The Epidemiology of the Acquisition of Bacteria in Hospitals: A Study Using Data from Hospital Information Systems

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ABSTRACT

Health-care associated infections (HAI) cause significant mortality and morbidity for many hospitalized patients and increase the cost of patient care. The incidence of HAI is particularly high in intensive-care units (ICU), affecting about 30% of ICU patients. The growing implementation and capabilities of hospital information systems provide vast amounts of information that could be used to control HAI, but these resources remain underused for this application. The goals of this thesis were 1) to explore how data from these information systems can be used to enable efficient surveillance of all bacteria types, and 2) to explore the potential of these data to inform infection control efforts by studying bacteria acquisition.

The goals were met in a series of three studies. The 'admission discharge transfer' information system was used to define a cohort of 65,124 patients admitted to two university hospitals (the Montreal General Hospital (MGH) and Royal Victoria Hospital (RVH)) over 2000-2005. Data from the laboratory information system were extracted, linked, grouped and analyzed. The first study demonstrates an approach to deriving population-level information about HAI from data held in hospital information systems and presents prevalence, rates, and time trends of bacteria and antibiotic resistance.

The subsequent studies focus on the 19,343 hospital admissions with ICU stays.

The second study evaluates the impact of a physical intervention: the re-opening of the MGH ICU in a new location with all private rooms, on bacterial acquisition rates. A substantially reduced rate of acquisition of infectious organisms following the intervention was found. Finally, the third study assesses the risk that a patient will acquire MRSA or C.*difficile* from a previous bed occupant who was positive for these bacteria. An increased risk for exposed patients in the RVH was found. At the MGH the risk for exposed patients was elevated only before the intervention to private rooms.

This thesis describes and shows how routinely collected electronic data from hospital information systems can be used to derive updated information on rates of organisms and susceptibility to antimicrobials, study infection control intervention, and support an individual assessment of the infection risk of a patient.

ABRÉGÉ

L'Épidémiologie de l'Acquisition des Bactéries dans les Hôpitaux : Une Étude Utilisant des Données de Systèmes d'Information Hospitaliers

Les infections nosocomiales (IN) causent une mortalité et une morbidité significatives chez les patients hospitalisés et augmentent le coût des soins aux patients. L'incidence des IN est particulièrement élevée dans les unités de soins intensifs (USI), affectant environ 30% des leurs patients. La croissance de l'implantation et des capacités des systèmes d'information hospitaliers procurent une vaste quantité d'informations pour contrôler les IN, mais ces ressources demeurent sous-utilisées pour cette application. Les buts de cette thèse étaient 1) d'explorer comment les données provenant de ces systèmes peuvent être utilisées pour permettre une surveillance efficace de tous les types de bactéries, et 2) d'explorer le potentiel de ces données pour les efforts de contrôle des infections en étudiant l'acquisition des bactéries.

Les buts ont été accomplis par une série de trois études. Le système d'information 'admission congé transfert' a été utilisé pour définir une cohorte de 65 124 patients admis à deux hôpitaux universitaires (l'Hôpital général de Montréal (HGM) et l'Hôpital Royal-Victoria (HRV)) durant la période 2000-2005. Des données du système d'information du laboratoire ont été extraites, liées, regroupées et analysées. La première étude démontre une approche pour dériver des informations à propos des IN au niveau de la population à partir de données contenues dans les systèmes d'information hospitaliers et présente la prévalence, les taux, et les tendances temporelles des bactéries et de la résistance aux antibiotiques. Les études subséquentes se concentrent sur 19 343 admissions dans les hôpitaux avec séjours dans les USI.

La deuxième étude évalue l'impact d'une intervention physique : la réouverture de l'USI de l'HGM dans un nouveau lieu avec chambres privées, sur le taux d'acquisition des bactéries. Une réduction substantielle du taux d'acquisition des organismes infectieux suite à l'intervention a été trouvée. Finalement, la troisième

étude évalue le risque qu'un patient acquiert le SARM ou le *C.difficile* d'un occupant précédent de son lit qui était positif pour ces bactéries. Un risque accru pour les patients exposés à l'HRV a été trouvé. À l'HGM, le risque pour les patients exposés a seulement été évalué avant l'intervention des chambres privées. Cette thèse présente comment la collecte routinière de données électroniques provenant des systèmes d'information hospitaliers peut être utilisée pour dériver des informations sur les taux des organismes et la réceptivité aux antimicrobiens, pour étudier une intervention de contrôle des infections, et pour supporter une évaluation individuelle du risque d'infection d'un patient.

Preface

Format of the Thesis

The format of this thesis is that of a manuscript-based thesis. It was prepared according to McGill University *Guidelines for the Thesis Preparation* found at:

http://www.mcgill.ca/gps/students/thesis/programs/guidelines/preparation/

The thesis consists of a collection of three papers for which I am the primary author, as well as separate chapters: Introduction, Background with a literature review, Objectives, Data description, and Discussion. The three manuscripts are related and complement each other to form a cohesive body of research that addresses the objectives of the thesis. Each manuscript corresponds to a chapter of the thesis. A preamble to each of the manuscripts explains its rationale and its relation to the other manuscripts and to the objectives of the thesis. Corresponding tables and figures are presented at the end of each chapter or manuscript. In addition, the second manuscript is followed by an appendix detailing the statistical approach that could not have been included in the journal article due to space limitations.

The background chapter provides more detailed information for each of the manuscripts in the thesis. Thus there is unavoidable repetition of some material. All publications cited in each of the manuscripts are listed in the References section at the end of the thesis.

Contributions of Authors

The idea of using the hospital laboratory information system (LIS) to generate prevalence information at the population level originated from the complaints of Dr. Peter Goldberg (director, RVH ICUs) to Dr. Vivian Loo (chief, department of Microbiology at the MUHC; her prior role was director of the infection prevention and control program) on the complete lack of capability by the LIS or any other hospital information system to provide summary rates.

This frustration led to the use of data from the RVH and MGH LIS in this research and to the focus on aggregated data at the population level. Dr. Loo's suggestion led to the focus on ICU patients. I further developed the study questions and chose to focus on prevalence of bacteria and bacterial acquisition rather than on infection rates, defined the thesis objectives, and conceived the second and third studies of this thesis.

The design of the studies, and the methods that were used in them were selected or developed by me with the guidance and advice of the thesis supervisors, Dr. David Buckeridge and Dr. James Hanley. The statistical methods were chosen, adjusted, and applied, and the results summarized and interpreted by me, with the guidance of the thesis supervisors.

Dr. Buckeridge obtained the LIS and ADT data, and I obtained the ICU data. I processed and linked all the data, and defined and built the database. Dr. Loo defined the infections groups of interest, determined the assignment of the tests codes into these groups, and grouped organisms into the organism groups that were used throughout the thesis.

I wrote the thesis including all the manuscripts. The thesis supervisors reviewed and edited the thesis and manuscripts both for content and for language. Dr. Loo, Dr. Goldberg and Dr. Ash Gursahaney (director, critical care medicine at the MGH), the collaborators on the manuscripts in this thesis provided clinical expertise, insight on the hospital environment, and input on the interpretation of the results. The collaborators of each manuscript provided feedback on it.

Statement of Originality

The work presented in this thesis constitutes original scholarship and advances the knowledge in the domain of hospital infectious diseases. The thesis contributes to the areas of health informatics and to the research of infection control.

The potential of hospital information systems for surveillance, prevention, and management of HAI is widely recognized but is infrequently utilized. The gap between the potential in the data and the realization of this promise has become a target for discussion and is the result of the considerable barriers imposed by such data. This thesis addresses those barriers, and demonstrates application of the data to the study of acquisition of bacteria in hospitals.

In the first manuscript, I focus on rates of bacteria with the purpose of describing the individualized exposure of patients to bacteria. Generally, studies focus on infection rates regardless of the purpose of the investigation.

The second manuscript describes the rate of acquisition of bacteria following room privatization in an ICU. Although this was studied before, most studies focus on MRSA rates alone, and measured *infection* rates. As a result, many failed to show any improvement and the results are inconsistent. I defined *acquisition* of bacteria rather than infection as the measured outcome, introduced the use of the distinction between exogenous and endogenous bacteria to the study of the impact of an intervention on acquisition of bacteria, and studied the impact for all common bacteria. With one of the study hospitals unchanged, we took advantage of experiment-like conditions and compared before and after rates in two hospitals using a semi-parametric model.

The third manuscript describes the risk of acquiring MRSA and *C.difficile* from a previous bed occupant positive to these organisms. To my knowledge, the risk had not been assessed for C.*difficile* in any published study. A single study which assessed this risk for MRSA did not consider important potential confounders.

Although this work would not have been possible without the guidance of the thesis supervisors and the input of the collaborators, the studies presented in the forthcoming chapters represent my own original work.

Statement of Financial Support

Various sources of financial support enabled me to pursue my doctoral studies. I am grateful for having received twice the Research Institute of the MUHC Studentship Award, and twice the McGill Faculty of Medicine Studentship Award. Dr. Buckeridge provided complementary funding which I am very grateful for. I am also thankful to have received funding from the CIHR New Emerging Team Grant and from a Max Stern Recruitment Fellowship Research Award from McGill University.

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I am heartily thankful to my thesis supervisors. I could not thank enough Dr. Jim Hanley, for his support, advice, and mentorship ever since he encouraged me to become part of the program when I first stepped into his office upon arriving in Montreal, to the very last days of the completion of this thesis. His enthusiasm in sharing insights and intuitive understanding of the most complicated concepts and statistical methods contributed to my training more than any formal teaching. I offer my sincere thanks to Dr. David Buckeridge. His thorough knowledge and understanding of informatics and infectious diseases in addition to epidemiology contributed tremendously to this work. His ability to better articulate any idea I expressed both in conversation and in writing improved my own skills and will always remain for me something to aspire to. I could not have asked for better supervisors.

I would like to extend sincere thanks to my collaborators including Dr. Peter Goldberg, whose dissatisfaction with the hospital information systems triggered the research plan. His clinical insight was invaluable. I would also like to thank Dr. Vivian Loo for her clinical expertise and for taking time from her busy schedule to sort through hundreds of test codes and helping me navigate through the maze of hundreds of bacteria names. I would also like to thank Dr. Ash Gursahaney for his time and clinical insight. I also thank Dr. Robyn Tamblyn, who recognized the potential in these data and first introduced me to Dr. Loo.

Sincere thanks to the administrative staff in Purvis, in 1140 Pine and in the hospitals, who helped with the challenge of working on the thesis remotely. A special thank also to Isabelle Lussier; with her help the ICU archives were the only pain free part of the data.

I am grateful for the fellow graduate students and friends who shared the PhD road with me. A huge thanks to Ella Huszti for giving me a base in so many visits to Montreal. A special thanks also to Raluca Ionescu-Itto for her help with the

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Finally, and most of all, I thank my husband, Alex for his love, enormous support and encouragement, and for always believing in me.

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Chapter 1 Introduction

Health-care associated infections (HAI) cause significant morbidity and mortality in hospitalized patients, and increase the cost of patient care. HAI affect approximately 2 million hospitalized patients each year in the United States (1) and are estimated to cost between 28 billion and 45 billion US dollars per year (2). In 1995 alone, nosocomial infections contributed to an estimated 88,000 deaths in the US (3); in Canada, a 2002 point prevalence survey within the Canadian Nosocomial Infection Surveillance Program (CNISP) found a HAI prevalence of 10.5% infected patients (4) resulting in an estimated excess of 8,000 deaths each year (5).

Intensive-care unit (ICU) patients are especially vulnerable to HAI. Healthcare associated infections occur in about 30% of ICU patients (6) and are associated with an increased length of stay (LOS) of 8-9 days (7) which costs an estimated 3.5 billion dollars per year in the United States (8). Ventilator associated pneumonia alone adds approximately 17,000 ICU days per year in Canada, and costs an additional estimated 46 million dollars per year (9). The rates of antibiotic resistance among bacteria that cause HAI are increasing with time (10), and this increase in resistant bacteria will increase the burden of HAI (11).

Current information on rates of bacterial infections and antibiotic resistance is crucial for empirical selection of antimicrobial therapy and is critical for infection control efforts. Changes over time, and variation among hospital wards and groups of individuals (12) in prevalence of bacterial infection and resistance make constant surveillance of HAI an important component of a comprehensive infection prevention and control programs (13). Manual surveillance is however labor-intensive, slow, and expensive, and cannot provide full, constant and updated monitoring of all bacteria rates in all sites.

There exists a considerable, and largely untapped, potential to obtain surveillance information on HAI from the growing number of increasingly sophisticated hospital information systems(14;15). Using these electronic data automatically should enable rapid and low-cost surveillance of all bacteria types. However,

most laboratory information systems were not designed to allow easy extraction of aggregated, standardized data for infection control purposes. Surveillance data at the population level and prevalence information for infection control personnel are not easily derived from the individual patient data in these systems and there exist no common mechanisms for extracting and transforming individual clinical data into aggregated data to support hospital epidemiology.

The first manuscript in this dissertation explores the steps needed to derive population level information from hospital information systems, and presents rates of bacteria and antibiotic resistance. Detailed information on the exposure of patients to bacteria in different hospital locations, and specifically in the ICUs, together with rates bacterial acquisition has the potential to advance infection control efforts.

One important control measure that is becoming more widespread is the construction of private ICU rooms. Such rooms may reduce the acquisition of certain pathogens, but the limited evidence on this topic is inconsistent (16-20). I take advantage of a window of opportunity that arose during the time-period I studied. In one of the two university hospitals I studied the ICU was reopened in a new location within the hospital and with all private rooms, replacing the older ICU which had two rooms of 12 patients each. A comparison of rates before and after the privatization with the rates in the ICU of another university hospital, while taking other factors and trends into account provided an opportunity to assess the effect of the intervention on acquisition rates. The breadth of the data available in hospital information systems provided an opportunity to study the effect of this intervention on the acquisition of all likely exogenous and exogenous/ endogenous organisms, in contrast to previous studies which focused on specific organisms. The second thesis manuscript describes the conduct and results of this study.

Residual bacterial contamination can persist in rooms, even after current cleaning practices are followed. However, transmission from previous room occupant to present occupant, although it can be mediated by health workers, is largely

environmental. This potentially important route of transmission has not received much study. MRSA and *C.difficile* are at the focus of infection control efforts, and are considered 'environmental'. Only one study has linked MRSA acquisition to MRSA in previous room occupant, but it did not account of potential bias due to selective room assignment and to confounding by prevalence. No studies have examined the potential risk of *C.difficile* from a previous patient who was colonized with the pathogen. In the third manuscript of this dissertation, I used the data from the same two university hospital ICUs to assess the risk that a patient will acquire MRSA or *C.difficile* from a previous bed occupant who was positive for these bacteria. Studying two ICUs in two hospitals that share infection control policies and cleaning practices, but have different physical infrastructure and patient populations, provided an opportunity to study potential modifiers for this risk.

Chapter 2 Background and Literature Review

2.1 Hospital Acquired Infections

The Center for Disease Control and Prevention (CDC) defines hospital acquired infections (HAI) for the purpose of surveillance in the acute care setting as a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s) (21). There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting. The CDC criteria of an HAI that are applied in the CDC-NNIS surveillance reports (22), and define an infection as hospital acquired if the onset is more than 48 hours after admission to the hospital, are derived from this principle. The term "HAI" has replaced the term "nosocomial", which is considered less generic.

HAI may be caused by infectious agents from endogenous or exogenous sources (21). Endogenous sources are body sites, such as the skin, nose, mouth, and gastrointestinal tract, or vagina that are normally inhabited by microorganisms. Exogenous sources are those external to the patient, such as patient care personnel, visitors, patient care equipment, medical devices, or the health care environment.

The CDC sets criteria for specific types of infection by body systems, and their reporting(21). Types of infections include urinary-tract infection, surgical site infection, bloodstream infection, pneumonia, bone and joint infection, central nervous system infection, cardiovascular system infection, eye, ear, nose, throat or mouth infection (EENT), gastrointestinal system infection, lower respiratory tract infection other than pneumonia, reproductive tract infection, skin and soft tissue infection, and systemic infection.

HAI affect approximately 2 million hospitalized patients each year in the United States(1) and are estimated to cost between 28 billion and 45 billion US dollars per year (2). In 1995 alone, nosocomial infections contributed to an estimated 88,000 deaths in the US(3) and the burden of HAI increases with the rise in resistance bacteria(11) In Canada, a point prevalence survey within the Canadian

Nosocomial Infection Surveillance Program (CNISP) found a HAI prevalence of 10.5% infected patients(4) resulting in an estimated excess of 8,000 deaths each year (5). Ventilator associated pneumonia alone adds approximately 17,000 ICU days per year in Canada, and costs an additional estimated 46 million dollars per year (9).

A cornerstone to the efforts to prevent HAI has been surveillance for HAI, so that the impact of infection control measures can be measured, risk factors assessed, treatment regimes optimized, and resources planned.

2.1.1 Manual Surveillance of Hospital Infections

Surveillance of (HAI) is an important component of comprehensive infection control and prevention efforts (13). The CDC has conducted surveillance of HAI since the 70th. The SENIC study in the 1970th confirmed the effectiveness of surveillance on reducing rates of HAI (13). It found an overall infection rate increase of 18% from 1970 to 1976, but also found that hospitals with effective infection control measures, that were not common back than, reduced hospital infection rates by 32%.

The most commonly used definitions for reporting HAI are the ones which were developed and used by the CDC. The CDC reports rely on manual collection of data based on HAI case definitions and methodology (23) developed by the CDC National Nosocomial infections Surveillance System (NNIS). The NNIS is an on-going collaborative surveillance system sponsored by the CDC to obtain national data on nosocomial infections (22). The data are used to estimate the magnitude of the nosocomial infection problem in the United States and to monitor trends in infections and risk factors.

Many surveillance studies are conducted regularly; among them are large studies that took place in Canada, in the US, and internationally. The SENTRY program is an international antimicrobial surveillance program funded by an educational/research grant from Bristol-Myers Squibb (24). Since 1997 it has

monitored pathogen frequency and antimicrobial susceptibilities in hospitalized patients. The specimens for the study were collected by participating hospitals and selected based on clinical criteria from the laboratory results of each month. The study results were reported through dozens of papers focusing on different pathogens, infections, antimicrobials, patient groups, and geographical areas.

The Canadian Ward Surveillance Study (CANWARD 2007) (25) is a national study of inpatient and outpatient pathogens and their resistance to antibiotic of blood, respiratory, urine and wound infections. The most common organism isolated from the Canadian hospitals in this study were (by % of total isolates) *Escherichia coli* 21.6%; Methicillin-sensitive *Staphylococcus aureus* (MSSA) 13.9%; *Streptococcus pneumoniae* 8.9%; *Pseudumonas aeruginosa* 8%; *Klebsiella pneumoniae* 5.8%; MRSA 4.9% *Haemophilus influenzae* 4.3; and CNS/*Staphylococcus epidermidis* 4% (26).

The gold standard for surveillance is prospective active surveillance. Although not as accurate as the traditional prospective method, prevalence surveys can provide baseline information about the occurrence and distribution of HAI within a healthcare institution (4). CNISP is a collaborative effort of the Canadian Hospital Epidemiology Committee, a subcommittee of the Association of Medical Microbiology and Infectious Disease Canada and the Public Health Agency of Canada (PHAC). Twenty-five acute-care CNISP member hospitals in eight provinces participated in a one-day HAI point prevalence survey occurring on any day between 5 and 8 February 2002. The study found a HAI prevalence of 11.6% (4) which was low compared to other studies.

Manual surveillance plays an essential role in infection control and prevention, but, the process of manually reviewing patient records, or sampling patients for the purpose of surveillance, is labour intensive, slow, and expensive, and even investing in frequent large scale studies cannot provide full, constant and updated monitoring of all bacteria rates in all sites.

2.1.2 Electronic Surveillance of Hospital Infections

The advantages of reliable automated surveillance of hospital infections are obvious in terms of speed, scope and cost of updated information. The potential to automate part of the surveillance process, and therefore attempts to exploit electronic data, have grown together with the increase in information system implementation in hospitals. Evans et al (27) demonstrated the potential of information systems utilization for infection control in hospitals in 1986, with an alerts system.

However, the progress has been slow and in most hospitals not only is this advanced functionality not available, but basic surveillance based on electronic data is not a common practice. Discharge codes have been available electronically in many hospitals, but they were found to be unreliable for HAI surveillance (28). Most electronic surveillance systems are based on positive microbiology culture results in laboratory information systems. But, as the goals of most systems are to track infection rates, identify early disease clusters, or alert on notifiable infections, correctly identifying hospital acquired infections in the data is the primary focus.

Different algorithms have been designed to address this challenge, aimed at distinguishing colonizations from infections and identifying primary acquired infections. An early example is the HELP system (29), developed in Salt Lake City, which utilized microbiology laboratory data and admission dates in a rule based system to identify hospital acquired infections with good accuracy. Another expert system was called the GermWatcher and was developed in Barnes hospital in 1990. It offered a similar functionality to the HELP system and in addition produced reports on positive cultures that were likely infections (30;31). Today, commercial applications to alert on significant positive tests are more common, and are usually based on simple rules that were shown to be reliable (30;32). Other systems have been developed to automate different aspects of surveillance such as cluster detection, or surveillance of specific types of infections (33;34).

New systems are being developed that can integrate input from additional electronic resources, such as radiology reports with free text (35), and new algorithms to better identify infections and even to identify transmission (36). Genetic data, which are likely to become more commonly available, have the potential to improve detection of transmission, and also to distinguish new infections from repeat infections in the same patient.

A comparison of these electronic-based results to rates from surveillance studies of infections is problematic. Infection rates that are estimated from electronic systems are necessarily different from those used in manual surveillance as they are based on different definitions. Woeltje et al. (37) go as far as to suggest that the terminology of 'electronic rate' or 'electronic index' to clarify that the HAI rate derived electronically cannot be directly compared with traditionally manually determined rates even when definitions are carefully followed.

2.1.3 ICU Acquired Infections

Patients who are admitted to the ICU are 5 to 10 times more likely to acquire an infection than other hospitalized patients (38). HAI occur in about 30% of ICU patients and are associated with substantial morbidity and mortality (6). In ICU patients, these infections are associated with an increased length of stay (LOS) of 8-9 days (7), and the resulting additional cost from excess stay alone is estimated at 3.5 billion dollars per year in the United States (8).

ICU patients are a vulnerable population, and are very susceptible to infections. The EPIC I and II studies (Extended Prevalence of Infection in the ICU) are point prevalence studies. EPIC II was conducted on May 2007 and included patients from 1265 ICUs (39). On the day of the study, 51% of the patients were considered infected; microbiological culture results were positive in 70% of the infected patients. However, not all infections were ICU acquired.

Patients develop infections while in ICUs both from organisms they were already colonized by when admitted to the ICU, and from organism they acquire while at

the ICU. Many studies that report infection rates in ICU patients do not have the data to estimate if the organisms that cause these infections were ICU acquired. The prevalence of organisms in a unit determines patient exposure to potentially new bacteria. The SENTRY study included a report on pathogens and resistance profiles among ICU patients (40). It included blood, respiratory tract, urine, and wound sites specimens from 25 ICUs in North America. *Staphylococcus aureus* was the most common pathogen (24.1%), followed by *Pseudomonas aeruginosa* (12.2%), *Escherichia coli* (10.1%), *Klebsiella* spp. (8.9%), *Enterococcus* spp. (7.2%), Coagulase-negative *Staphylococci* (7%) and *Enterobacter* spp. (7%).

In a study of the acquisition and cross‐transmission of *Staphylococcus aureus* in different ICUs (41), higher colonization pressure and a greater number of beds per nurse correlated with a higher rate of acquisition for both MSSA and MRSA. The type of ICU setting (private vs. bay rooms) affected MRSA acquisition only, and the amount of hand disinfectant used affected MSSA acquisition only. In 40% of the cases of *S. aureus* acquisition, cross‐transmission from another patient was possible.

The incidence of infections caused by antibiotic-resistant pathogens in ICU patients is increasing (42). These pathogens include MRSA, VRE, and extended-spectrum β-lactamase-producing Gram-negative bacilli. In most cases resistant pathogens are acquired by patients during the hospital stay, often during an ICU stay (43).

In order to reduce transmission of resistant bacteria, an effective infection control program has to be in place (44). Isolation of patients is an important part of such infection control programs.

2.1.4 MRSA in ICU Patients

MRSA is a coined acronym term for the pathogen, *Staphylococcus aureus*, which has developed broad-based resistance to β-lactam antibiotics. Methicillin (or oxacillin) resistance has been universally accepted as a descriptor to indicate

the β-lactam resistant phenotype of this staphylococcus (45). It was first described in 1961, but became a major problem starting on the 1990s and has increased in prevalence since then. MRSA studies sometimes separate the hospital-acquired strains (HA-MRSA) from the community-acquired strains (CA-MRSA), but following Lin et al. (46), because they seem to cause a similar spectrum of nosocomial infection in ICUs and because few prior epidemiologic studies of MRSA have distinguished between the strains, I will discuss both together as MRSA.

Staphylococcus aureus (*S. aureus*) is a gram-positive coccus that grows in pairs, short chains and clusters, cocci, and can be found in the colonised (or carriage) state on skin and in nasal passages in a large fraction (25% – 30%) of the healthy population (45). It has a good ability to adapt to hostile environments.

Studies that perform serial surveillance cultures for MRSA, upon hospital admission and at regular intervals thereafter, have provided estimates of both MRSA admission prevalence and incidence (acquisition rate) in ICUs. In U.S. adult ICUs, the average admission prevalence of MRSA colonization is around 8% (46). Marshall et al. found a 7% colonization rate on admission to the ICU and an 11% acquisition rate during the ICU stay (47). The 2003 National Nosocomial Infections Surveillance (NNIS) System Report showed that from January 1998 through June 2003, 26% of all S. *aureus* isolates from outpatients were methicillin-resistant, 42% of all S. *aureus* isolates from non-ICU inpatients were MRSA, and 52% of all S aureus isolates from ICU patients were MRSA(22). MRSA is rapidly becoming a common pathogen in ICUs worldwide; a 1992 study on the prevalence of S aureus infections in over 1400 European ICUs showed that S aureus was responsible for 30% of all ICU infections; of these 70% were caused by MRSA (48).

MRSA causes skin and soft tissue infections, complicated urinary tract infections, kidney infections, catheter-associated infections, bacteremia, endocarditis and respiratory tract infections (including hospital ventilator-associated pneumonia) (45). Compared with MSSA infections, MRSA infections are associated with

increased morbidity and mortality in critically ill patients (38;49). Infections due to MRSA are also associated with prolonged length of hospital stay, and increased costs (49).

2.1.5 *C.difficile* in ICU Patients

Clostridium difficile (*C.difficile*) is a toxigenic, spore-forming anaerobic bacterium that is the primary cause of health care facility-associated diarrhea in North America.

Clostridium difficile-associated disease (CDAD) is defined by the presence of diarrhea and a positive assay for *C. difficile* toxin A, toxin B, or both.

In the United States, the number of hospital discharges for which C.difficile infection was listed as one of the diagnoses increased from 82,000 in 1996 to 178,000 in 2003 and to more than 250,000 in 2005, and there was an increase in severity of the disease. (50). Much of the change in CDAD epidemiology is thought to be because of the emergence of a hypervirulent, epidemic strain, (known as the North American PFGE type 1, restriction enzyme analysis type BI, and PCR ribotype 027 (NAP1/BI/027)), which caused CDAD outbreaks in a number of hospitals in Quebec from late 2003 through 2004 (51). The exact cause of hypervirulence in this train is not known; however, the strain does produce greater levels of toxins A and B in vitro and produces an extra toxin known as binary toxin. This strain was uncommon as a cause of human disease prior to 2001 but has become widespread coincident with its development of high levels of fluoroquinolone resistance (50;51).

The mortality rate associated with *C.difficile* diarrhea has been estimated at 25-28% (51;52). Age-specific incidence of CDAD increased markedly after the age of 50 years and the attributable mortality rate increased after the age of 60 years (51). CDAD was associated with $5042-$7179 (48%-53% increase in cost) attributable inpatient costs over 180 days (53).

