1 * time_t + \beta_2 * intervention_t + \beta_3 * time\ after\ intervention_t + e_t$$

Where:
- $Rate_t$ is the rate of nosocomial MRSA at time t
- β_0 estimates the baseline nosocomial MRSA rate at the beginning of the intervention period
- β_1 estimates the change in the nosocomial MRSA rates that occur with each month before the intervention (pre-intervention slope)
- *time* is a continuous variable indicating the number of months prior to and after the intervention. It ranges from -24 months to 19 months
- β_2 estimates the change in the nosocomial MRSA rate immediately following the intervention (change in level)
- *intervention* indicates whether or not the intervention had taken place during that time period (before the intervention is coded as $intervention_t = 0$ and after the intervention is coded as $intervention_t = 1$)
- β_3 estimates the change in the slope after the intervention compared to the slope before the intervention
- *time after intervention* is a continuous variable indicating the number of months that have passed since the intervention was implemented. This is coded as zero for all time periods prior to the intervention
- e_t represents the random error.

SAS PROC GENMOD was used to fit the initial model and to produce the predicted rates and 95% confidence intervals required to generate the statistical graphs. A similar approach was used to analyze and generate graphs for nosocomial CDAD rates, regional MRSA rates and mupirocin usage. We used PROC AUTOREG to fit the final models, as this procedure (unlike Genmod) is capable of accounting for autocorrelation. In both procedures, the log-link function was specified and patient-days was specified as the offset. A 2-sided p value of < 0.05 in the best fitting model was deemed a priori to be statistically significant. SAS statistical software, version 9.1.3 (SAS Institute) was used for all analyses.

3.4 Results

3.4.1 Description of the Ottawa Hospital population

Between January 2006 and August 2009, the Ottawa Hospital admitted 147,975 patients. During our study period, there were no clinically significant differences in the hospital population in the pre- and post-intervention periods (Table 3.0). Approximately 57% of the in-patient hospital population were female with a mean age of 55 years. The average patient was admitted for approximately 8 days and nearly five percent of patients were admitted to the intensive care unit (ICU) during their encounter. Approximately four percent of in-patients died during their hospitalization.

TABLE 3.0
CHARACTERISTICS OF PATIENTS AT THE OTTAWA HOSPITAL[¥]
January 2006 – August 2009

CHARACTERISTIC	TOTAL* (N=147975)	PRE INTERVENTION (N=76273)	POST INTERVENTION (N=68067)
Female (%)	85077 (57.5)	43958 (57.6)	39064 (57.4)
Age (mean ± SD)	55.4 ± 20.2	55.2 ± 20.2	55.6 ± 20.2
(median, IQR, Q1-Q3)	57.0, 35.0, 37.0-72.0	57.0, 35.0, 37.0-72.0	57.0, 35.0, 37.0-72.0
Length of stay (mean ± SD)	7.8 ± 15.6	7.9 ± 16.9	7.6 ± 14.0
(median, IQR, Q1-Q3)	3.0, 5.0, 2.0-7.0	3.0, 5.0, 2.0-7.0	3.0, 6.0, 2.0-8.0
ICU days (%)	6820 (4.6)	3612 (4.7)	3028 (4.5)
Acute care days (mean ± SD)	6.9 ± 11.1	6.7 ± 10.8	7.0 ± 11.3
(median, IQR, Q1-Q3)	3.0, 5.0, 2.0-7.0	3.0, 5.0, 2.0-7.0	3.0, 5.0, 2.0-7.0
Crude mortality (%)	6118 (4.1)	3166 (4.2)	2797 (4.1)
Campus (%)			
General	69097 (46.7)	35722 (46.8)	31715 (46.6)
Civic	58608 (39.6)	29821 (39.1)	27356 (40.2)
Heart Institute	20270 (13.7)	10730 (14.1)	8996 (13.2)
Charlson index (%)			
0	81472 (55.1)	41917 (55.0)	37600 (55.2)
1-2	33964 (23.0)	17367 (22.8)	15715 (23.1)
3-4	14572 (9.9)	7496 (9.8)	6727 (9.9)
5+	17967 (12.0)	9493 (12.4)	8025 (11.8)

* Pre & Post Intervention totals will not add to Total as January 2008 was excluded from intervention months to allow for an integration period. There were 3635 admissions during this month.
¥ Excludes newborns

In regards to the number of patients screened in both periods, 22271 (29.2%) of patients were screened in the pre intervention period, compared with 51815 (83.8%) in the post intervention period (Table 3.1). A total of 745 and 1621 MRSA positive cases were detected during the pre intervention and post intervention periods, respectively. This results in a detection rate of 9.8 per 1,000 admitted patients pre intervention and 26.2 per 1,000 admitted patients post intervention.

TABLE 3.1
RESULTS OF SCREENING FOR MRSA AT THE OTTAWA HOSPITAL¥
January 2006 – August 2009

	PRE INTERVENTION	POST INTERVENTION
Number of Admitted Patients	76259	61782
Number screened (%)	22271 (29.2)	51815 (83.8)
Total MRSA positive cases at screening (% of admissions)	745 (1.0)	1621 (2.6)
New cases (% of MRSA positive)	132 (17.7)	273 (16.8)
Previously Known (% of MRSA positive)	175 (23.5)	327 (20.2)
False Positives (% of MRSA positives)	438 (58.8)	1021 (63.0)
MRSA Detection Rate (per 1,000 admissions)	9.8	26.2

¥ Excludes newborns

3.4.2 Description of nosocomial MRSA within the Ottawa Hospital

During our study period, there were a total of 644 nosocomial MRSA cases, 323 cases in the pre intervention period and 321 in the post intervention period for an incidence rate of 41.8 per 100,000 patient days and 47.5 per 100,000 patient days, respectively (Table 3.2). MRSA bacteremia occurred in 28 patients, 14 in each study period for an incidence rate of 1.8 per 100,000 patient days in the pre intervention period and 2.1 per 100,000 patient days in the post intervention period.

TABLE 3.2
SUMMARY OF NOSOCOMIAL MRSA CASES AT THE OTTAWA HOSPITAL¥
(PER 100,000 PATIENT DAYS)
January 2006 – August 2009

	PRE INTERVENTION	POST INTERVENTION	TOTAL
Nosocomial MRSA Cases	323	321	644
Nosocomial MRSA rate	41.8 / 100,000 pt days	47.5 / 100,000 pt days	
MRSA Bacteremia Cases	14	14	28
MRSA Bacteremia rate	1.8 / 100,000 pt days	2.1 / 100,000 pt days	
Patient Days	773072	675416	1448488

¥ Excludes newborns, pt = patient

3.4.3 Statistical analysis

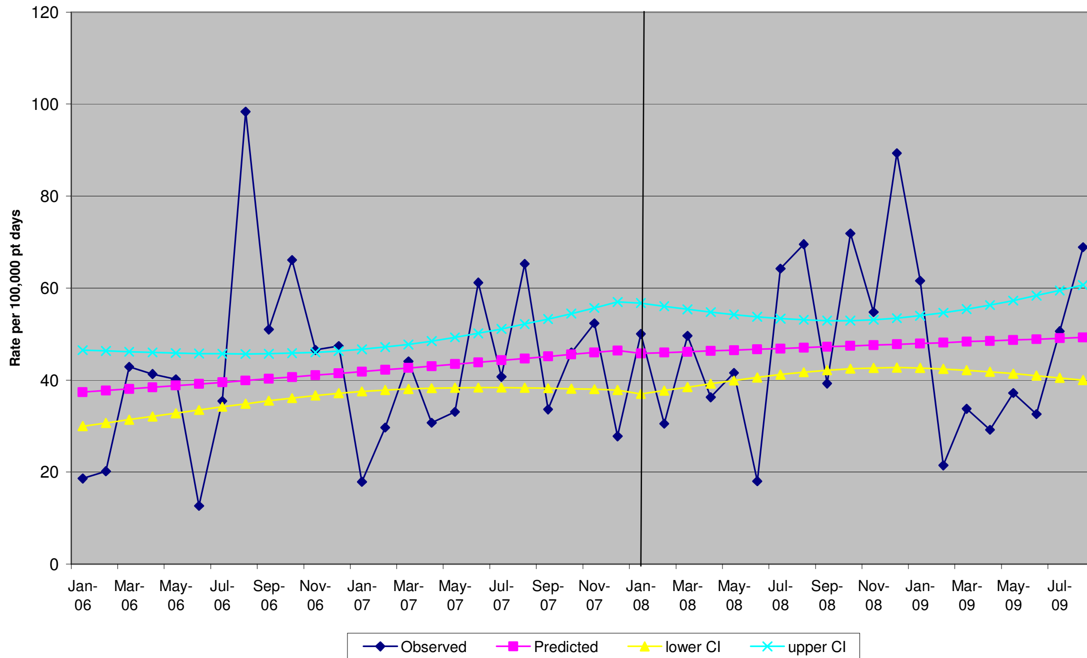
The statistical analysis component of this thesis consisted of two steps. The first step of the statistical analysis included a visual inspection of the data by means of graphical representation of the data which was produced using SAS and is shown below. The second step involved generating inferential statistics (p-values) using a segmented Poisson regression model.

3.4.3.1 Visual Inspection of Data

<u>Nosocomial MRSA rates</u>

The graph representing the rates of nosocomial MRSA (per 100,000 patient-days) pre and post intervention (Figure 3.0) shows an increasing trend in the monthly nosocomial MRSA rate prior to the intervention. Post-intervention, there continues to be a slight increasing trend in the slope with virtually no change in the level, suggesting that the MRSA screening intervention did not have an effect in decreasing the nosocomial transmission/acquisition of MRSA within the hospital. However, further statistical analysis was conducted to determine the effectiveness of the intervention.

FIGURE 3.0
NOSOCOMIAL MRSA RATES PRE- AND POST-INTERVENTION, THE OTTAWA HOSPITAL[¥]
(PER 100,000 PATIENT DAYS)
January 2006 – August 2009



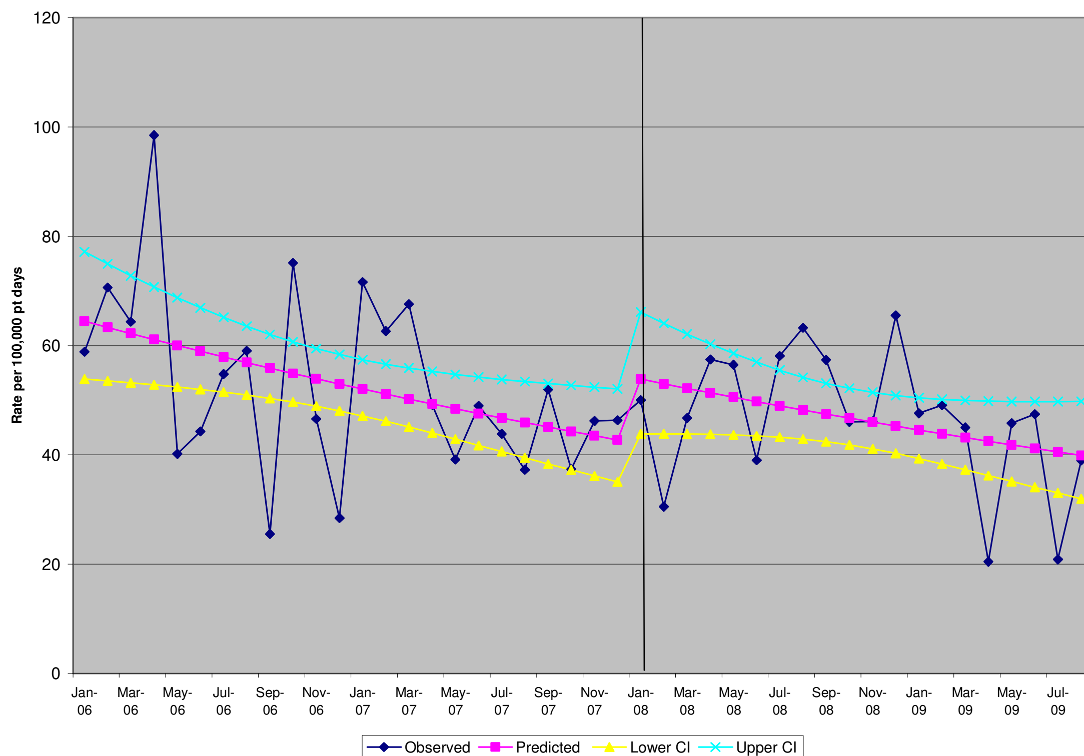
¥ Excludes newborns

Nosocomial CDAD rates – Internal Control Group

The graphical presentation of pre- and post-intervention nosocomial CDAD rates (per 100,000 patient-days) shows near-identical pre- and post-intervention trends (Figure 3.1). This is an important finding which speaks to the internal validity of the intervention. Based on the visual inspection alone, it is believed that there were no changes in factors or practices other than the intervention, which could have had a dramatic effect on infection control practices during our intervention: any extraneous factors (such as improved infection control practices, environmental cleaning, hand hygiene) that could have influenced MRSA rates would be expected to influence CDAD rates in the same manner. The lack of any noticeable overall change in the CDAD rates before and after

the intervention suggest the absence of any such factors that could threaten the internal validity of the study.

FIGURE 3.1
NOSOCOMIAL CDAD RATES PRE- AND POST-INTERVENTION, THE OTTAWA HOSPITAL[¥]
(PER 100,000 PATIENT DAYS)
January 2006 – August 2009



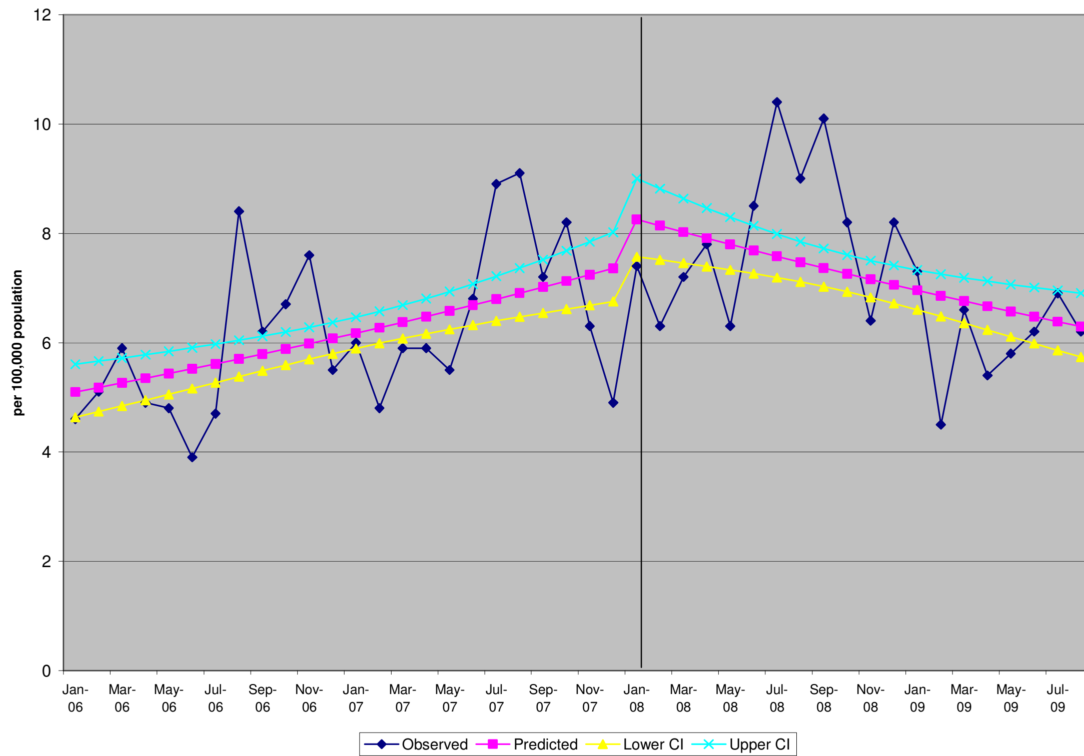
¥ Excludes newborns

<u>Regional Rates of MRSA – External Control Group</u>

The graph representing the regional MRSA rates (per 100,000 population) pre and post intervention suggests an increasing trend in monthly rates prior to the intervention and a decreasing trend in monthly rates after the intervention (Figure 3.2). This finding suggests that regional rates of MRSA were declining in the post intervention period. Thus, because regional rates were declining while the rates at our institution were stable

or increasing, it supports the conclusion that the intervention was not effective. If the rate in our institution was declining at the same rate as the region, it would be unclear whether the reduction is due to the intervention or due to factors external to our institution. However, further analysis follows to determine the significance of these findings.