Previous antibiotic exposure was an important risk factor for patients who develop the disease during a hospital stay (54). Specifically, previous use of fluoroquinolones increased the risk of CDAD (55). Other risk factors were CDAD-associated disease pressure (see section 2.3), histamine-2 blockers, proton pump inhibitors, and IV vancomycin, while previous use of metronidazole had a protective effect (55).

Potential sources of infection for susceptible patients (potential reservoirs) are cross infection between patients, the environment, and carriage on the hands of hospital personnel. Handwashing with soap and water was found to be superior to alcohol-based handrubs in removal of *C.difficle* on hands (56). Skin contamination often persists on patients' chests and abdomens after resolution of diarrhea (57), so isolation of patients has been recommended beyond the duration of diarrhea.

2.2 ICU Private Rooms and the Rate of Infections

Isolation of ICU patients in private rooms is a common infection control recommendation intended to limit the transmission of infectious organisms to patients by facilitating better infection control practices by health care workers (58) and allow for better isolation of patients from hospital-borne infectious agents (59). It is hypothesized that single rooms facilitate more frequent hand washing by health care workers and are also easier to clean (59;60). In units comprising a mix of private and non-private rooms, the private rooms serve as isolation rooms and infected or colonized patients are transferred in and out of these rooms in order to isolate them or protect other patients from them. Units that comprise only single rooms reduce the number of these patient transfers which leads to reduced exposure of patients to cross transmission.

Current guidelines on the design and construction of hospitals and health care facilities, issued by the American Institute of Architects for health with assistance from the U.S. Department of Health, recommend single-patient rooms in new constructions and in renovations (61). A literature review from 2007 that

examined the benefit from single rooms to hospitalized patients on multiple outcomes found a moderate effect on patient satisfaction with care, noise and quality of sleep, and the experience of privacy and dignity, but found conflicting results on hospital infection rates (18). This study also found that many of the reviewed opinion-articles advocated the concept of single rooms mostly by reasoning instead of by evidence. In the conclusion of the study, the authors recommend that the gap between research and policy should be bridged.

In a systematic review, only 3 of 8 studies reviewed found a statistically significant reduction in the rate of infections in ICU patients following an intervention to change the facilities' architecture (20). Cepeda et al. found that isolation of ICU patients in a private room did not decrease the rate of MRSA acquisition (16). Their study however was based on transfer of patients to private rooms for isolation upon colonization, not on continued stay in private rooms. Bracco et al. found reduced rates of MRSA, *Pseudomonas aeruginosa,* and *Candida* acquisition in ICU patients in single rooms compared to bay rooms (17). Most previous studies were limited in their scope to specific types of bacteria or infection. The majority examined MRSA (20) and only a few studies considered the effect of a physical intervention on vancomycin resistant *Enterococcus* (VRE) (62) and *C. difficile* (63). Preston et al. studied the effect of conversion of an ICU from an open unit to isolation rooms on acquisition rates of several organisms (64). Despite the fact that patients were screened every four days, and several organisms were considered, no reduction in acquisition rates was evident. They attributed this lack of improvement to insufficient hand washing by health care workers.

In summary, results from studies are inconclusive regarding the effect of private rooms on infection rates and there is a gap between evidence and policy.

2.3 Transmission of Bacteria in Hospitals

The factors that influence the acquisition of an HAI bacterial infection are a patient's individual level factors such as age, severity of illness and co-

morbidities, and as a precursor, whether the patient is colonized with the bacteria in question or the patient is otherwise exposed to it. The factors that influence patient's colonization with bacteria are facility-level factors(65). These factors are: hand disinfection, use of gloves, gowns, and masks, isolation of colonized patients, crowding, nurse-patient ratios, health care workers compliance, patient attitude towards isolation, and environmental contamination.

Colonization pressure represents the prevalence of bacteria in the surrounding environment of the patient that can lead to patient-to-patient transmission. The importance of 'Colonization pressure' as a risk factor for bacterial transmission was first described by Bonten et al. for VRE (66). Colonization pressure was found to the most important variable affecting acquisition of VRE. The study by Merrer et al. on a medical ICU found weekly colonization pressure, defined as the fraction of MRSA positive patient days out of the total number of patient days, to be the only independent predictor of MRSA acquisition (67). The risk of MRSA acquisition was 5.8 times higher (95% CI 1.7, 20.1) when colonization pressure was over 40% compared to when it was less than 10%. Risks increased gradually with the increase in colonization pressure. A modified form of colonization pressure was an important risk factor for CDAD (68), which was chosen because screening of C.difficile asymptomatic carriers is not part of most routine infection control practices. In another study (69) physical proximity to a patient with CDAD, especially in a neighbouring bed, was found to be a risk factor for acquisition of CDAD with a risk ratio of 3.4 (95% CI 1.95, 5.9). The risk from a roommate with CDAD was not as high, and the risk according to the colonization pressure was not studied.

Colonized and infected inpatients are the major institutional reservoir and are responsible for the colonization of their environment. Transient carriage on the hands of hospital personnel is the most common mechanism of patient-to-patient transmission for MRSA(70).

Several studies proposed algorithms for the analysis of transmission of bacteria in hospitals. Pelupessy et al. suggest an algorithm using a Markov chains model to

assess the relative importance of different colonization routes of pathogens (71). They tested the algorithm on datasets on VRE and Pseudomonas with genotyping information, and obtained a good estimate of the percent of cross-transmission. Bootsma et al. estimated the importance of the endogenous bacterial acquisition route vs. the exogenous one of third-generation cephalosporin-resistant Enterobacteriaceae in two ICUs using a Markov model (72). The analysis using traditional statistical methods agreed with the result of the model on the endogenous route being the predominant one. Cooper et al. suggested a method for analysis of nosocomial infection data, including estimation of transmission (36). Their approach used Markov chains Monte Carlo algorithm (in a Bayesian framework) and it was applied to illustrative data of VRE transmission. These algorithms show promise, and could be used as a tool in infection control investigations, but in the present, demand more adjustment and careful consideration than can be implemented in an automated system for surveillance of electronic data.

2.3.1 Residual Contamination

Patients who are colonized or infected with organisms that are 'environmental', such as MRSA, VRE, *C.difficile*, or *Acinetobacter* shed these organisms onto surfaces in their immediate environment (73;74).

Certain nosocomial pathogens, including MRSA and *C.difficile* spores, can persist on inanimate surfaces for weeks or even months (75), and may not be eradicated by conventional cleaning (76;77). Bacteria contaminate furniture including bed rails, curtains, and surfaces, medical equipment, gowns and gloves of healthcare workers, and computers keyboards and mice (46;78-81).

The bacteria can than be transmitted to new patients directly or through the hands of healthcare workers (82;83). Indeed, one intervention to improve cleaning practices reduced patient acquisition of VRE (84). Physical proximity increased transmission risk: sites near a colonized patient were more frequently

contaminated, and sites close to the patient hand-touch were regarded as a particular risk (81).

2.3.2 Acquisition from Previous Bed Occupant

Only one previous study assessed the risk of MRSA acquisition to MRSA in the previous room occupant (85). In this study Huang et al. studied the risk of acquisition of MRSA and VRE in ICU patients in 8 hospitals using a retrospective cohort. They found an adjusted odds ratio of 1.4 (95% CI 1.0, 1.8) of MRSA acquisition among patients whose prior room occupant was MRSA positive compared to patients whose prior room occupant was MRSA negative. For VRE the odds ratio was 1.4 (95% CI 1.0, 1.9). Fourteen percent of ICU bed occupants had a prior occupant who was MRSA positive. These patients' risk of MRSA acquisition was 3.9% vs. a risk of 2.9% in the non-exposed. The excess risk accounted for 5.1% of all incident MRSA cases. Patients' age, the pre-ICU hospital length of stay, and leukemia were predictors of MRSA acquisition, in addition to the prior occupant MRSA status. The paper does not report prevalence (over the 20 months of the study), or room assignment being considered as possible confounders.

While one other study (in addition to Huang et al.) reported risk from previous VRE colonized room occupant (85;86) no previous study assessed this risk for *C.difficile*.

In summary then, there are large gaps in our knowledge regarding the transmission of bacteria in hospitals, and specifically in ICUs. The upcoming chapters show how, once the under-utilized data in HIS have been harnessed some of these gaps can be addressed.

Chapter 3 Study Objectives

The objectives of this thesis were to:

1) Explore how data from hospital information systems can be used to enable parallel efficient surveillance of all bacteria types.

2) Explore how these data could inform infection control efforts by studying bacteria acquisition.

Chapter 4 Data Description and Processing

The data for this thesis were extracted from three hospital information systems at the McGill University Health Centre (MUHC): the laboratory information system (LIS); the admission, discharge, transfer (ADT) information system; and the ICU information system. All the data were recorded in these sources systems as part of routine clinical care. The data, availability, and data fields are described in the data description section.

The main barriers to widespread use of similar data are the ability to access and process the data. The data in the laboratory information system are generated through the routine processing of specimens. Data are stored as records of transactions with the system, and the system is designed to allow humans to read data on screen, one record at a time. Unfortunately, the data are not recorded in a standard manner, and this lack of a uniform structure poses a great challenge to automated processing of the data, while the volume of the data makes non-automated processing infeasible. Although the problems that make these data difficult to process are pervasive across hospital information systems, the processing itself had to be tailored to the local implementation. The processing of the data used in this dissertation is described in the data processing section and examples of the records can be found in Appendix 2. A relational database was built to store the data, because it enables fast and flexible querying of the data, as well as reliable and efficient storage. The description of the database can be found in Appendix 1.

We grouped the tests in the LIS by body systems and specific organisms according to the codes that were used to order the tests. In some cases, additional fields, such as the body site from which the test was obtained, were used to complete the definition. The complete list of test groups, codes, and frequencies used in this research can be found in Appendix 3. Bacteria were grouped into groups of organisms. The complete list of bacteria and bacteria names as appear

in the records, and their grouping can be found in Appendix 4. The list of names used in the records for antimicrobials can be found in Appendix 5.

Data Description

Microbiology lab tests orders and Microbiology lab tests results

Availability: 1/2000 - 12/2005 from the RVH and the MGH. 704,477 tests were ordered; (439,080 in the RVH; 265,397 in the MGH). 661,770 of these were ordered for inpatients (390,150 RVH; 271,620 MGH).

Data were generated as part of routine clinical care. The lab results were reported electronically through a lab information (and management) system (LIS or LIMS), no paper trail was generated. The data are entered as part of routine specimen processing. Drop-down menus are available as the laboratory technician enters data, but free-text data entry is also possible.

Fields: Patient Medical Record Number (MRN); Patient type (inpatient, outpatient); Type of test; Description; Order date; Specimen source; Specimen site; Specimen location; Date received; Date reported; Results: Isolates, infectious organism, antibiotic resistance.

Admission Discharge Transfer (ADT)

Availability: 1/2000 - 12/2005 from the RVH and the MGH. 381,186 records (277,802 RVH 103,384 MGH).

Fields: MRN; Sex; Date of birth; Case number (of hospitalization); Location: ward room and bed; Admission date and time; Discharge date and time.

ICU

Availability: RVH from 4/2000 to 12/2005. 2298 complications; 2478 infections upon admission. MGH from 2/2003 to 12/2005. 1436 complications; 579 infections upon admission.

The information is entered at the end of each day by a medical data archivist based on paper records and electronic information on tests orders and results.

Fields: MRN; Age; Sex ; Date of ICU admission; Date of ICU discharge; Operative status; ICU admission Dx Code; ICU admission Dx Description; Secondary ICU admission Dx Code; Secondary ICU admission Dx Description; Complication Code; Complication; Complication Date; Patient's origin; ApacheII; GCS; ICU Team; ICU Attending; Allergies; Immuno-compromised.

Data Processing and Database Development

Database definition

A relational database model was used and the database schema was defined to support a decision support database with minimal redundancy permitted. The main entities were defined as patient, bacterium, antibiotic (the set that appear in the susceptibility testing), beds location, ICU admissions indication, ICU complication, microbiology tests type, and hospital service. Relations were defined to describe ordered cultures, the different results of the test, infections of ICU patients, etc. For example, the relation of patients with beds locations (and a date attribute) is used to represent ADT data. Constraints are defined only in the database building process, not on the tables.

I used MYSQL database on Linux. The schema was defined in SQL using the emacs editor. See Appendix 1 for the entities-relationships diagram.

Data parsing and entry into the database

The data from the microbiology system and the ADT system were available only as large text files containing 'screen dumps' of the entire set of records as one file. The files were parsed using a custom computer program to identify records, and to process the information in each record. Examples of the records can be found in Appendix 2. The ICU data were available as consistent comma separated values (CSV) (or Excel Files) which made the processing more straightforward. Almost no data cleaning was necessary for the ICU data. Parsing was performed using Perl.

The records of the orders of the tests and the ADT records were parsed to separate fields, but were consistent in their structure.

The microbiology lab tests results were available in the form of large files of screen shot "dumps" extracted from a mainframe computer. The records followed a general structure, but the format of each record varied by the hospital, the date and in many cases by the type/code of the test (there were more than 400 types; relevant tests can be found by groups in Appendix 3). The records also included free text with typographical errors, alternative spelling of names (see lists in appendices) and special tabs which added to the complexity of the parsing. The number of the records – more than 600,000 tests with a valid specimen, out of more than 700,000 tests that were ordered, required the processing to be fully automated.

Validation of the processing

Validation of the automated parsing was performed to ensure the consistency and completeness of the data and the data processing. Validation of the data processing was performed both automatically and manually.

Automated validation included comparison of the number of records of orders and results, the use of detailed logs of the parsing process with automatic and manual examination of the log files, and checking of every record for which the parsing process failed. The original records are stored in the database and were used routinely to verify the accuracy of the parsing. No errors were detected through this continues validation which included hundreds of records.

Manual validation included sampling records of the original data files for each type and format, and manually comparing that the resulting database records were correct and complete.

Records indexing and linkage

The medical record number (MRN) was used as a unique key for each patient, to identify data from different sources on the same patient. The case number - the number of the hospitalization together with the hospital name, is a unique key for a hospitalization. Each test has a unique identifier within each hospital. A unique specimen was identified by the key for the test combined with the name of the agent found. Each report of antibiotic susceptibility was identified by the isolate and the name of the tested antibiotic. Within each hospital the location name was a unique key for each hospital bed.

Each data source was parsed separately, and inserted into one or more database tables. No additional linking was required.

Data storage, management, and security

Once built, the database does not have to be updated unless new data are added. Some fields, such as groups and flags, might be updated if data definitions are changed. Data for more hospitals or more years could be added using the existing software if provided at the previous formats.

The original data files as well as the database were stored on a secure server. Access to the data was by secured connection only, and physical as well as electronic access is limited to authorized personnel only.

Data Definitions

Test types by codes

The microbiology lab tests were ordered using codes that describe the test type in the system. The data included tests that were ordered using 420 different codes, representing the method of testing, suspected organisms, method of procuring the test, and sometimes information on the body site. The codes that were used and the frequency of their use also varied between the hospitals.

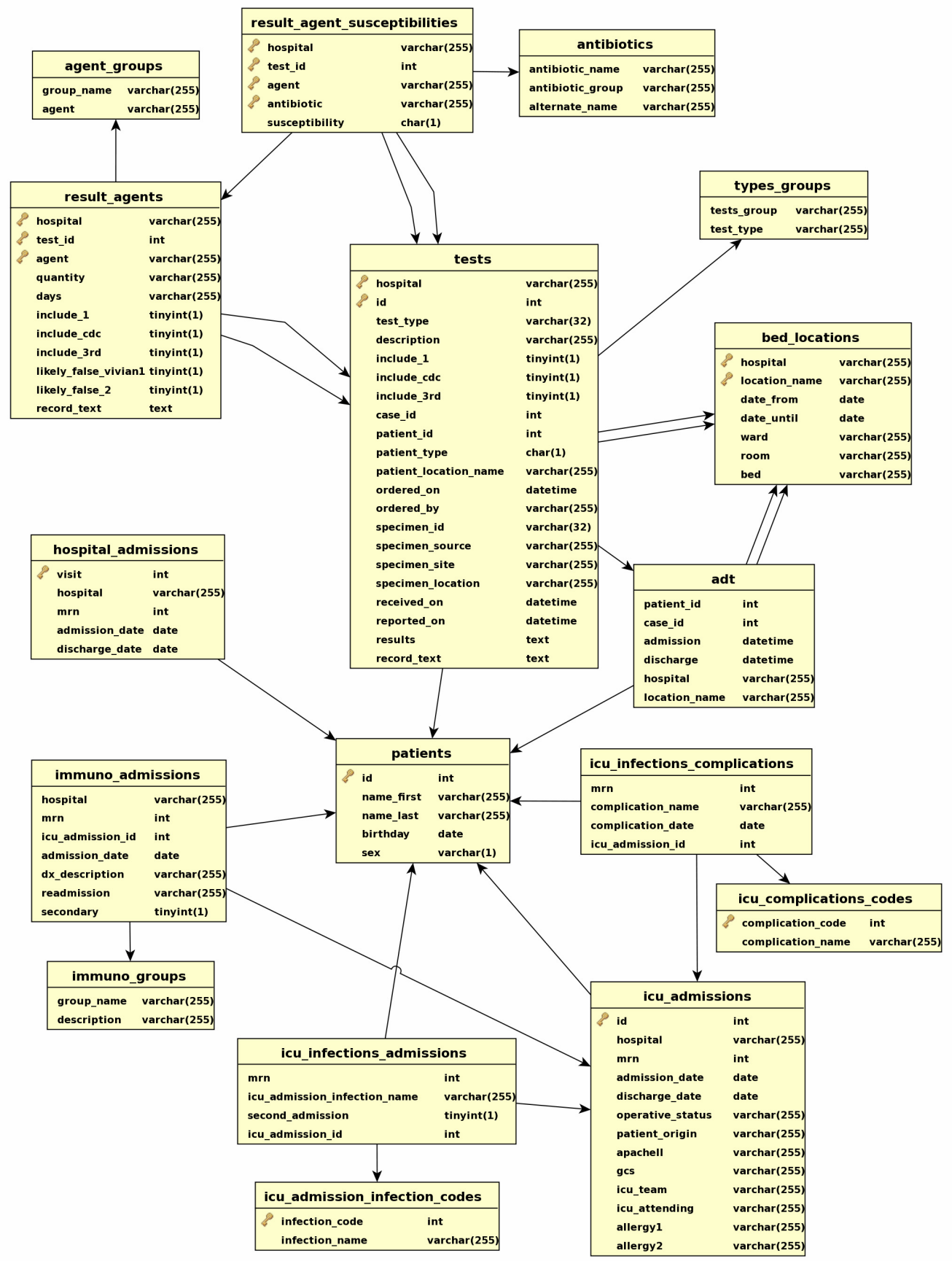
Grouping of tests

All the codes were reviewed with a microbiology and infectious diseases expert. The 65 codes for bacterial testing were categorized into 13 groups representing body systems, specimen source (blood, urine), or specific bacteria of special interest for infection control: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus* (VRE) and Clostridium *difficile* (C.*difficile*). Many of the codes did not map to any of these groups, and represent tests that are not in the scope of any of the studies. Such codes included codes for ordering tests for viruses, screening blood bank products, and ordering tests for fungi and parasites. The list of the groups, codes in each group and frequencies of tests with valid results can be found in Appendix 3.

Grouping of organisms

Bacteria, yeast, and fungi, were grouped with the help of a microbiology and infectious disease expert by the closeness of the types and other considerations such as the typical level of similarity in the antibiotic resistance profile and the level of identification that is routinely performed at the lab. The complete list of organisms and their assigned group can be found in Appendix 4.

Appendix 1 - Entity Relationship Diagram of the Database Schema



Appendix 2 - Examples of Records

Records were anonymised. Identifying information was replaced by xxx.

Records of tests orders (3 records)

```
XXXXXX^XXX00009913265200000xxxxx023136060200408050603197209^XXXX
XX, XXXXXURINEFREEFORMTEXTPUI14W1439 C
XXXXXX^XXXXXX000099300695000000xxxxx016440547200010010957100033^
XXXXXXXX,XXXXX-URINEMIDSTREAMURINEPUI13E1305 C
XXXXXXX^XXXXXX000099300695000000xxxxx016478406200010100815100033
^XXXXXXXX,XXXXX-RESPIRATORYSPUTUMPSPI13E1305 C
```

Records from the ADT system (4 records)

```
0000000xxxxx000099122971xxxxxxxxxxxx1840AMBUAMBU03
0000000xxxxx000099087413200506081412 15E1521 A
xxxxxxx|M|19281224|000099107166| 12W1235
B|200505040653|200505081356
xxxxxxx|M|19381015|000099075426|19TH1926
A|200509140840|200509211459
```

Records of tests results

Record 1

```
00000xxxxxxx011699282T001                SPECIMEN ID xxxxx FINAL
CULTURE RESULTS
00000xxxxxxx011699282T002       PAT.NAME: XXXXXX, XXXXXX LOC: R05
39 01 MRN: xxxxxxx TYPE: I
00000xxxxxxx011699282T003       WOUND CULTURE WITH GRAM STAIN
RECEIVED: FRI 19-MAY-2000
00000xxxxxxx011699282T004       SOURCE: SWAB
SITE: BACK WOUND
00000xxxxxxx011699282T005       COLLECT LOCATION: R05 39 01
REPORTED: THU 25-MAY-2000
00000xxxxxxx011699282T006GRAM STAIN:
00000xxxxxxx011699282T007        3+ WHITE BLOOD CELLS , 2+ GRAM
POSITIVE COCCI
00000xxxxxxx011699282T008        2+ GRAM NEGATIVE ROD
00000xxxxxxx011699282T009AEROBIC AND ANAEROBIC CULTURE RESULTS:
00000xxxxxxx011699282T010        1+ LACTOBACILLUS SPECIES
00000xxxxxxx011699282T011        2+ PSEUDOMONAS AERUGINOSA X2
TYPES
00000xxxxxxx011699282T012SENSITIVITIES: ANTIBIOTICS
00000xxxxxxx011699282T013               CEFTAZIDIME
S
00000xxxxxxx011699282T014               CIPROFLOXACIN
S
00000xxxxxxx011699282T015               TICARCILLIN/CLAVULANIC A
S
00000xxxxxxx011699282T016               AMIKACIN
S
```

```
00000xxxxxxx011699282T017               GENTAMICIN
S
00000xxxxxxx011699282T018               TOBRAMYCIN
S
00000xxxxxxx011699282T019               IMIPENEM
S
00000xxxxxxx011699282T020SENSITIVITIES: ANTIBIOTICS
00000xxxxxxx011699282T021               CEFTAZIDIME
S
00000xxxxxxx011699282T022               CIPROFLOXACIN
S
00000xxxxxxx011699282T023               TICARCILLIN/CLAVULANIC A
S
00000xxxxxxx011699282T024               AMIKACIN
S
00000xxxxxxx011699282T025               GENTAMICIN
S
00000xxxxxxx011699282T026               TOBRAMYCIN
S
00000xxxxxxx011699282T027               IMIPENEM
S
00000xxxxxxx011699282T028        1+ ANAEROBIC GRAM POSITIVE COCCI
```

Record 2

```
00000xxxxxxx011455676T001                 SPECIMEN ID xxxxx FINAL
CULTURE RESULTS
00000xxxxxxx011455676T002       PAT.NAME: XXXXXX, XXXXXX LOC:
TICU ICU 2 MRN: xxxxxxx TYPE: I
00000xxxxxxx011455676T003       SPUTUM CULTURE WITH GRAM STAIN
RECEIVED: MON  3-APR-2000
00000xxxxxxx011455676T004       SOURCE: TTA
SITE: LUNG
00000xxxxxxx011455676T005       COLLECT LOCATION: TICU ICU 2
REPORTED: FRI  7-APR-2000
00000xxxxxxx011455676T006GRAM STAIN:
00000xxxxxxx011455676T007        3+ WHITE BLOOD CELLS ,3+ GRAM
POSITIVE COCCI IN CLUSTERS
00000xxxxxxx011455676T008CULTURE RESULTS:
00000xxxxxxx011455676T009        2+ NORMAL FLORA
00000xxxxxxx011455676T010        1+ STAPHYLOCOCCUS AUREUS
00000xxxxxxx011455676T011SENSITIVITIES: ANTIBIOTICS
00000xxxxxxx011455676T012               PENICILLIN G
R
00000xxxxxxx011455676T013               OXACILLIN
S
00000xxxxxxx011455676T014               CEFAZOLIN
S
00000xxxxxxx011455676T015               ERYTHROMYCIN
S
00000xxxxxxx011455676T016               CLINDAMYCIN
S
00000xxxxxxx011455676T017               TRIMETHOPRIM/SULFAMETHOX
S
00000xxxxxxx011455676T018               VANCOMYCIN
S
```

```
00000xxxxxxx011455676T019        1+ SERRATIA MARCESCENS
00000xxxxxxx011455676T020SENSITIVITIES: ANTIBIOTICS
00000xxxxxxx011455676T021               AMPICILLIN
R
00000xxxxxxx011455676T022               CEFAZOLIN
R
00000xxxxxxx011455676T023               TRIMETHOPRIM/SULFAMETHOX
S
00000xxxxxxx011455676T024               CIPROFLOXACIN
S
00000xxxxxxx011455676T025               GENTAMICIN
S
00000xxxxxxx011455676T026               TOBRAMYCIN
S
00000xxxxxxx011455676T027               TICARCILLIN/CLAVULANIC A
I
00000xxxxxxx011455676T028               CEFTRIAXONE
S
00000xxxxxxx011455676T029               CEFTAZIDIME
S
00000xxxxxxx011455676T030               IMIPENEM
S
```

Record 3

```
00000xxxxxxx019993701T001WEST NILE VIRUS - SEROLOGY
00000xxxxxxx019993701T002                              1st Serum
2nd Serum
00000xxxxxxx019993701T003                              ID#   xxxxx
ID#
00000xxxxxxx019993701T004
Date:20040901        Date:
00000xxxxxxx019993701T005                              Req# A685217
Req#
00000xxxxxxx019993701T006VNO/MAC-EIA IgM               NON REACTIF
00000xxxxxxx019993701T007Flavivirus/EIA IgG
00000xxxxxxx019993701T008Comment:
00000xxxxxxx019993701T009Test done at the LSPQ with a detection
kit used for research only.
00000xxxxxxx019996863T001                  Specimen ID xxxxx FINAL
Culture Results
```

Record 4

```
00000xxxxxxx022308296T001
Microbiology Report
00000xxxxxxx022308296T002               PROCEDURE: Urine culture
COLL: 2005/09/27 20:42
00000xxxxxxx022308296T003                  SOURCE: U Cath
00000xxxxxxx022308296T004               BODY SITE: Bladder
ACCESSION: MB-05-000728
00000xxxxxxx022308296T005         Additional Info:
00000xxxxxxx022308296T006    *** FINAL REPORT ***
00000xxxxxxx022308296T007    Final Report
00000xxxxxxx022308296T008    Verified:2005/09/29 15:43
```

```
00000xxxxxxx022308296T009    10e6 cfu/L x3types. Mixed culture.
Results suggest contamination.
00000xxxxxxx022308296T010    Please repeat if clinically
indicated.
00000xxxxxxx022308296T011
00000xxxxxxx022308296T012    *** Order Comments***
00000xxxxxxx022308296T013    (1)Antibiotics: NONE/
00000xxxxxxx022308296T014
00000xxxxxxx022308296T015
```

Record 5

```
00000xxxxxxx023263157T001*** COLLECTION DATE:  01-SEP-2004
COLLECTION TIME: 08:59   ID: xxxx
00000xxxxxxx023263157T002    CULTURE TYPE: MRSA           SOURCE:
NOSE
00000xxxxxxx023263157T003   FINAL CULTURE
Date : 05-SEP-2004 10:54
00000xxxxxxx023263157T004   Isolate #1 <METHICILLIN RESISTANT
STAPHYLOCOCCUS AUREUS>
00000xxxxxxx023263157T005                    ====> SENSITIVITY
PROFILE MATRIX <====
00000xxxxxxx023263157T006ISOLATE #          1
00000xxxxxxx023263157T007                   KB MIC
00000xxxxxxx023263157T008CIPROFLOXACIN       R
00000xxxxxxx023263157T009CLOXACILLIN         R
00000xxxxxxx023263157T010CEFAZOLIN           R
00000xxxxxxx023263157T011CLINDAMYCIN         R
00000xxxxxxx023263157T012ERYTHROMYCIN        R
00000xxxxxxx023263157T013FUSIDIC ACID        S
00000xxxxxxx023263157T014MUPIROCIN           S
00000xxxxxxx023263157T015PENICILLIN          R
00000xxxxxxx023263157T016RIFAMPIN            S
00000xxxxxxx023263157T017TETRACYCLINE        S
00000xxxxxxx023263157T018SEPTRA              S
00000xxxxxxx023263157T019VANCOMYCIN          S
00000xxxxxxx023263157T020LINEZOLID           S
00000xxxxxxx023263157T021                 ========> Sensitivity
Legend  <========
00000xxxxxxx023263157T022  S = Sensitive    I = Intermediate
R = Resistant
00000xxxxxxx023263157T023   COMMENTS: MULTIPLY-RESISTANT ORGANISM
00000xxxxxxx023263157T024             ISOLATION PRECAUTIONS MUST
BE INSTITUTED
00000xxxxxxx023263157T025   MICRO STATUS : DONE
```

Record 6

```
00000xxxxxxx022305401T001
Microbiology Report
00000xxxxxxx022305401T002                PROCEDURE: Ear Discharge
bacterial culturCOLL: 2005/09/27 16:14
00000xxxxxxx022305401T003                   SOURCE: Ear
00000xxxxxxx022305401T004                BODY SITE: Ear
ACCESSION: MB-05-000656
```

```
00000xxxxxxx022305401T005         Additional Info:
00000xxxxxxx022305401T006    *** FINAL REPORT ***
00000xxxxxxx022305401T007    Final Report
00000xxxxxxx022305401T008    Verified:2005/10/03 10:55
00000xxxxxxx022305401T009    2+ Klebsiella species
00000xxxxxxx022305401T010    3+ Coagulase negative Staphylococcus
species
00000xxxxxxx022305401T011    3+ Enterococcus species
00000xxxxxxx022305401T012
00000xxxxxxx022305401T013    *** SUSCEPTIBILITY RESULTS ***
00000xxxxxxx022305401T014    Klebsiella species
00000xxxxxxx022305401T015    ___________________
00000xxxxxxx022305401T016
Interpretation
00000xxxxxxx022305401T017    Ampicillin                    R
00000xxxxxxx022305401T018    Cefazolin                     S
00000xxxxxxx022305401T019    Ceftriaxone                   S
00000xxxxxxx022305401T020    Ciprofloxacin                 S
00000xxxxxxx022305401T021    Gentamicin                    S
00000xxxxxxx022305401T022    Trimethoprim/Sulfa            S
00000xxxxxxx022305401T023    Ticarcillin/Clavulanate       S
00000xxxxxxx022305401T024    Tobramycin                    S
00000xxxxxxx022305401T025
00000xxxxxxx022305401T026    Enterococcus species
00000xxxxxxx022305401T027    ____________________
00000xxxxxxx022305401T028
Interpretation
00000xxxxxxx022305401T029    Ampicillin                    S
00000xxxxxxx022305401T030    Vancomycin                    S
00000xxxxxxx022305401T031
00000xxxxxxx022305401T032    Coagulase negative Staphylococcus
species
00000xxxxxxx022305401T033
_________________________________________
00000xxxxxxx022305401T034
Interpretation
00000xxxxxxx022305401T035    Cefazolin                     S
00000xxxxxxx022305401T036    Trimethoprim/Sulfa            S
00000xxxxxxx022305401T037    Vancomycin                    S
00000xxxxxxx022305401T038    Erythromycin                  R
00000xxxxxxx022305401T039    Oxacillin                     S
00000xxxxxxx022305401T040    Penicillin                    S
00000xxxxxxx022305401T041
00000xxxxxxx022305401T042
```

Record 7

```
00000xxxxxxx023280034T001*** COLLECTION DATE:  04-SEP-2004
COLLECTION TIME: 11:51   ID: xxxxx
00000xxxxxxx023280034T002    CULTURE TYPE: BACT-PUS-DEEP  SOURCE:
LEFT FOOT/ANKLE
00000xxxxxxx023280034T003   GRAM STAIN: NO WBC
00000xxxxxxx023280034T004               GRAM POSITIVE COCCI (2+)
00000xxxxxxx023280034T005               GRAM NEGATIVE BACILLI
(2+)
```

```
00000xxxxxxx023280034T006   PRELIMINARY CULTURE (1)
Date : 08-SEP-2004  11:20
00000xxxxxxx023280034T007   Isolate #1 <STAPHYLOCOCCUS AUREUS> 2+
00000xxxxxxx023280034T008   Isolate #2 PROTEUS MIRABILIS 2+
00000xxxxxxx023280034T009   Isolate #3 LACTOSE FERMENTING
COLIFORMS 1+
00000xxxxxxx023280034T010   Isolate #4 LACTOSE FERMENTING
COLIFORMS 1+
00000xxxxxxx023280034T011   FINAL CULTURE
Date : 10-SEP-2004 12:20
00000xxxxxxx023280034T012   Isolate #1 <METHICILLIN RESISTANT
STAPHYLOCOCCUS AUREUS> 2+
00000xxxxxxx023280034T013              INDUCIBLE RESISTANCE TO
CLINDAMYCIN, USE WITH CAUTION.
00000xxxxxxx023280034T014   Isolate #2 PROTEUS MIRABILIS 2+
00000xxxxxxx023280034T015   Isolate #3 LACTOSE FERMENTING
COLIFORMS 1+
00000xxxxxxx023280034T016   Isolate #4 LACTOSE FERMENTING
COLIFORMS 1+
00000xxxxxxx023280034T017              NO ANAEROBES ISOLATED
00000xxxxxxx023280034T018                    ====> SENSITIVITY
PROFILE MATRIX <====
00000xxxxxxx023280034T019ISOLATE #          1         2         3
4
00000xxxxxxx023280034T020                  KB MIC    KB MIC
KB MIC    KB MIC
00000xxxxxxx023280034T021AMIKACIN                     S
S         S
00000xxxxxxx023280034T022AMPICILLIN                   R
R         R
00000xxxxxxx023280034T023CEFOTAXIME                   S
S
00000xxxxxxx023280034T024CIPROFLOXACIN       R        I
S         S
00000xxxxxxx023280034T025CLOXACILLIN         R
00000xxxxxxx023280034T026CEFAZOLIN           R        S
S         R
00000xxxxxxx023280034T027CEFTAZIDIME                  S
S         S
00000xxxxxxx023280034T028CLINDAMYCIN         S
00000xxxxxxx023280034T029ERYTHROMYCIN        R
00000xxxxxxx023280034T030FUSIDIC ACID        S
00000xxxxxxx023280034T031GENTAMICIN                   R
S         S
00000xxxxxxx023280034T032IMIPENEM                     S
S         S
00000xxxxxxx023280034T033MUPIROCIN           R
00000xxxxxxx023280034T034PENICILLIN          R
00000xxxxxxx023280034T035PIPERACILLIN                 S
S         S
00000xxxxxxx023280034T036RIFAMPIN            S
00000xxxxxxx023280034T037TETRACYCLINE        S
00000xxxxxxx023280034T038SEPTRA              S        R
S         S
00000xxxxxxx023280034T039TOBRAMYCIN                   R
S         S
00000xxxxxxx023280034T040VANCOMYCIN          S
```

```
00000xxxxxxx023280034T041PIPERACILLIN/TAZOBA          S
S         S
00000xxxxxxx023280034T042LINEZOLID          S
00000xxxxxxx023280034T043TICARCILLIN/CLAVULA          S
S         S
00000xxxxxxx023280034T044               ========> Sensitivity
Legend  <========
00000xxxxxxx023280034T045  S = Sensitive    I = Intermediate
R = Resistant
00000xxxxxxx023280034T046   COMMENTS: SWAB UNSUITABLE FOR
ANEROBES. SEND TISSUE OR FLUID IN
00000xxxxxxx023280034T047             SEALED SYRINGE W/O NEEDLE
OR IN STERILE CONTAINER
00000xxxxxxx023280034T048   COMMENTS: MULTIPLY-RESISTANT ORGANISM
00000xxxxxxx023280034T049             ISOLATION PRECAUTIONS MUST
BE INSTITUTED
```

Record 8

```
00000xxxxxxx025714065T001
Microbiology Report
00000xxxxxxx025714065T002               PROCEDURE: MRSA screen
COLL: 2006/01/24 11:41
00000xxxxxxx025714065T003                  SOURCE: Peg Site
00000xxxxxxx025714065T004               BODY SITE: Peg Site
ACCESSION: MB-06-006295
00000xxxxxxx025714065T005         Additional Info:
00000xxxxxxx025714065T006    *** FINAL REPORT ***
00000xxxxxxx025714065T007    Final Report
00000xxxxxxx025714065T008    Verified:2006/01/28 09:47
00000xxxxxxx025714065T009    Methicillin-Resistant Staphylococcus
aureus isolated
00000xxxxxxx025714065T010    Multiple resistant organism.
Isolation precautions must be instituted.
00000xxxxxxx025714065T011    Specimen pooled with Accession #
#6296 and #6297
00000xxxxxxx025714065T012    Inducible resistance to Clindamycin,
use with caution.
00000xxxxxxx025714065T013
00000xxxxxxx025714065T014    *** SUSCEPTIBILITY RESULTS ***
00000xxxxxxx025714065T015    Staphylococcus aureus
00000xxxxxxx025714065T016    ____________________
00000xxxxxxx025714065T017                                   MIC
Result   Interpretation
00000xxxxxxx025714065T018
(mg/L)       MIC
00000xxxxxxx025714065T019    Clindamycin
<=0.25       R
00000xxxxxxx025714065T020    Erythromycin                   >=8
R
00000xxxxxxx025714065T021    Fusidic Acid                   <=0.5
S
00000xxxxxxx025714065T022    Gentamicin                     <=0.5
S
00000xxxxxxx025714065T023    Linezolid                      4
S
```

```
00000xxxxxxx025714065T024    Oxacillin                      >=4
R
00000xxxxxxx025714065T025    Penicillin                     >=0.5
R
00000xxxxxxx025714065T026    Quinapristin/Dalfopristin
<=0.25       S
00000xxxxxxx025714065T027    Rifampin                       <=0.5
S
00000xxxxxxx025714065T028    Trimethoprim/Sulfa             <=10
S
00000xxxxxxx025714065T029    Vancomycin                     <=1
S
00000xxxxxxx025714065T030
00000xxxxxxx025714065T031    *** MRSA screen
Interpretive Results
00000xxxxxxx025714065T032    * Non-commercialized kit used,
validated by a Microbiologist
00000xxxxxxx025714065T033
00000xxxxxxx025714065T034
```

Record 9

```
00000xxxxxxx019685689T001*** COLLECTION DATE:  25-AUG-2002
COLLECTION TIME: 16:12   ID: xxxxx
00000xxxxxxx019685689T002    CULTURE TYPE: BACT-PUS-SUPER SOURCE:
SURGICAL WOUND
00000xxxxxxx019685689T003   GRAM STAIN: NO WBC
00000xxxxxxx019685689T004               GRAM NEGATIVE BACILLI
(1+)
00000xxxxxxx019685689T005   FINAL CULTURE
Date : 30-AUG-2002 12:09
00000xxxxxxx019685689T006   Isolate #1 <STAPHYLOCOCCUS AUREUS>
(2+)
00000xxxxxxx019685689T007   Isolate #2 LACTOSE FERMENTING
COLIFORMS (2+)
00000xxxxxxx019685689T008   Isolate #3 NON LACTOSE FERMENTING
COLIFORMS (2+)
00000xxxxxxx019685689T009                    ====> SENSITIVITY
PROFILE MATRIX <====
00000xxxxxxx019685689T010ISOLATE #          1         2         3
00000xxxxxxx019685689T011                   KB MIC    KB MIC
KB MIC
00000xxxxxxx019685689T012AMPICILLIN                    R
R
00000xxxxxxx019685689T013CIPROFLOXACIN                 S
S
00000xxxxxxx019685689T014CLOXACILLIN          S
00000xxxxxxx019685689T015CEFAZOLIN            S         S
R
00000xxxxxxx019685689T016CLINDAMYCIN          S
00000xxxxxxx019685689T017ERYTHROMYCIN         S
00000xxxxxxx019685689T018GENTAMICIN                    S
S
00000xxxxxxx019685689T019PENICILLIN           R
00000xxxxxxx019685689T020PIPERACILLIN                  S
S
```

```
00000xxxxxxx019685689T021TETRACYCLINE        S
00000xxxxxxx019685689T022SEPTRA              S         S
S
00000xxxxxxx019685689T023VANCOMYCIN          S
00000xxxxxxx019685689T024PIPERACILLIN/TAZOBA           S
S
00000xxxxxxx019685689T025TICARCILLIN/CLAVULA           S
S
00000xxxxxxx019685689T026                ========> Sensitivity
Legend  <========
00000xxxxxxx019685689T027  S = Sensitive    I = Intermediate
R = Resistant
00000xxxxxxx019685689T028   MICRO STATUS : DONE
```

Record 10

```
00000xxxxxxx023136060PU   T001*** COLLECTION DATE:  05-AUG-2004
COLLECTION TIME: 06:03   ID: xxxxx
00000xxxxxxx023136060PU   T002    CULTURE TYPE: BACT-URINE
SOURCE: URINE
00000xxxxxxx023136060PU   T003   MICROSCOPY: LEUCOESTERASE SCREEN
POSITIVE (REAGENT STRIP)
00000xxxxxxx023136060PU   T004   PRELIMINARY CULTURE (1)
Date : 10-AUG-2004  13:45
00000xxxxxxx023136060PU   T005   Isolate #2 PRESUMPTIVE
ESCHERICHIA COLI 100x10E6  (10E8) CFU/L
00000xxxxxxx023136060PU   T006   FINAL CULTURE
Date : 11-AUG-2004 11:28
00000xxxxxxx023136060PU   T007   Isolate #1 KLEBSIELLA OXYTOCA
100x10E6  (10E8) CFU/L
00000xxxxxxx023136060PU   T008   Isolate #2 PRESUMPTIVE
ESCHERICHIA COLI 100x10E6  (10E8) CFU/L
00000xxxxxxx023136060PU   T009                    ====>
SENSITIVITY PROFILE MATRIX <====
00000xxxxxxx023136060PU   T010ISOLATE #          1         2
00000xxxxxxx023136060PU   T011                   KB MIC    KB MIC
00000xxxxxxx023136060PU   T012AMIKACIN                     S
00000xxxxxxx023136060PU   T013AMPICILLIN          R         R
00000xxxxxxx023136060PU   T014CEFOTAXIME                   S
00000xxxxxxx023136060PU   T015CIPROFLOXACIN       S         R
00000xxxxxxx023136060PU   T016CEFAZOLIN           S         R
00000xxxxxxx023136060PU   T017CEFTAZIDIME                  S
00000xxxxxxx023136060PU   T018GENTAMICIN          S         S
00000xxxxxxx023136060PU   T019IMIPENEM                     S
00000xxxxxxx023136060PU   T020NITROFURANTOIN      S         R
00000xxxxxxx023136060PU   T021PIPERACILLIN        S         S
00000xxxxxxx023136060PU   T022SEPTRA              S         R
00000xxxxxxx023136060PU   T023TOBRAMYCIN                   S
00000xxxxxxx023136060PU   T024PIPERACILLIN/TAZOBA S         S
00000xxxxxxx023136060PU   T025TICARCILLIN/CLAVULA S         S
00000xxxxxxx023136060PU   T026                ========>
Sensitivity Legend  <========
00000xxxxxxx023136060PU   T027  S = Sensitive    I = Intermediate
R = Resistant
00000xxxxxxx023136060PU   T028   MICRO STATUS : DONE
```

Record 11

```
00000xxxxxxx026421693CBLD1T001
Microbiology Report
00000xxxxxxx026421693CBLD1T002                PROCEDURE: Blood
culture(aerobic btl onlyCOLL: 2006/05/23 10:34
00000xxxxxxx026421693CBLD1T003                   SOURCE: Blood
00000xxxxxxx026421693CBLD1T004                BODY SITE:
Peripheral Lt Arm        ACCESSION: MB-06-070518
00000xxxxxxx026421693CBLD1T005          Additional Info: Taken
from FEM line
00000xxxxxxx026421693CBLD1T006    *** FINAL REPORT ***
00000xxxxxxx026421693CBLD1T007    Final Report
00000xxxxxxx026421693CBLD1T008    Verified:2006/05/27 12:13
00000xxxxxxx026421693CBLD1T009    Serratia marcescens isolated
00000xxxxxxx026421693CBLD1T010    Staphylococcus epidermidis
isolated
00000xxxxxxx026421693CBLD1T011    in 1 of 1 bottle
00000xxxxxxx026421693CBLD1T012
00000xxxxxxx026421693CBLD1T013    *** SUSCEPTIBILITY RESULTS ***
00000xxxxxxx026421693CBLD1T014    Serratia marcescens
00000xxxxxxx026421693CBLD1T015    ____________________
00000xxxxxxx026421693CBLD1T016
MIC Result   Interpretation
00000xxxxxxx026421693CBLD1T017
(mg/L)       MIC
00000xxxxxxx026421693CBLD1T018    Amoxicillin/Clavulanate
>=8          R
00000xxxxxxx026421693CBLD1T019    Ampicillin                    4
R
00000xxxxxxx026421693CBLD1T020    Cefazolin
>=64         R
00000xxxxxxx026421693CBLD1T021    Ceftriaxone
<=1          S
00000xxxxxxx026421693CBLD1T022    Cephalothin(1)
>=64         R
00000xxxxxxx026421693CBLD1T023    Ciprofloxacin
<=0.25       S
00000xxxxxxx026421693CBLD1T024    Gentamicin                    2
S
00000xxxxxxx026421693CBLD1T025    Imipenem
<=1          S
00000xxxxxxx026421693CBLD1T026    Piperacillin/Tazobactam
<=4          S
00000xxxxxxx026421693CBLD1T027    Trimethoprim/Sulfa
<=20         S
00000xxxxxxx026421693CBLD1T028    Ticarcillin/Clavulanate
<=8          S
00000xxxxxxx026421693CBLD1T029
00000xxxxxxx026421693CBLD1T030    Staphylococcus epidermidis
00000xxxxxxx026421693CBLD1T031    ___________________________
00000xxxxxxx026421693CBLD1T032
MIC Result   Interpretation
00000xxxxxxx026421693CBLD1T033
(mg/L)       MIC
```

```
00000xxxxxxx026421693CBLD1T034    Trimethoprim/Sulfa
<=10         S
00000xxxxxxx026421693CBLD1T035    Clindamycin
<=0.25       S
00000xxxxxxx026421693CBLD1T036    Erythromycin
<=0.25       S
00000xxxxxxx026421693CBLD1T037    Oxacillin(2)
>=4          R
00000xxxxxxx026421693CBLD1T038    Penicillin
>=0.5        R
00000xxxxxxx026421693CBLD1T039    Vancomycin                    2
S
00000xxxxxxx026421693CBLD1T040
00000xxxxxxx026421693CBLD1T041    *** Order Comments***
00000xxxxxxx026421693CBLD1T042    (1)Antibiotics: CIPRO/
00000xxxxxxx026421693CBLD1T043
00000xxxxxxx026421693CBLD1T044    *** Result Comments ***
00000xxxxxxx026421693CBLD1T045    (1)Cephalothin is used to
predict susceptibility to Cephalexin and
00000xxxxxxx026421693CBLD1T046    Cefadroxi
00000xxxxxxx026421693CBLD1T047    (2)Cefazolin susceptibility is
dependent on Oxacillin interpretation
00000xxxxxxx026421693CBLD1T048
00000xxxxxxx026421693CBLD1T049
```

Record 12

```
00000xxxxxxx022170112PFLD T001*** COLLECTION DATE:  18-JAN-2004
COLLECTION TIME: 20:26   ID: xxxxx
00000xxxxxxx022170112PFLD T002    CULTURE TYPE: BACT-FLUID
SOURCE: PAD FLUID
00000xxxxxxx022170112PFLD T003   MACROSCOPY: 15 CC RECEIVED
00000xxxxxxx022170112PFLD T004               BLOODY
00000xxxxxxx022170112PFLD T005               CENTRIFUGED
00000xxxxxxx022170112PFLD T006   GRAM STAIN: WBC (4+)
00000xxxxxxx022170112PFLD T007               GRAM POSITIVE COCCI
(2+)
00000xxxxxxx022170112PFLD T008               YEAST CELLS SEEN
(2+)
00000xxxxxxx022170112PFLD T009   PRELIMINARY CULTURE (1)
Date : 20-JAN-2004  09:16
00000xxxxxxx022170112PFLD T010             LF 3+
00000xxxxxxx022170112PFLD T011             CANDIDA SPECIES 3+
00000xxxxxxx022170112PFLD T012   PRELIMINARY CULTURE (2)
Date :  21-JAN-2004 11:42
00000xxxxxxx022170112PFLD T013   Isolate #1 KLEBSIELLA PNEUMONIAE
3+
00000xxxxxxx022170112PFLD T014   Isolate #2 ENTEROCOCCI SPECIES
3+
00000xxxxxxx022170112PFLD T015   Isolate #3 CANDIDA SPECIES (3+)
00000xxxxxxx022170112PFLD T016   FINAL CULTURE
Date : 23-JAN-2004 11:24
00000xxxxxxx022170112PFLD T017   Isolate #1 KLEBSIELLA PNEUMONIAE
3+
00000xxxxxxx022170112PFLD T018   Isolate #2 ENTEROCOCCI SPECIES
3+
```

```
00000xxxxxxx022170112PFLD T019   Isolate #3 CANDIDA SPECIES,
OTHER THAN CANDIDA ALBICANS 3+
00000xxxxxxx022170112PFLD T020   Isolate #4 ESCHERICHIA COLI 2+
00000xxxxxxx022170112PFLD T021   Isolate #5 COAGULASE NEGATIVE
STAPHYLOCOCCUS 2+
00000xxxxxxx022170112PFLD T022              NO ANAEROBES ISOLATED
00000xxxxxxx022170112PFLD T023                    ====>
SENSITIVITY PROFILE MATRIX <====
00000xxxxxxx022170112PFLD T024ISOLATE #          1         2
4
00000xxxxxxx022170112PFLD T025                  KB MIC    KB MIC
KB MIC
00000xxxxxxx022170112PFLD T026AMPICILLIN          R         S
S
00000xxxxxxx022170112PFLD T027CIPROFLOXACIN       S
S
00000xxxxxxx022170112PFLD T028CEFAZOLIN           S
S
00000xxxxxxx022170112PFLD T029GENTAMICIN          S
S
00000xxxxxxx022170112PFLD T030PIPERACILLIN        R
S
00000xxxxxxx022170112PFLD T031SEPTRA              S
S
00000xxxxxxx022170112PFLD T032VANCOMYCIN                   S
00000xxxxxxx022170112PFLD T033PIPERACILLIN/TAZOBA S
S
00000xxxxxxx022170112PFLD T034TICARCILLIN/CLAVULA S
S
00000xxxxxxx022170112PFLD T035               ========>
Sensitivity Legend  <========
00000xxxxxxx022170112PFLD T036  S = Sensitive    I = Intermediate
R = Resistant

00000xxxxxxx022170112PFLD T037   MICRO STATUS : DONE
```

Appendix 3 - List of Tests Codes by Groups of Tests

The numbers represent frequencies of tests with valid results.

MRSA:

'MRSA culture'	87299
'MRSA'	52247
'MRSA screen'	19453
Total:	**158999**

VRE:

'VANCOMYCIN RESISTANT CULTURE'	38346
'VRE'	26029
'VRE culture'	9567
'VRE screen'	4953
'VRE OTHER THAN STOOL & RECTAL'	28
Total:	**78923**

C.Diff:

'CLOSTRIDIUM DIFFICILE TOXIN ASSA'	13081
'CLOS'	12315
'C.Difficile Toxin assay'	5813
'CLOSTRIDIUM TOXIN ASSAY'	526
'Clostridium difficile toxin Rapi'	6
'C.Difficile Toxin Rapid test'	4
Total:	**31745**

Mycology:

‘MYCOLOGY-DEEP’	1682
‘RESPIRATORY CULTURE/MYCOLOGY’	1555
'BODY FLUID MYCOLOGY'	1079
'Fungus / Deep culture'	838
'TISSUE MYCOLOGY'	746
'STOOL MYCOLOGY'	406
‘Mycoplasma /Ureaplasma culture’	294
'Fungus / Sterile Body Fld'	290
'CSF FOR MYCOLOGY WITH INDIA INK'	276
'BACT-BLOOD MYC'	233
‘MYCOLOGY-SUPER’	222
'WOUND MYCOLOGY'	219
'URINE MYCOLOGY'	213
‘YEAST CULTURE’	194
'BLOOD MYCOLOGY'	185
‘Fungus / Yeast culture’	96
'THROAT MYCOLOGY'	96
'Fungus / Blood culture'	90
‘MYCO’	37
Total:	**8751**

Blood:

'BLOOD CULTURE'	44269
'BACT-BL.AER+AN'	27199
'BACT-AEROBIC'	18341
'Blood culture(aero+anaerobic b'	10981
'Blood culture(aerobic btl only'	7208

Total:	**107998**

Urine: (not including chlamydia in urine or gonorrhea)

'Urine culture'	50688
'BACT-URINE'	35985
'BACT-UR'	45
Total:	**86718**

Deep wound:

'BACT-PUS-DEEP'	7327
'SBF CULTURE WITH GRAM STAIN'	5012
'BACT-FLUID'	3307
'Pus Deep culture'	1888
'SBF Culture'	1683
'BIOPSY/TISSUE CULTURE'	964
'Tissue culture'	363
'BACT-BIOPSY/TI'	133
'PATIENT PROSTHESIS'	27
Total:	**20704**

Superficial wound:

'WOUND CULTURE WITH GRAM STAIN'	8292
'BACT-PUS-SUPER'	6392
'Pus Superficial culture'	1925
'SKIN (SUPERFICIAL)'	1854
'Eye culture'	1309
'BACT-EYE'	223
'EAR CULTURE'	73
'BACT-EAR'	36
'Ear Discharge bacterial cultur'	28
'BACT-PUS'	10
Total:	**20142**

Respiratory: separated to throat and all other (lower + sputum)

Throat:

'BACT-THROAT'	1020
'THROAT GENERAL'	747
'BACT-NOSE'	487
'Throat culture'	471
'Nose culture'	175
'BACT-THROAT-GC'	40
Total:	**2940**

Lower respiratory:

'SPUTUM CULTURE WITH GRAM STAIN'	14785
'BACT-RESP'	12757
'Sputum culture'	4485
'BAL WITH GRAM STAIN'	899
'LEGIONELLA'	452
'BACT-BR.WASH'	420
'BACT-BRONCHIO-'	382
'Bronchio-alveolar lavage'	198
'Bronchial Washing culture'	116
'Sputum /CF (r/o B.cepacia&Pseudo'	71
'Sputum culture / Systic fibros'	56

'QUANTITATIVE CULTURE*'	31
'Quantitative culture'	23
'BACT-BRONCHIAL'	9
Total:	**34684**

Digestive: (not include gastric aspirate and Ova or bile)

'Stool culture'	4735
'BACT-FAECES'	2691
Total:	**7426**

Vaginal:

'GENITAL VAGINAL'	1341
'BACT-VAG'	1012
'Vaginal culture'	842
'GR. B STREP / VAGINAL-RECTAL'	746
'CHLAMYDIA BY PCR'	696
'MYCOPLASMA / UREAPLASMA'	582
'Chlamydia Trachomatis DNA'	497
'Strep group B screen'	420
'Chlamydia / N.gono DNA'	170
'GENITAL URETHRAL'	115
'BACT-CERVIX-GC'	47
'BACT-VAG FOR S'	31
Total:	**6499**

CSF:

'CSF CULTURE WITH GRAM STAIN'	2916
'BACT-CSF'	1325
'CSF Culture'	976
Total:	**5217**

Medical devices: (central lines catheters central jugulars etc.)