FIGURE 3.2
REGIONAL MRSA RATES, CHAMPLAIN LOCAL HEALTH INTEGRATION (LHIN)
(PER 100,000 POPULATION)
January 2006 – August 2009



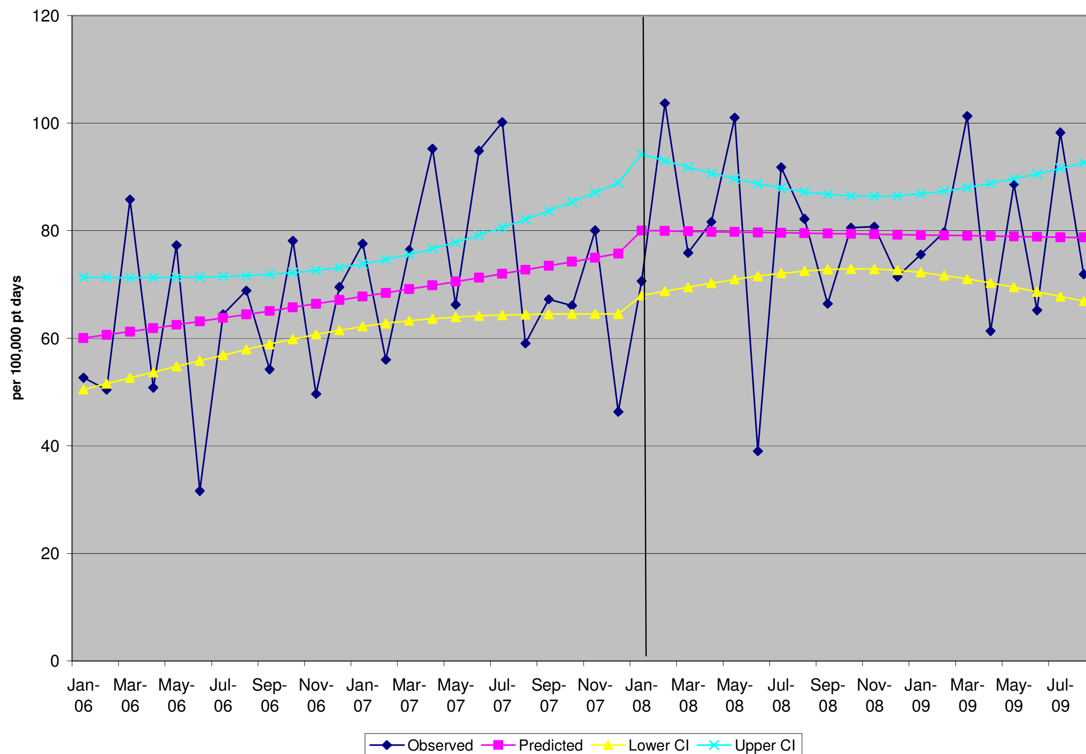
¥ Excludes newborns

Mupirocin usage

The graph representing mupirocin usage pre and post intervention suggests an increasing trend in slope prior to the intervention and a steady slope in the post intervention period (Figure 3.3). However, overall it appears that mupirocin usage was increased in the post

intervention period which suggests that decolonization therapy may have been utilized more in the universal MRSA screening intervention period than in the selective screening period. Further analysis was conducted to determine the significance of this finding.

FIGURE 3.3
MUPIROCIN ORDERS, THE OTTAWA HOSPITAL[¥]
(PER 100,000 PATIENT DAYS)
January 2006 – August 2009



¥ Excludes newborns

3.4.3.2 Model creation

In addition to the visual inspection of the data, the statistical models were also tested for overdispersion, autocorrelation, and seasonality to aid in the development of the final statistical model.

Overdispersion

The Poisson model was estimated both with and without accounting for over-dispersion to assess the goodness of fit of the models (Table 3.3).[79] The estimate of dispersion is measured by both the deviance and Pearson's chi-square divided by their degrees of freedom. If this statistic is not close to 1, then the data may be overdispersed if the dispersion estimate is greater than 1 (or underdispersed if the dispersion estimate is less than 1).[79] It was decided to present only the results accounting for overdisperson as it is a more conservative approach which accounts for any variability that may have occurred due to uncontrolled factors.[79]

TABLE 3.3
ASSESSING THE MODELS FOR OVERDISPERSION, CRITERIA IN ASSESSING GOODNESS OF FIT

	CRITERION	DF	VALUE	VALUE/DF	P VALUE	RESULT
MRSA	Deviance	42	329.7754	7.8518	0.0730	Overdispersed
	Pearson Chi Sq	42	343.1275	8.1697		
MRSA	Deviance	42	42.000	1.0000	0.5224	Overdispersion
DScale	Pearson Chi Sq	42	43.7005	1.0405		Accounted for
CDAD	Deviance	42	191.1217	4.5505	<0.0001	Overdispersed
	Pearson Chi Sq	42	189.9792	4.5233		
CDAD	Deviance	42	42.000	1.0000	0.0596	Overdispersion
DScale	Pearson Chi Sq	42	41.7489	0.9940		Accounted for
Mupirocin	Deviance	42	156.4251	3.7244	0.0011	Overdispersed
	Pearson Chi Sq	42	151.7895	3.6140		
Mupirocin	Deviance	42	42.000	1.0000	0.0910	Overdispersion
DScale	Pearson Chi Sq	42	40.7554	0.9704		Accounted for
Regional	Deviance	42	13.7048	0.3263	0.3303	Underdispersed
	Pearson Chi Sq	42	14.1967	0.3380		
Regional	Deviance	42	42.000	1.0000	0.0883	Underdispersion
DScale	Pearson Chi Sq	42	43.5075	1.0359		Accounted for

Autocorrelation

Autocorrelation was detected using two methods, visually (not shown) and using the Durbin-Watson statistic (Table 3.4). Autocorrelation exists when consecutive residuals

are similar to one another. Negative autocorrelation, for example, exists when residuals tend to lie on the different sides of the regression line, whereas positive autocorrelation suggests that the health outcomes at two time points may be more similar as they lie on the same side of the line.[78] The Durbin-Watson statistics for both MRSA and CDAD were not significant indicating that no autocorrelation exists. However, the Durbin-Watson statistics for mupirocin and regional MRSA rates suggest that there is negative autocorrelation noted with mupirocin usage (Pr > DW = 0.0203) and positive autocorrelation noted with the regional MRSA rates (Pr < DW = 0.001). Due to the evidence of autocorrelation, PROC AUTOREG will be utilized in the final model for all parameters to ensure a more conservative approach.

TABLE 3.4
ASSESSING THE MODELS FOR AUTOCORRELATION, DURBIN-WATSON

	DURBIN-WATSON	PR < DW POSITIVE	PR > DW NEGATIVE	RESULT
MRSA	1.6811	0.0593	0.9407	No autocorrelation
CDAD	2.2527	0.6459	0.3541	No autocorrelation
Mupirocin	2.7271	0.9797	0.0203	Negative autocorrelation
Regional	1.2573	0.0010	0.9990	Positive autocorrelation

Seasonality

As time series sometime exhibit seasonal fluctuations, it was important to test for and account for any seasonality that may influence the true effects of the intervention.[78] The Dickey-Fuller test was utilized as a method to test for seasonality. As noted in Table 3.5, seasonality did not influence the true effects of our intervention in this model.

TABLE 3.5
ASSESSING THE MODELS FOR SEASONALITY

	DICKEY-FULLER P VALUE* PR < TAU	RESULT
MRSA	0.0001	Do not need to correct for seasonality
CDAD	0.0001	Do not need to correct for seasonality
Mupirocin	0.0001	Do not need to correct for seasonality
Regional	0.0074	Do not need to correct for seasonality

* null is that tau is not stationary

3.4.3.3 Regression Analysis

The following segmented regression analyses were produced using SAS 9.1 PROC AUTOREG.

Nosocomial MRSA

The intercept variable (measuring our level) shows that just before the beginning of our observation period, the rate of nosocomial MRSA was 46.79 per 100,000 pt days (Table 3.6). The relative_time variable (measuring trend) shows that before the intervention, there was no significant month-to-month change in our trend (p value for baseline trend = 0.4818). The inter variable (measuring our level after the intervention), shows that immediately following the intervention the nosocomial rate dropped by 1.1 per 100,000 pt days but this change was not statistically significant (p value = 0.9234). The time_passed variable (measuring the difference in trend after the intervention) shows no significant change in the month-to-month trend in the mean number of nosocomial cases after the intervention (p value for trend change = 0.8255). Therefore, the analysis concludes that the intervention did not decrease the level nor the trend in the monthly incidence of nosocomial MRSA cases.

TABLE 3.6
SAS ANALYSIS OUTPUT, NOSOCOMIAL MRSA RATES

VARIABLE	ESTIMATE	P VALUE
Intercept (level)	46.79	<0.0001
Relative_time (trend)	0.4002	0.4818
Inter (change in level after intervention)	-1.1147	0.9234
Time_passed (change in trend after intervention)	-0.2067	0.8255

Nosocomial CDAD

The intercept variable (measuring our level) shows that just before the beginning of our intervention period, the rate of nosocomial CDAD was 41.00 per 100,000 pt days (Table 3.7). The relative_time variable (measuring trend) shows that before the intervention, there was significant month-to-month change in our trend (p value for baseline trend = 0.0260). The inter variable (measuring our level after the intervention), shows that immediately following the intervention the nosocomial rate increased by 12.52 per 100,000 pt days but was not statistically significant (p value = 0.1423). The time_passed variable (measuring our trend after the intervention) shows no significant change in the month-to-month trend in the mean number of nosocomial cases after the intervention (p value for trend change = 0.7534). Overall, the intervention did not alter the nosocomial rate of CDAD and we can conclude that, using this method, there were no threats to the internal validity of the study.

TABLE 3.7
SAS ANALYSIS OUTPUT, NOSOCOMIAL CDAD RATES

VARIABLE	ESTIMATE	P VALUE
Intercept (level)	41.0073	<0.0001
Relative_time (trend)	-0.9462	0.0260
Inter (change in level after intervention)	12.5226	0.1423
Time_passed (change in trend after intervention)	0.2139	0.7534

Mupirocin Usage

The intercept variable (measuring our level) shows that just before the beginning of our study period, the number of mupirocin orders was 76.22 per 100,000 pt days (Table 3.8). The relative_time variable (measuring trend) shows that before the intervention, there was no significant month-to-month change in our trend (p value for baseline trend = 0.1553). The inter variable (measuring change in level after the intervention), shows that immediately following the intervention the usage of mupirocin increased by 3.93 orders (per month) however, was not significant (p value = 0.6940). The time_passed variable (measuring change in trend after the intervention) shows no significant change in the month-to-month trend in the mean number of mupirocin orders after the intervention (p value for trend change = 0.3312). Therefore, mupirocin usage was not significantly altered throughout the study period and it is unlikely that decolonization therapy affected our results.

TABLE 3.8
SAS ANALYSIS OUTPUT, MUPIROCIN USAGE

VARIABLE	ESTIMATE	P VALUE
Intercept (level)	76.2239	<0.0001
Relative_time (trend)	0.7028	0.1553
Inter (change in level after intervention)	3.9307	0.6940
Time_passed (change in trend after intervention)	-0.7887	0.3312

Regional MRSA Rates

The intercept variable (measuring our level) shows that at the beginning of our intervention period, the number of MRSA cases in the region was 7.39 per 100,000 population (Table 3.9). The relative_time variable (measuring trend) shows that before

the intervention, there was significant month-to-month change in our trend (p value for baseline trend = 0.0172). The inter variable (measuring our level after the intervention), shows that immediately following the intervention the regional rates increased by 0.8 per 100,000 population however, was not significant (p value = 0.3158). The time_passed variable (measuring change in trend after the intervention) shows significant change in the month-to-month trend (decrease) in the regional rates after the intervention (p value for trend change = 0.0037). Overall, the regional rates of MRSA began to significantly decrease in the post intervention period. This finding suggests that, using this method, the external control group (regional MRSA rates) did not affect the internal validity of the study. However, as rates at our institution were stable or increasing while regional rates were declining, we can conclude that the intervention was not effective.