'LINE/TIP/CATHETER CULTURE'	4579
'BACT-STERILITY'	2973
'Catheter bacterial culture'	1357
Total:	**8909**

Appendix 4 - List of the Names of Organisms (as They Appear in the Records) and Organisms Groups

Bacteria:	Bacteria Group:
ABIOTROPHIA ADIACENS	ABIOTROPHIA ADIACENS
ACANOBACTERIUM BERNARDIAE	ACANOBACTERIUM BERNARDIAE
ACHROMOBACTER SPECIES	ACHROMOBACTER SPECIES
ACHROMOBACTER XYLOSOXIDANS	ACHROMOBACTER SPECIES
ACINETOBACTER	ACINETOBACTER SPECIES
ACINETOBACTER BAUMANII	ACINETOBACTER SPECIES
ACINETOBACTER BAUMANNII	ACINETOBACTER SPECIES
ACINETOBACTER CALCOACETICUS	ACINETOBACTER SPECIES
ACINETOBACTER HAEMOLYTICUS	ACINETOBACTER SPECIES
ACINETOBACTER LWOFFI	ACINETOBACTER SPECIES
ACINETOBACTER LWOFFII	ACINETOBACTER SPECIES
ACINETOBACTER SPECIES	ACINETOBACTER SPECIES
ACINETOBACTER URSINGII	ACINETOBACTER SPECIES
ACTINOMYCES	ACTINOMYCES SPECIES
ACTINOMYCES ISRAELII	ACTINOMYCES SPECIES
ACTINOMYCES ODONTOLYTICUS	ACTINOMYCES SPECIES
ACTINOMYCES SPECIES	ACTINOMYCES SPECIES
AEROCOCCUS SPECIES	AEROCOCCUS SPECIES
AEROCOCCUS VIRIDANS	AEROCOCCUS SPECIES
AEROMONAS	AEROMONAS SPECIES
AEROMONAS HYDROPHILA	AEROMONAS SPECIES
AEROMONAS HYDROPHILIA	AEROMONAS SPECIES
AEROMONAS SALMONICIDA	AEROMONAS SPECIES
AEROMONAS SOBRIA	AEROMONAS SPECIES
AEROMONAS SPECIES	AEROMONAS SPECIES
ALCALIGENES	ALCALIGENES SPECIES
ALCALIGENES FAECALIS	ALCALIGENES SPECIES
ALCALIGENES SPECIES	ALCALIGENES SPECIES
ALCALIGENES XYLOSOXIDANS	ALCALIGENES SPECIES
ALPHA HAEMOLYTIC STREPTOCOCC	STREPTOCOCCUS SPECIES
ALPHA HEMOLYTIC STREP	STREPTOCOCCUS SPECIES
ALPHA STREPTOCCI	STREPTOCOCCUS SPECIES
ANAEROBIC COCCI	ANAEROBIC COCCI
ANAEROBIC GRAM POSITIVE BACILLI	ANAEROBIC GRAM POSITIVE BACILLI
ANAEROBIC GRAM POSITIVE COCCI	ANAEROBIC GRAM POSITIVE COCCI
ASPERGILLUS	ASPERGILLUS SPECIES
ASPERGILLUS FLAVUS	ASPERGILLUS SPECIES
ASPERGILLUS FUMIGATUS	ASPERGILLUS SPECIES
ASPERGILLUS NIDULANS	ASPERGILLUS SPECIES
ASPERGILLUS NIGER	ASPERGILLUS SPECIES
ASPERGILLUS SPECIES	ASPERGILLUS SPECIES
ASPERGILLUS TERREUS	ASPERGILLUS SPECIES
ASPERGILLUS VERSICOLOR	ASPERGILLUS SPECIES
BACILLUS	BACILLUS SPECIES

BACILLUS CEREUS	BACILLUS SPECIES
BACILLUS CIRCULANS	BACILLUS SPECIES
BACILLUS FRAGILIS	BACILLUS SPECIES
BACILLUS SPECIES	BACILLUS SPECIES
BACILLUS SPHAERICUS	BACILLUS SPECIES
BACTERIODES FRAGILIS	BACTEROIDES SPECIES
BACTEROIDES	BACTEROIDES SPECIES
BACTEROIDES FRAGILIS	BACTEROIDES SPECIES
BACTEROIDES SPECIES	BACTEROIDES SPECIES
BACTEROIDES THETAIOTAOMICRON	BACTEROIDES SPECIES
BACTEROIDES UREOLYTICUS	BACTEROIDES SPECIES
BACTEROIDES VULGATUS	BACTEROIDES SPECIES
BETA HEMOLYTIC STREPTOCOCCI, GROUP C	GROUP C STREP
BETA HEMOLYTIC STREPTOCOCCI, GROUP G	GROUP G STREP
BETA HEMOLYTIC STREPTOCOCCI,GROUP A	GROUP A STREP
BETA HEMOLYTIC STREPTOCOCCI,GROUP B	GROUP B STREP
BETA LACTAMASE NEGATIVE	BETA LACTAMASE NEGATIVE
BETA LACTAMASE POSITIVE	BETA LACTAMASE POSITIVE
BURKHOLDERIA CEPACIA	BURKHOLDERIA CEPACIA
C.DIFFICILE	CLOSTRIDIUM DIFFICILE
CAMPYLOBACTER	CAMPYLOBACTER
CANDIDA ALBICANS	CANDIDA SPECIES
CANDIDA CIFIRII	CANDIDA SPECIES
CANDIDA DUBLINIENSIS	CANDIDA SPECIES
CANDIDA GLABRATA	CANDIDA SPECIES
CANDIDA KRUSEI	CANDIDA SPECIES
CANDIDA LUSITANIAE	CANDIDA SPECIES
CANDIDA PARAPSILOSIS	CANDIDA SPECIES
CANDIDA SPECIES	CANDIDA SPECIES
CANDIDA TROPICALIS	CANDIDA SPECIES
CAPNOCYTOPHAGA SPECIES	CAPNOCYTOPHAGA SPECIES
CHROMOGENIC NEISSERIA	CHROMOGENIC NEISSERIA
CHRYSEOBACTERIUM INDOLOGENES	CHRYSEOBACTERIUM SPECIES
CHRYSEOBACTERIUM MENINGOSEPTICUM	CHRYSEOBACTERIUM SPECIES
CHRYSEOBACTERIUM SPECIES	CHRYSEOBACTERIUM SPECIES
CHRYSEOMONAS LUTEOLA	CHRYSEOMONAS LUTEOLA
CITROBACTER	CITROBACTER SPECIES
CITROBACTER AMALONATICUS	CITROBACTER SPECIES
CITROBACTER BRAAKII	CITROBACTER SPECIES
CITROBACTER DIVERSUS	CITROBACTER SPECIES
CITROBACTER FARMERI	CITROBACTER SPECIES
CITROBACTER FREUNDII	CITROBACTER SPECIES
CITROBACTER KOSERI	CITROBACTER SPECIES
CITROBACTER SPECIES	CITROBACTER SPECIES
CITROBACTER YOUNGAE	CITROBACTER SPECIES
CLOSTRDIUM SPECIES	CLOSTRDIUM SPECIES
CLOSTRIDIUM	CLOSTRDIUM SPECIES
CLOSTRIDIUM BARATII	CLOSTRDIUM SPECIES
CLOSTRIDIUM BIFERMENTANS	CLOSTRDIUM SPECIES
CLOSTRIDIUM BIFERMENTENS	CLOSTRDIUM SPECIES
CLOSTRIDIUM CARDAVERIS	CLOSTRDIUM SPECIES
CLOSTRIDIUM CLOSTRIDIIFORME	CLOSTRDIUM SPECIES
CLOSTRIDIUM CLOSTRIDIOFORM	CLOSTRDIUM SPECIES
CLOSTRIDIUM DIFFICILE	CLOSTRIDIUM DIFFICILE
CLOSTRIDIUM LINOSUM	CLOSTRDIUM SPECIES
CLOSTRIDIUM PARAPUTRIFICUM	CLOSTRDIUM SPECIES

CLOSTRIDIUM PERFRINGENS	CLOSTRDIUM SPECIES
CLOSTRIDIUM PERFRINGES	CLOSTRDIUM SPECIES
CLOSTRIDIUM RAMOSUM	CLOSTRDIUM SPECIES
CLOSTRIDIUM SEPTICUM	CLOSTRDIUM SPECIES
CLOSTRIDIUM SPECIES	CLOSTRDIUM SPECIES
CLOSTRIDIUM TERTIUM	CLOSTRDIUM SPECIES
CLOSTRIDIUM WELCHII	CLOSTRDIUM SPECIES
COAGULASE NEGATIVE	COAGULASE NEGATIVE
COLIFORM	COLIFORM
COLIFORMS NON LACTOSE FERMENTER	COLIFORM
COMAMONAS ACIDOVORANS	COMAMONAS ACIDOVORANS
COORYNEBACTERIUM JEIKEIUM	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM JEIKEIUM	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM MACGINGLEYI	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM MACGINLEYI	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM PSEUDODIPHTHERITICUM	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM SPECIES	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM STRIATUM	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM UREALYTICUM	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM UREALYTICUS	CORYNEBACTERIUM SPECIES
CORYNEBACTERIUM XEROSIS	CORYNEBACTERIUM SPECIES
CRYPTOCOCCUS NEOFORMANS	CRYPTOCOCCUS NEOFORMANS
DIPHTHEROIDS	DIPHTHEROIDS
EIKENELLA CORRODEN	EIKENELLA CORRODEN
ENTERBACTER SPECIES	ENTEROBACTER SPECIES
ENTEROBACTER	ENTEROBACTER SPECIES
ENTEROBACTER ABSURIAE	ENTEROBACTER SPECIES
ENTEROBACTER AEROGENES	ENTEROBACTER SPECIES
ENTEROBACTER AGGLOMERANS	ENTEROBACTER SPECIES
ENTEROBACTER AMIGENUS	ENTEROBACTER SPECIES
ENTEROBACTER AMNIGENUS	ENTEROBACTER SPECIES
ENTEROBACTER ASBURIAE	ENTEROBACTER SPECIES
ENTEROBACTER CANCEROGENES	ENTEROBACTER SPECIES
ENTEROBACTER CLOACAE	ENTEROBACTER SPECIES
ENTEROBACTER CLOCAE	ENTEROBACTER SPECIES
ENTEROBACTER GERGOVIAE	ENTEROBACTER SPECIES
ENTEROBACTER HORMACCHEI	ENTEROBACTER SPECIES
ENTEROBACTER SAKAZAKII	ENTEROBACTER SPECIES
ENTEROBACTER SPECIES	ENTEROBACTER SPECIES
ENTEROBACTER TAYLORAE	ENTEROBACTER SPECIES
ENTEROCOCCI	ENTEROCOCCUS SPECIES
ENTEROCOCCI AVIUM	ENTEROCOCCUS SPECIES
ENTEROCOCCI CASSELIFLAVUS	ENTEROCOCCUS SPECIES
ENTEROCOCCI FAECALIS	ENTEROCOCCUS SPECIES
ENTEROCOCCI FAECIUM	ENTEROCOCCUS SPECIES
ENTEROCOCCI FEACALIS	ENTEROCOCCUS SPECIES
ENTEROCOCCI GALLINARIUM	ENTEROCOCCUS SPECIES
ENTEROCOCCI SPECIES	ENTEROCOCCUS SPECIES
ENTEROCOCCUS	ENTEROCOCCUS SPECIES
ENTEROCOCCUS AVIUM	ENTEROCOCCUS SPECIES
ENTEROCOCCUS CASSELIFLAVUS	ENTEROCOCCUS SPECIES
ENTEROCOCCUS DURANS	ENTEROCOCCUS SPECIES
ENTEROCOCCUS FAECALIS	ENTEROCOCCUS SPECIES
ENTEROCOCCUS FAECIUM	ENTEROCOCCUS SPECIES
ENTEROCOCCUS GALLINARUM	ENTEROCOCCUS SPECIES

ENTEROCOCCUS SPECIES	ENTEROCOCCUS SPECIES
ERYSIPELOTHRIX RHUSIOPATHIAE	ERYSIPELOTHRIX RHUSIOPATHIAE
ESCHERICHIA COLI	ESCHERICHIA COLI
ESCHERICHIA HERMANNII	ESCHERICHIA
ESCHERICHIA VULNERIS	ESCHERICHIA
EUBACTERIUM	EUBACTERIUM SPECIES
EUBACTERIUM LENTUM	EUBACTERIUM SPECIES
EUBACTERIUM SPECIES	EUBACTERIUM SPECIES
FLAVIMONAS ORYZIHABITANS	FLAVIMONAS ORYZIHABITANS
FLAVOBACTERIUM	FLAVOBACTERIUM SPECIES
FLAVOBACTERIUM INDOLOGENES	FLAVOBACTERIUM SPECIES
FLAVOBACTERIUM MENINGOSEPTICUM	FLAVOBACTERIUM SPECIES
FLAVOBACTERIUM SPECIES	FLAVOBACTERIUM SPECIES
FUNGI	FUNGI
FUNGUS	FUNGI
FUSOBACTERIUM	FUSOBACTERIUM SPECIES
FUSOBACTERIUM NECROPHORUM	FUSOBACTERIUM SPECIES
FUSOBACTERIUM NUCLEATUM	FUSOBACTERIUM SPECIES
FUSOBACTERIUM SPECIES	FUSOBACTERIUM SPECIES
FUSOBACTERIUM VARIUM	FUSOBACTERIUM SPECIES
GARDNERELLA VAGINALIS	GARDNERELLA VAGINALIS
GEMELLA HAEMOLYSANS	GEMELLA SPECIES
GEMELLA MORBILLORUM	GEMELLA SPECIES
GEMELLA SPECIES	GEMELLA SPECIES
GEOTRICHUM SPECIES	GEOTRICHUM SPECIES
GRANULICATELLA ADIACENS	GRANULICATELLA ADIACENS
GROUP A STREP	GROUP A STREP
GROUP B STREP	GROUP B STREP
HAEM.STREPT.GROUP A	GROUP A STREP
HAEM.STREPT.GROUP B	GROUP B STREP
HAEM.STREPT.GROUP C	GROUP C STREP
HAEM.STREPT.GROUP F	GROUP F STREP
HAEM.STREPT.GROUP G	GROUP G STREP
HAEMOPHILUS	HAEMOPHILUS SPECIES
HAEMOPHILUS APHROPHILUS	HAEMOPHILUS SPECIES
HAEMOPHILUS INFLUENZAE	HAEMOPHILUS SPECIES
HAEMOPHILUS PARAHAEMOLYTICUS	HAEMOPHILUS SPECIES
HAEMOPHILUS PARAINFLUENZAE	HAEMOPHILUS SPECIES
HAEMOPHILUS PARAPHROPHILUS	HAEMOPHILUS SPECIES
HAEMOPHILUS SPECIES	HAEMOPHILUS SPECIES
HAFNIA ALVEI	HAFNIA ALVEI
HAFNIA ALVRI	HAFNIA ALVEI
KLEBSIELLA	KLEBSIELLA SPECIES
KLEBSIELLA ORNITHICOLYTICA	KLEBSIELLA SPECIES
KLEBSIELLA ORNITHINOLYTICA	KLEBSIELLA SPECIES
KLEBSIELLA OXYTOCA	KLEBSIELLA SPECIES
KLEBSIELLA OZAENAE	KLEBSIELLA SPECIES
KLEBSIELLA OZONAE	KLEBSIELLA SPECIES
KLEBSIELLA PNEUMONIA	KLEBSIELLA SPECIES
KLEBSIELLA PNEUMONIAE	KLEBSIELLA SPECIES
KLEBSIELLA SPECIES	KLEBSIELLA SPECIES
KLEBSIELLA TERRIGENA	KLEBSIELLA SPECIES
LACTOBACILLUS	LACTOBACILLUS SPECIES
LACTOBACILLUS ACIDOPHILUS	LACTOBACILLUS SPECIES
LACTOBACILLUS CASEI	LACTOBACILLUS SPECIES
LACTOBACILLUS SPECIES	LACTOBACILLUS SPECIES

LECLERCIA ADECARBOXYLATA	LECLERCIA ADECARBOXYLATA
LEGIONELLA	LEGIONELLA
LEUCONOSTOC	LEUCONOSTOC SPECIES
LEUCONOSTOC SPECIES	LEUCONOSTOC SPECIES
LISTERIA	LISTERIA SPECIES
LISTERIA MONOCYTOGENES	LISTERIA SPECIES
LISTERIA SPECIES	LISTERIA SPECIES
METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS	MRSA
METHYLOBACTERIUM MESOPHILICUM	METHYLOBACTERIUM MESOPHILICUM
MICRO-AEROPHILIC STREP	MICROAEROPHILIC STREP
MICROAEROPHILIC STREP	MICROAEROPHILIC STREP
MICROAEROPHILIC STREPTOCOCCUS	MICROAEROPHILIC STREP
MICROCOCCUS	MICROCOCCUS SPECIES
MICROCOCCUS LUTEUS	MICROCOCCUS SPECIES
MICROCOCCUS SPECIES	MICROCOCCUS SPECIES
MORAXELLA	MORAXELLA SPECIES
MORAXELLA CATARRHALIS	MORAXELLA SPECIES
MORAXELLA CATHARRALIS	MORAXELLA SPECIES
MORAXELLA LACUNATA	MORAXELLA SPECIES
MORAXELLA SPECIES	MORAXELLA SPECIES
MORGANELLA	MORGANELLA SPECIES
MORGANELLA MORGANII	MORGANELLA SPECIES
MORGANELLA SPECIES	MORGANELLA SPECIES
MRSA	MRSA
NEISSERIA	NEISSERIA SPECIES
NEISSERIA MENINGITIDIS	NEISSERIA SPECIES
NEISSERIA SPECIES	NEISSERIA SPECIES
NOCARDIA	NOCARDIA SPECIES
NOCARDIA ASTEROIDES	NOCARDIA SPECIES
NOCARDIA FARCINICA	NOCARDIA SPECIES
NOCARDIA OTITIDISCAVIARUM	NOCARDIA SPECIES
NOCARDIA SPECIES	NOCARDIA SPECIES
NON-HEMOLYTIC STREPTOCOCCI	NON-HEMOLYTIC STREPTOCOCCI
OCHROBACTRUM ANTHROPI	OCHROBACTRUM ANTHROPI
PANTOEA	PANTOEA SPECIES
PANTOEA AGGLOMERANS	PANTOEA SPECIES
PANTOEA SPECIES	PANTOEA SPECIES
PASTEURELLA	PASTEURELLA SPECIES
PASTEURELLA SPECIES	PASTEURELLA SPECIES
PASTEURELLA MULTOCIDA	PASTEURELLA SPECIES
PASTEURELLA SPECIES	PASTEURELLA SPECIES
PEDIOCOCCUS	PEDIOCOCCUS
PEPTOCOCCUS NIGER	PEPTOCOCCUS NIGER
PEPTOSTREPTOCOCCUS SPECIES	PEPTOSTREPTOCOCCUS SPECIES
PEPTOSTREPTOCOCCUS ANAEROBIUS	PEPTOSTREPTOCOCCUS SPECIES
PEPTOSTREPTOCOCCUS ASACCHAROLYTICUS	PEPTOSTREPTOCOCCUS SPECIES
PEPTOSTREPTOCOCCUS MAGNUS	PEPTOSTREPTOCOCCUS SPECIES
PEPTOSTREPTOCOCCUS MICROS	PEPTOSTREPTOCOCCUS SPECIES
PEPTOSTREPTOCOCCUS SPECIES	PEPTOSTREPTOCOCCUS SPECIES
PLESIOMONAS SHIGELLOIDE	PLESIOMONAS SHIGELLOIDE
PORPHYROMONAS ENDODONTALIS	PORPHYROMONAS ENDODONTALIS
PREVOTELLA	PREVOTELLA SPECIES
PREVOTELLA BIVIA	PREVOTELLA SPECIES
PREVOTELLA BUCCAE	PREVOTELLA SPECIES
PREVOTELLA MELANINOGENICA	PREVOTELLA SPECIES

PREVOTELLA SPECIES	PREVOTELLA SPECIES
PROPIONIBACTERIUM	PROPIONIBACTERIUM SPECIES
PROPIONIBACTERIUM ACNES	PROPIONIBACTERIUM SPECIES
PROPIONIBACTERIUM SPECIES	PROPIONIBACTERIUM SPECIES
PROPRIONIBACTERIUM SPECIES	PROPIONIBACTERIUM SPECIES
PROTEUS	PROTEUS SPECIES
PROTEUS MIRABILIS	PROTEUS MIRABILIS
PROTEUS PENNERI	PROTEUS PENNERI
PROTEUS SPECIES	PROTEUS SPECIES
PROTEUS VULGARIS	PROTEUS VULGARIS
PROVIDENCIA	PROVIDENCIA SPECIES
PROVIDENCIA RETTGERI	PROVIDENCIA SPECIES
PROVIDENCIA SPECIES	PROVIDENCIA SPECIES
PROVIDENCIA STUARTII	PROVIDENCIA SPECIES
PROVOTELLA BUCCEA	PROVOTELLA SPECIES
PROVOTELLA SPECIES	PROVOTELLA SPECIES
PSEUDOMONAS	PSEUDOMONAS SPECIES
PSEUDOMONAS AERUGINOSA	PSEUDOMONAS SPECIES
PSEUDOMONAS ALCALIGENES	PSEUDOMONAS SPECIES
PSEUDOMONAS CEPACIA	PSEUDOMONAS SPECIES
PSEUDOMONAS FLUORESCENS	PSEUDOMONAS SPECIES
PSEUDOMONAS PUTIDA	PSEUDOMONAS SPECIES
PSEUDOMONAS SPECIES	PSEUDOMONAS SPECIES
PSEUDOMONAS STUTZERI	PSEUDOMONAS SPECIES
RAHNELLA AQUATILIS	RAHNELLA AQUATILIS
ROSEOMONAS GILARDII	ROSEOMONAS GILARDII
ROTHIA DENTOCARIOSA	ROTHIA
ROTHIA MUCILANGINOSA	ROTHIA
SALIVARIUS	SALIVARIUS
SALMONELLA	SALMONELLA
SALMONELLA SPECIES GROUP B	SALMONELLA
SERRATIA	SERRATIA SPECIES
SERRATIA FICARIA	SERRATIA SPECIES
SERRATIA FONTICOLA	SERRATIA SPECIES
SERRATIA LIQUEFACIENS	SERRATIA SPECIES
SERRATIA MARCESCENS	SERRATIA SPECIES
SERRATIA MARCESENS	SERRATIA SPECIES
SERRATIA ODORIFERA	SERRATIA SPECIES
SERRATIA PLYMUTHICA	SERRATIA SPECIES
SERRATIA SPECIES	SERRATIA SPECIES
SHEWANELLA PUTREFACIENS	SHEWANELLA PUTREFACIENS
SHIGELLA	SHIGELLA
SPHINGOMONAS	SPHINGOMONAS SPECIES
SPHINGOMONAS PAUCIMOBILS	SPHINGOMONAS SPECIES
SPHINGOMONAS SPECIES	SPHINGOMONAS SPECIES
STAMATOCCUS SPECIES	STAMATOCCUS SPECIES
STAPH. AUREUS MRSA POSITIVE	MRSA
STAPHYLOCOCCUS	STAPHYLOCOCCUS SPECIES
STAPHYLOCOCCUS AUREUS	STAPHYLOCOCCUS AUREUS
STAPHYLOCOCCUS AURICULARIS	STAPHYLOCOCCUS AURICULARIS
STAPHYLOCOCCUS CAPITIS	STAPHYLOCOCCUS CAPITIS
STAPHYLOCOCCUS CHROMOGENES	STAPHYLOCOCCUS CHROMOGENES
STAPHYLOCOCCUS COAGULASE NEGATIVE	COAGULASE NEGATIVE
STAPHYLOCOCCUS COHNII	STAPHYLOCOCCUS COHNII
STAPHYLOCOCCUS EPIDERMIDIS	STAPHYLOCOCCUS EPIDERMIDIS
STAPHYLOCOCCUS EPIDERMITIDI	STAPHYLOCOCCUS EPIDERMIDIS

STAPHYLOCOCCUS HAEMOLYTICUS	STAPHYLOCOCCUS HAEMOLYTICUS
STAPHYLOCOCCUS HOMINIS	STAPHYLOCOCCUS HOMINIS
STAPHYLOCOCCUS INTERMEDIUS	STAPHYLOCOCCUS INTERMEDIUS
STAPHYLOCOCCUS LUGDONENSIS	STAPHYLOCOCCUS LUGDUNENSIS
STAPHYLOCOCCUS LUGDUNENSIS	STAPHYLOCOCCUS LUGDUNENSIS
STAPHYLOCOCCUS SACCHAROLYTICUS	STAPHYLOCOCCUS SACCHAROLYTICUS
STAPHYLOCOCCUS SAPROPHYTICUS	STAPHYLOCOCCUS SAPROPHYTICUS
STAPHYLOCOCCUS SCHLEIFERI	STAPHYLOCOCCUS SCHLEIFERI
STAPHYLOCOCCUS SIMULANS	STAPHYLOCOCCUS SIMULANS
STAPHYLOCOCCUS SPECIES	STAPHYLOCOCCUS SPECIES
STAPHYLOCOCCUS SPECIES COAGULASE NEGATIVE	COAGULASE NEGATIVE
STAPHYLOCOCCUS WARNERI	STAPHYLOCOCCUS WARNERI
STAPHYLOCOCCUS XYLOSUS	STAPHYLOCOCCUS XYLOSUS
STENOTROPHOMONAS MALTOPHILIA	STENOTROPHOMONAS MALTOPHILIA
STOMATOCOCCUS	STOMATOCOCCUS SPECIES
STOMATOCOCCUS SPECIES	STOMATOCOCCUS SPECIES
STREPTOCOCCI, GROUP D	GROUP D STREP
STREPTOCOCCI, GROUP F	GROUP F STREP
STREPTOCOCCUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS ACIDOMINIMUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS ADJACENS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS AGALACTIAE	STREPTOCOCCUS SPECIES
STREPTOCOCCUS AGINOSIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS ANGINOSUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS BOVIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS CONSTELATTUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS CONSTELLATUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS EQUINUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS FAECALIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS FAECIUM	STREPTOCOCCUS SPECIES
STREPTOCOCCUS GORDONII	STREPTOCOCCUS SPECIES
STREPTOCOCCUS GROUP A	GROUP A STREP
STREPTOCOCCUS GROUP B	GROUP B STREP
STREPTOCOCCUS GROUP C	GROUP C STREP
STREPTOCOCCUS GROUP D	GROUP D STREP
STREPTOCOCCUS GROUP F	GROUP F STREP
STREPTOCOCCUS GROUP G	GROUP G STREP
STREPTOCOCCUS INTERMEDIUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS MICROAEROPHILIC	STREPTOCOCCUS SPECIES
STREPTOCOCCUS MILLERI	STREPTOCOCCUS SPECIES
STREPTOCOCCUS MITIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS MUTANS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS ORALIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS PASTEURIANUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS PNEUMONIA	STREPTOCOCCUS SPECIES
STREPTOCOCCUS PYOGENES	STREPTOCOCCUS SPECIES
STREPTOCOCCUS SALIVARIUS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS SANGUINIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS SANGUIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS SPECIES	STREPTOCOCCUS SPECIES
STREPTOCOCCUS VESTIBULARIS	STREPTOCOCCUS SPECIES
STREPTOCOCCUS VIRIDANS	STREPTOCOCCUS SPECIES
TRICHOSPORON ASAHII	TRICHOSPORON SPECIES
TRICHOSPORON SPECIES	TRICHOSPORON SPECIES
VANCOMYCIN RESISTANT ENTEROCOCCUS	VRE
VANCOMYCIN-RESISTANT ENTERCOCCI	VRE

VANCOMYCIN-RESISTANT ENTEROCOCCI	VRE
VEILLONELLA	VEILLONELLA SPECIES
VEILLONELLA SPECIES	VEILLONELLA SPECIES
VRE	VRE
VRE FAECALIS	VRE
VRE FAECIUM	VRE
WOLINELLA	WOLINELLA SPECIES
WOLINELLA SPECIES	WOLINELLA SPECIES
YEAST	YEAST
YERSINIA	YERSINIA

Appendix 5 - List of Antimicrobials (as Appear in the Antibiograms)

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'5-Fluorocytosine',
'Amikacin',
'Amoxicillin/Clavulanic a',
'Amoxicillin/Clavulanate',
'Amphothericin B',
'Amphotericin B',
'Ampicillin',
'Aztreonam',
'Bacitracin',
'Cefazolin',
'Cefepime',
'Cefotetan',
'Cefoperazone',
'Cefotaxime',
'Cefoxitin',
'Ceftazidime',
'Ceftriaxone',
'Cefuroxime',
'Cephalothin',
'Chloramphenicol',
'Ciprofloxacin',
'Clarithromycin',
'Clindamycin',
'Cloxacillin',
'Colistin',
'Doxycycline',
'Erythromycin',
'Fluconazole',
'Fusidic Acid',
'Gatifloxacin',
'Gentamicin',
'High level Gentamicin',
'Gentamicin synergy',
'Imipenem',
'Itraconazole',
'Levofloxacin',
'Linezolide',
'Linezolid',
'Meropenem',
'Metronidazole',
'Minocycline',
'Moxifloxacin',
'Mupirocin',
'Nalidixic Acid',
'Nitrofurantoin',
'Novobiocin',
'Oxacillin',
'Penicillin G',
'Penicillin',
'Piperacillin',
'Piperacillin.Tazobactam',
'Quinupristine/dalfoprist',
'Quinapristin/Dalfopristin',
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'Rifampin',
'Septra',
'Streptomycin 2000',
'Streptomycin synergy',
'High level Streptomycin',
'Sulfamethoxazole',
'Synercid',
'Teicoplanin',
'Tetracycline',
'Ticarcillin/Clavulanic a',
'Ticarcillin/Clavulanate',
'Tobramycin',
'Trimethoprim/Sulfamethox',
'Trimethoprim/Sulfa',
'Vancomycin',
'Voriconazole'
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Chapter 5 Trends in the Prevalence of Bacteria and of Antibiotic Resistance in 2 Canadian Hospitals 2000-2005: Data from Routine Clinical Care

Preamble to Manuscript 1

The first manuscript explores how data that are collected routinely as part of patient care and stored in laboratory information system can be used to enable efficient surveillance of all bacteria types. The goal is to have better information on the true exposure of each individual patient to bacteria for the purpose of studying transmission and improving infection control. In this manuscript the main focus is on prevalence estimates of bacteria and antibiotic resistance, and more briefly, on some of the required steps for deriving prevalence information from individual patient records.