TABLE 3.9
SAS ANALYSIS OUTPUT, REGIONAL MRSA RATES

VARIABLE	ESTIMATE	P VALUE
Intercept (level)	7.3942	<0.0001
Relative_time (trend)	0.0989	0.0172
Inter (change in level after intervention)	0.8258	0.3158
Time_passed (change in trend after intervention)	-0.2026	0.0037

3.5 Discussion

The statistical analysis demonstrates that the universal MRSA screening intervention was not effective in reducing the number of nosocomial MRSA cases within the Ottawa Hospital. The conclusions of the analysis involving nosocomial CDAD rates suggest that there were no threats to the internal validity of the intervention by means of competing programs (i.e. improved hand hygiene, housekeeping methods, etc.). The hospital does

not routinely order decolonization of MRSA positive patients (mupirocin), and the consistent and unchanged mupirocin usage throughout the study period suggests that decolonization would not have affected the effectiveness of the intervention. Our external control, regional MRSA rates, significantly decreased in the post intervention period. This supports the conclusion that the universal MRSA screening intervention was unsuccessful in decreasing the nosocomial MRSA rates within the hospital as it would be expected that decreasing community rates would be mirrored within the institution as well, which was not the case here. The reasons for the decline in regional MRSA rates are not clear as there was no region-wide intervention introduced during this time period. However, similar declines were noted in certain regions in Canada during this period.[87]

These results are surprising as it would be expected that as more MRSA cases were found and subsequently isolated in the intervention period, rates of nosocomial MRSA would decline. There are several potential explanations. First, perhaps the intervention did not show a decrease in nosocomial MRSA rates as hand hygiene compliance was suboptimal. Nicolau et al. suggest that for every 1% increase in hand hygiene compliance, MRSA rates may decrease by as much as 7%.[86] This finding is echoed in several studies and mathematical models.[5,81,82] Allegranzi et al. suggest that hand hygiene compliance may be more likely to impact the MRSA rate than the CDAD rate.[83] Hand hygiene audits were not consistently performed throughout our study periods. However, periodic audits estimate hand hygiene compliance to be 26-79% prior to the intervention (2005-varies by health care provider and unit, average of 50.3%) and during the intervention 40-71% (2009-varies by health care provider and unit, average of 49.5%).[85] Conclusions from the

hand hygiene audits, in relation to the effects of hand hygiene compliance on our intervention, are difficult to make as the audits were not routinely performed throughout both periods and were not conducted on the same in-patient units. In addition, compliance with contact precautions may have been less than ideal during our intervention, also influencing the transmission of MRSA within the facility. While we attempted to control for these factors by utilizing an internal control group, it is possible that the effects were more noticeable within the MRSA rates than the CDAD rates.

Second, the imperfect admission screening compliance may have also had an effect on our results. Pre-intervention, the compliance with risk-factor based screening was approximately 54%; throughout the intervention period compliance with universal MRSA screening was approximately 84%. While this represents a realistic portrayal of hospital function, it does not allow us to determine the intervention's effectiveness had a higher percentage of the inpatient population been screened upon admission (although this is addressed in the economic analysis – Chapter 4). Perhaps, a higher compliance with admission screening may have identified more MRSA cases and reduced the transmission by means of isolating patients sooner upon positive result.

Third, it is unclear whether the length of the intervention was appropriate. Due to the nature of the study design, a sample size could not be produced prior to the study implementation and therefore the length of the study was dependent on administration support. However, the length of our intervention was comparable to other published studies, which had intervention lengths between 7.5 months and 15 months.[1,34]

Fourth, the prevalence of MRSA within the Ottawa region, while continuing to rise, was still relatively low. Spiegelhalter suggests that infectious diseases rates have far more variability within them than would normally be expected due to chance alone and therefore a significant effect (i.e. altered infection rates) as a result of an intervention is less likely to be noted.[84] Additionally, other studies have suggested that this type of intervention may only be beneficial in areas where the prevalence of MRSA is much higher.[13,35] In fact Murthy et al. suggested that areas with higher endemicity might benefit from a universal MRSA screening intervention. The prevalence of MRSA on admission in the Murthy et al. study was 5.1% [35] which is considerably higher than the prevalence on admission to our hospital of 2.6%.

Finally, there were several MRSA outbreaks in both study periods. An outbreak was defined as two or more nosocomial MRSA cases epidemiologically linked to the same hospital unit. During the pre-intervention period, there were a total of 42 outbreaks involving a total of 203 patients. Four of the outbreaks in this period involved 10 or more patients, with the largest two outbreaks involving 19 and 29 patients respectively. In the post-intervention period, there were 36 outbreaks involving 164 patients with three of these outbreaks involving 10 or more patients (17 patients in the largest outbreak). While it is possible that a single large uncontrolled MRSA outbreak could have nulled the effects of our universal MRSA screening intervention, this scenario seems unlikely as there were more outbreaks involving more patients in the pre intervention period than the post period thus making outbreaks less likely to have affected our intervention results.

3.6 Limitations

While every effort was made to follow sound epidemiological principals in the design and analysis of this study, some limitations were noted. First, as discussed above, the overall compliance with the universal MRSA screening protocol was less than ideal. However, following universal MRSA screening, there were more than two times the number of patients screened on admission with no apparent effect on the rate of nosocomial MRSA. It is also possible that patients were swabbed for MRSA $\geq$ 48 hours after admission due to a clinical change or as a result of an outbreak investigation. Second, while not apparent, there may have been other practice changes that occurred during the intervention which may have altered the results. However, it is unlikely this was the case as major factors were accounted for in the analysis. Finally, the data for the regional rates of MRSA was voluntary and incomplete as data were missing from one of the area hospitals for the final two months of the study period. While this is unlikely to have a significant impact on the overall regional rates, it can not be discounted. It is unlikely that this would have an effect on the primary outcome of this analysis.

3.7 Conclusions

The statistical analysis suggests that the universal MRSA screening intervention was unsuccessful in decreasing the nosocomial rates of MRSA within our institution when compared to a risk factor-based screening program after ruling out potential threats to validity such as infection control measures, decolonization, and MRSA rates in the community.

4.0 Chapter 4 - Economic Evaluation

4.1 Chapter overview

An economic analysis was undertaken to examine the cost-effectiveness of a universal MRSA screening intervention on the nosocomial rate of MRSA within the Ottawa Hospital. This analysis was done from the perspective of the health care organization. Overall, the MRSA screening program costs the Ottawa Hospital approximately $1.16 million ($CAD) annually.

4.2 Problem stated

The economic analysis was performed to assess the cost effectiveness of a universal MRSA screening intervention versus a risk factor-based screening program. The cost effectiveness was determined by comparing the associated costs of both screening programs per patient screened and by examining the nosocomial MRSA rate in both periods.

4.2.1 Rationale

The decision to include an economic analysis as part of this project was based on the need for cost data upon which to base healthcare policy decisions. We chose to determine if the intervention was clinically effective *and* cost effective as policy makers and funding agencies require evidence that a program is beneficial or non-beneficial in all aspects. A systematic review of the literature conducted by Wilton et al. (2002) determined that the majority of studies examining the effectiveness of interventions aimed at reducing antimicrobial-resistant organisms within health-care settings did not adequately assess the cost effectiveness of the interventions.[26] Therefore, this project

examined the cost effectiveness of the screening intervention using a cost-effectiveness analysis and Markov models incorporating both hospital and societal perspectives.

4.3 Methods

4.3.1 Background

A cost-effectiveness analysis from the perspective of the health care organization and society was used to measure the economic impacts of our screening intervention. This type of analysis allowed us to determine whether the net costs of our program outweighed the associated net benefits.[88]

A decision analytic approach was chosen as it allows for a variety of information to be combined in a cohesive manner with the intention of summarizing this information to reach conclusions, generate hypotheses and guide future research.[89] This approach can be used to assess the value of various options in regards to either patient-specific or population-specific policies.[89] A decision analysis involves the development of a decision tree, consisting of various nodes (strategies/options) which break the tree into branches, each branch has a probability assigned and results in various outcomes.[89]
The sum of each branch must equal 1. While it is important and more accurate to utilize local data where available, data to complete the tree may also be pulled from the available literature or, if the literature is insufficient, ‘expert opinion’ may be used.[89,90] Local data were extensively used throughout this project when available.

Once the tree has been populated with the appropriate data, the analysis can be performed. The value of each outcome is multiplied by the probabilities associated with achieving that particular outcome, and these values are them summed at the chance node (branch) that led to the outcome.[89]

A Markov model is a form of decision analysis that is utilized to examine various scenarios that involve transitions between several states of health and is utilized in this thesis.[89] A Markov model allows for the effect of time.[89,90] The development of the Markov model began with the identification of the health states that defined the clinical scenario,[89] in this instance MRSA infection/colonization, for example. Lines are drawn between states to represent the direction or transition from one state to another.[89] Each state in the model is associated with various costs, probability of transitioning from one state to the next and outcomes.[91] The values for the model may be derived from the literature.[89]

4.3.2 Patient-based Model

An economic analysis was conducted to evaluate the short-term patient-based cost impact of a universal MRSA screening intervention, and calculate a net cost from a health care system's perspective. The analysis considered:

- operating costs to the hospital to implement the universal screening program, including laboratory costs for testing and nursing costs for specimen collection

- costs of management of new cases discovered by the universal MRSA screening intervention (infection control costs, housekeeping costs, isolation costs for MRSA patients)
- decreased cost of fewer nosocomial cases (healthcare costs associated with MRSA colonization and infection)
- use of modeling to estimate the decreased costs of future MRSA infections and transmission

4.3.2.1 Health states

A patient's admission to hospital and whether or not they were screened for MRSA was considered to be the first step in the model (Figure 4.0). The patient moves throughout the varying states within the model with death or discharge from hospital being the final absorbing states in this model, one in which the patient cannot leave (in order to terminate the Markov process).[92] Each state incorporated costs associated with increased length of hospital stay (LOS), laboratory testing costs and control costs, when applicable. Sixteen health states were included and are described in Table 4.0. It should be noted that the 'screening' state was captured in two different phases (pre and post) to represent the difference in the probability of a patient being screened upon admission within the pre and post intervention periods. The model was structured in Microsoft Excel XP.

FIGURE 4.0 PATIENT-BASED MODEL

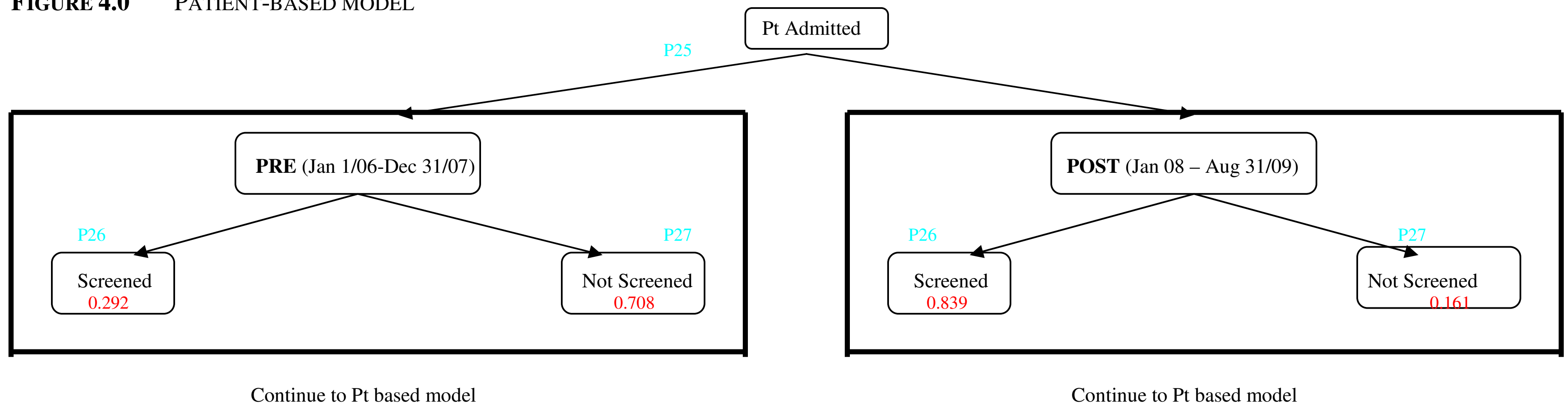


FIGURE 4.0 PATIENT-BASED MODEL (CONTINUED)

P26 Screened

P27 Not Screened

P28 Negative PCR 0.955

P29 Positive PCR 0.045

P30 MRSA negative 0.9516

P31 Known MRSA positive 0.03

P32 Unknown MRSA positive 0.0184

P33 True Neg 0.98

P34 False Neg 0.02

P45 Positive C/S 0.65

P46 Negative C/S 0.35

Control costs

P49 Do not Acquire MRSA 0.995

P50 Acquire MRSA 0.005

P51 Infected 0.043

P52 Colonized 0.957

P40 Infected 0.043

↑ LOS Control costs

P39 Colonized 0.957

P41 Death 0.13

P42 Discharge 0.87

P43 Death 0.033

P44 Discharge 0.967

P47 Discharge 0.967

P48 Death 0.033

↑ LOS Control costs

P55 Death 0.033

Discharge 0.967

P53 Death 0.13

P54 Discharge 0.87

P56

P35 Do not Acquire MRSA 0.995

P36 Acquire MRSA 0.005

MRSA POSITIVE

P37 Discharge 0.967

P38 Death 0.033

P57 Infected 0.043

P58 Colonized 0.957

Control costs ↑ LOS

Control costs

P59 Death 0.13

P60 Discharge 0.87

P61 Death 0.033

P62 Discharge 0.967

TABLE 4.0
PATIENT-BASED ECONOMIC MODEL, HEALTH STATES

HEALTH STATE	DESCRIPTION	REFERENCE TO MODEL DIAGRAM
Screened	Patient screened for MRSA	P26/P27
	Cost of laboratory supplies, nursing time to obtain swab etc. associated with this state.	
Negative PCR	Patient's preliminary screen for MRSA is negative.	P28
	Cost of performing a preliminary screen for MRSA associated with this state.	
	Negative PCR requires no further action.	
Positive PCR	Patient's preliminary screen for MRSA is positive.	P29
	Cost of performing a preliminary screen for MRSA is associated with this state.	
	Positive PCR requires further action (culture).	
Negative culture	Patient's culture for MRSA is negative.	P46
	Cost of performing a culture is associated with this state.	
Positive culture	Patient's culture for MRSA is positive.	P45
	Cost of performing a culture is associated with this state.	
MRSA negative	Patient is MRSA negative, but has not undergone testing at admission.	P30
	This assumption is based on likelihood of MRSA positive status in general population studies	
	No additional costs associated with this state.	
Known MRSA positive	Patient has been previously identified as MRSA positive.	P31
	Assumption based on population prevalence studies.	
	Control costs and increased length of stay costs associated with this state.	

Health State	Description	Reference to model diagram
Unknown MRSA positive	Patient's MRSA status unknown. Assumption based on prevalence studies. No cost associated with this state.	P32
True Negative	Patient is MRSA negative based on sensitivity of PCR test. No additional cost associated with this state.	P33
False Negative	Patient is MRSA positive despite PCR negative result. This is a function of the sensitivity of the PCR test. No additional cost associated with this state.	P34
Do not acquire MRSA	Patient remains MRSA negative during hospital admission. No cost associated with this state.	P35/P49
Acquire MRSA	Patient was initially negative upon hospital admission but acquired MRSA during their stay. Control costs are associated with this state.	P36/P50
Infected	Patient confirmed infected with MRSA bacteremia. Control costs and increased length of stay costs associated with this state.	P40/P51/P57
Colonized	Patient is colonized with MRSA. Control costs are associated with this state.	P39/P52/P58
Discharge	Patient is discharged from hospital. This is an absorbing state. No cost associated with this state, however length of stay varied among average patient and MRSA infected patient.	P37/P42/P44/ P47/P54/P56/ P60/P62
Death	Patient died during hospital admission. This is an absorbing state. No cost associated with this state.	P38/P41/P43/ P48/P53/P55/ P59/P61

4.3.2.2 Probabilities – Patient-based model

After a review of the available literature and the patient data captured as a result of this project, both models were populated with probabilities which best represented the nodes in the models. An explanation of how each probability was obtained for the patient-based model follows and is summarized in Table 4.1.

<u>Screened Upon Admission</u>

The probability of screening upon admission was pulled directly from the study population for both periods. The probability of an admitted patient being screened upon admission was 29.2% in the pre intervention period (22271/76259) and averaged 83.8% in the post intervention period (51815/61782).

<u>Positive PCR</u>

The probability that a screened patient would be PCR positive for MRSA was 4.5%. This probability was obtained from the Microbiology department of the Ottawa Hospital during our study period.

<u>Known MRSA Positive</u>

The likelihood of a hospital knowing a patient is MRSA positive when the patient was not screened (based on MRSA results from a previous hospital admission) was derived from Conterno's unpublished work at the Ottawa Hospital.[93] As there is no known published literature regarding an unscreened patient's likelihood of having MRSA, this estimate is based on the likelihood of a screened patient having MRSA. Therefore, it was determined that 3% of the patient population would have a positive MRSA test.

Unknown MRSA Positive

As above, there are no published estimates, to our knowledge, that describe the probability of a patient being MRSA positive unbeknownst to the institution. However, this scenario may occur, thus making MRSA transmission to unassuming patients and staff possible. We expect that, with a universal MRSA screening intervention, the likelihood that a patient would be positive for MRSA but unknown to the institution is the same as the proportion of known MRSA positive patients. To associate a probability to this state, we added the true MRSA positive patients (i.e. total number MRSA PCR positives multiplied by the total MRSA culture positives) and the false MRSA negative patients (i.e. total MRSA PCR negatives multiplied by the false negatives) to get the total number of MRSA positives in screened population. This number was then subtracted by the already known MRSA positives to estimate the unknown MRSA positive patients.

Positive MRSA Culture

This probability was derived from unpublished work of Conterno at the Ottawa Hospital.[93] Conterno discovered that 65% of screening cultures for MRSA yield a positive result in our patient population.

MRSA Acquisition

The probability of an inpatient acquiring MRSA during their hospital stay was determined by utilizing the nosocomial rate of MRSA within the Ottawa Hospital. This was produced from OHDW during our study period. It was determined that the probability of a patient acquiring MRSA while in hospital was 0.5%.

MRSA Infected

In order to determine an accurate representation of MRSA infected versus colonized, MRSA bacteremia rates were used. Blood cultures are considered to be from a sterile site and thus represent true infection, whereas MRSA isolated from non-sterile sites requires a subjective assessment to determine if the patient is infected or colonized. Thus, using bacteremia as a measure of true MRSA infection yields a conservative, but objective, estimate.[94] Bacteremia rates have been utilized in the literature to confirm a patient's MRSA infection status. Our bacteremia rates were pulled from the OHDW during our study period; 4.3% (28/644) of MRSA positive patients had a positive blood culture for MRSA.

False Negative (PCR)

The probability that an MRSA PCR test would yield a false negative result was derived from Conterno's unpublished work at the Ottawa Hospital. Conterno found that 2% of PCR tests yielded a false negative result.[93]

Death (MRSA Infected)

Coello et al. reported that 13% of their MRSA infected population died during that hospital admission.[95] This probability was supported by several studies, stating that between 15-23% of MRSA positive patients will die during their hospitalization.[14,96,97] The Coello et al. study was utilized as it had the best study design and most appropriate study population.

Death (MRSA Colonized)

It was assumed that an MRSA colonized patient would have the same likelihood of death as any other hospitalized patient. There has not been any published literature, to our knowledge, that would suggest otherwise. Van Walraven et al. conducted a study within our institution which concluded that 3.3% of inpatients die during their admission at the Ottawa Hospital.[98]

Death (MRSA Negative)

The likelihood that a hospitalized patient would die during their admission was derived form the Van Walraven study (as mentioned above). Within the Ottawa Hospital 3.3% of in patients would die during their hospital stay.[98] This figure is slightly lower than in other studies which reported that hospital deaths occurred in 5.9-6.5% of patients, however we chose to use the van Walraven data as it was based on our specific patient population.[99,100]

Length of Stay

In order to address the potential for increased length of stay attributed to an MRSA infection, the literature was reviewed to determine the average number of additional days an MRSA infected patient would acquire due to the illness. For the purpose of this model, 17 additional hospital days were attributed to each MRSA infected patient to account for additional costs of the infection.[108] This data was drawn from a study, conducted in a comparable Toronto hospital, which found that the average patient length

of stay was 7 days and the average length of stay for MRSA infected patients was 24 days.[108]

It should be noted that in this model, unlike the population-based model, the likelihood of decolonization is not addressed as the length of stay for MRSA infected patients (17 days) is considerably shorter than the length of time required to clear MRSA as suggested by the literature.[101]

TABLE 4.1
PATIENT-BASED ECONOMIC MODEL, PROBABILITIES

PROBABILITY	ESTIMATE	DESCRIPTION	SOURCE	SAMPLE SIZE	REFERENCE TO MODEL	
Screened upon admission to hospital – Pre Intervention	0.29	Likelihood of being screened for MRSA within 48 hours of admission	OHDW 2006-2009	22271/ 76259	P26	ACTUAL
Screened upon admission to hospital – Post Intervention	0.84	Likelihood of being screened for MRSA within 48 hours of admission	OHDW 2006-2009	51815/ 61782	P26	ACTUAL
Positive PCR	0.045	Likelihood of preliminary screen resulting in a positive outcome	Microbiologist 2006-2009	N/A	P29	ACTUAL
Known MRSA positive	0.03	Likelihood of the hospital already knowing the positive MRSA status of an admitted patient	Conterno et al.	232/ 8528	P31	DERIVED (from TOH data)
Unknown MRSA positive	0.0184	Likelihood of a patient who was not screened being MRSA positive	Calculated: (PCR positive x MRSA culture positive) + (PCR negative x False negative) to = all MRSA positive in screened population, then subtract those known MRSA positive	(0.045 * 0.65) + (0.955 * 0.02) = 0.0484 all cases (0.0484) – known positive (0.03) = 0.0184	P32	DERIVED (from TOH data)
Positive MRSA culture	0.65	Likelihood of a patient's culture resulting in a positive outcome	Conterno et al.	Not specified	P45	DERIVED (from TOH data)
MRSA acquisition	0.005	Likelihood of a patient who was MRSA negative on admission acquiring MRSA while admitted to hospital	OHDW- TOH nosocomial MRSA rate	644/ 138041	P36 P50	ACTUAL
MRSA infected	0.043	Likelihood of a patient screened positive being infected with MRSA	OHDW 2006-2009 Bacteremia rate	28/644	P40 P51 P57	ACTUAL

PROBABILITY	ESTIMATE	DESCRIPTION	SOURCE	SAMPLE SIZE	REFERENCE TO MODEL	
False Negative (PCR)	0.02	Likelihood of an MRSA PCR test reading negative when it was actually positive.	Conterno (Unpublished)	Not specified	P34	DERIVED (from TOH data)
Death (MRSA Infected)	0.13	Likelihood that an infected patient would die while in hospital.	Coello et al. 1989-1992	62/476	P41 P53 P59	DERIVED
Death (MRSA colonized)	0.033	Likelihood that a colonized patient would die while in hospital.	Van Walraven et al. 1998-2002	3074/ 94273 3114/ 94488	P43 P48 P55 P61	DERIVED (from TOH data)
Death (MRSA negative)	0.033	Likelihood that a hospitalized patient would die while in hospital	Van Walraven et al. 1998-2002	3074/ 94273 3114/ 94488	P38	DERVIED (from TOH data)

OHDW = Ottawa Hospital Data Warehouse, TOH = The Ottawa Hospital

4.3.2.3 Costing – Patient-based model

The monetary values in the patient-specific model (i.e. cost of swabs, gowns etc.) were either obtained from a recent study conducted at the Ottawa Hospital[24] or were obtained from the appropriate department within the Ottawa Hospital (Table 4.2). Up-dated laboratory costs were obtained from a microbiologist in the Ottawa Hospital laboratory department. Costs associated with average hospital stay costs, private room costs and beds blocked due to isolation precautions were obtained from the Hospital's Finance department. All costs were obtained in and/or adjusted to the current year, 2010.[102]

TABLE 4.2
PATIENT-BASED MODEL, COSTS

SERVICE	COST	SOURCE
Administrative costs		
Time to obtain specimen (min)	6	Conterno
Cost of nursing time/hr	$34.98	ONA[¥]
Cost of nursing time/culture	$3.50	
Total Administrative costs	***$38.48***	
Cost of Contact Precautions (CP)		
No. of contacts / pt / day	50	Conterno*
Gowns @ $0.50 each	$25.00	Conterno*
Gloves @ $0.15 each	$7.50	Conterno*
Mask @ $0.13 each	$6.50	Conterno
Material cost of CP / pt / day	$39.00	
Time to put on CP (min)	1	Conterno
Cost of nursing time / pt on CP/ day	$29.15	
Total Cost of CP / pt / day	***$68.15***	
Lost revenue due to private room use		
Per diem cost / room	$220.00	The Ottawa Hospital

Lost revenue due to blocked bed		
Cost / bed	$180.00	The Ottawa Hospital
Infection Control Time		
Cost of infection control professional/hr	$41.07	Infection Control Dept. & ONA^
Time / new case of MRSA (min)	30	Conterno
Time / false positive and known MRSA case (min)	15	Conterno
Cost of new case	***$20.54***	
Cost of false positive case	***$10.27***	
Housekeeping costs		
Cleaning regular room	$42.62	Conterno*
Cleaning isolation room	$66.69	Conterno*
Difference	$24.07	Conterno*
Hospital stay costs		
Medical/surgical stay cost / pt / day	$1 219	The Ottawa Hospital
Laboratory costs		
MRSA PCR cost		
Supply cost	$17.68	
Labour cost	$2.24	
Total MRSA PCR cost	***$19.92***	The Ottawa Hospital
PCR positive / Culture (new pt)		
Supply cost	$7.06	
Labour cost	$9.53	
Total PCR positive / Culture cost (new pt)	***$16.59***	The Ottawa Hospital
PCR positive / culture negative	***$3.93***	The Ottawa Hospital
PCR positive / culture positive $19.92 + $16.59	***$36.51***	The Ottawa Hospital
PCR positive culture negative $19.92 + $3.93	***$23.85***	The Ottawa Hospital

* costs adjusted from 2005 to 2010 rates using Bank of Canada Inflation calculator
^ Hourly wage calculated using average of top three tiers of 2010 nursing salary (ONA)
¥ Hourly wage calculated using average of all tiers of 2010 nursing salary (ONA)
pt = patient, CP = contact precautions

It should be noted that additional lab equipment was purchased prior to the start of the screening intervention to accommodate the increased demand on the laboratory system at an approximate cost of $97 000. However, since the equipment costs could not be attributed solely to the intervention as the equipment would be utilized after the intervention period and would have been required regardless of the implementation of a universal screening program, capital costs were not included in the model.

4.3.2.4 Sensitivity analysis – Patient-based model

A sensitivity analysis (one-way) of the patient-based model was performed. This was undertaken as the potential exists for additional costs to be incurred in the pre period that are not captured in the model. The populations of interest in the sensitivity analysis are: (1) patients unscreened for MRSA and therefore not known to carry MRSA; and (2) patients with false-negative screening tests. For instance, an 'unscreened' patient who was unknowingly MRSA positive upon admission (P32 in Patient-based model diagram) may not have incurred costs in the original model as we were not aware of his status. However, upon suspicion of an infection, this patient might subsequently have a clinical culture taken during his hospital stay deeming him MRSA infected and thus incurring costs. The same might be true for a false negative patient (P34 in Patient-based model diagram) who may, in fact, be MRSA infected and have additional costs attributed to his care.

As these costs were not documented or easily supported by the literature, they could not be included in the original patient model. Therefore, a separate economic analysis was

conducted to demonstrate the effect that these potential added costs would have on the universal MRSA screening intervention.

In addition to the above analysis, in order to test the robustness of the findings, further sensitivity analysis was conducted. Probabilities were altered across all states in the patient-based model to demonstrate the effect of uncertainty on our results. As noted below, the items altered in the sensitivity analysis include; screening, MRSA PCR negative, true MRSA negative, positive MRSA culture, acquisition of MRSA, MRSA infected risk of death, MRSA colonized risk of death and MRSA infection rate.

Unscreened, unknown MRSA positive, infected patient

The methods used to derive the number of patients who were not screened and unknown MRSA positive who became infected is summarized in Table 4.3.

TABLE 4.3 NUMBER OF PATIENTS WHO WERE NOT SCREENED AND UNKNOWN MRSA POSITIVE WHO BECAME INFECTED

	PRE	POST
Total number of Pts admitted	76259	61782
Total Number of Pts Screened	22271 (29.2%)	51815 (83.8%)
Total Number of Pts not screened	53988	9967
Total number of Pts estimated to be MRSA positive	972 (1.8%)	179 (1.8%)
Total number of Pts estimated to be MRSA infected	42 (4.3%)	8 (4.3%)

Pts = patients

The associated costs applied to this population were as in the original model, minus the cost of the screening specimen.

False negative patients

The methods used to derive the number of false negative cases is summarized in Table 4.4.

TABLE 4.4 NUMBER OF PATIENTS WHO WERE FALSE NEGATIVE WHO BECAME INFECTED

	PRE	POST
Total number of screened pts	22271	51815
Total number of negative screens	21893 (95.5%)	51068 (95.5%)
Estimated total number of false negatives	438 (2%)	1021 (2%)

Pts = patients

The associated costs applied to this population were as in the original model.