Infections can result in severe consequences, and colonization puts a patient at an increased risk of infection, but colonization by itself does not result in clinically apparent symptoms, and as a result is seldom measured as an outcome. Most research to date directed at enabling surveillance of bacteria using electronic data has focused on identifying infections, given their clinical significance. However, for the purpose of studying transmission and acquisition of bacteria in hospitals the mere presence of bacteria is important, not only the clinical manifestations of infection. The overall prevalence of bacteria in a hospital or hospital ward will determine patient exposure, not just the bacteria present in infected patients.

Comprehensive assessment of the overall prevalence of bacteria would be studied ideally through systematic and repeated screening of all patients and staff in the hospital for all bacteria, as well as sampling of environmental cultures from all surfaces, medical equipment, water supply, the air, etc. Data of this nature are collected as part of short term active surveillance studies, but they are not routinely available. Exploiting the data that are collected routinely as part of clinical care and are available in electronic information systems, may provide the closest available substitute to the ideal data. Using data from hospital information systems requires consideration of all the results, not just those that likely represent infections, and also adjustment to account for repeat samples

and other artefacts of clinical practice patterns. Periodic rates of bacterial prevalence and antibiotic resistance calculated from these data, as is the output of the first study, can serve as a proxy for general prevalence of bacteria in the hospital. When analyzed by patient location and time at the hospital, these data provide a comprehensive picture of the true bacterial exposure of a patient during a hospital stay. These analyses could have been performed automatically using the steps described in this study, in many settings where information systems are implemented, if not for the data processing barriers.

The data in the laboratory information system is generated through the routine processing of specimens. It is stored record by record in the system, and designed to be read by humans on screen, one record at a time. Unfortunately, the insufficient standards for the contents of each record, the lack of uniform structure, and problems with consistency, pose a great challenge to automated processing of the data. The volume of the data makes non-automated processing non-feasible. Though the problems that make these data difficult to process are widespread, the processing itself had to be tailored to the local implementation. The specificity of the processing to each hospital, time period, type of tests etc., is the reason I don't describe it in the manuscript. Chapter 4 of the thesis describes this process. Aspects of the data aggregation process that affect the resulting rates and that are of general applicability, such as the criteria for categorization and exclusion of isolates that were adopted, are discussed in the manuscript. Apart from discussing criteria for categorization and exclusion of isolates, the manuscript is structured to be a mainly substantive report.

Uniform standards across hospitals and adherence to uniform, consistent structure and terminology will ultimately enable wide-spread implementation of automatic surveillance applications based on data from hospital laboratory systems.

Title Page

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Title: Trends in the Prevalence of Bacteria and of Antibiotic Resistance in 2 Canadian Hospitals 2000-2005: Data from Routine Clinical Care

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Abstract

Health-care associated infections (HAI) cause significant mortality and morbidity in hospitalized patients and increase the cost of patient care. There is a considerable, largely untapped potential for information on HAI in the growing implementation and capabilities of hospital information systems. We demonstrate an approach to deriving population-level information about HAI from such systems, and focus on an analysis of prevalence and time trends of bacteria and antibiotic resistance.

We constructed a retrospective cohort of all patients admitted to two university hospitals over the interval 2000-2005. Data from the laboratory information system and the admission discharge transfer system were extracted, linked, grouped and analyzed. The data were summarized and prevalence, rates, and time trends in the rates of bacteria and antibiotic resistance were calculated.

We present the number of non-repeating isolates of the different organisms by body site. Fifty nine different organisms are represented with 15 or more positive isolates during the study period. We calculated the level of susceptibility to antibiotics of selected organisms. We also calculated the time trends of antibiotic susceptibility levels over all bacteria, and for specific selected bacteria. Time trends of rates of MRSA, VRE and C.*difficile* are presented as well.

Data collected in hospital information systems can be used to derive rates of organisms and susceptibility to antimicrobials. Routine analysis of these data has the potential to improve empirical selection of antimicrobial therapy and may complement information from other resources used to guide comprehensive infection prevention and control efforts. However, considerable effort will need to be devoted to the standards and record structure in laboratory information systems if such routine analysis is going to be available in 'close to real-time'.

Introduction

Health-care associated infections (HAI) add significant morbidity and mortality to hospitalized patients, and add substantial cost to the treatment of these patients. HAI affect approximately 2 million hospitalized patients each year in the United States (1) and are estimated to cost between 28 billion and 45 billion US dollars per year (2). In 1995 alone, nosocomial infections contributed to an estimated 88,000 deaths in the US (3) and the burden of HAI increases with the rise in resistance bacteria (11). In Canada, a 2002 point prevalence survey conducted through the Canadian Nosocomial Infection Surveillance Program (CNISP) found a HAI prevalence of 10.5% (4) corresponding to an estimated excess of 8,000 deaths each year (5). Ventilator associated pneumonia alone adds approximately 17,000 ICU days per year in Canada, and costs an estimated 46 million dollars per year (9).

Timely information on rates of bacterial infections and antibiotic resistance is crucial for empirical selection of antimicrobial therapy and for monitoring of trends of infection and resistance. However, given that the prevalence of bacterial infection and resistance vary over time and place, regional and national estimates, especially if dated, may be inaccurate for any given hospital. The antibiotic resistance rate is increasing with time (10), although it varies among hospital wards and patient populations (12). Surveillance of HAI is therefore an important component of a comprehensive infection prevention and control program (13).

Typically, studies of bacterial infections and antibiotic resistance rates are performed by sampling patients or manually reviewing paper records. This process is labor intensive, slow, and expensive. As a result, large studies are conducted infrequently (4;22;39) and most studies are restricted to a specific infection or pathogen at a specific time period.

There exists however a rapidly growing and largely untapped reserve of clinical information that is collected routinely through laboratory information systems as part of patient care. Furthermore, the volume of available data will continue to grow through efforts both in the US (14) and in Canada (15) to support wide scale implementation of clinical information systems. The prospect is that electronic data in hospitals will become

more abundant and more accessible than ever. Using these electronic data automatically should enable rapid and low-cost surveillance of all bacteria types.

Although this approach holds promise, surveillance data including prevalence estimates for infection control personnel are not derived routinely from these electronic patient data. Most laboratory information systems were not designed to allow extraction and analysis of aggregate data for infection control purposes. Moreover, the recent availability of these data has provided little time for the development and evaluation of methods for transforming individual-level clinical data into aggregated indicators for hospital infection control.

To date, most efforts aimed at utilizing information from laboratory information systems have focused on reporting to public health departments of notifiable infections or fast identification of epidemics (37). The tendency of these applications to depend on computerized algorithms to distinguish between infection and colonization, and to identify correctly a primary hospital acquired infection, has driven the development of methods to enable detection of individual cases of infection (87). Our focus however, is on methods to estimate and monitor the general prevalence of bacteria with the purpose of studying transmission and informing infection control efforts. Colonized patients are a reservoir of bacteria and can potentially infect other patients. Therefore, all positive cultures are informative when assessing patients' exposure.

We demonstrate how individual patient information from hospital laboratory information systems can be used to derive prevalence estimates of bacterial and antibiotic resistance in hospitals over time. These estimated rates can be used to present information to prescribing physicians, and inform infection control personnel.

Methods

We conducted a retrospective cohort study of all patients admitted to two sites of the McGill University Health Centre (MUHC), the Royal Victoria Hospital (RVH) and the Montreal General Hospital (MGH), over a 6 year period (2000-2005).

We extracted from the MUHC laboratory information system (LIS) records of all Microbiology tests orders and results for all patients admitted during the study period. In addition, we extracted records from the admission, discharge, and transfer (ADT) information system to estimate lengths-of-stay at locations within the hospitals. A relational database (using MySQL database) was built from LIS and ADT records.

More than 400 different types of Microbiological test codes were used during the study period to order tests in the hospital laboratory information system. The 65 codes for bacterial testing were categorized into 13 groups representing body systems, specimen source (blood, urine), or specific bacteria of special interest for infection control: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus* (VRE) and *Clostridium difficile* (*C.difficile*). Other codes were used for purposes such as ordering tests for viruses, screening blood bank products, and ordering tests for fungi and parasites.

During the study interval, routine screening was performed for MRSA and VRE. Testing for C.*difficile* and other suspected infections was initiated based on clinical signs of infection. Most diagnostic tests were cultures with possible multiple isolates. Antibiograms were reported for most cultured isolates. Tests for *C.difficile* were toxin screen assays. Tests for MRSA and VRE were cultures or a positive/negative screen only.

Bacteria species were categorized by an infectious diseases expert according to similarity, lab procedures and clinical considerations. The NNIS criteria (23) were followed to define repeated results per patient per infection. Results of tests repeated within a month in the same patient for the same type of infection were excluded.

Antibiotic susceptibility percentages: Antibiograms were used to calculate the percent of susceptibility to different bacteria. Following the Clinical and Laboratory Standards Institute (CLSI) guidelines for reporting cumulative antimicrobial sensitivity test data(88)

we report the percent of isolates sensitive to an antibiotic. When 30 isolates or fewer were reported, the estimated prevalence was considered too vulnerable to random noise and was not reported. In keeping with these guidelines, the isolates with intermediate resistance were considered resistant and repeated tests from the same patient per bacteria per calendar year were excluded. Results of screening tests (as opposed to diagnostic tests) were excluded. The number of strains is the number of isolates for the antibiotic for which the number of reported isolates that are included is the highest (following the CLSI guidelines).

Time trends of positive rates of bacteria over the study period were plotted. We also present figures for resistant bacteria that were the focus of infection control efforts. Bacteria rates were calculated based on the incidence of new patients with positive isolates in diagnostic and screening tests aggregated for each month of each calendar year (following the CDC criteria). For the denominators, we calculated the number of patient days for each calendar month. We used the R (2.7.1) statistical software for creating the figures. Moving averages with a symmetrical window of 3 months were used to smooth the monthly rates.

We calculated time trends of susceptibility to each antibiotic over all bacteria over the 6 years of the study. We calculated the percent susceptibility to antibiotic over time of selected bacteria as MRSA and Pseudomonas. For certain antimicrobial combinations we calculated the percent of susceptibility to any of the drugs over time.

Results

During the 6 years of the study period, 546,641 tests were ordered for 65,124 hospitalized patients in the two hospitals. From the tests ordered, 82,490 were positive, resulting in the identification of 113,481 isolates for 23,925 patients. The numbers of tests ordered are presented in Table 1 for twelve body systems and organisms.

The average number of isolates and the rate of negative tests varied considerably among the different body sites (Table 5.1). Most positive tests consisted of a single isolate (74.6%). 17.5% had 2 isolates; 5.3% had 3 isolates; 2% had 4 isolates. Less than 1% (681 tests) had 5 isolates or more, up to a maximum of 9 isolates. Most of the tests with multiple isolates were for wounds. The average number of repeats per patient and infection varied among the different sites and different test types, making the calculations sensitive to the exclusion criteria for repeated positives. Patients were screened weekly for MRSA and VRE. However, many patients with a short length-of-stay and almost all emergency room patients were not screened.

Fifty nine organism groups (bacteria groups, yeast and fungi) were isolated in at least 15 instances during the study period (Table 5.2). The large variety in the infecting organisms can be seen through all common sites. In some groups (blood in particular) the number of probable contaminants, such as the skin organisms is very large. For organisms in which the common site of infection or colonization is not presented in table 2, as for C.*difficile* and the digestive system, the 'other' site column is high in comparison to the numbers in the row. Tests that were ordered under codes specific for MRSA screening (e.g. 'MRSA culture') are categorized under the 'other' column as well.

The number of total isolates (Table 5.2) is greater than the number of unique (non-repeat) isolates (Table 5.1) due to the routine performance of repeat tests for some indications. For blood, only approximately half of the isolates are included when repeats are excluded (6,477/11,684=0.55) but for urine only 15% are repeats (22,529/26,596=0.85).

The antibiotic susceptibilities percentages of selected bacteria are presented in Table 5.3. The maximal number of strains is the number of included isolates and for some bacteria and antimicrobials, such as MRSA and VRE with Vancomycin, the maximum was usually observed. However, the number of strains can be much lower: the panel of

antimicrobials that bacteria are tested for differs with the type of the infection, the body system, and the specimen type. In addition, some of the antimicrobials tested might be considered second or third lines of treatment and omitted from the report. In comparison to Table 5.2, where the NNIS exclusion criteria are followed resulting in less isolates excluded, isolates numbers are much smaller. Common Gram-negative organisms' susceptibilities are presented in Table 5.3a. Selected Gram-positive organisms' susceptibilities are presented in Table 5.3b.

Rates of bacteria that were the focus of infection control efforts during the study period are presented in Figure 5.1. The trends in the two hospitals were similar, and so results aggregated across hospitals are presented. The hospitals experienced a *C.difficile* epidemic during 2002-2004 as can be seen in Figure 5.1a. MRSA rates (Figure 5.1b) increased during the study period, most notably during 2002-2003, and somewhat decreased thereafter, possibly due to enhanced infection control efforts that followed the *C.difficile* epidemic. A rise in VRE coincided with a rise in *C.difficile* (Figure 5.1c). The rates of MSSA were largely unchanged during the study period but fluctuated and were much higher than the rate of MRSA, which resulted in a noisy MRSA to MSSA ratio (Figure 5.1d).

The percent susceptibility to selected antibiotics over time is presented in Figure 5.2. Susceptibility levels of cephalosporins over all bacteria remained unchanged during the study period with 68% susceptibility to Cefazolin and close to a 100% to Cefuroxime (Figure 5.2a). Susceptibility to ticarcillin/clavulanic acid over all bacteria also remained unchanged, but susceptibility to tetracycline decreased from around 78% to 67% (Figure 5.2c). The level of susceptibility to a combination of Erythromycin and Clindamycin followed closely the level of susceptibility to Clindamycin over all bacteria (Figure 5.2c). In MRSA the levels of susceptibility to this combination is almost identical to the level of susceptibility to Clindamycin. The level of Erythromycin susceptibility of MRSA was very low (less than 2%) and hardly added to the susceptibility of the drug combination. The resistance levels to Clindamycin both over all bacteria and in MRSA increased over the study period, especially during the period of 2004-2005. Susceptibility levels to antimicrobials in Pseudomonas remained largely unchanged over the study period, with a possible decrease in the susceptibility to Imipenem (Figure 5.2d).

Discussion

We have demonstrated how individual patient information from hospital laboratory information systems, collected as part of routine clinical care, can be used to derive the prevalence of bacteria and antibiotic resistance in a hospital over time. We presented the information available in a typical laboratory information system, and summarized the prevalence of different organisms, and the antimicrobial susceptibility of selected bacteria. We also presented time trends over six years of selected multi-drug resistant organisms and time trends of susceptibility to antimicrobials.

In modern hospitals, all microbiology lab tests ordered and their results are stored in a laboratory information system. Hospital information systems, however, are configured to enable presentation of an individual test record on a screen, and they often possess a limited capability to aggregate and extract data of epidemiological interest. To conduct this study, we therefore extracted all the records from the system and built a database to enable maximum flexibility in data integration and analysis according to a range of variables. Extracting and processing this type of non-structural data is in general one of the largest barriers to making use of LIS data, and was the first challenge we encountered. The translation of individual data that were not collected as part of a planned study into valid prevalence information that would be comparable to data collected prospectively also posed several challenges.

An important challenge was the interpretation of the codes used to order tests. These codes are necessary to allow grouping of tests into infection types. The assignment of codes to groups was not always straightforward, and some codes had to be analyzed and tests assigned by other information in the record such as specimen location and body site. This is not solely the result of imprecise code choices when tests are ordered. It also points out the importance of adopting a clear and consistent coding system when the system is implemented, with population level as well as individual patient level information in mind. The lack of consistency across systems can make working with data across hospitals, and within hospitals over time, challenging.

Another challenge was that records in the hospital information systems were not the result of an active sample of all patients at specific time points according to specific

protocol. Rather, tests were ordered according to clinical need at the time of care. Consequently, only patients suspected of having an infection were tested (with the exception of MRSA and VRE screening). This situation is however similar to the protocol used in many studies, which dictate collection of specimens only from patients with symptomatic infections. On the other hand, routine data contain many repeat tests for the same patients over a short time frame. In order to present a valid summary, repeat tests must be identified and excluded.

The large range in the number of isolates and tests (Tables 5.2 and 5.3) is due to the different exclusion criteria of isolates that were followed, and to differences in reporting antibiograms. The exclusion criteria of the CDC-NNIS surveillance reports (22) were designed for reporting different types of infections while the criteria that were followed for calculating percent resistance (Table 5.3) were geared towards susceptibility patterns and therefore include only the first isolate per bacteria regardless of body system. In addition, not all isolates are tested for all antibiotics, and some antibiotic testing is not reported (as the reports are designed with specific clinical goals and might omit second and third line treatments). In addition some isolates have no antibiogram reported at all. As a result the number of strains reported in Table 5.3 can be much lower than the number of included isolates.

A comparison of the results in the present study with rates from surveillance studies of infections is problematic. Infection rates that are estimated from electronic systems are necessarily different from those used in manual surveillance as they are based on different definitions. Woeltje et al.(37) go as far as suggesting the terminology of ‘electronic rate’ or ‘electronic index’ to clarify that the HAI rate derived from data in a hospital information system cannot be compared directly with manually determined rates even when definitions are carefully followed. We present results of positives without an attempt to ‘correct’ the rates to exclude colonizations, which adds additional complexity to comparison to infection surveillance studies. Indeed, a comparison of the relative frequency of bacteria to results from the CANWARD study (26) indicates a general similarity in the most frequent organisms. One exception is the difference in the frequency of coagulase-negative *Staphyloccuccus*, which is probably a colonizing bacteria and not a cause of an infection in most patients. MRSA rates are relatively higher

when screening results are included and lower when only diagnostic results are included. Results of trends, even if not directly comparable to results that are derived with different methodology, are internally consistent over time and are useful for study of changes in time.

We followed the method recommended by the National Committee for Clinical Laboratory Standards (NCCLS) for reporting antimicrobial susceptibility test data for identifying and excluding duplicate isolates for reporting antimicrobial resistance patterns (88). There is conflicting evidence as to the level of influence the method for duplicate isolates exclusion has on the antibiotic resistance rates (89-92). The NCCLS method is an accepted standard that does not over-represent resistant strains due to repeat testing.

Some aspects of data that are not actively collected limit the utility of the data. A positive screening test result indicates colonization by an organism. But, an isolate from a diagnostic test can indicate colonization or infection. There is also no guarantee that an isolate indicates a new infection rather than an existing one. This ambiguity makes the data better suited for deriving prevalence rather than incidence rates. In some cases, not all the antimicrobials tested are reported. Selective reporting of second and third line antimicrobials only in cases where a more resistant strain is present can lead to over estimation of resistance rates. Reporting is however largely standard across each organism. Other limitations are not different from the ones faced by all studies that rely on microbiological diagnostic tests: inaccuracy of the results with false positive and false negative rates that can be high, and contaminants.

Despite the limitations discussed, the types of data used for this study possess considerable advantages. Relying on the information that is collected routinely in hospital information systems makes it possible to present results on a wide breadth of organisms and antimicrobials over a long period of time. In this paper, we chose to focus on bacteria and selected antimicrobials and only space limitations prevented the presentation of time trends for all organisms and antimicrobials. Other potential analysis could include exploring in more detail trends of antimicrobial resistance for specific bacteria and in specific infection sites or specimen types (as respiratory or blood isolates). It is also possible to examine isolates from different hospital wards, nursing units, or hospital

services, or to stratify by patient time in the hospital. These data can also be used in the development of empirical antimicrobial treatment algorithms for patients in specific units with specific infections, and to examine components of infection control policies such as the frequency of MRSA and VRE screening.

There is a targeted effort in Canada (15) as well as in the US (14) towards wide implementation of clinical information systems. The prospect is that electronic data in hospitals will become more abundant and more accessible than ever. Using available electronic data, in an automatic manner can enable efficient parallel surveillance of all bacteria types by utilizing existing resources. This updated aggregated local information on rates of infections with different bacteria and their antibiotic resistance has the potential to improve empirical selection of antimicrobial therapy. In addition, it can be used to complement information from other resources as part of comprehensive infection prevention and control efforts.

Tables

Table 5.1: Tests by specimen site and type of culture (without excluding any repeats or similar tests)

	Tests Ordered		Positive Results	
Site / test type	# Tests	# Patients	# Tests	# Isolates
Blood	89,873	22,539	9,578	11,684
Urine	72,089	32,097	21,785	26,596
Respiratory (lower)	25,092	10,377	11,006	15,963
Throat	2,338	2,117	361	429
Wound deep	17,021	8,515	6,465	11,927
Wound superficial	17,660	8,236	12,195	24,941
Medical devices	7,641	4,077	1,982	2,651
Digestive (Stool)	6,157	4,443	533	551
CSF	4,376	2,271	420	456
C. difficile	25,599	11,467	4,287	4,287
Total	267,846	106,139*	68,612	99,485
Screening tests	# Tests	# Patients	# Positive Tests	# Patients Positive
MRSA	127,542	33,261	12,381	3,294
VRE	63,426	31,412	1,611	525

Not presented are tests for Mycology, viruses, and the group of vaginal tests.
* Patients are not distinctive among categories

Table 5.2: Numbers of isolates of common organisms in selected sites, excluding repeats, ordered by total frequency

Organisms	Site						Total
	Blood	Urine	Respiratory (lower)	Wound Deep	Wound Superficial	Other	
TOTAL	**6,477**	**22,529**	**11,737**	**8,839**	**19,091**	**13,236**	**81,909**
Coagulase-negative *Staphylococcus*	1,779	1,639	192	1,448	3,491	1,220	9,769
Enterococcus species	449	4,869	236	1,071	2,366	250	9,241
Escherichia species	787	5,961	592	699	950	67	9,056
MRSA	318	472	802	319	961	5,460	8,332
Yeast*	335	2,199	1,687	389	767	534	5,911
Staphylococcus aureus	598	487	1,220	798	2,072	224	5,399
Klebsiella species	485	2,281	1,007	431	976	144	5,324
Pseudomonas species	183	1,154	2,136	351	1,300	134	5,258
C. difficile	1	0	0	2	2	3,456	3,461
Enterobacter species	145	719	578	260	619	75	2,396
Corynebacterium species	87	144	26	331	1,424	112	2,124
Streptococcus viridans	316	189	35	717	786	49	2,092
Proteus mirabilis	82	791	139	124	394	35	1,565
Haemophilus species	22	1	877	79	89	6	1,074
VRE	10	15	1	4	5	958	993
Citrobacter species	36	394	142	93	198	11	874
Group B *strep*	46	288	103	116	306	14	873
Serratia species	63	182	244	67	195	37	788
Bacteroides species	81	0	2	302	354	2	741
Stenotrophomonas maltophilia	37	44	376	72	142	16	687
Anaerobic *cocci*	54	0	2	170	360	3	589
Streptococcus pneumoniae	116	0	411	21	27	12	587

Acinetobacter species	28	65	179	51	153	22	498
PropionIbacterium species	50	0	0	153	117	65	385
Morganella species	16	139	35	53	106	8	357
Lactobacillus species	20	87	2	101	109	3	322
Group A *strep*	26	3	31	50	121	85	316
Clostridium species	43	0	1	89	117	4	254
Bacillus species	26	2	98	49	43	30	248
Moraxella species	7	1	207	5	18	3	241
Proteus species	10	141	11	12	55	8	237
Proteus vulgaris	2	43	17	21	65	5	153
Group G *strep*	21	8	14	25	74	10	152
Fungi*	1	6	107	25	11	1	151
Group C *strep*	8	4	19	28	27	22	108
Neisseria species	18	3	25	22	33	7	108
Providencia species	5	43	6	6	41	3	104
Group F *strep*	1	1	8	54	21	1	86
Salmonella	27	2	0	5	0	43	77
Group D *strep*	3	37	0	12	18	0	70
Micrococcus species	18	6	1	21	15	7	68
Aeromonas species	7	0	3	14	16	24	64
Staphylococcus saprophyticus	5	58	0	0	1	0	64
Prevotella species	13	0	1	21	21	0	56
Alcaligenes species	8	13	10	10	12	1	54
Hafnia alvei	1	9	17	9	13	1	50
Fusobacterium species	11	0	0	16	23	0	50
non-hemolytic *Streprococci*	0	10	0	12	9	1	32
Pasteurella species	3	0	5	5	15	0	28

Campylobacter	5	0	0	1	0	21	27
Veillonella species	2	0	1	12	12	0	27
Listeria species	15	0	1	2	2	1	21
Actinomyces species	0	0	3	14	4	0	21
Shigella	0	0	0	0	0	20	20
Pantoea species	2	4	1	5	6	0	18
Flavobacterium species	3	2	6	4	1	1	17
Eikenella corroden	0	0	2	9	6	0	17
Staphylococcus lugdunensis	7	1	0	6	1	1	16
Stomatococcus species	7	0	4	1	3	0	15
Other	28	12	114	52	18	19	243
TOTAL	**6,477**	**22,529**	**11,737**	**8,839**	**19,091**	**13,236**	**81,909**

*The results for fungi and yeast represent only isolates from test groups that were included in the study. Tests for other organisms than bacteria (such as tests for yeast only) are not included.