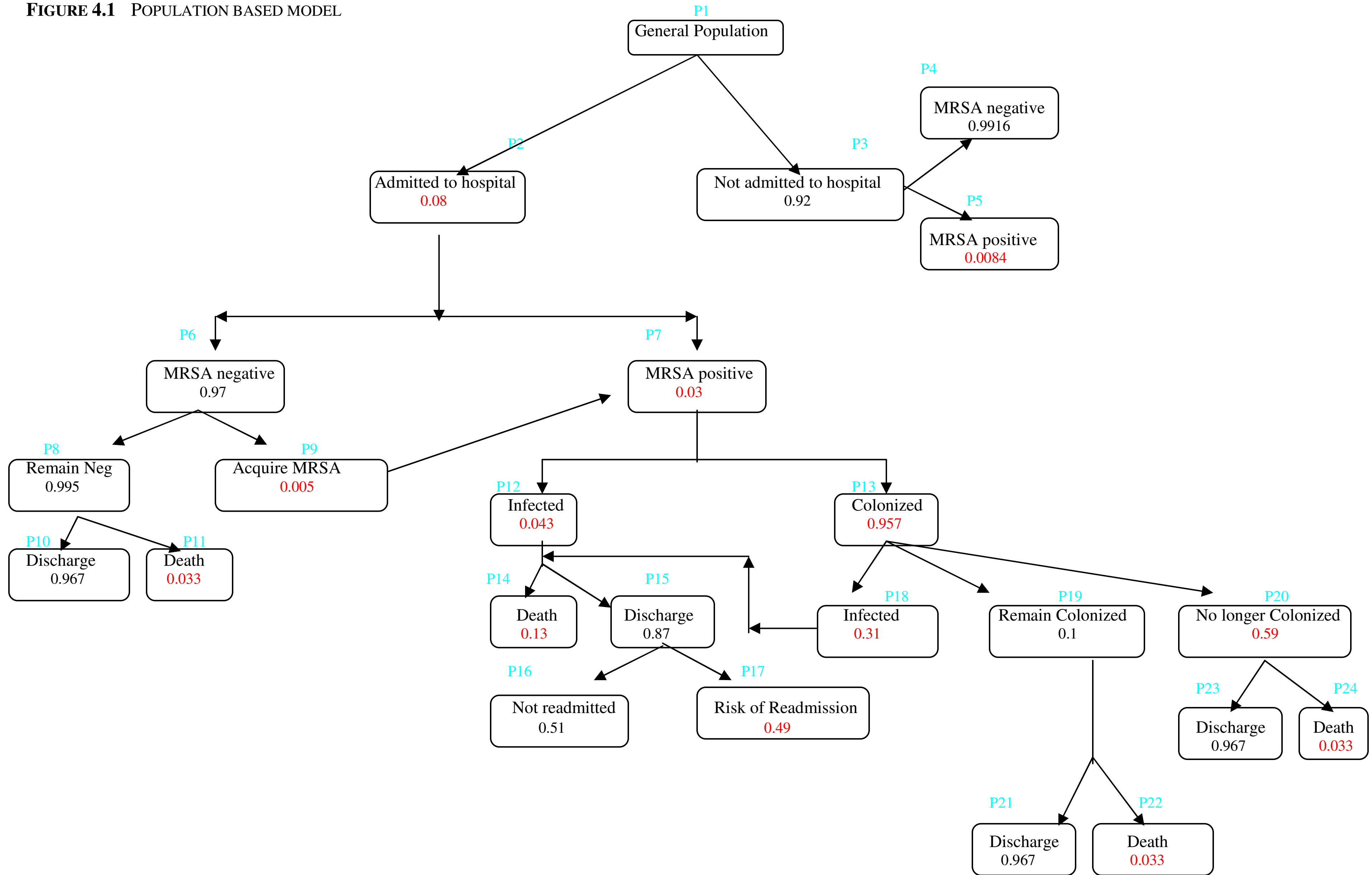
4.3.3 Design of a Population-based model

A second economic model was designed to illustrate how the long-term population-based costs associated with MRSA infection or colonization from a societal perspective could be assessed (Figure 4.1). Because both the statistical analysis in Chapter #3 concluded that the intervention was unsuccessful in decreasing the nosocomial rate of MRSA within the facility, and the patient-based model failed to demonstrate cost-effectiveness (see section 4.4.1), full analysis of the model was unnecessary. However, a brief description of how a model could be developed follows. The description explains how the transition probabilities could be obtained but further exploration of costs and utilities is not included. Within the population model, terminal nodes representing death, MRSA complications and transmission were proposed with incorporation of quality adjusted life years (QALYs), increased length of stay (LOS), readmission rates, complications, and

likelihood of transmission to other patients. Literature searches were conducted to obtain representative information regarding these short and long term outcomes. As with the patient-based model, the majority of the probabilities used for this analysis were based on a relevant study conducted in our institution.[24] Further probabilities were obtained from recent, relevant and comparable Canadian literature when available.

For this model, the length of the cycle was set at one year (as this model was expected to span the entire life history of the patient), in order to determine the societal impact of MRSA, which is a relatively low risk event. The one year length of the cycle was deemed relevant according to the literature.[92]

FIGURE 4.1 POPULATION BASED MODEL



4.3.3.1 Health States

The likelihood of a member of the general population being admitted to hospital was considered the first step in this population-based model (Figure 4.2). The person would move throughout the model with death or discharge from hospital being the final absorbing state for those persons with no MRSA or MRSA colonization. The risk of readmission versus no readmission was the final state for persons with MRSA infection as it was important to illustrate that these persons may endure several more rounds through the cycle as a result of their MRSA infected status. Each state incorporated costs associated with increased length of hospital stay (LOS), laboratory testing costs, control costs, decreased quality adjusted life years (QALY), decreased income and decreased societal contribution, when applicable. Fourteen health states were included and are described in Table 4.5. The model was structured in Microsoft Excel XP.

4.3.3.2 Probabilities – Population-based model

After a review of the available literature, the model was populated with probabilities which best represented the states/nodes in the model. An explanation of how each probability was obtained for the population-based model follows and is summarized in Table 4.6.

Admitted to hospital

This probability was obtained utilizing Canadian Institute of Health Information (CIHI) data. In 2006-07, CIHI reported that approximately 8 in 100 Canadians were hospitalized.[103]

TABLE 4.5
POPULATION-BASED ECONOMIC MODEL, HEALTH STATES

HEALTH STATE	DESCRIPTION	REFERENCE TO DIAGRAM
Admitted to hospital	Person requires admission to hospital Costs associated with patient care during hospital stay are associated with this state. Deceased QALY, loss of income and loss of societal contribution are associated with this state.	P2
Not admitted to hospital	Person does not require admission to hospital. There are no costs/concerns associated with this state.	P3
MRSA negative	Person is MRSA negative upon screening/testing. Cost of running laboratory tests are associated with this state.	P4/P6
MRSA positive	Person is MRSA positive upon screening/testing. Control costs are associated with this state.	P5/P7
Remain MRSA negative	Person remains MRSA negative throughout their hospital admission There are no additional costs associated with this state	P8
Acquire MRSA	Person initially negative for MRSA, but becomes MRSA positive during hospital admission. Controls costs and additional laboratory testing associated with this state.	P9
Infected with MRSA	Person confirmed positive with MRSA bacteremia. Control costs and increased length of stay costs associated with this state.	P12/P18
Colonized with MRSA	Person is colonized with MRSA. Control costs are associated with this state.	P13
Remain colonized with MRSA	Person continues to be colonized with MRSA. Control costs and additional laboratory testing are associated with this state.	P19
No longer colonized with MRSA	Person is no longer MRSA colonized. Additional laboratory testing is associated with this state.	P20
Discharge	Person is discharged from hospital. There are no costs associated with this state. This is an absorbing state for those who were MRSA negative/MRSA colonized.	P10/P15/P23
Death	Person died during hospital admission. Loss of life, loss of societal contribution are associated with this state. This is an absorbing state.	P11/P14/P24
Readmission	Person requires readmission to hospital after earlier discharge from hospital. Control costs, laboratory testing, decreased QALY, loss of income and loss of societal contribution are associated with this state. This is an absorbing state for those who were MRSA infected. Person restarts model.	P17
No readmission	Person does not require readmission to hospital after earlier discharge from hospital. There are no costs associated with this state. This is an absorbing state for those who were MRSA infected.	P16

General Population – MRSA positive

The probability that a member of the general population would be MRSA positive was challenging to identify. There were only a handful of U.S. reports which specified the likelihood of a person having MRSA within the general population. In 2001-02 the National Health and Nutrition Examination Survey (NHANES) identified that approximately 0.84% of the general population was MRSA positive.[104] While this is based on U.S. data, we utilized this probability as it was the only option to help identify the likelihood of MRSA positive status within our Canadian population. It is likely an overestimate in our population and is, therefore, a conservative approach.

Hospital Population – MRSA positive

The likelihood that a hospitalized patient would test positive for MRSA was derived from Conterno et al. The authors determined that approximately 3% of patients test positive for MRSA and was based on a sample of Ottawa Hospital patients.[24]

Acquire MRSA

The Ottawa Hospital's nosocomial MRSA rate was utilized as the probability of acquiring MRSA while admitted to hospital. The data were pulled from the OHDW during our study period. Therefore, the probability of acquiring MRSA was 0.5%.

Death – hospitalized patient

The likelihood of dying while admitted to hospital was 3.3%. This probability was derived from the literature and was based on the Ottawa Hospital population in

2001/02.[98]

MRSA infected

The MRSA bacteremia rate was utilized to define the probability of an MRSA positive patient being infected with MRSA versus colonized. These data were pulled from the OHDW during our study period. The MRSA bacteremia rate was 4.3%. As previously mentioned, the rate of bacteremia is an objective measure of MRSA infection that has been utilized in the literature.[94]

MRSA colonized becoming infected

The likelihood that an MRSA colonized patient would become infected with MRSA was derived from the literature. Huang et al. reported that 31% of those colonized with MRSA became infected with MRSA.[94] The literature supports this finding as, the risk of an MRSA colonized individual becoming subsequently infected with MRSA was reported to be between 13-29% in several studies, justifying the probability of 31%.[105,106] The Huang article was chosen as it had the best study design and most comparable study population.

MRSA colonized – no longer colonized

Marschall et al. identified that 59% of their study population became MRSA negative after initially being colonized with MRSA.[101] The likelihood of an MRSA colonized person clearing their colonization was supported in the literature. Approximately 32-41% of patients will remain colonized with MRSA after detection.[33,107] Therefore, a

subsequent 59-68% were no longer colonized with MRSA. The Marschall et al. study was chosen as it had a stronger study design and study population and had the longest follow-up period (one year).[101]

Infected risk of readmission

The likelihood of an MRSA infected person being readmitted after previous discharge was 49%. This probability was derived from Datta & Huang who found that 49% of MRSA patients who were discharged from hospital required readmission within one year.[97]

Infected risk of death

The likelihood that an MRSA infected patient would die during their hospitalization was 13%. Coello et al. reported that 13% of their MRSA infected population died during that hospital admission.[95] The probability of being MRSA positive and dying was supported by several studies, stating that between 15-23% of MRSA positive patients will die.[14,96,97] The Coello et al. study was utilized as it had the best study design and most comparable study population.

TABLE 4.6
POPULATION-BASED MODEL, PROBABILITIES

PROBABILITY	ESTIMATE	DESCRIPTION	SOURCE	SAMPLE SIZE	REFERENCE TO MODEL	
Admitted to hospital	0.08	Likelihood of a person being admitted to a hospital	CIHI highlights 2006/07	DAD/NACR database	P2	DERIVED
General population - MRSA positive	0.0084	Likelihood of a person in the general population being MRSA positive	Mainous et al. (Used NHANES data 2001/02)	9 622	P5	DERIVED
Hospital population – MRSA positive	0.03	Likelihood of a hospitalized patient being MRSA positive	Conterno et al.	232/ 8528	P7	DERIVED (from TOH data)
Acquire MRSA while in hospital	0.005	Likelihood of an in patient acquiring MRSA while in hospital. (Nosocomial MRSA rate)	OHDW 2006-2009	644/ 138041	P9	ACTUAL
Death – average hospital patient	0.033	In patient mortality 3.3%	Van Walraven 1998-2003	3074/94273 3114/94488	P11 P22 P24	DERIVED (TOH data)
MRSA infected	0.043	Likelihood on an MRSA positive person having an MRSA infection	OHDW 2006-2009 Bacteremia rate	28/644	P12	ACTUAL
MRSA colonized becoming infected	0.31	Risk of an MRSA colonized patient becoming infected with MRSA	Huang et al. 2000	209	P18	DERIVED
MRSA colonized, no longer colonized	0.59	Likelihood of a patient who was colonized with MRSA, being cleared of the disease	Marschall et al. 2000-2003	116	P20	DERIVED
Infected, risk of readmission after discharge	0.49	Likelihood of an MRSA person being readmitted once discharged	Datta & Huang 2002-2005	32/65	P17	DERIVED
Infected risk of death	0.13	Likelihood that an MRSA infected would die while admitted to hospital	Coello et al. 1989-1992	62/476	P14	DERIVED

4.4 Results

4.4.1 Patient-based model

Overall, it was estimated that the universal MRSA screening intervention incurred an additional cost of $1.67 million over 20 months compared to the risk factor-based screening method utilized over 24 months in the pre period (Table 4.7). The annual costs for screening in the pre period were estimated at $783 773.64/year compared to $1 942 892.13/year in the post intervention period, representing an additional cost of $1.16 million/year for the universal MRSA screening intervention. The estimated additional cost per patient screened was $17.76. This cost was derived from the assigned probabilities and costs associated with each health state in the model (Table 4.8).

As expected, the laboratory costs were greater in the post intervention period during the universal MRSA screening intervention as more screening tests were conducted. An increase of nearly $600 000 was noted in regards to lab costs from the pre to post periods, which is equivalent to nearly $400 000 per year. Loss of revenue due to private room use for MRSA patients was the next highest cost to the hospital in the post intervention period, and represents the highest annual cost. Infection Control measures of contact precautions, additional housekeeping and private room usage together increased costs by approximately $775 000 from the pre to the post intervention period, which is equivalent to nearly $550 000 per year.

TABLE 4.7
UNIVERSAL MRSA SCREENING INTERVENTION COSTS

COSTS		ACTUAL PRE PERIOD COSTS (24 MONTHS)	ACTUAL POST PERIOD COSTS (20 MONTHS)	ACTUAL DIFFERENCE PRE-POST (PERIOD)	ESTIMATED PRE PERIOD ANNUAL COSTS	ESTIMATED POST PERIOD ANNUAL COSTS	ESTIMATED ANNUAL DIFFERENCE PRE-POST
Length of Stay	Total	$273 604.74	$534 653.40	-$261 048.66	$136 802.37	$320 792.04	-$183 989.67
	Infected	$273 604.74	$534 653.40	-$261 048.66	$136 802.37	$320 792.04	-$183 989.67
	Colonized	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Laboratory**	Total	$444 012.45	$1 032 927.26	-$588 914.81	$222 006.23	$619 756.32	-$397 750.09
	Infected	$357.20	$708.69	-$351.49	$178.60	$425.21	-$246.61
	Colonized	$5 853.34	$11 438.06	-$5 584.72	$2 926.67	$6 862.84	-$3 936.17
Contact Precautions**	Total	$184 997.54	$362 610.09	-$177 612.55	$92 498.77	$217 566.05	-$125 067.28
	Infected	$15 296.28	$29 890.59	-$14 594.31	$7 648.14	$17 934.35	-$10 286.21
	Colonized	$160 202.88	$313 053.84	-$152 850.96	$80 101.44	$187 832.30	-$107 730.86
Housekeeping	Total	$25 364.16	$50 123.40	-$24 759.24	$12 682.08	$30 074.04	-$17 391.96
	Infected	$1 017.17	$2 003.16	-$985.99	$508.59	$1 201.90	-$693.31
	Colonized	$22 638.01	$44 581.95	-$21 943.94	$11 319.01	$26 749.17	-$15 430.16
Private Room**	Total	$597 781.66	$1 171 764.00	-$573 982.34	$298 890.83	$703 058.40	-$404 167.57
	Infected	$49 379.03	$96 492.00	-$47 112.97	$24 895.52	$57 895.20	-$32 999.68
	Colonized	$517 162.63	$1 010 592.00	-$493 429.37	$258 581. 32	$606 355.20	-$347 773.88
Overall**	**Total**	**$1 567 547.33**	**$3 238 153.55**	**-$1 670 606.22**	**$783 773.67**	**$ 1 942 892.13**	**-$1 159 118.46**
	Infected	$405,346.90	$792,133.59	-$386 786.69	$202 673.45	$475 280.15	-$272 606.70
	Colonized	$705,856.86	$1,379,665.85	-$673 808.94	$352 928.43	$827 799.48	-$474 871.05

** infected and colonized totals will not add up to total due to false positive and negative screen costs

TABLE 4.8
COST OF PATIENT CARE AND ASSOCIATED PROBABILITIES IN VARIOUS HEALTH STATES WITH THE PATIENT-BASED MODEL

State	Cost / pt	Pre Intervention Probability	Post Intervention Probability	Pre Intervention Cost	Post Intervention Cost	Reference to model
Screened for MRSA – PCR neg. – True neg. – No acquisition – Discharged	$19.92	0.261142165	0.756411788	$5.20	$15.07	P37
Screened for MRSA – PCR neg. – True neg. – No acquisition - Death	$19.92	0.00891178	0.025813432	$0.18	$0.51	P38
Screened for MRSA – PCR neg. - False neg. - Infected - Death	$19.92	3.0963E-05	8.9686E-05	$0.00	$0.00	P41
Screened for MRSA – PCR neg. - False neg. - Infected - Discharge	$19.92	0.000207214	0.000600206	$0.00	$0.01	P42
Screened for MRSA – PCR neg. - False neg. - Colonized - Death	$19.92	0.000174927	0.000506686	$0.00	$0.01	P43
Screened for MRSA – PCR neg. - False neg. - Colonized - Discharge	$19.92	0.005125896	0.014847422	$0.10	$0.30	P44
Screened for MRSA - PCR pos. – Culture neg. - Discharge	$811.97	0.004416773	0.01279341	$3.59	$10.39	P47
Screened for MRSA - PCR pos. – Culture neg. - Death	$811.97	0.000150728	0.00043659	$0.12	$0.35	P48
Not screened for MRSA – MRSA neg. - No acquisition - Discharge	$0.00	0.650073312	0.146495394	$0.00	$0.00	P47
Not screened for MRSA– MRSA neg. - No acquisition - Death	$0.00	0.022184508	0.004999326	$0.00	$0.00	P48
Not screened for MRSA - Unknown MRSA status - Infected - Death	$0.00	7.30278E-05	1.6457E-05	$0.00	$0.00	P53
Not screened for MRSA - Unknown MRSA status - Infected - Discharge	$0.00	0.000488724	0.000110135	$0.00	$0.00	P54
Not screened for MRSA - Unknown MRSA status - Colonized - Death	$0.00	0.000412574	9.29745E-05	$0.00	$0.00	P55
Not screened for MRSA - Unknown MRSA status - Colonized - Discharge	$0.00	0.012089674	0.002724434	$0.00	$0.00	P56
Screened for MRSA – PCR neg. - True neg. - Acquire MRSA - Infected - Death	$25,949.36	7.58594E-06	2.19731E-05	$0.20	$0.57	P59
Screened for MRSA – PCR neg.- True neg. - Acquire MRSA - Infected - Discharge	$25,949.36	5.07674E-05	0.00014705	$1.32	$3.82	P60
Screened for MRSA – PCR neg. - True neg. - Acquire MRSA - Colonized - Death	$2,616.42	4.28572E-05	0.000124138	$0.11	$0.32	P61
Screened for MRSA – PCR neg. - True neg. - Acquire MRSA - Colonized - Discharge	$2,616.42	0.001255844	0.003637618	$3.29	$9.52	P62
Screened for MRSA – PCR pos. – Culture pos. - Infected - Death	$25,819.46	4.74172E-05	0.000137346	$1.22	$3.55	P59
Screened for MRSA – PCR pos. – Culture pos. - Infected - Discharge	$25,819.46	0.00031733	0.000919164	$8.19	$23.73	P60
Screened for MRSA – PCR pos. – Culture pos. - Colonized - Death	$2,494.26	0.000267886	0.000775945	$0.67	$1.94	P61
Screened for MRSA – PCR pos. – Culture pos. - Colonized – Discharged	$2,494.26	0.007849867	0.022737545	$19.58	$56.71	P62
Not screened for MRSA- MRSA neg. - Acquire MRSA- Infected - Death	$25,929.44	1.8884E-05	4.25556E-06	$0.49	$0.11	P59
Not screened for MRSA – MRSA neg. - Acquire MRSA - Infected - Discharge	$25,929.44	0.000126378	2.84795E-05	$3.28	$0.74	P60
Not screened for MRSA – MRSA neg. - Acquire MRSA - Colonized - Death	$2,596.50	0.000106686	2.4042E-05	$0.28	$0.06	P61
Not screened for MRSA – MRSA neg. - Acquire MRSA - Colonized - Discharge	$2,596.50	0.003126232	0.000704503	$8.12	$1.83	P62
Not screened for MRSA - Known MRSA pos. - Infected - Death	$25,698.51	0.000119067	0.000026832	$3.06	$0.69	P59
Not screened for MRSA - Known MRSA pos. - Infected - Discharge	$25,698.51	0.000796833	0.000179568	$20.48	$4.61	P60
Not screened for MRSA - Known MRSA pos. - Colonized - Death	$2,382.16	0.00067078	0.000152536	$1.60	$0.36	P61
Not screened for MRSA - Known MRSA pos. - Colonized - Discharge	$2,382.16	0.019711425	0.004442011	$46.96	$10.58	P62
TOTAL		**1**	**1**	**$128.03**	**$145.79**	**(-$17.76)**

Pt = patient, neg. = negative, pos = positive

4.4.2 Sensitivity analysis – Patient-based model

After the patient-based economic model was completed, a sensitivity analysis was conducted to determine if various factors might alter the costs associated with the universal MRSA screening intervention (Table 4.9). As expected, overall program costs could be decreased if fewer patients were MRSA PCR positive (1-3%), that is if fewer patients were MRSA positive at admission, and could save between $3.03 and $30.75 per patient screened. Conversely, higher probabilities of PCR positive patients would dramatically increase the cost of the intervention by as much as $93.98 per patient screened (10% PCR positive). As the probability of positive culture confirmation increases to 80%, the cost increases from $17.76 per screened patient to $27.72 per screened patient. As there were no additional costs attributed to death, the probability of death did not alter the cost of the intervention. In addition, the probability of MRSA acquisition and percentage of infected (versus colonized) did not dramatically alter costs according to this sensitivity analysis. Interestingly, only when acquisition rates are very high does the intervention becomes less costly as a higher proportion of patients are infected.

TABLE 4.9
SENSITIVITY ANALYSIS RESULTS, PATIENT-BASED MODEL (PER PATIENT SCREENED)

ACTUAL OTTAWA HOSPITAL MODEL					SENSITIVITY ANALYSIS			
Probability	**Actual Probability**	**Actual Cost Pre Intervention**	**Actual Cost Post Intervention**	**Actual Cost Pre-Post**	**Estimated Probability**	**Estimated Cost Pre Intervention**	**Estimated Cost Post Intervention**	**Estimated Cost Pre-Post**
Screening	Pre 29% Post 84%	$128.03	$145.79	-$17.76	Post 75%	$128.03	$142.88	-$14.85
					95%	$128.03	$149.34	-$21.31
PCR Negative	96%	$128.03	$145.79		90%	$168.22	$262.20	-$93.98
					92%	$153.61	$219.87	-$66.26
					94%	$138.99	$177.54	-$38.54
					97%	$117.07	$114.04	$3.03
					98%	$109.76	$92.87	$16.89
					99%	$102.46	$71.70	$30.75
True Negative	98%	$128.03	$145.79		90%	$127.63	$144.63	-$17.00
					95%	$127.88	$145.35	-$17.47
					99%	$128.08	$145.93	-$17.85
Positive Culture	65%	$128.03	$145.79		40%	$119.27	$120.41	-$1.14
					50%	$122.78	$130.56	-$7.79
					60%	$126.28	$140.71	-$14.43
					70%	$129.78	$150.86	-$21.08
					80%	$133.29	$161.01	-$27.72
Acquire MRSA	0.5%	$128.03	$145.79		0.25%	$119.51	$137.34	-$17.83
					1%	$145.08	$162.68	-$17.60
					5%	$281.45	$297.80	-$16.36
					10%	$451.91	$466.71	-$14.80
					60%	$2156.50	$2155.76	$0.74
Infected risk of death	13%	$128.03	$145.79		6%	$128.03	$145.79	-$17.76
					20%	$128.03	$145.79	-$17.76
Colonized risk of death	3.3%	$128.03	$145.79		1.6%	$128.03	$145.79	-$17.76
					5%	$128.03	$145.79	-$17.76
MRSA infected	4.3%	$128.03	$145.79		2%	$109.52	$127.51	-$18.00
					3%	$117.57	$135.46	-$17.89
					6%	$141.72	$159.29	-$17.57
					8%	$157.82	$175.18	-$17.37
					15%	$214.17	$230.80	-$16.63

Further sensitivity analysis included costs for those patients who may have not had costs attributed to them in the original model. The inclusion of ‘false negative’ and ‘unknown’ ‘unscreened’ MRSA infected cases into the patient-based model added 71 patients in the pre period (42 unscreened/unknown, 19 false negative) and 52 in the post period (8 unscreened/unknown, 44 false negative). An additional $1.6 million and $1.3 million in costs would have been incurred in the pre and post periods respectively, which is equivalent to $790,000 and $800,000 per year, respectively (Table 4.10). When these costs are factored in, the total universal MRSA screening intervention would cost an additional $1.4 million dollars (or $1.2 million per year) compared to the risk factor-based program previously utilized. The addition of these cases would alter the cost per patient screened from an additional $17.76, as noted in the original analysis, to an additional $18.18 per patient screened (Table 4.11).

TABLE 4.10
SENSITIVITY ANALYSIS RESULTS, PATIENT-BASED MODEL

	ACTUAL PRE PERIOD COSTS (24 MONTHS)	ACTUAL POST PERIOD COSTS (20 MONTHS)	ACTUAL DIFFERENCE PRE-POST (PERIOD)	ESTIMATED ANNUAL PRE PERIOD COSTS	ESTIMATED ANNUAL POST PERIOD COSTS	ESTIMATED ANNUAL DIFFERENCE PRE-POST
Additional costs associated with 'unscreened', 'unknown MRSA positive' 'infected' pts	42 pts x $25 929.44 = $1 089 036.48	8 pts x $25 929.44 = $207 435.52	$881 600.96	$544 518.20	$124 461.31	$420 056.89
Additional costs associated with 'false negative' pts	19 pts x $25 932.77 = $488 417.79	44 pts x $25 932.77 =$1 138 526.40	-$650 108.61	$244 208.90	$683 115.84	-$438 906.94
Total additional costs	$1 577 454.27	$1 345 961.92	$231 492.35	$788 727.14	$807 577.15	-$18 850.01
Original costs (as noted Table 4.7)	$1 567 547.33	$3 238 153.55	-$1 670 606.22	$783 773.67	$1 942 892.13	-$1 159 118.46
Combined Overall Total	**$3 145 001.50**	**$4 584 115.47**	**-$1 439 113.97**	**$1 572 500.75**	**$2 750 469.28**	**-$1 177 968.53**

Pts = patients

TABLE 4.11

COST OF PATIENT CARE AND ASSOCIATED PROBABILITIES IN VARIOUS HEALTH STATES WITH THE SENSITIVITY ANALYSIS OF THE PATIENT-BASED MODEL

State	Cost / pt	Pre Intervention Probability	Post Intervention Probability	Pre Intervention Cost	Post Intervention Cost	Reference to model
Screened for MRSA – PCR neg. – True neg. – No acquisition – Discharged	$19.92	0.261142165	0.756411788	$5.20	$15.07	P37
Screened for MRSA – PCR neg. – True neg. – No acquisition - Death	$19.92	0.00891178	0.025813432	$0.18	$0.51	P38
Screened for MRSA – PCR neg. - False neg. - Infected - Death	**$25,932.77**	3.0963E-05	8.9686E-05	**$0.80**	**$2.33**	P41
Screened for MRSA – PCR neg. - False neg. - Infected - Discharge	**$25,932.77**	0.000207214	0.000600206	**$5.37**	**$15.57**	P42
Screened for MRSA – PCR neg. - False neg. - Colonized - Death	$19.92	0.000174927	0.000506686	$0.00	$0.01	P43
Screened for MRSA – PCR neg. - False neg. - Colonized - Discharge	$19.92	0.005125896	0.014847422	$0.10	$0.30	P44
Screened for MRSA - PCR pos. – Culture neg. - Discharge	$811.97	0.004416773	0.01279341	$3.59	$10.39	P47
Screened for MRSA - PCR pos. – Culture neg. - Death	$811.97	0.000150728	0.00043659	$0.12	$0.35	P48
Not screened for MRSA – MRSA neg. - No acquisition - Discharge	$0.00	0.650073312	0.146495394	$0.00	$0.00	P47
Not screened for MRSA– MRSA neg. - No acquisition - Death	$0.00	0.022184508	0.004999326	$0.00	$0.00	P48
Not screened for MRSA - Unknown MRSA status - Infected - Death	**$25,929.44**	7.30278E-05	1.6457E-05	**$1.89**	**$0.43**	P53
Not screened for MRSA - Unknown MRSA status - Infected - Discharge	**$25,929.44**	0.000488724	0.000110135	**$12.67**	**$2.86**	P54
Not screened for MRSA - Unknown MRSA status - Colonized - Death	$0.00	0.000412574	9.29745E-05	$0.00	$0.00	P55
Not screened for MRSA - Unknown MRSA status - Colonized - Discharge	$0.00	0.012089674	0.002724434	$0.00	$0.00	P56
Screened for MRSA – PCR neg. - True neg. - Acquire MRSA - Infected - Death	$25,949.36	7.58594E-06	2.19731E-05	$0.20	$0.57	P59
Screened for MRSA – PCR neg.- True neg. - Acquire MRSA - Infected - Discharge	$25,949.36	5.07674E-05	0.00014705	$1.32	$3.82	P60
Screened for MRSA – PCR neg. - True neg. - Acquire MRSA - Colonized - Death	$2,616.42	4.28572E-05	0.000124138	$0.11	$0.32	P61
Screened for MRSA – PCR neg. - True neg. - Acquire MRSA - Colonized - Discharge	$2,616.42	0.001255844	0.003637618	$3.29	$9.52	P62
Screened for MRSA – PCR pos. – Culture pos. - Infected - Death	$25,819.46	4.74172E-05	0.000137346	$1.22	$3.55	P59
Screened for MRSA – PCR pos. – Culture pos. - Infected - Discharge	$25,819.46	0.00031733	0.000919164	$8.19	$23.73	P60
Screened for MRSA – PCR pos. – Culture pos. - Colonized - Death	$2,494.26	0.000267886	0.000775945	$0.67	$1.94	P61
Screened for MRSA – PCR pos. – Culture pos. - Colonized – Discharged	$2,494.26	0.007849867	0.022737545	$19.58	$56.71	P62
Not screened for MRSA- MRSA neg. - Acquire MRSA- Infected - Death	$25,929.44	1.8884E-05	4.25556E-06	$0.49	$0.11	P59
Not screened for MRSA – MRSA neg. - Acquire MRSA - Infected - Discharge	$25,929.44	0.000126378	2.84795E-05	$3.28	$0.74	P60
Not screened for MRSA – MRSA neg. - Acquire MRSA - Colonized - Death	$2,596.50	0.000106686	2.4042E-05	$0.28	$0.06	P61
Not screened for MRSA – MRSA neg. - Acquire MRSA - Colonized - Discharge	$2,596.50	0.003126232	0.000704503	$8.12	$1.83	P62
Not screened for MRSA - Known MRSA pos. - Infected - Death	$25,698.51	0.000119067	0.000026832	$3.06	$0.69	P59
Not screened for MRSA - Known MRSA pos. - Infected - Discharge	$25,698.51	0.000796833	0.000179568	$20.48	$4.61	P60
Not screened for MRSA - Known MRSA pos. - Colonized - Death	$2,382.16	0.00067078	0.000152536	$1.60	$0.36	P61
Not screened for MRSA - Known MRSA pos. - Colonized - Discharge	$2,382.16	0.019711425	0.004442011	$46.96	$10.58	P62
TOTAL		1	1	**$148.77**	**$166.95**	**(-$18.18)**