Table 5.3a: Percent susceptibility* to common antibiotics of selected gram negative bacteria over the study period

		% susceptibility														
Organisms	# Strains†	amikacin	Ampicillin	cefazolin	cefotaxime	ceftazidime	ceftriaxone	ciprofloxacinn	gentamicin	imipenem	nirtofurantoin	piperacillin	septra	tobramycin	Ticarcillin/ clavulanic a.	trimethoprim-sulfamethoxazole
Escherichia species	7224	99.5	62	92.8	16.2	90.1	93.4	89.9	95.2	99.9	96.1	98	83.2	93	90.2	80.4
Klebsiella species	3794	100	0.8	91.9	95.5	95.7	95.2	94.5	97.6	99.7	48.8	97.1	95.9	93.1	93.1	87.5
Pseudomonas species	2592	90.4	-	-	-	93.6	-	82.3	85.6	88.3	4.4	95.9	-	89	78.5	-
Enterobacter species	1786	100	1.8	10.7	80*	79.3	78.3	94.1	98.2	99.6	49.8	86	96.1	98.1	75.5	90.4

* Susceptibility percentages for each organism/antimicrobial were generated by including the first isolate of that organism per patient per year in the study

† Number of strains is the number of included isolates tested for the most commonly reported antimicrobial for a specific organism

Table 5.3b: Percent susceptibility* to common antibiotics of selected gram positive bacteria over the study period

		% susceptibility																		
Organisms	# Strains†	ampicillin	Cefazolin	chloramphenicol	ciprofloxacinn	clindamycin	erythromycin	Fusidic acid	gentamicin	levofloxacin	linezolid	mupirocin	nirtofurantoin	oxacillin	penicillin	Quinapristin/ dalfoprist	septra	tetracycline	trimethoprim-sulfamethoxazole	vancomycin
Enterococcus species	5339	89.3	-	-	23.1	-	-	-	64.5	59.8	-	-	94.6	-	-	-	-	25.8	-	99.3
MRSA	3622	-	0.5	-	1.1	17.4	1.2	98	96.6	100	99.9	90.7	98.7	0	0.1	-	98.6	98.6	98	100
Staphylococcus aureus	3820	-	99.8	-	-	89.7	76.4	-	100	-	-	-	99.5	99.5	14.3	-	99.1	97.4	98.5	100
VRE	498	7.8	-	96.8							98.6					96.1		52.8		0

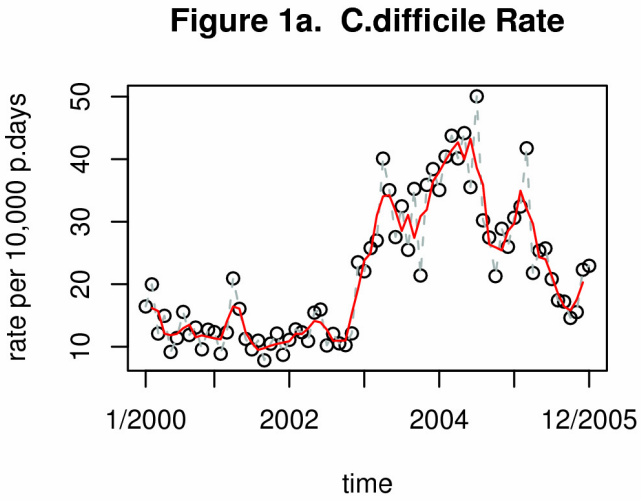
* Susceptibility percentages for each organism/antimicrobial were generated by including the first isolate of that organism per patient per year in the study

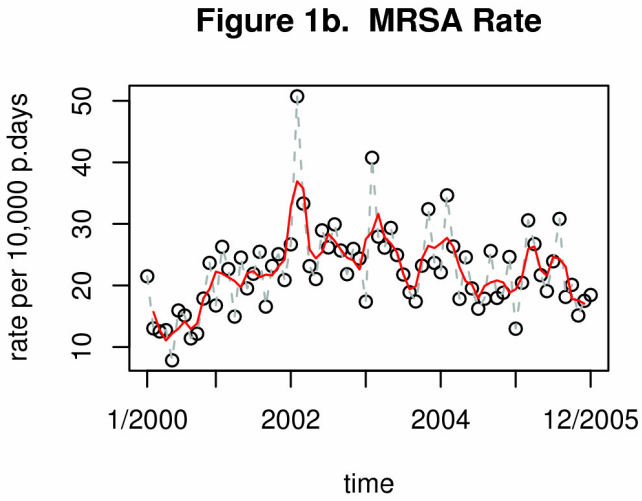
† Number of strains is the number of included isolates tested for the most commonly reported antimicrobial for a specific organism

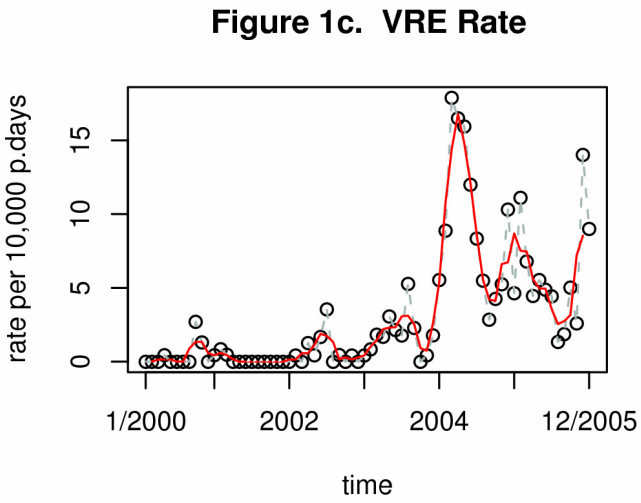
Figures

Figure 5.1: Rate of selected bacteria over the study period by month.

5.1a: MRSA; 5.1b: C.*difficile*; 5.1c: vre; 5.1d: MRSA to MSSA ratio







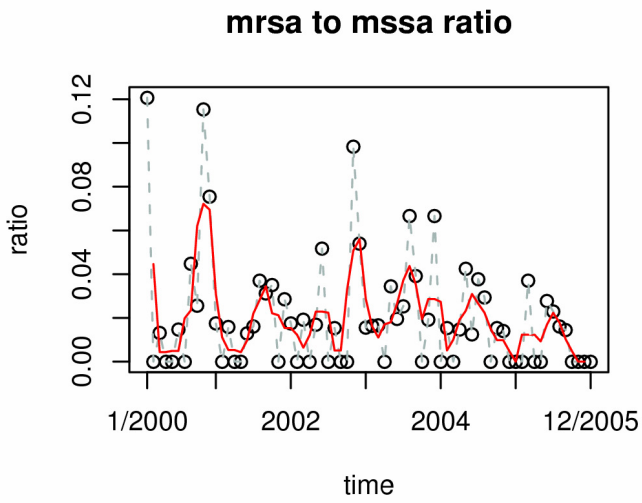


Figure 5.2: Percent susceptibility (%S) to antibiotic over time.

5.2a: Percent susceptibility over all bacteria to Cafazolin; Ceftriaxone; Ceftazidime; Cefotaxime; Cefuroxime

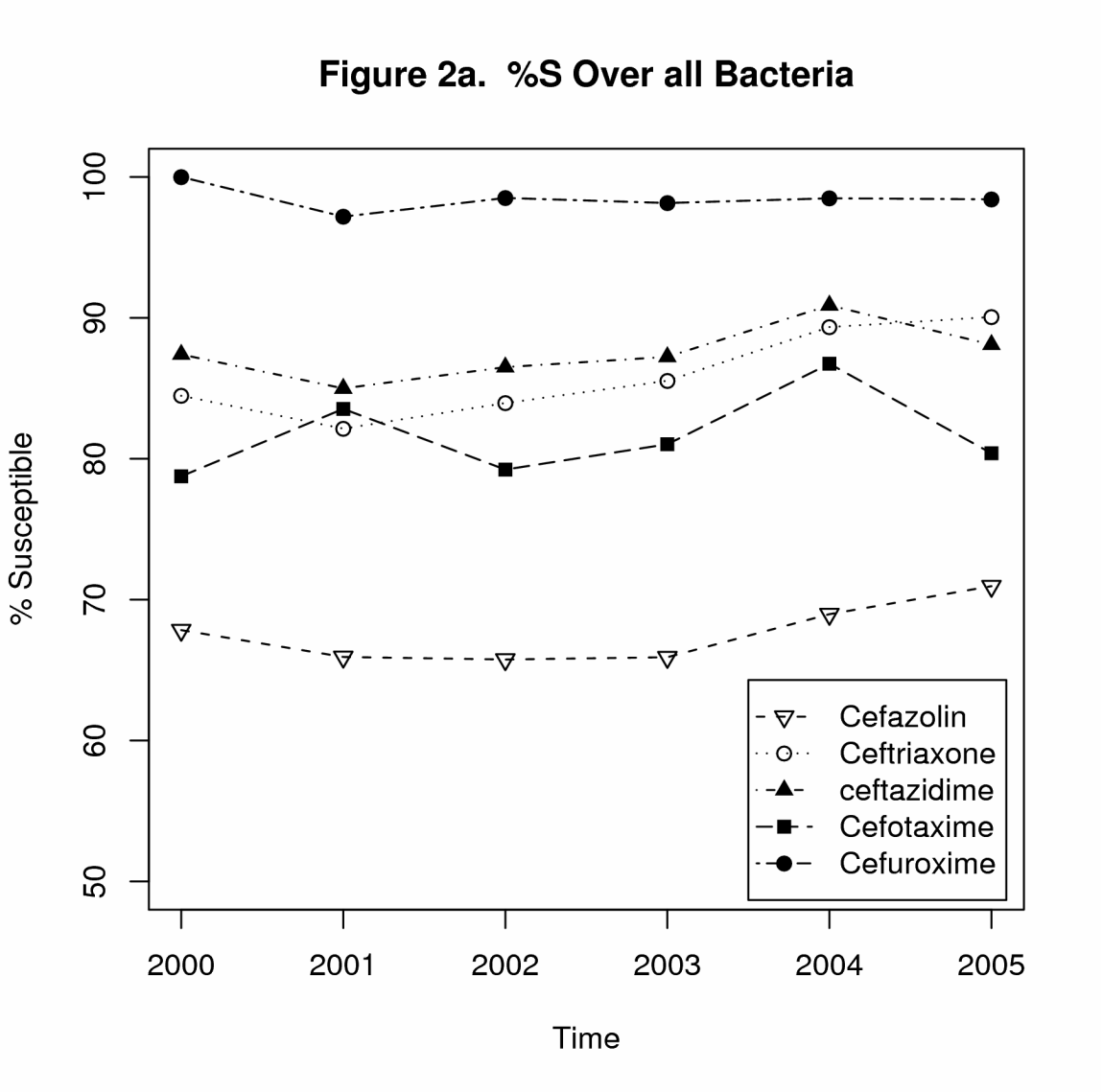


Figure 5.2b: Percent susceptibility (%S) over all bacteria to Ciprofloxacin; Vancomycin; Tetracyclin; Ticarcillin/Clavulanate

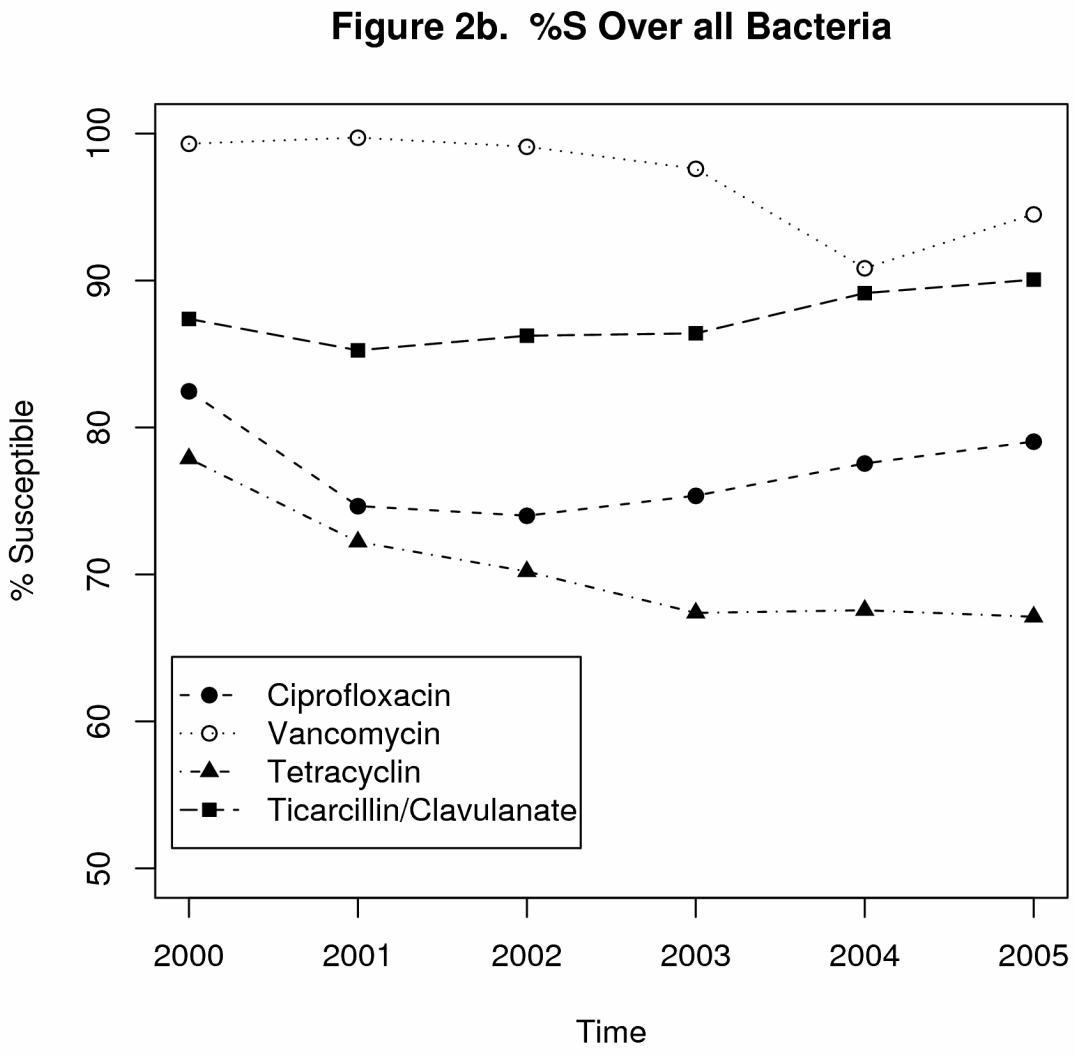


Figure 5.2c: Percent susceptibility (%S) over all bacteria and in MRSA to Erythromycin and/or Clindamycin

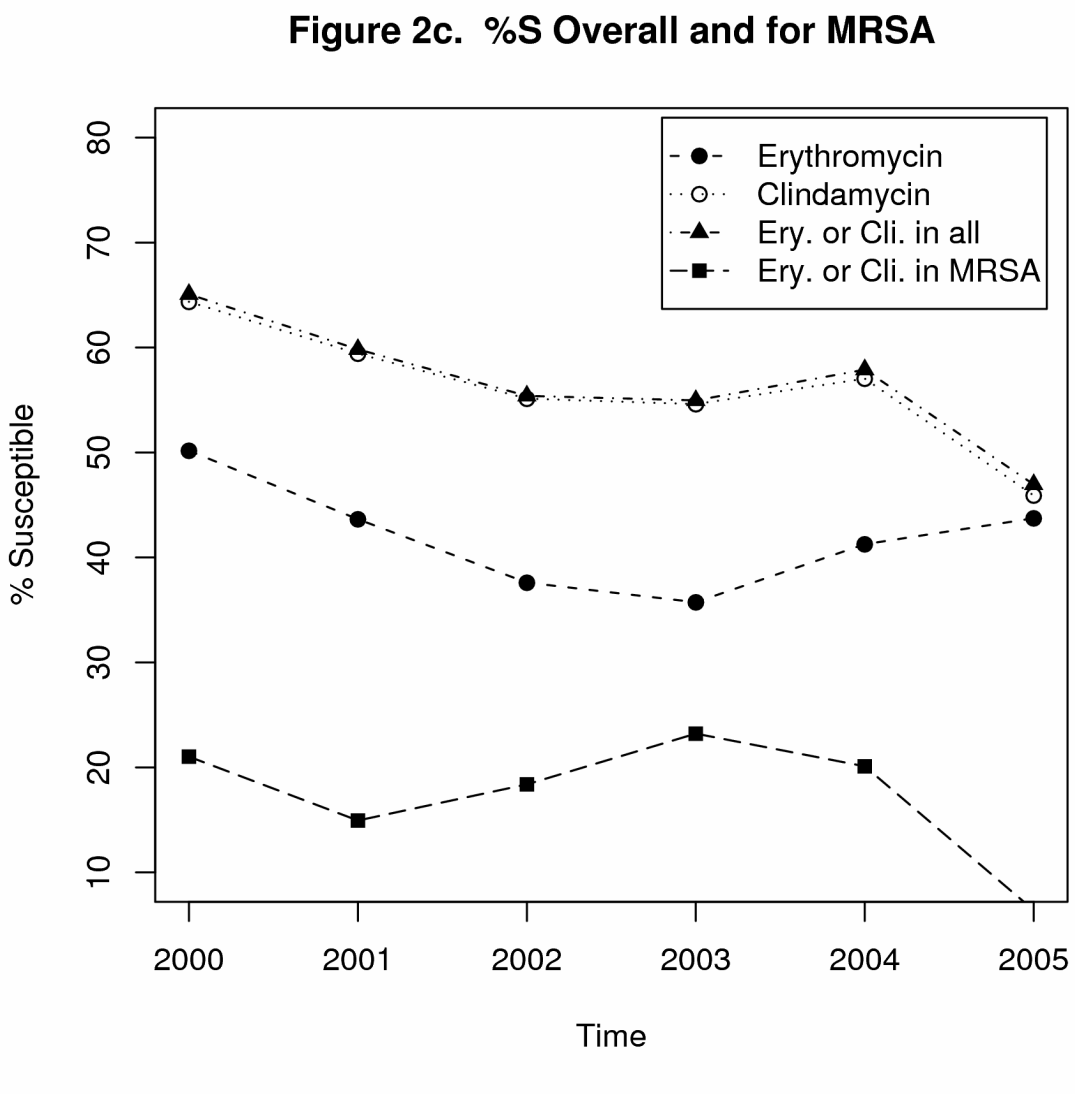
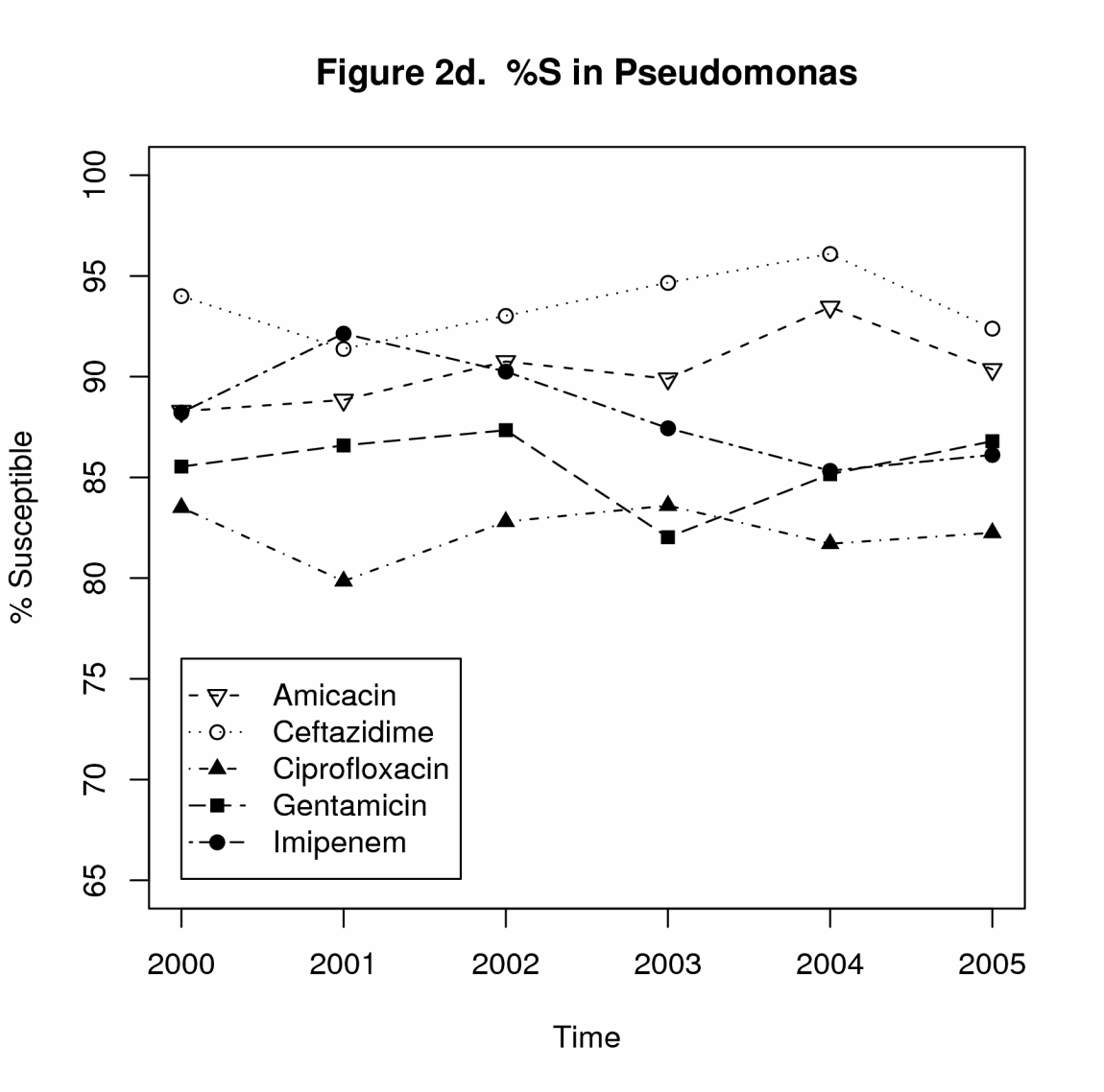


Figure 5.2d: Percent susceptibility (%S) in Pseudomonas to Amicacin; Ceftazidime; Ciprofloxacin; Gentamicin; Imipenem;



Chapter 6 Infection Acquisition following Intensive Care Unit Room Privatization

Preamble to Manuscript 2

The second goal of the thesis was to explore the potential of electronic data from hospital information systems to study patterns of bacterial acquisition in ICU settings. In the second manuscript, I describe a study of the impact of a physical intervention on bacterial acquisition rates. The re-opening of the ICU in one of the study hospitals in a new location within the hospital part way through the study period with all private rooms, replacing the older ICU which had two rooms of 12 patients each, provided an opportunity to study the impact of this intervention on bacterial acquisition rates. A comparison of rates before and after the privatization with the rates in the ICU of the second study hospital, which was unchanged during the study period, while taking other factors and trends into account, provided an opportunity to isolate the effect of the intervention from other factors and time trends.

The breadth of the data available through hospital information systems enabled the study of a wide range of infectious organisms. Previous studies focused on few bacteria, and in most cases, on MRSA alone. This study introduces the use of the classification of bacterial acquisition as likely exogenous or endogenous to study the effect of a physical intervention on acquisition. Likely exogenous bacteria have been studied most commonly in this context. The comparison of the effect of the intervention on both exogenous and endogenous bacteria, however, is a useful mechanism to validate the methodology.

Previous studies of similar interventions have measured the effect on the level of infection. However, this type of intervention has the potential to reduce bacterial transmission, and many factors that have nothing to do with transmission influence the chances that an exposed patient will develop an infection following acquisition of bacteria. Important factors include the patient's age and general health status, co-morbidities, procedures that were performed and medications taken. The direct outcome that is measured is acquisition of bacteria by patients. The first positive test of patients for

a type of bacteria is a sensitive measure of bacterial acquisition, and therefore of bacterial transmission. The study is based on the same electronic data from the laboratory information system that were described in the first manuscript with data from two additional hospital information systems. The interpretation of the outcome of change in bacterial acquisition is discussed in the manuscript. Results of a validation study with infections as recorded in an information system that is maintained in the ICUs are also discussed.

Title Page

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Title: Infection Acquisition following Intensive Care Unit Room Privatization

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Abstract

Background Patients in intensive care units (ICU) commonly acquire infections, which impose a heavy human and financial burden. The use of private rooms may reduce the acquisition of certain pathogens, but the limited evidence on this topic is inconsistent.

Methods We compared the rates of acquisition of infectious organisms in an ICU before and after a change from multi-bed to single rooms. As a control, we used acquisition rates in the ICU of a second, nearby university teaching hospital, which contained both multi-bed and single rooms throughout the study period. We used a statistical model to adjust for background time trends common to both hospitals.

Results The adjusted rate of acquisition of *C.difficile*, VRE, and MRSA combined decreased by 54% (95% CI: 29%-70%) following the intervention. The MRSA acquisition rate fell by 47% (1%-71%), the *C.difficile* acquisition rate fell by 43% (7%-65%), and the yeast acquisition rate fell by 51% (34%-64%). Twelve common and likely exogenous organisms and exogenous/endogenous organisms had a reduction in acquisition rate following the intervention; for six of them, this reduction was statistically significant. No effect was observed on the acquisition rate of Coagulase-negative *Staphylococcus*, the most common endogenous organism, for which no change would be expected. The adjusted rate ratio of the average length of stay in the ICU was 10% (0%-20%) lower following the intervention.

Conclusions Conversion to single rooms can substantially reduce the rate at which patients acquire infectious organisms while in the ICU.

Introduction

Healthcare associated infections occur in about 30% of patients in intensive-care units and are associated with substantial morbidity and mortality (6). In ICU patients, these infections are associated with an increased length of stay (LOS) of 8-9 days (7), and the resulting additional cost from excess stay alone is estimated at 3.5 billion dollars per year in the United States (8).

Isolation of ICU patients in private rooms is a common infection control recommendation intended to limit the transmission of infectious organisms to patients by facilitating infection control practices by health care workers (58). Current guidelines on the design and construction of hospitals and health care facilities, issued by the American Institute of Architects for health with assistance from the U.S. Department of Health, recommend single-patient rooms in new constructions and in renovations (61).

However, results from studies are inconclusive regarding the effect of private rooms on infection rates (16-19). In a systematic review, only 3 of 8 studies reviewed found a statistically significant reduction in the rate of infections in ICU patients following an intervention to change the facilities' architecture (20).

Most previous studies were limited in their scope to specific types of bacteria or infection. The majority examined methicillin-resistant *Staphylococcus aureus* (MRSA) (20) and only a few studies considered the effect of a physical intervention on vancomycin resistant *Enterococcus* (VRE) (62) and *Clostridium difficile* (*C. difficile*) (63).

Private rooms are believed to facilitate better infection control practices and allow for better isolation of patients from hospital-borne infectious agents (59). A sensitive measure of transmission of bacteria and yeast is the first or incident acquisition of those organisms by a patient. Acquisition of an infectious organism is a necessary precursor to infection. Once acquired, the organism may result in colonization of the patient, where no symptoms are evident, or it may lead to symptomatic infection. The association between colonization and future infection is well demonstrated for many bacteria, (93-96) and the colonization rate is therefore clinically important.

Bacteria may be acquired from exogenous sources, such as the physical environment, other patients, or health workers. In addition, acquisition can also be from an endogenous source such as the patient's own flora. Infection control efforts such as patient isolation are directed towards preventing the transmission of exogenous bacteria. A comparison of an intervention's effect on likely exogenous versus likely endogenous colonization rates gives direct evidence of an intervention's success in achieving reduced exposure of patients to hospital-borne organisms.

On the second of March 2002, a new ICU with all private rooms opened at the Montreal General Hospital in Montreal, replacing the older ICU which had rooms of 12 patients. The presence of a second university teaching hospital, under the same McGill University academic department of medicine, less than a mile (about 1.4 km) away and serving the same community, presented a valuable opportunity to examine the effect of private rooms on bacterial acquisition rates. A comparison of rates before and after the privatization, while taking other factors and trends into account provides an opportunity to assess the effect of the intervention on acquisition rates.

Methods

Setting and Study Design

The Montreal General Hospital – the "intervention" hospital, and the Royal Victoria Hospital – the "comparison" hospital, are two McGill-University hospitals serving the same Montreal region. The hospitals have a single, common infection control service with one director and they have shared infection control policies and practices. The hospitals experienced similar trends in the rates of bacterial infection and outbreaks of *C.difficile* during the study period.