Pt = patient, neg. = negative, pos = positive

4.5 Discussion

To our knowledge, this is the first large-scale study to examine the cost-effectiveness of a hospital-wide universal MRSA screening intervention versus a risk-based program. While the results of the analysis were not favourable, this is an important finding. The majority of universal MRSA screening studies in the literature valued the intervention based on a purely clinical perspective and did not account for the cost effectiveness of the intervention.[31,32,34,64] Furthermore, studies that included a cost component included total costs and not a formal economic analysis.[1]

Clancy et al. concluded that universal screening in high-risk intensive care units may be a cost avoidant strategy to decrease MRSA infections in their hospital.[1] The authors stated that a cost of $19 714/ month was averted in the intensive care units due to a reduction in the mean number of MRSA infections of 2.5 per month following the screening program. However, this study was unit-specific and contrasted the results with a 'no screening' method, limiting direct comparison to our study.

Murthy et al. conducted a study with a more formal economic component.[35] The results from this study are difficult to compare with ours as well, however, as the authors chose to assess three screening strategies on a surgical population: (1) a universal MRSA screening intervention for MRSA (2) risk factor-based screening and pre emptive isolation, and (3) standard admission with 'no screening'. The authors found that while universal screening for MRSA reduced the risk of MRSA infection, it was not cost

effective at their centre as they had low prevalence of MRSA, successful hand hygiene measures and good compliance with infection control policies.

Lee et al. utilized a computer simulation model to determine whether active MRSA screening would be beneficial at various prevalence and acquisition rates within a healthcare institution.[65] They concluded that a universal MRSA screening intervention appeared to be cost effective. The authors suggested that institutions compare their individual conditions to those utilized in their model to determine which screening approach to take. Our results may differ from Lee et al. as they compared universal MRSA screening to 'no screening' and used computer modelling, whereas we used the current standard of risk-based screening as our comparator and based our findings on real-time hospital data.

Comparisons with other studies should be interpreted with caution as previous studies utilized various costs methods, varying laboratory methods, and various populations. Our economic models were strengthened by the fact that they were designed with the goal of capturing the effects of a universal MRSA screening intervention from both the hospital and societal perspective. This micro- and macroeconomic approach to the intervention is another important contribution to the available literature. The majority of studies which examined MRSA screening interventions chose only to document the effects of the intervention from the hospital's perspective. [1,31,32,34,35,64,65] While this is an important perspective, the societal perspective should be examined to demonstrate the long term implications and effects of MRSA infection (i.e. hospital readmission).

Although our population-based model was not populated as this would not yield useful information for an intervention not shown to be effective, the model itself could be useful for settings where the intervention is found to be effective (e.g. high prevalence settings) to guide policy and program implementation.

4.6 Limitations

There were several challenges associated with this economic analysis. One of the major limitations of this economic analysis was gathering accurate data on patients' MRSA status in the pre period. As the institution performed risk factor-based screening in the pre period, populating the patient-based model was more challenging in the sense that detailed descriptive statistics were not available for the number of patients who were not screened in this period. Some of the factors were assumed, including the likelihood of being MRSA positive but not screened, as mentioned previously.

Secondly, assigning of probabilities in instances where we were unable to use real numbers from our institution was challenging, as this was the first study of its kind to conduct a thorough economic analysis on a universal MRSA screening intervention. These probabilities were using the best literature available, however, some were based on U.S. data or slightly dated studies.

Third, MRSA bacteremias were used as a measure of MRSA infection and thus excluded other potential infections (wounds, UTI, pneumonia, etc). This is a potential limitation to note, as the most comparable study to ours utilized all infections.[33] However, we chose

to utilize MRSA bacteremia rates as it was the most objective measure of true MRSA infection and is always clinically significant. As previously mentioned, blood cultures are considered to be from a sterile site representing true infection, whereas MRSA isolated from a non-sterile sites requires a subjective assessment to determine if the patient is infected or colonized.[94] The decision to include bacteremias as our standard for MRSA infection is supported in the literature and yields a conservative, but objective, estimate of MRSA infection.[13,67,96]

Another limitation was addressed with the sensitivity analysis of the patient-based model, but is still of note. As some of our probabilities in the model were based on 'unknown' cases, assigning costs to these cases was challenging. The concern was that the model may be missing those cases that were 'not screened' or falsely negative and therefore, unknown MRSA positive cases. These patients would attribute costs once their MRSA infected status became known (upon positive clinical culture after infection or illness suspected). This in turn, may have falsely elevated the costs in the post period as these patients were identified upon admission screening but the pre period screening regimen neglected to catch similar patients and their associated costs in the pre period. Based on the premise that these cases are 'unknown', they could not be accounted for in the original analysis as they were not based on evidence. In addition, this issue has yet to be appropriately addressed in the literature.

The final limitation of this project was the incomplete population-based analysis. As previously mentioned, it was decided that running the complete population-based

economic model would not yield additional useful information. However, the model has been populated and can be easily translated for the benefit of other institutions or for further studies and/or economic analysis.

4.7 Conclusions

The economic analysis concluded that overall, an additional $1.7 million dollars was required to implement the universal MRSA screening intervention over 20 months with an estimated increase of $17.76 per patient screened compared to risk factor-based screening. On average, the program cost an estimated $1.9 million per year, representing an excess cost of $1.16 million per year compared to the previous screening method. When this factor is combined with the knowledge from the preceding chapter suggesting that the nosocomial rate of MRSA did not decrease, it is apparent that the universal MRSA screening intervention was not clinically or economically effective. This finding is an important contribution to the current literature as it begins to shed light on the costs associated with MRSA screening interventions, which are poorly understood. As this appears to be the first study to adequately examine the cost effectiveness of a hospital-wide universal MRSA screening intervention, further research is required to verify/dispute these findings in other settings.

Chapter 5 – Summary & Conclusions

Methicillin-resistant *Staphyloccocus aureus* (MRSA) is a pathogen which places logistical and financial strain on the healthcare system. Institutions are challenged with implementing effective interventions to prevent the transmission of MRSA to vulnerable patients within their facilities. The objective of this thesis was to measure the clinical and cost-effectiveness of a universal MRSA screening intervention within a large tertiary care facility. A multi-method approach was utilized, and included: (1) a literature review of the existing MRSA screening options with a focus on universal screening, (2) a statistical analysis of a pre and post universal screening intervention and, (3) an economic analysis of a hospital wide universal screening intervention.

As stated in section 1.2, the specific objectives of this thesis were to:

1. Determine if a universal MRSA screening intervention reduced the incidence of nosocomial MRSA over time in a large tertiary care facility compared to regional rates.
2. Determine the cost effectiveness of implementing a universal MRSA screening intervention using both patient-based and population-based approaches.

The hypothesis to be tested in this thesis, as stated in section 1.3.6, was that a universal MRSA screening intervention would be effective in reducing the nosocomial spread of MRSA within the Ottawa Hospital. This would then merit the conduct of a full economic analysis.

5.1 Background – MRSA Screening

A review of the current literature identified three main screening interventions (risk factor-based screening, search and destroy theory, and universal screening) and synthesized what was known about the effectiveness and economic impact of universal MRSA screening interventions. The literature review identified a total of 472 published studies which matched the search criteria. Of these, 17 studies examining some form of universal MRSA screening intervention were further explored. Sixty five percent (11/17) of the identified studies suggested that universal screening is an effective way to reduce the number of MRSA cases within a facility.[1,25,31-33,59-64] However, only three of the studies were conducted on a hospital wide population [33,65,71] and of these, two concluded that universal screening was an effective approach to MRSA screening.[33,65] Furthermore, the studies had limitations which preclude direct comparisons with our study as discussed in the following sections.

The literature review of the economic impacts of a universal screening intervention identified a total of 42 studies. Eight studies assessed the economic impacts of MRSA in hospitals and were further explored; of these, four conducted a quality economic analysis which included an economic model, probability assignment and explanation of detailed costs.[35,65,66,69] A universal screening intervention was deemed cost effective in 50% (2/4) of the reports.[66,66] Again, limitations of these studies, including use of computer simulation rather than real-world data, made direct comparison with our results challenging.

5.2 Evaluation of a Universal MRSA Screening Intervention

The universal screening intervention at the Ottawa Hospital aimed to statistically analyze the effectiveness of the universal MRSA screening intervention in reducing the nosocomial transmission of MRSA at the Ottawa Hospital. The retrospective population-based observational study consisted of two periods. In the first period (24 months), patients admitted to the Ottawa Hospital underwent risk factor-based screening. These patients were screened for MRSA based on the following certain pre-defined risk factors: previous hospitalization in past 6 months, direct transfer from another healthcare facility, or history of MRSA colonization or infection. In the second period (20 months), universal MRSA screening was implemented in which all patients admitted to the Ottawa Hospital were screened for MRSA upon admission. Data for the analysis were extracted from the Ottawa Hospital Data Warehouse.

During the first period, 22271 (29.2%) patients were screened compared with 51815 (83.8%) in the post intervention period. The MRSA detection rate was 9.8 per 1,000 admitted patients pre intervention and 26.2 per 1,000 admitted patients post intervention. Furthermore, during our study there were a total of 644 nosocomial MRSA cases (323 cases in the pre intervention period and 321 in the post intervention period) for an incidence rate of 41.8 per 100,000 patient days and 47.5 per 100,000 patient days, respectively. MRSA bacteremia occurred in 28 patients, 14 in each study period for an incidence rate of 1.8 per 100,000 patient days in the pre intervention period and 2.1 per 100,000 patient days in the post intervention period.

The statistical analysis demonstrated that the universal MRSA screening intervention was not effective in reducing the number of nosocomial MRSA cases within the Ottawa Hospital. Threats to the internal and external validity were accounted for using internal (CDAD rates) and external (regional rates) control groups and did not impact the results.

5.3 Economic Analysis

An economic analysis was conducted which examined the cost-effectiveness of a universal MRSA screening intervention on the nosocomial rate of MRSA within the Ottawa Hospital from the perspective of the health care organization. Two models were created, one to evaluate the short-term patient-based cost impact of a universal MRSA screening intervention, and one to assess the long-term population-based costs associated with an MRSA infection or colonization from a societal perspective.

5.3.1 Patient-Based Model

The patient-based model was populated with probabilities using data from our specific project, where available, Ottawa Hospital data, or data derived from other sources. Cost estimates were based on Ottawa Hospital data. Overall, it was estimated that the universal MRSA screening intervention incurred an additional cost of nearly $1.7 million over 20 months compared to the risk factor-based screening method utilized over 24 months in the pre period. The annual costs for screening in the pre period were estimated at $783 773.64/year compared to $1 942 892.13/year in the post intervention period, representing an additional cost of $1.16 million/year for the universal MRSA screening intervention. The estimated additional cost per patient screened was $17.76.

5.3.2 Population-Based Model

The second economic model to assess the long-term population-based costs associated with MRSA infection or colonization from a societal perspective was populated using probabilities which were based on a relevant study conducted in our institution.[24] However, after the segmented regression analysis determined no decrease in the nosocomial MRSA rates within the facility, the population-based economic analysis was not performed.

5.3.3 Sensitivity Analysis of Patient-Based Model

A sensitivity analysis (one-way) was conducted to demonstrate the effect of uncertainty on our results. The sensitivity analysis, probabilities were altered across all states in the patient-based model. Items incorporated in the sensitivity analysis included: the probability of being screened MRSA PCR negative, true MRSA negative, positive MRSA culture, acquisition of MRSA, MRSA infected risk of death, MRSA colonized risk of death and MRSA infection rate.

Overall, the results of the sensitivity analysis revealed that:

- Program costs could be decreased if fewer patients were MRSA PCR positive (i.e. fewer MRSA positives upon admission)
- Higher probabilities of PCR positive patients, detected due to screening on admission, increase the cost of the intervention
- The cost increases as the probability of a true positive (positive PCR & positive culture) increases

- The probability of death did not alter the cost of the intervention
- The percentage of MRSA infected (versus colonized) did not significantly alter he costs of the intervention
- The probability of nosocomial MRSA acquisition did not dramatically alter costs
- When nosocomial acquisition rates are very high (≈ 60%), the intervention becomes cost saving

A further sensitivity analysis of the patient-based model was performed due to the potential for additional costs to be incurred in the pre-intervention period which may not have been captured in the model. The populations of interest in the sensitivity analysis were: (1) patients unscreened for MRSA and therefore not known to carry MRSA; and (2) patients with false-negative screening tests. As previously explained in section 4.3.2.4, an 'unscreened' patient who was unknowingly MRSA positive upon admission may not have incurred costs in the original model. Upon suspicion of an infection, this patient might have had a clinical culture taken during his hospital stay deeming him MRSA infected and thus incurring costs. The same might be true for a false MRSA negative patient who may, in fact, be MRSA infected and have additional costs attributed to his care. However, as these costs were not documented or easily supported by the literature, they could not be included in the original patient model. Therefore, this separate economic analysis was conducted to display the effect that these potential added costs may have on the universal MRSA screening intervention.