The 25-bed adult ICU of the comparison hospital remained unchanged during 2000-2005 and had rooms with 2, 5 or 6 beds and eight single rooms. Prior to the intervention the 24-bed adult ICU at the intervention hospital consisted of two large rooms of 12 beds and 2 private rooms within each larger room and a total of 4 sinks. In March 2002, the intervention hospital ICU was moved to a new location with 24 beds, each in a private room containing a sink, and 2 additional sinks in an area outside the private rooms.

The nursing ratio was the same in both hospitals and remained constant during the study period. This ratio was 1:1 for 30% of beds and 2:1 for 70% of beds. This ratio was maintained even through temporary shortage in nurses by intermittent bed closing. Alcohol-based hand gels were available throughout the study in a ratio of one per two beds in both hospitals. The products that were used were identical between the two hospitals.

We studied the cohorts of patients who were admitted to these two ICUs during 2000-2005.

Patients and Test Results

We measured the incidence rates of positive microbiological test results for all patients in the cohort. Test results for specimens collected during the first 48 hours after ICU admission were excluded. The initial positive test result per patient per organism was counted regardless of the specimen type. An ICU patient was considered at risk of colonization separately with every bacteria group for which she had not previously tested positive.

Results from tests that were ordered up to 48 hours after a patient was discharged from the ICU were considered as ICU acquired. Studies that rely on data recorded in the ICU alone do not routinely include cases identified after discharge from the ICU. We therefore also performed a sensitivity analysis, by including only cases that would have been captured at the ICU alone for MRSA.

Infectious Organisms

Bacteria, yeast and molds were divided into likely exogenous or endogenous source of infection (97-100). An organism was considered exogenous if it was likely to be transmitted to a patient through contact with contaminated equipment, the environment or another patient or staff in the ICU. An organism was considered endogenous if it was likely to be present in the patient's own flora on admission to the ICU, for example Coagulase negative Staphylococcus (Table 4).

Data

The data for the study were obtained from three hospital information systems. ICU patients were identified and admission times in the ICU were obtained from the admission discharge transfer (ADT) database. The ADT system contained the location information over time for all admitted patients. Every admission to a specific bed within the hospital, move to another bed, and discharge is recorded with its precise time.

Microbiology test results were obtained from the laboratory information system. Patients were universally screened for MRSA and VRE upon ICU admission. Contacts of index cases were re-screened. The same protocol applied to both hospitals during the entire study period. Other Microbiology testing was initiated upon suspicion of an infection. Stool samples were tested routinely for *C.difficile* in patients with diarrhea.

Information on patients' infections was obtained from the ICU information system and was used to validate our approach of using the first positive Microbiology result. The ICU database is maintained by an archivist who records all infections identified for patients during an ICU stay. MRSA and VRE positives are recorded as well as *C.difficile* colitis cases. For these 3 organisms, we validated cases detected using the Microbiology tests results against cases recorded in the ICU information system. We computed

sensitivity and specificity of case detection via the Microbiology tests using the ICU system as gold standard. The system was in place during almost the entire study period at the comparison hospital and from February of 2003 at the intervention hospital.

Data Analysis

In order to isolate the effect of the intervention from other changes and trends that took place over the study period we took advantage of the fact that, aside from the intervention, both hospitals experienced similar trends and changes. Rather than compute 2 separate pre-post rate ratios for each of the two hospitals, and then compare the two pre-post rate ratios, we compared the 26 monthly pre-intervention ratios of rates (monthly intervention vs. comparison to adjust for time trends and other common hospital factors) with the corresponding 46 post-intervention ones. Thus, we used the 72 monthly rates for each organism in each hospital, to calculate 72 rate ratios (intervention vs. comparison hospital). We fitted a logistic regression model to estimate the post-intervention change in the level of these rate ratios in order to evaluate the effect of the intervention. The numbers of cases in the 2 hospitals combined served as the binomial 'denominators' and the numbers of cases in the intervention hospital as numerators, with the ratios scaled by the numbers of patient days in the contrasted hospitals. Thus, the model posited one rate ratio pre- and a second rate ratio post-intervention; the complement of the ratio of the two was taken as an estimate of the percentage reduction in the rate in the intervention hospital due to the intervention. Robust confidence intervals were constructed using the sandwich estimator (101). We used the R (version 2.7.1) statistical software for fitting the parameters of the model and for the data analysis.

We also evaluated the average number of days a patient spent in the ICU during a hospitalization pre and post intervention. We applied a similar (linear) regression approach to the logs of the 72 (intervention vs. comparison) ratios of the average LOS in the ICU during a hospitalization, comparing the ratios pre and post intervention.

The transfer to the new ICU was done overnight on March 2nd 2002. The change to all private rooms was hypothesized to have an immediate and a constant affect on the infection rate. To account for the possibility that the new environment was cleaner, and that the cleaner environment had an effect that faded with time, an alternative model was

tested. This second model allowed the effect of the new environment to fade with time, with the incidence rate falling post intervention, than reaching a new plateau, lower than the original one. The first model assumed that any observed reduction is attributable to decreased person-to-person transmission and to private rooms (facilitating better hand hygiene by hospital staff). The second model assumed that some of any observed reduction is attributable to a temporary decreased environment to person transmission due to moving to a new and presumably uncontaminated environment. We tested several versions of the second model, representing several rates of environment contamination, ranging from two weeks to three months. The second model did not describe the data any better than the simple one and so results are not presented.

There were no other major events during the study period such as changes in antibiotic prescribing or infection control policies. A *C.difficile* epidemic that occurred during 2003-2004 led to some enhancement in infection control practices, but changes were the same in both hospitals.

Models for endogenous organisms were analyzed as a 'negative' comparison where no change in the rate of acquisition was expected as a result of the intervention. An analysis for MRSA, *C.difficile*, and VRE combined was performed in addition to a separate analysis for each organism. These three organisms are a focus of infection control efforts and are very likely due to exogenous bacteria.

Results

A total of 19,343 admissions to both ICUs contributed 85,995 patient-days at risk. The patient population within each ICU remained essentially constant before and after the intervention (Table 6.1).

In the intervention hospital, a total of 3,084 incident positive cultures for different bacteria, yeast, and fungi were detected in the ICU during the study period, and the corresponding number in the comparison hospital was 3,513. Table 6.2 presents the counts and rates of incident positives cultures for the most common organisms.

In a comparison with ICU data on patients' infections, our method of defining a case was found to be advantageous. We captured 91% of MRSA noted in the ICU system, 98% of *C.difficile* cases, and 100% of VRE cases reported in the ICU system. Our method captured additional cases that emerged from the ICU, for which the tests results became available only once patients were already discharged from the ICU. When not accounting for the post-ICU captured cases (which the ICU system did not capture), the specificity of our method compared to the ICU system was 0.96 for *C.difficile*, 0.72 for MRSA, and 0.88 for VRE. The cases that emerged at the 48 hours post ICU discharge were, however, considered as true positives and included in the analysis.

Table 6.3 shows additional details about the frequency and rates of positive culture results for selected bacteria by year. In the interval 2002-2004, both hospitals experienced an epidemic of *C.difficile* and an increase in the number of MRSA and VRE cases. 59% of MRSA positives were identified through diagnostic tests (57.5% in the intervention hospital and 61% at the comparison hospital) and 41% through screening tests. Screening tests identified all but one of the VRE cases.

The average number of days in the ICU during a hospital stay increased steadily during the study period for patients at the comparison hospital (Table 6.3). At the intervention hospital the average number of days at the ICU fluctuated, but did not increase during the study period. The adjusted average ICU LOS fell by an estimated 10% (relative ratio of 0.90 with 95% CI of 0.80-1.0) following the intervention. The decrease was borderline statistically significant.

The adjusted rate of acquisition of *C.difficile*, VRE, and MRSA combined decreased after the intervention by 54% (rate ratio 0.46, 0.30 - 0.71 CI) (Table 6.4). The numbers of VRE alone were too small to obtain precise estimates, but the model for the combined data showed an additional decrease over and above the decrease in MRSA (47%) and *C.difficile* (43%) when VRE were also included. Of the other likely exogenous organisms, *Stenotrophomonas maltophilia* had a reduction that was not statistically significant, and the rate of acquisition of *Acinetobacter* species fell by 53%. The number of fungal infections was relatively small, resulting in wide confidence intervals.

The acquisition of most of the organisms in the exogenous/endogenous group fell following the intervention (Table 6.4). Three organisms had statistically significant reductions: yeast acquisition fell by 51%; *Enterobacter* species fell by 38%; *Klebsiella* species fell by 38%. *Enterococcus* species, *Escherichia* species, and *Serratia* species fell by 23%, 11%, 23% respectively; these reductions were not statistically significant. The numbers of new acquisitions of *Citrobacter* species, *Proteus mirabilis*, and *Morganella* species were relatively small, resulting in wide confidence intervals. *Staphylococcus aureus*, and *Pseudomonas* species did not show any significant change in the rate of incident acquisitions.

The effect of the intervention on Coagulase-negative *Staphylococcus*, the most common organism, was not statistically significant, as expected (Table 6.4). Coagulase-negative *Staphylococcus* was considered a likely endogenous organism and was tested as a negative comparison. *Streptococcus viridans*, another likely endogenous organism also did not show a reduction in acquisition rates with the ICU intervention, but *Haemophilus* species did have a statistically significant reduction.

Our sensitivity analysis excluding MRSA cases that were captured in the 48 hours following discharge from the ICU revealed the importance of including those cases. With these cases excluded, the estimated adjusted decrease in MRSA cases was 31% (compared to 43% when the cases are included), and the reduction was no longer statistically significant.

Comment

Following the change of an ICU to all private rooms, we found that the rate of acquisition of bacteria decreased by more than half. An ICU environment with private rooms may facilitate better infection control practices, therefore reducing the transmission of infectious organisms.

In our study, after adjustment for common outside temporal factors, *C.difficile*, MRSA, Yeast, *Acinetobacter* , *Klebsiella*, and *Enterobacter* all had significant reductions in acquisition rates. Other likely exogenous organisms such as *Stenotrophomonas maltophilia*, *Enterococcus* species, *Escherichia* species, and *Serratia* species had reductions that were not statistically significant. Yeast is the only one of these organisms (apart from MRSA, VRE and *C.difficile*) that other studies have reported to have a reduction in rate following a physical intervention.

Pseudomonas and *Staphylococcus aureus* did not show any reduction following the intervention despite the fact that they are considered possibly exogenous. A study that used routine screening and typing for these two organisms found that almost all *Pseudomonas* and *Staphylococcus aureus* positives in surgical ICU patients were of endogenous sources (102). *Pseudomonas aeruginosa* is commonly isolated from patients who have been hospitalized longer than one week (103). Most ICU patients spend time in hospital wards prior to their ICU stay. Patients are not routinely cultured upon admission to the ICU, which is a limitation of our data. Therefore, a possible explanation is that many of the patients acquired those organisms prior to their ICU stay.

The rates of Coagulase-negative *Staphylococcus* and *Streptococcus viridans* were not affected by the intervention, as expected. However, *Haemophilus* species which were also considered likely endogenous organisms decreased significantly. A possible explanation lies in the rate of detection and the lack of screening for all organisms which is a limitation of the data. *Haemophilus* species positives arise from cultures of the respiratory system. A decrease in testing because of fewer cases of suspected infections will result in a decrease in the detection of endogenous *Haemophilus*.

The observed decrease in ICU LOS is consistent with knowledge that infections in ICU patients increase the average ICU and hospital LOS (7). Acquisition is on the causal

pathway to LOS, but there are many other important factors affecting LOS. Acquisition, as a more direct outcome than LOS had a stronger correlation with the intervention. In addition, the results of the sensitivity analysis of exclusion of post-ICU cases, suggest that part of the benefit from reduced acquisition will take effect after the ICU stay. On the other hand, we do not have overwhelming evidence to suggest that a significant decrease in LOS occurred as a result of the intervention. The data are noisy and could also be consistent with a small temporal trend. A larger study is needed in order to measure with adequate precision the effect of such an intervention on LOS.

Many previous studies were based on ICU identified cases alone. In our sensitivity analysis, excluding likely ICU-acquired MRSA cases that were detected within 48 hours of ICU discharge resulted in a change in the MRSA acquisition rate that was not significant. This observation may explain why some previous studies that were focused on the rates of MRSA alone failed to show any significant decrease of rates as a result of a physical intervention.

The use of acquisition rather than infection as an outcome measure is a potential limitation of the study. However, using acquisition is a sensitive method for detecting transmission of bacteria to patients, and reducing this transmission is the target of most physical interventions. Studies that rely upon infection rates also suffer from the imprecision in the timing of the outcome. The interval between the acquisition and colonization of a patient by a specific pathogen and the development of an infection depends on factors independent of transmission.

In view of the epidemic that affected both hospitals in the post-intervention period, the unpredictable nature of such events, and the difficulty in adequately reflecting the volatility in the statistical standard errors, a much longer series would have been desirable. However data prior to 2000 were not available. Recently, the two hospitals have instituted even greater co-operation and joint management by transferring patients to the other ICU when one is full, thereby precluding any chance to extend the data series. Despite these real-world limitations, and despite the noise, the patterns in Figure 6.1 are clear.

The transfer to the new ICU was done overnight with all the old equipment and beds moved to the new location. We assume that this is the reason that the effect of the new facility remained constant after the move, without any additional effect of the 'newness' of the facility that would be expect to wane with time.

The older ICU had a small number of sinks, which were not easily accessible. The new ICU environment might have resulted in improved infection control practices, as it is hypothesized that single rooms facilitate more frequent hand washing by health care workers and are also easier to clean (59;60). They also reduce the number of patient transfers among rooms. Further research is needed to determine the mechanisms through which the transmission is reduced. Better knowledge on the routes of transmission could assist in developing improved infection control policies.

The drastic improvement in the physical facility of the ICU from common rooms to private rooms yielded a dramatic reduction in the transmission of bacteria and yeast. Our approach of looking at all potentially exogenous bacteria and our modeling approach that adjusted for background time trends and other factors allowed for a comprehensive demonstration of this improvement. The effect of a physical intervention in other settings may vary depending on many local characteristics. This study demonstrates the potential benefit of single rooms in reducing the transmission of infections in ICU settings.

Tables

Table 6.1: The patient populations* in the ICUs before and after room privatization

Hospital	Intervention		Comparison	
Period relative to 2002-03-02	Pre	Post	Pre	Post
Hospital admissions with ICU stay	2732	5468	4167	6976
Mean age (y)	59.6	59.4	60.1	60.9
Female N (%)	973 (36)	1874 (34)	1624 (39)	2690 (39)

* The approximate mix of patients remained largely constant within each ICU throughout the study period. At the intervention hospital general medical patients accounted for 25% of admissions and 27% of patient days; non-trauma surgery for 30% of admissions; trauma patients for 21% of patient days; and, cardiac surgery for 21% of admissions and 15% of patient days. At the comparison hospital, general medical patients accounted for 14% of admissions; non-trauma surgery for 37% of admissions and 33% of patient days; cardiac surgery accounted for 44% of admissions; solid organ transplantation account for 4% of admissions and 5% of the patient days; and, hematology oncology patients accounted for 1% of admissions..

Table 6.2: Numbers and rates of initial positive culture test results for common organisms

Organism	Hospital	
	Intervention	Comparison
	N (Rate per 10,000 patient days)	N (Rate per 10,000 patient days)
Coagulase-negative *Staphylococcus*	471 (119.0)	536 (116.2)
Enterococcus species	257 (64.9)	317 (68.7)
Yeast	245 (61.9)	594 (128.7)
Escherichia species	205 (51.8)	209 (45.3)
Klebsiella species	190 (48.0)	280 (60.7)
Staphylococcus aureus	190 (48.0)	126 (27.3)
Enterobacter species	176 (44.5)	175 (37.9)
Pseudomonas species	156 (39.4)	221 (47.9)
Haemophilus species	150 (37.9)	74 (16.0)
MRSA	141 (35.6)	62 (13.4)
Clostridium difficile	130 (32.9)	135 (29.3)
Streptococcus viridans	94 (23.8)	56 (12.1)
Corynebacterium species	87 (22.0)	106 (23.0)
Acinetobacter species	71 (17.9)	30 (6.5)
Stenotrophomonas maltophilia	61 (15.4)	78 (16.9)
Serratia species	48 (12.1)	75 (16.3)
Citrobacter species	43 (10.9)	53 (11.5)
Proteus mirabilis	33 (8.3)	73 (15.8)
Streptococcus pneumoniae	37 (9.3)	12 (2.6)
Morganella species	21 (5.3)	22 (4.8)
Group B *strep*	21 (5.3)	14 (3.0)
Bacteroides species	17 (4.3)	30 (6.5)
Fungi	12 (3.0)	22 (4.8)
VRE	10 (2.5)	16 (3.5)
Lactobacillus species	12 (3.0)	18 (3.9)
Neisseria species	15 (3.8)	7 (1.5)
Moraxella species	9 (2.3)	22 (4.8)
Anaerobic *cocci*	8 (2.0)	23 (5.0)

Table 6.3: Number of incident positive culture results and rates for selected organisms by year 2000-2005 and average length of patient stay at the ICU during a hospitalization.

Hospital	Year	Avg. ICU LOS	N First Positives (rate per 10,000 patient days)				
			C.difficile.	MRSA	VRE	Other	Total
Int.	2000	4.9	18 (33.6)	24 (44.9)	0 (0)	441 (824.3)	483 (902.8)
	2001	4.7	18 (27.5)	35 (53.5)	0 (0)	513 (784.5)	566 (865.6)
	2002	5.0	20 (29.0)	35 (50.8)	0 (0)	445 (645.4)	500 (725.2)
	2003	4.7	23 (32.6)	21 (29.8)	2 (2.8)	509 (722.1)	555 (787.3)
	2004	4.6	29 (43.2)	14 (20.9)	3 (4.5)	430 (640.6)	476 (709.2)
	2005	4.9	22 (32.3)	12 (17.6)	5 (7.3)	465 (682.8)	504 (740.1)
	Total	4.8	130 (33)	141 (35.8)	10 (2.5)	2,803 (712.2)	3,084 (783.6)
Comp.	2000	3.8	19 (25.3)	3 (4)	0 (0)	527 (701.5)	549 (730.7)
	2001	3.9	8 (11.0)	15 (20.7)	0 (0)	491 (677.7)	514 (709.5)
	2002	4.1	12 (15.6)	14 (18.3)	4 (5.2)	638 (831.9)	668 (871)
	2003	4.2	39 (49.5)	12 (15.2)	5 (6.3)	577 (731.7)	633 (802.7)
	2004	4.5	30 (39.7)	11 (14.6)	1 (1.3)	527 (697.6)	569 (753.1)
	2005	4.7	27 (30.8)	7 (8)	6 (6.8)	540 (615.7)	580 (661.3)
	Total	4.2	135 (28.9)	62 (13.3)	16 (3.4)	3,300 (707.6)	3,513 (753.2)

Table 6.4: Rate ratios* - the change in acquisition rates of the organisms post privatization in the ICU.

Organisms	Rate Ratio (95% CI)†	
Likely Exogenous		
C.difficile +MRSA + VRE	0.46	(0.30 - 0.71)
C.difficile	0.57	(0.35 - 0.93)
MRSA	0.53	(0.29 0.99)
VRE	NA	
Acinetobacter species	0.47	(0.24 - 0.92)
Stenotrophomonas maltophilia	0.48	(0.21 - 1.07)
Fungi – Molds	1.23	(0.75 - 2.03)
Exogenous/ Endogenous		
Yeast	0.49	(0.36 - 0.66)
Enterococcus species	0.77	(0.56 - 1.06)
Enterobacter species	0.62	(0.42 - 0.93)
Escherichia species	0.89	(0.55 - 1.44)
Staphylococcus aureus	1.02	(0.67 - 1.54)
Pseudomonas species	1.0	(0.63 - 1.57)
Klebsiella species	0.62	(0.38 - 0.99)
Serratia species	0.77	(0.41 - 1.43)
Citrobacter species	1.36	(0.74 - 2.50)
Proteus mirabilis	0.69	(0.38 - 1.24)
Morganella species	0.57	(0.30 - 1.06)
Likely Endogenous		
Coagulase-negative *Staphylococcus*	0.96	(0.76 - 1.20)
Haemophilus species	0.53	(0.30 - 0.95)
Streptococcus viridans	1.03	(0.56 - 1.90)

* Rate ratios are estimated through logistic regression based on the split of each monthly cases (see text) between the 2 hospitals, pre and post intervention

† Confidence intervals based on robust SE

Figures

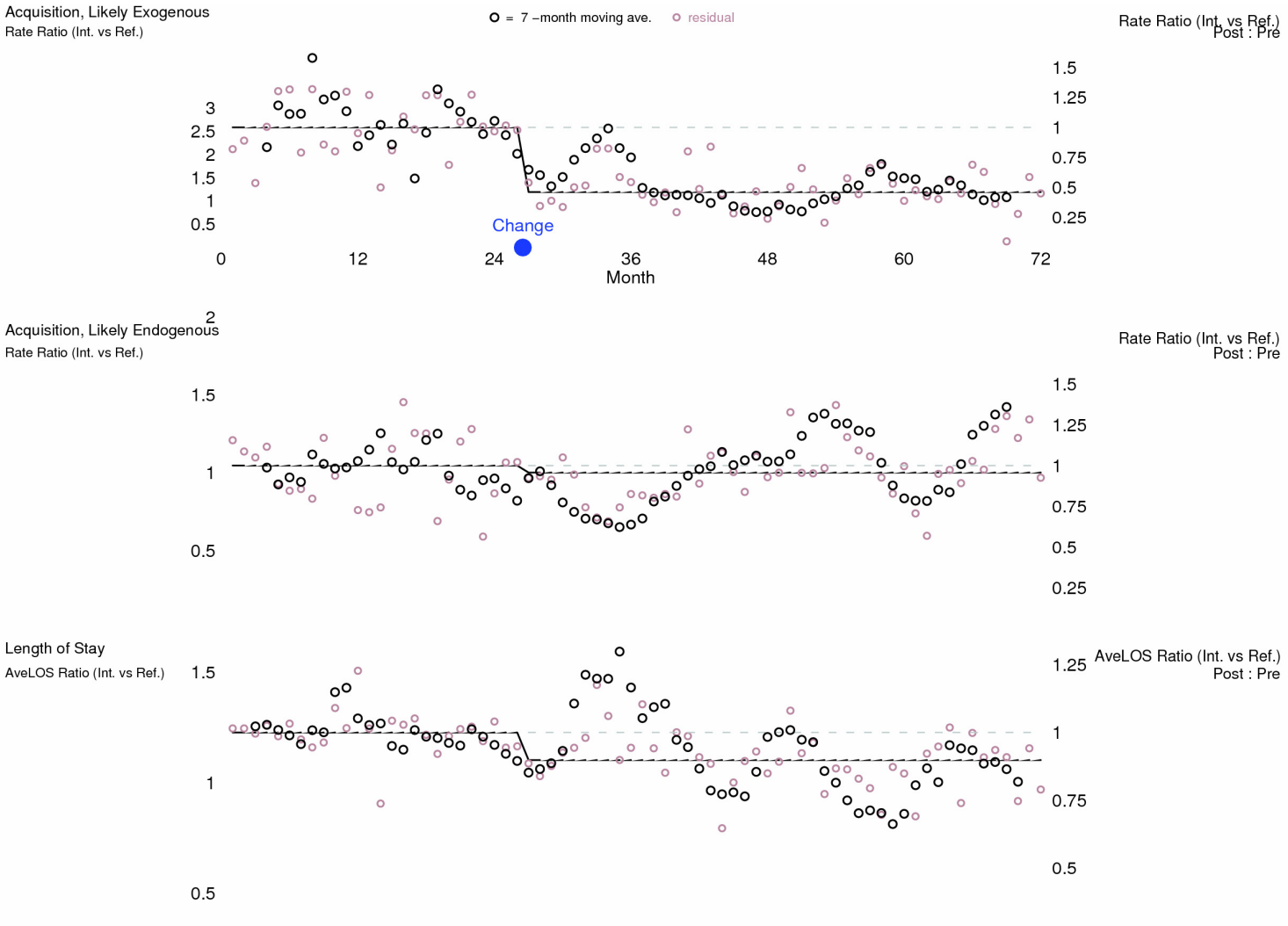
Figure 6.1: Monthly contrasts of event rates and LOS in the intervention versus comparison hospital, pre- and post-intervention.

Black circles represent ratios within each month, brighter circles the fitted residuals. On the left is the axis of the ratios, on the right, the magnitude of the change in the average ratios pre/post intervention.

(a) Monthly ratios of acquisition rates of likely exogenous organisms.

(b) Monthly ratios of acquisition rates of likely endogenous organisms

(c) Monthly ratios of average length of stay.


Acquisition, Likely Exogenous
Rate Ratio (Int. vs Ref.)
= 7 –month moving ave.
residual
Rate Ratio (Int. vs Ref.)
Post : Pre
Change
Month
Acquisition, Likely Endogenous
Rate Ratio (Int. vs Ref.)
Length of Stay
AveLOS Ratio (Int. vs Ref.)
AveLOS Ratio (Int. vs Ref.)

Appendix for: ICU Private Rooms and the Rate of Bacterial Acquisition

The two hospitals represent similar environments. But, while one did not undergo the change during the study period, the other did. The objective of the design and data analysis is to isolate the effect of the intervention from other changes and trends that took place over the study period. For example, similar sized epidemics of *C.difficile* took place in both hospitals at around the same time. Also, during the study period the rates of several bacteria increased, and then decreased. Therefore it is difficult to specify a smooth in time (i.e. parametric) form for the absolute rate in each hospital, and so instead we adopted a semi-parametric approach. In this approach, even if the absolute rates fluctuate with time, the closeness of the two hospitals, the stable population base, and the same seasonal and other temporal influences mean that the ratio of rates – in the absence of the intervention – were assumed to remain constant over time. Our approach therefore relies on within- month rate ratios and on the change in these rates post (and presumably because of the) intervention.

Notation and Interpretation of Parameters

$Y_{i,m}$; $Y_{c,m}$: Numbers of new acquisitions in the intervention hospital (i) and comparison hospital (c) in month m (m= 1,..72)

$Den_{i,m}$; $Den_{c,m}$: ICU patient days at risk in month *m*, in the intervention and comparison hospitals

$Rate_{i\text{-}m}$; $Rate_{c\text{-}m}$:Rate of new acquisitions in the intervention and comparison hospitals in month *m*

$Rate_{i,m} / Rate_{c,m}$: The within month rate ratio is assumed to be constant (K) until the time of the intervention; it takes on a different value after the time of the intervention

RR = $Rate_{i,m} / Rate_{c,m}$ =Kθ After the intervention

θ=1 if the intervention had no effect
θ < 1 if the intervention had positive effect

I_m : Intervention indicator for month *m*

$$I_m = \begin{cases} 1 & \textit{If post intervetion month} \\ 0 & \textit{Otherwise} \end{cases}$$

Statistical Models for Y's and for the Estimation of Intervention Effect Parameter θ

$Y_{i,m} \sim \text{Poisson}(\mu_{i,m})$; $Y_{c,m} \sim \text{Poisson}(\mu_{c,m})$

$$Y_i \mid (Y_i + Y_c) \sim \text{Binomial}(\text{'n'} = Y_{i\text{-}m} + Y_{c\text{-}m}, \Pi = \mu_{i,m} \Big/ \mu_{c,m} + \mu_{i,m})$$

$$\text{Log}\left(\mu_{i,m} \Big/ \mu_{c,m}\right) = \text{Log}\left(Den_{i,m} * Rate_{i,m} \Big/ Den_{c,m} * Rate_{c,m}\right) = \text{Log}\left(Den_{i,m} \Big/ Den_{c,m}\right) + \text{Log}\left(Rate_{i,m} \Big/ Rate_{c,m}\right)$$

$$= \text{'offset'} + \text{Log}(K) + \text{Log}(\theta) * I_m$$

$$\Rightarrow \text{Log}\left(Rate_{i,m} \Big/ Rate_{c,m}\right) = \text{Log}(K) + \text{Log}(\theta) * I_m$$

To estimate θ we fitted a logistic regression model to the series of 72 $Y_{i\text{-}m}$ using as binomial 'denominators' the total cases for each of these 72 months and using

$\text{Log}\left(Den_{i,m} \Big/ Den_{c,m}\right)$ for each of these months as the offsets. The exponentiated regression coefficient associated with I_m is the point estimate of θ.