The inclusion of ‘false negative’ and ‘unknown / unscreened’ MRSA infected cases into the patient-based model added 71 patients in the pre period (42 unscreened/unknown, 19 false negative) and 52 in the post period (8 unscreened/unknown, 44 false negative), contributing an additional $1.6 million and $1.3 million in costs in the pre and post periods respectively. Annually, this was equivalent to $790,000 (pre period) and $800,000 (post period) per year, thus bringing the overall total of the universal MRSA screening intervention to an additional $1.4 million dollars (or $1.18 million per year) compared to the risk factor-based program previously utilized. The addition of these cases would alter the cost per patient screened from an additional $17.76, as noted in the original analysis, to an additional $18.18 per patient screened.

5.4 Discussion

Our study builds upon the findings of the other studies identified in the literature review by including a hospital-wide universal MRSA screening program, having both internal and external controls, and examining the economic impacts in more detail. The findings of our study are in line with the findings of other research which suggests that universal screening for MRSA was not beneficial.[34-36,64,71,72] However, direct comparisons can only be made with one of these studies as it also included *all* adult hospital admissions.[71]

Robotham et al. examined the effects of both random and universal MRSA screening methods and determined that random screening was more efficient than universal screening and allowed for effective nosocomial control.[71] The authors concluded that admission screening, in their model, would not prevent nosocomial MRSA transmission

within a facility even if 100% of patients are screened on admission. Furthermore, the authors state that admission screening alone cannot be used to manage any epidemic which is driven by in-patient transmission. There are, however, several limitations of this study. First, the model did not take into account that an MRSA positive patient may have a potentially longer length of stay which could affect within-hospital transmission rates. Second, the model compared random screening to universal screening. Random screening is not equivalent to risk factor-based screening; it is simply a random screening of patients at a given time. It is unlikely that an institution would chose to randomly screen patients given the absence of evidence supporting the effectiveness of this approach over risk-factor based screening. Finally, it should be emphasized that the authors used a stochastic computer model to analyse the two interventions which makes the comparison to our real-time hospital study challenging.

There continues to be considerable debate around the effectiveness of universal screening for MRSA. In contrast to our results, several studies found universal screening to be beneficial in their institution.[1,25, 31-33,59-63,65,72] However, as previously mentioned, the majority of these studies evaluated the effects of universal screening on only selected populations/departments within a facility. Only two of the studies which found universal screening to be beneficial examined *all* adult hospital admissions,[33,65] and of these, only one used real hospital patient data.[33]

Robicsek et al. (2008) examined the effects of two expanded surveillance interventions on MRSA disease over four years in a 3-hospital organization in the US. The study

involved three periods. The first was a baseline period in which no active surveillance was conducted, the second introduced universal screening into the ICU and the third involved universally screening all admissions to hospital. The study concluded that screening for MRSA was associated with a substantial reduction in rates of MRSA clinical infection.[33] However, the investigators did not utilize robust internal or external control measures to account for other possible factors that could have led to these results. Furthermore, the authors did not perform an economic evaluation of the intervention which could have contributed to their conclusions.

Lee et al. evaluated the cost effectiveness of a universal MRSA surveillance program at various prevalence and reproductive rates. A computer simulation model was used to evaluate the effects of universally screening all adults at hospital admission. The authors concluded that a universal MRSA screening intervention is cost effective at a variety of prevalence and reproductive rates.[65] There were two limitations noted. First, the project compared universal screening to no screening at all making the results of the project less generalizable, as most hospitals have some form of screening program in place for MRSA. Second, it was a computer simulation model, which as mentioned, makes the comparison to our real-time hospital study challenging.

Several factors may explain why this intervention did not prove beneficial in our patient population, as discussed in Section 3.5. Infection control practices play an extremely important role in any infection control strategy and as a result, any changes with these practices within intervention periods may affect the results of the intervention. While we

attempted to control for these factors by utilizing an internal control group, it is possible that the effects were more noticeable within the MRSA rates than the CDAD rates. In addition, studies have suggested that this type of intervention may only be beneficial in areas where the prevalence of MRSA is much higher and therefore the lower regional incidence of MRSA in Ottawa may have sheltered the effects of the intervention. [9,16] Furthermore, MRSA outbreaks, the laboratory method utilized and the length of the intervention may have factored into the effectiveness of the intervention, although it is unlikely these factors alone would have significantly altered the outcome of the intervention. Finally, while our compliance averaged approximately 84% and is a realistic portrayal of hospital function, it was not 100%. This factor does not allow us to determine the intervention's effectiveness had a higher percentage of the inpatient population been screened upon admission and as a result, it cannot be discounted that a higher compliance with admission screening may have altered our results.

5.5 Conclusions

Overall, an additional $1.7 million dollars was required to implement the universal MRSA screening intervention over 20 months with an estimated increase of $17.76 per patient screened compared to risk factor-based screening. On average, the program cost an estimated $1.9 million per year, representing an excess cost of $1.16 million per year compared to the previous screening method. When the results from the economic analysis are combined with the statistical analysis (not resulting in decrease the nosocomial MRSA rate), it is apparent that the universal MRSA screening intervention was not clinically or economically effective. As this appears to be the first study to

adequately examine the cost effectiveness of a hospital-wide universal MRSA screening intervention, further research is required to verify/dispute these findings in other settings. Nonetheless, this thesis represents an important contribution to the current literature as it fills a large gap in the knowledge relating to the combined clinical and economic costs effectiveness associated with an MRSA universal screening intervention.

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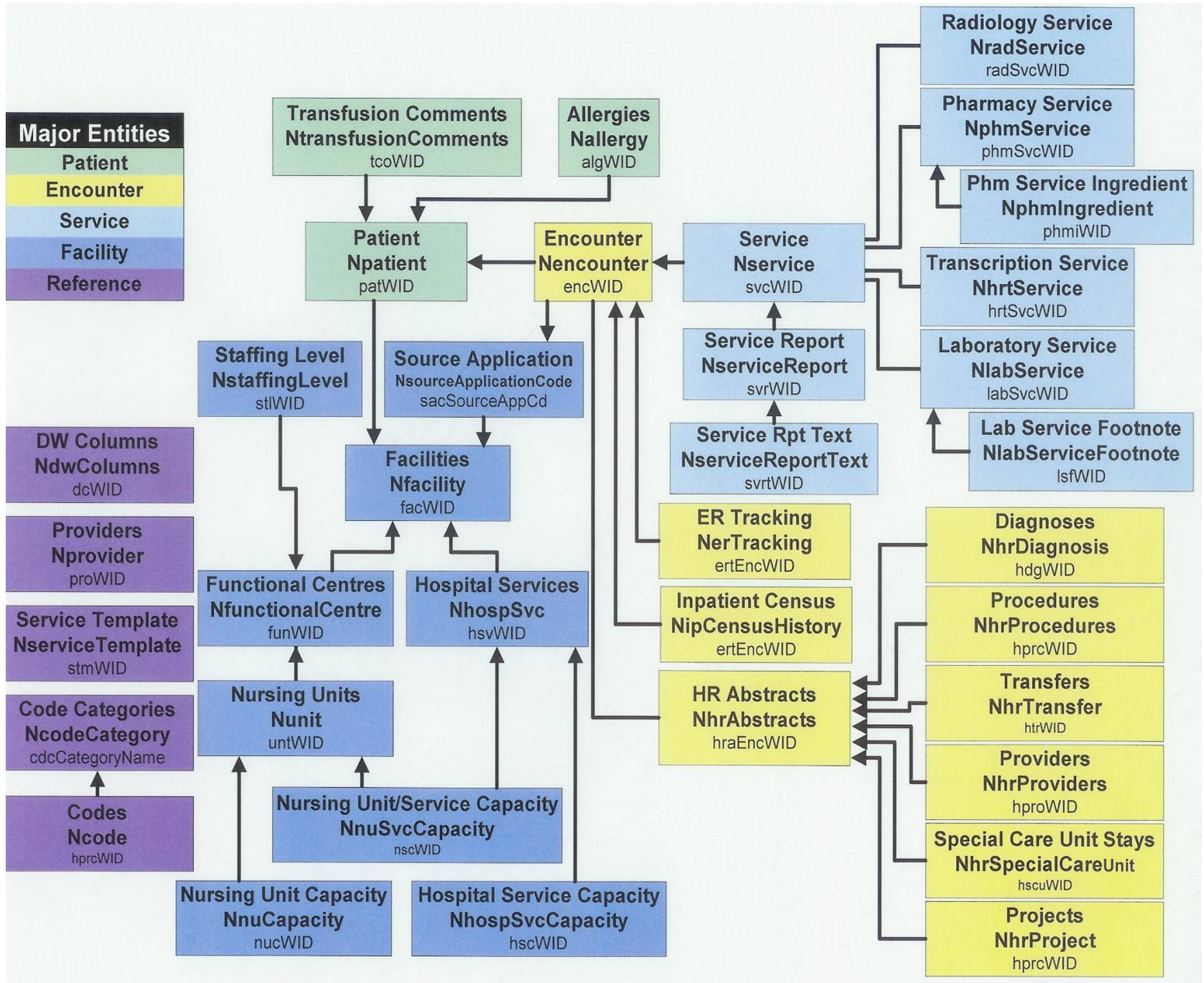
APPENDIX A DESCRIPTION OF TABLES/VARIABLES UTILIZED FROM THE OTTAWA HOSPITAL DATA WAREHOUSE

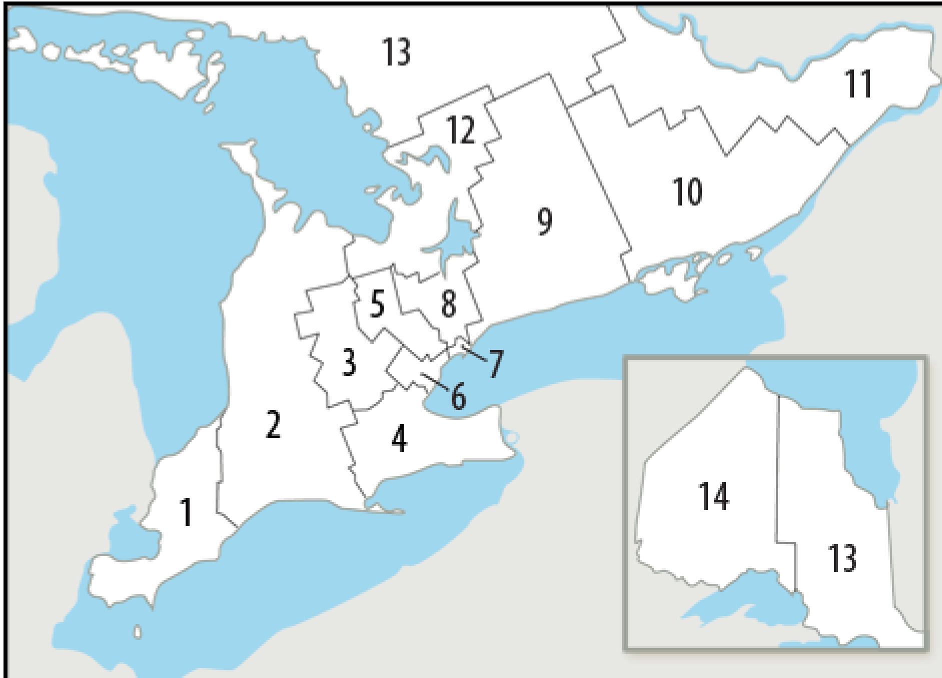
TABLE	DESCRIPTION	MAIN VARIABLES UTILIZED
Encounter Table	Contains a list of all patient encounters within the hospital and allowed for a list of patients to be generated based on specific dates and criteria of interest. This table links to several other tables of interest, including the service table, inpatient census table and the abstract table, among others.	The main variables accessed through this table included; *the encounter unique identifier*, which is an unidentifiable number sequentially assigned to each row of the table which allowed for the identification of each patient encounter and the linking of that encounter with other services and data of interest. The *encounter type code*, which identifies the type of encounter the patient had (i.e. in-patient, emergency, daycare) and was used to determine our population of interest (i.e. those admitted as in-patients to hospital). The *encounter start and end date/time* was utilized to determine if certain laboratory tests were performed within the hospital admission of interest and was also used to correct certain values which were missing or invalid
Service Table	Contains information about services a patient may have received during their hospital encounter (i.e. lab testing, diagnostic testing, pharmacy etc.) and is the highest level table in the service category. The Service Table has eight sub-tables including, radiology services, laboratory services and pharmacy services. This table was mainly linked with the Encounter Table to determine which services were performed for each patient encounter, as well as, to the Service Report Table (houses information on all lab reports), Pharmacy Service Table, and Laboratory Service Table.	The main variables utilized from this table included the *service unique identifier*, for linking purposes, *service performed date/time* which indicates when a service was performed and the *service template unique identifier*, which identifies individual hospital services a patient may have received. For example, a service template unique identifier of '8510' indicates an MRSA screen was performed, whereas, a code of '7065' indicates a blood culture was performed. These codes also translate into other sub-tables of the service table, for example, a code of '12163' indicates that the patient was prescribed a drug called Mupirocin, listed in the Pharmacy Service Table.
Lab Service Table	A sub table of the Service Table and houses laboratory specific information regarding services performed during patient encounters. This table lists specific tests performed, dates the test was performed and laboratory results.	The main variables utilized from this table were the *laboratory specimen date/time* which captures the date and time the laboratory test was performed, and the *service unique identifier* which links to the service table
Service Report Text Table	Another sub table of the Service Table. The Service Report Text Table contains the text or documented results of hospital service reports. For example, it will list the text of reports associated with laboratory results (i.e. Moderate growth of Methicillin-resistant staph aureus detected). Due to the nature of the data in this table when entered into the OHDW, a single report is often several lines of text representing multiple observations for each patient in the table. Therefore, part of the complex SAS code associated with this table included wrapping the text so that it appeared compact and together as a single observation.	The main variables of interest used in this table included the *service unique identifier,* for linking purposes and the *report text* variable which contained the text for the services of interest.
Pharmacy Service Table	A sub table under the Service Table and provides pharmacy specific information regarding drugs received by patients during their hospital encounter.	The main variables utilized in this table were the *service unique identifier*, for linking purposes and the *pharmacy order description* to identify specific generic drugs prescribed to the population of interest.

APPENDIX B DIAGRAM OF OTTAWA HOSPITAL DATA WAREHOUSE



Reference: Ottawa Hospital Data Warehouse

Appendix C Map of Local Health Integration Networks in Ontario



Local Health Integration Network

1. Erie St.Clair
2. South West
3. Waterloo Wellington
4. Hamilton Niagara Haldimand Brant
5. Central West
6. Mississauga Halton
7. Toronto Central
8. Central
9. Central East
10. South East
11. Champlain
12. North Simcoe Muskoka
13. North East
14. North West

Reference: http://www.champlainlhin.on.ca/map.aspx#champlain