The percent reduction is $100(1-\hat{\theta})$.

Chapter 7 The Risk of *Clostridium difficile* and MRSA Acquisition by ICU Patients from Previous Bed Occupant

Preamble to Manuscript 3

In the third manuscript, the goal of exploring the potential of electronic data from hospital information systems to inform infection control efforts by studying bacteria acquisition is further addressed. The study utilized the data to estimate individualized exposure measures, in addition to hospital and ward-level exposures, according to the specific location of a patient over time within an ICU. Specifically, I assessed the risk that a patient will acquire MRSA or *C.difficile* from a previous bed occupant who was positive for these bacteria. The outcome is acquisition of bacteria, as in my second manuscript, and the first positive test result for a type of bacteria was used as a sensitive measure. The precise time and location at which the data were recorded in the admission discharge transfer information system were used to identify exposure windows and the times tests were ordered were used to identify likely times of acquisition.

Title Page

To be submitted to the Annals of Internal Medicine

Title: The Risk of *Clostridium difficile* and MRSA Acquisition by ICU Patients from Previous Bed Occupant

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Abstract

Introduction

MRSA and *C.difficile* are frequently acquired in intensive care units (ICUs) and account for considerable morbidity, mortality and cost.

Residual bacterial contamination can persist in rooms after an infected or colonized patient has left the room even if current cleaning practices are followed, placing subsequent occupants of the room at a potentially increased risk of acquiring these bacteria. This potentially important route of transmission has not received much study.

Methods

We studied retrospectively the cohort of disease free ICU bed stays at 2 university hospitals (MGH and RVH) over 6 years (2000-2005), using data obtained from the admission, discharge, and transfer database, and from the microbiology laboratory information system. Crude and adjusted relative risks of MRSA/*C.difficile* acquisition were calculated to quantify the additional risk to patients who occupied a bed location in which the previous occupant was positive for MRSA/*C.difficile*, while accounting for unit prevalence, room type, patient age, hospital LOS, and immune status.

Results

MRSA exposure: At the RVH, 4.3% (794 of 18,413) of susceptible ICU bed stays were in a bed location where the previous occupant was MRSA positive; at the MGH the frequency of this exposure was 8% (779 of 9,693 patient bed stays). *C.difficile* exposure: At the RVH, some 3.5% (654 of 18,493) were exposed; at the MGH 3.5% (352 of 10,201).

MRSA acquisition: Exposed patients at the RVH were 2.6 times more likely to acquire MRSA relative to unexposed patients (95% CI 1.1, 5.9) and the attributable risk among the exposed was 62%. The risk ratio in both hospitals combined was 2.3 (1.2, 4.2) when adjusted for prevalence, patient age, private room, and hospital. At the MGH physical intervention with room privatization during the study period modified the relative risk associated with exposure to a previous bed occupant from 2.6 (1.4, 4.7) pre-privatization to a non-significant 0.7 post-privatization.

C.difficile acquisition: The crude risk ratio at the RVH was 1.8 (0.9, 3.6) and the prevalence adjusted risk was 1.5. Among patients exposed to a bed where the previous occupant was colonized or infected, immune-compromised patients had a four fold higher risk (RR: 4.1 CI: 1, 16) to acquire *C.difficile*.

Conclusions

Patients admitted to an ICU bed previously occupied by an MRSA or *C.difficile* positive patient were at increased risk of acquiring these bacteria. The risk was higher for MRSA and higher for patients in non-private rooms.

Introduction

MRSA and *C.difficile* are acquired frequently by patients in ICUs and they result in considerable morbidity, mortality and cost (46;49) (51;52). Together with VRE, these organisms are a central focus of infection control efforts. They are also considered 'environmental' bacteria, which can persist on inanimate surfaces for weeks or even months (75).

Transmission of infectious organisms from one patient to other patients in the same unit, is both direct and environmental, but is largely mediated through intermediary health workers (70). Transmission from a previous to current room occupant, although possibly mediated by health workers, is more likely to be due to environmental exposure. Patients infected or colonized with MRSA or *C.difficile* shed these organisms onto surfaces in their environment (73;74). Residual bacterial contamination can persist in rooms for weeks or even months (75), even after current cleaning practices are followed (76;77). Environmental contamination from *C.difficile* occurs in the form of spores on surfaces, furniture, bathtubs and equipment when cleaning is not sufficient (81). This residual environmental contamination places the subsequent bed occupant at risk of acquiring these bacteria (82;83), and the risk is higher when the physical proximity to the source of the contamination is higher (81).

This potentially important route of transmission has not been well studied. One study has linked MRSA acquisition to MRSA in a previous room occupant (85), but it did not account for potential bias due to selective room assignment and to confounding by prevalence. Unless the prevalence was constant over time, lack of control for the prevalence in the unit would introduce a false association between the status of the prior patient and the status of the following patient. This false association would result in a spurious finding of elevated risk. No studies have examined the potential risk of *C.difficile* from a previous patient who was colonized with the pathogen.

We therefore studied if patients occupying certain bed locations at certain times were at increased risk of acquiring MRSA and *C.difficile*. The time-and location-specific elevated risks were postulated to be those in which the immediately previous patient in the same bed location had been colonized with the organism in question. We studied the ICU units

of two hospitals that share infection control policies and cleaning practices, but varied in their physical infrastructure and patient population. These circumstances provided an opportunity to study potential modifiers of the risk of acquiring bacteria from a previous bed occupant.

Methods

Overview and Study Design

We studied the cohort of all patients admitted to the ICUs of two university hospitals over 6 years: 2000-2005. We compared the risk of acquiring MRSA and *C.difficile* in "exposed" patients -- patients who occupied a bed where the prior occupant was positive for these pathogens -- to patients who were not exposed in this way.

VRE burden is low in Canada, and therefore acquisition risk of VRE through this route of transmission was not studied.

Setting

We studied patients admitted to the ICUs of two McGill university hospitals, the Montreal General Hospital (MGH), and the Royal Victoria Hospital (RVH) that serve the same Montreal region. The hospitals have a single, common infection control service with one director and they have shared infection control policies and practices. The hospitals experienced similar trends in the rates of bacterial infection and outbreaks of *C.difficile* during the study period.

The 25-bed adult ICU of the RVH remained unchanged during 2000-2005 and had eight single rooms, and rooms with 2, 5 or 6 beds. The 24-bed adult ICU at the MGH was moved to a new location in the hospital on March 2002 with 24 beds, each in a private room containing a sink, and 2 additional sinks in an area outside the private rooms. Prior to this intervention, the ICU consisted of two large rooms of 12 beds and 2 private rooms within each larger room and a total of 4 sinks.

The nursing ratio was the same in both hospitals and remained constant during the study period. This ratio was 1:1 for 30% of beds and 2:1 for 70% of beds. This ratio was maintained even through temporary shortage in nurses by intermittent bed closing.

Alcohol-based hand gels were available throughout the study in a ratio of one per two beds in both hospitals. Cleaning procedures were standardized across the MGH and RVH, and the two ICUs shared the same housekeeping manager during the study period. In all rooms, the germicide used was a quaternary ammonium. Surfaces were cleaned daily. Floors were visually inspected and cleaned if soiled. All rooms were cleaned upon

patient discharge. In addition, beginning in 2000, rooms of *C.difficile* positive patients were cleaned with diluted bleach solution at 500 PPM. From 2001 to 2007 the same bleach solution was used in all patient rooms on alternate days. In 2004 the liquid bleach was replaced by chlorine disinfectant tablets diluted to 500 PPM.

The approximate population mix at the RVH ICU was: general medical patients accounted for 14% of admissions; non-trauma surgery for 37% of admissions (and 33% of patient days); cardiac surgery accounted for 44% of admissions; solid organ transplantation accounted for 4% of admissions (and 5% of the patient days); and, hematology oncology patients accounted for 1% of admissions. At the MGH general medical patients accounted for 25% of admissions (and 27% of patient days); non-trauma surgery patients accounted for 30% of admissions; trauma patients accounted for 21% of patient days; and, cardiac surgery patients accounted for 21% of admissions (and 15% of patient days).

Data

The data for the study were obtained from three hospital information systems. ICU patients were identified and admission times in the ICU and specific bed locations were obtained from the admission discharge transfer (ADT) database. The ADT system contained the location information of all admitted patients, recording the precise time of every admission to a specific bed within the hospital, move to another bed, and discharge. Microbiology tests results were obtained from the laboratory information system. Patients were screened universally for MRSA upon ICU admission. Contacts of index cases were re-screened. Other microbiology testing was initiated upon suspicion of an infection. Stool samples were tested routinely for *C.difficile* in patients with diarrhea. Data from an information system that is maintained in the ICU were used to identify patients who were immuno-compromised at the time of an ICU bed stay.

Bed-stays Inclusion/Exclusion

An eligible bed-stay was defined as a disease-free patient at a specific bed location. A patient could have multiple eligible bed stays even within the same ICU stay. A patient was considered MRSA/*C.difficile* free and a candidate to acquire these bacteria if she never tested positive for MRSA/*C.difficile* respectively.

Outcome

The main outcome was the first positive result per patient per bacteria recorded. The use of first result ever is a strict criterion, which may have missed patients with true repeat acquisition. However, given that the half life of MRSA carriage is approximately 40 months (104), we felt this strict criterion to be justified. Following the CDC standard, a patient who tested positive to a bacteria 48 hours after admission and up to 48 hours after discharge from an ICU location, was considered to have acquired the bacteria during the bed-stay. Tests results from the first 48 hours were excluded. As a result, patients who tested positive on the first MRSA screening on admission to the ICU were excluded from the numerator, and we have greater confidence that subsequent positive results truly acquired MRSA in the ICU. The 48 hours exclusion criterion applied from the beginning of any bed-stay.

Exposure

Exposure status: A bed location was considered positive for MRSA/*C.difficile* if the most recent occupant of the bed tested positive sometime during the month prior to the bed-stay or during the bed-stay. The subsequent patient at this bed location was considered exposed to MRSA/*C.difficile* respectively during the hospitalization if that patient was susceptible (i.e., not previously infected themself).

Bed Stays of Immuno-compromised Patients

Bed stays of hemato-oncology patients, patients post organ transplant, or HIV-positive patients were considered bed stays of immuno-compromised patients.

Data Analysis

The unit of analysis was a patient's bed-stay i.e. a patient stay at a specific bed location at the ICU. Multiple bed-stays of the same patient were counted as separate units, even within the same ICU stay, as long as the patient remained MRSA/*C.difficile* free. The numbers of exposed/unexposed stays (denominator) and the numbers of patients who became positive to bacteria (numerator) within these stays were aggregated by calendar month.

Relative risks, comparing the risk in exposed bed stays with that in unexposed bed stays, were calculated for each pathogen separately. Since prevalence changed over time, we adjusted the comparisons by using a Mantel-Haenszel summary estimate that grouped the 72 monthly observations into 3 strata representing months with low, medium, and high prevalence. We also examined the applicability of adjusting for calendar time by grouping the 72 months into 18 strata, each consisting of 3 consecutive months. We also calculated the percent attributable risk of acquisition in the exposed and in the overall population.

We estimated the distribution of the bed locations where patients potentially acquired bacteria, to assess whether certain beds were repeatedly more 'risky' or were occupied by the more susceptible patients. We looked to see whether certain beds were routinely more likely to contain exposed candidates, or whether patients were more likely to acquire bacteria at specific beds. Comparing acquisition rates both in the exposed and unexposed according to room was important as specific rooms might be harder to clean and therefore pose more often a potential environmental hazard regardless of selective room assignment.

We compared the level of exposure and the risk for patients in private and non-private rooms in the RVH ICU, which was comprised of private and non-private rooms throughout the study period. In the MGH ICU, which was re-opened with all private room part way through the study period, we compared the risk before and after the privatization of rooms.

We used logistic regression to test potential covariates of acquisition. Univariate logistic regression was used to separately test the impact of hospital, patient age (over and under 65), the length of stay at the hospital prior to the bed stay in question, level of prevalence at the unit, private room at the RVH (through an interaction term), room privatization at the MGH (interaction with hospital), and immuno-compromised status. A multivariate logistic regression model was used to test the adjusted impact of the exposure and other potential covariates.

The R statistical software (version 2.10.0) was used for data analysis.

Results

Exposure of Susceptible Patients

MRSA: There were 18,413 hospital bed stays of MRSA-susceptible patients at the RVH during the study period (Table 7.1a). For 794 of them (4.3%), the patient was "exposed" i.e., the susceptible patient occupied a bed location in which the previous occupant was MRSA positive. At the MGH the level of exposure was higher: 8% of stays (779 patients out of 9,693) involved a bed location where the previous occupant tested positive.

C.difficile: There were 18,493 hospital bed stays involving *C.difficile*-susceptible patients at the RVH during the study period (Table 7.1b). 654 of them (3.5%) were exposed in that the previous bed location occupant was *C.difficile* positive. At the MGH 352 (3.5% of 10,201) eligible patients were classified as exposed.

In general, the age of the exposed groups was slightly higher than that of the unexposed groups (Table 7.1). The mean hospital length of stay prior to the ICU bed stay in question was higher for the exposed group for MRSA at the RVH, and the proportion of immuno-compromised patients slightly higher (0.09 among exposed vs. 0.07 among all patients).

Acquisition of Infectious Organisms

MRSA: At the RVH, some 57 patients acquired MRSA during a bed stay, and 140 at the MGH. Thus, overall the risk was 0.7%. Exposed patients -- susceptible patients who stayed at a bed location at the RVH where the previous occupant of the same bed location was MRSA positive -- had a risk ratio of 2.6 (95% CI 1.1-5.9) for acquiring MRSA during the hospital bed stay at that location (Table 7.2). The prevalence adjusted risk ratio was 2.5 (1.1-5.9). At the MGH, neither the risk ratio at 1.5 (95% CI 0.9-2.5) nor the prevalence adjusted risk ratio at 1.3 (95% CI 0.7-2.1), were significantly elevated.

C.difficile: 131 patients acquired *C.difficile* during a bed stay at the RVH and 126 at the MGH over the 6 years of the study. Thus the overall risk was 0.9%. Exposed patients -- patients who stayed at a bed location at the RVH, where the previous occupant of the same bed location was *C.difficile* positive -- had a higher risk to acquire *C.difficile* during the hospital bed stay at that location (Table 7.2a), with a crude risk ratio of 1.8 (95% CI 0.9-3.6). The prevalence adjusted risk ratio was 1.5 (95% CI 0.9-3.6). The very small

number of incident exposed cases at the MGH resulted in a very imprecise risk estimate (0.7 with 95% CI 0.2-2.1) with no evidence of change in the risk.

The crude rate-ratios were consistently higher than the adjusted ones (Table 7.2), consistent with some confounding by prevalence. The results of the prevalence adjusted risk and the calendar time adjusted risk (in three months intervals) gave similar estimates of risk ratios.

Attributable Risk of Exposure and Influence of Specific Rooms

Most of the 8 MRSA cases among the exposed at the RVH were likely due to the exposure with an attributable risk in the exposed of 62% (95% CI, 11%-84%) (Table 7.2). Out of the entire eligible patients it was 7% (95% CI -2% to 14%). At the MGH the attributable risk for MRSA was not statistically significant at 33%. For *C.difficile* the attributable risk among the exposed was 44% and was not statistically significant.

The frequency of "exposure" of patients in private rooms at the RVH was higher than in the shared rooms for both MRSA and *C.difficile*. The associated risk ratios contrasting exposed to non-exposed patients in private to non-private rooms were 7.1 (95% CI 6.1, 8.3) and 2.9 (95% CI 2.5, 3.4) for the two respective bacteria. However, the distribution of bed locations where patients became positive for MRSA and *C.difficil*e did not show a similar over-representation of isolation rooms (relative to those in non-private rooms, patients in private rooms were 2.2 and 1.1 times more likely to acquire these bacteria respectively). Examination of the exposed patients' bed locations for MRSA or *C.difficile* at the MGH, and comparison to bed locations where patients acquired these bacteria also revealed no bias as a result of room assignment.

Modifying Effect of Physical Intervention at One Hospital

A large majority of MRSA exposed cases at the MGH (12 out of 16 over the entire study period) acquired MRSA during a bed stay before the physical intervention of the MGH ICU to a new location with all private rooms (Table 7.3). The level of exposure among eligible patients remained constant at 0.8%. The risk ratio of MRSA acquisition – i.e., contrasting those exposed to previous positive bed stay with those not exposed - was 2.6 (95% CI 1.4 - 4.7) prior to room privatization with a statistically significant 61%

attributable risk in the exposed and a statistically significant 10% attributable risk in the population. The risk ratio post privatization was 0.7 (95% CI 0.2 – 1.8). Due to the timing of the *C.difficile* epidemic, acquisition rate of *C.difficile* was higher post 2002 i.e. post privatization. There were few *C.difficile* exposed cases overall at the MGH, with a pre-intervention rate ratio of 2.2 (95% CI 0.5 – 9.1).

Univariate Analysis of Risk Factors and Multivariate Analysis of Effect of Exposure

In a univariate logistic regression analysis, previous MRSA positive bed occupant, age older than 65, and higher MRSA prevalence increased the risk of a patient acquiring MRSA (Table 7.4). The rate of acquisition at the MGH was higher than at the RVH, but the risk of acquisition at the MGH decreased following the room privatization in March of 2002. A stay at a private room in the RVH increased the risk of acquisition in comparison to a stay at a non-private room in the univariate analysis, where the higher prevalence in private rooms was unaccounted for.

Patient age older than 65, prolonged hospital stay prior to the ICU bed stay, higher prevalence of *C.difficile*, and immuno-supression significantly increased the risk of *C.difficile* acquisition. The overall increase in the risk from exposure to a *C.difficile* positive previous bed occupant was small and statistically non-significant. The rate of acquisition was higher at the MGH.

In a multivariate analysis of MRSA acquisition, the risk ratio associated with a previous positive MRSA bed occupant was 2.3 (95% CI 1.2, 4.2) (see Table 7.5). Higher prevalence, older age, a stay at the MGH, a stay at a private room at the RVH, and a stay before the privatization at the MGH (March 2002) significantly increased the risk of acquisition. The privatization at the MGH modified the risk from exposure to a previous MRSA positive patient – with a risk ratio of 0.17 (95% CI 0.08, 0.36) (Table 7.5 footnotes); thus, the privatization was significantly and highly protective against this exposure. At the RVH, no risk modification was noted after the date when the privatization was carried out at the MGH.

Discussion

We found at one hospital, that patients hospitalized in an ICU bed location in which the previous patient was positive for MRSA or *C.difficile*, were at increased risk of acquiring these pathogens. At a second hospital, a physical intervention to move the ICU to a new location within the hospital with all private rooms part way through the study period modified the effect of exposure. Patients with ICU stays before this intervention were found to be at increased risk to acquire MRSA and *C.difficile*, while patients with stays after the intervention were not.

MRSA and *C.difficile* are considered 'environmental' bacteria. Residual contamination with these pathogens can remain in a room after a patient has left (75), and in some cases after standard cleaning procedures are applied (76;77). This residual contamination can put other patients at risk (82;83). Our findings suggest that environmental contamination was present after patients were discharged, and this contamination placed patients at increased risk of MRSA and *C.difficile*. The results of this study also suggest that change to a new ICU environment with private rooms enabled cleaning sufficient to interrupt this route of transmission.

The attributable risk fractions in the exposed were high (62% for MRSA in the RVH), but low in the population (6.5% for MRSA in the RVH and statistically non-significant). This risk from previous bed occupant provided a good explanation for the route of transmission for a small number of cases, because the frequency of exposure in the population was low. However, the rising prevalence of MRSA will result in the exposure becoming more common (38).

Patients in "exposed" bed stays were slightly older on average than unexposed patients. MRSA exposed patients at the RVH had a longer mean hospital length of stay prior to the ICU bed stay than the comparison group, and the proportion of immuno-compromized patients was slightly higher. In the RVH where the ICU comprised both private and shared rooms throughout the study period, the frequency of exposed patients in the private rooms was higher. The difference in the composition of the exposed group is probably a result of an attempt to protect the more vulnerable patients in private rooms, or a result of the isolation of sick patients (with infection other than MRSA) in order to

protect other patients. In the multivariate model LOS and immuno-compromized status were not statistically significant predictors of the risk of acquiring MRSA. The adjusted risk ratio, accounting for all potential confounders was 2.3 (95% CI 1.2, 4.2) whereas it was 2.1 at the univariate model. The higher risk might be due to the effect of private rooms which were protective against the exposure to a previous positive occupant. It could also be the result of residual confounding by prevalence, explaining the post room privatization term in the multivariate model which indicates a small protective effect (0.7).

There was a *C.difficile* epidemic in Quebec during the study period starting around 2003 and subsiding after 2004 (51). There was also an increase in the rates of MRSA during the years of the study (105). To control for potential confounding by prevalence, we calculated the calendar time and the prevalence adjusted risk ratios. The risks were slightly lower, suggesting some confounding from prevalence, slightly more pronounced for *C.difficile* than MRSA. This difference is expected as the fluctuations in the rate of *C.difficile* throughout the study period were stronger than for MRSA as a result of the epidemic.

The distribution of *C.difficile* cases over the study years together with the protective effect of the privatization against acquisition from previous bed occupant may explain the low number of *C.difficile* exposed cases at the MGH. Most *C.difficile* cases occurred starting in 2003, so the number of cases before the intervention of privatization in 2002 is small, and so is the potential for risk from a previous bed occupant.

A potential source of bias in the study is selective room assignment of at-risk patients to isolation rooms. Under this situation, patients who are developing an infection, or at increased risk of developing one, will be admitted to the same isolation rooms where there was a higher chance the previous occupant was also colonized or infected with these bacteria. We found that at the RVH the frequency of exposure to these bacteria was higher in private rooms, probably because they are used as isolation rooms for positive patients. Even with the higher exposure frequency, and a more vulnerable patient population on average, the increase in the rate ratios of acquisition in private rooms was modest given the high exposure risk in a private room. This finding suggests that the

observed increase in the risk was not a result of room assignment bias, but rather that private rooms offered a cleaner environment on average.

The MRSA screening policy created an ideal situation for detection of newly infected patients in our study. The measurement error of *C.difficile* was probably larger than for MRSA and could have led to a statistically non-significant result and an attenuated estimate of the risk. It is possible however that cleaning practices were better at preventing residual contamination of *C.difficile* and that the higher risk ratio estimates for MRSA represent a truly higher risk.

Only a single previous study has examined the potential risk from a previous bed occupant and found an increased risk of MRSA colonization by current room occupants following a previous room occupant positive for MRSA (the adjusted risk ratio found was 1.4). However that study did not adjust for the prevalence at each unit at any time. If the prevalence is not constant during the entire study period, it can lead to an over estimation of the risk. More than that, fluctuations in the unit prevalence will result in different levels of colonization pressure for different patients. MRSA colonization pressure is the most important predictor for MRSA acquisition (67), and when prevalence is high, it is also more likely that the previous occupant was MRSA positive by chance alone. The previous study also did not address the potential bias due to selective room assignment.

A limitation of our study is the lack of environmental samples. Environmental contamination is hypothesized as a likely route of transmission, but cannot be observed directly. Prior room contamination with VRE was highly predictive of VRE acquisition, whether measured via environmental cultures or prior room occupancy by VRE-colonized patients (86). Typing data could have provided stronger evidence of transmission of the same strain from one patient to the subsequent bed occupant. Because of the lack of environmental samples and typing data, this link is hypothesized, but cannot be proven. The small number of exposed cases allow for only limited testing of the factors that modify the risk. A larger study would enable us to better explore risk factors that modify the risk of acquisition from previous bed occupant beyond the privatization of rooms at the MGH.

The difference in risk ratios of MRSA and *C.difficile* acquisition following an MRSA/ *C.difficile* positive patient between the two hospitals and before and after room privatization suggest that residual environmental contamination does not depend on the cleaning procedures and infection control policies alone. These policies and procedures were shared between the two hospitals in the study. Some rooms might be more difficult to clean, and in some units the practices are followed to a larger extent. In both hospitals private rooms likely offered protection against increased risk conferred by a previous occupant. The threshold for risk from residual contamination might also vary for different groups of patients, as seen from the increased risk to immuno-compromised patients. Study of more ICUs will enable this route of transmission to be assessed under more settings with varying conditions and different compositions of patients.

Tables

Table 7.1a: Characteristics of the ICU bed stays of eligible MRSA free patients, classified by hospital and exposure.

Hospital	Exposure Status	Number of ICU bed-stays	Mean age (y) of patients	Female patients N (%)	Mean Hospital LOS[1]	Immuno-compromised patients
RVH	Exposed	794	61.8	322 (40.6)	9.7	73
	Unexposed	17,600	61.2	6,771 (38.5)	7.7	1,186
	Total	**18,394**	**61.2**	**7,093 (38.6)**	**7.8**	**1,259**
MGH	Exposed	779	59.7	309 (39.7)	4.2	0
	Unexposed	8,914	59.3	3,040 (34.1)	4.3	2
	Total	**9,693**	**59.4**	**3,349 (34.6)**	**4.3**	**2**

[1] Prior to the ICU bed stay

Table 7.1b: Characteristics of the ICU bed stays of eligible C.*difficile* free patients, classified by hospital and exposure.

Hospital	Exposure Status	Number of ICU bed-stays	Mean age (y) of patients	Female patients N	Female patients (%)	Mean Hospital LOS*	Immuno-compromised patients
RVH	Exposed	654	61.6	246	(37.6)	7.2	49
	Unexposed	17,839	61.3	6,850	(38.4)	7.1	1,120
	Total	**18,493**	**61.3**	**7,096**	**(38.4)**	**7.1**	**1,169**
MGH	Exposed	352	61.4	124	(35.2)	4.2	0
	Unexposed	9,849	59.7	3,407	(34.6)	4.6	2
	Total	**10,201**	**59.7**	**3,531**	**(34.6)**	**4.6**	**2**

* Prior to the ICU bed stay

Table 7.2: The risk of acquiring MRSA and C.*difficile* in ICU patients who occupied a bed location in which the immediately previous occupant was MRSA/ C.*difficile* positive ("exposed" bed stays) versus MRSA/ C.*difficile* negative ("unexposed" bed stays).

			Risk Ratio			Attributable Risk Percent	
Bacteria	Hosp.	Acquired* (exposed)	Crude RR (CI)	Prevalence Adjusted (CI)	Time Adjusted – 3 Months Interval (CI)	In entire Population	In the Exposed
MRSA	RVH	57 (6)	2.6 (1.1-6.1)	2.5 (1.1-5.9)	2.6 (1.1-6.2)	6.5% (-2.2, 14.4)	61.7% (10.9- 83.5)
	MGH	140 (16)	1.5 (0.9-2.5)	1.3 (0.7-2.1)	1.3 (0.8-2.2)	3.7% (-2.2, 9.2)	32.3% (-13.4, 59.6)
C. *difficile*	RVH	129 (8)	1.8 (0.9-3.6)	1.5 (0.7-3.1)	1.4 (0.7-2.9)	2.7% (-1.7, 6.8)	43.6% (-14.8, 72.3)
	MGH	126 (3)	0.7 (0.2-2.1)	0.7 (0.2-2.1)	0.6 (0.2-1.9)	0.0% (-0.3, 0.3)	-46.5% (-358.3, 53.2)

* The total number of patients who acquired the bacteria in question (the number of patients exposed to a positive previous bed location occupant who acquired it)

Table 7.3: Numbers and risks of MRSA exposed patient bed stays and MRSA incident cases before and after the physical intervention at the MGH ICU

	Number of Bed Stays (percent)*				
Intervention	Acquired MRSA	Exposed to MRSA	Incident Cases among the Exposed	Total	Risk Ratio (CI)
Pre	70 (1.9)	274 (8)	12 (0.33)	3,647	2.6 (1.4, 4.7)
Post	70 (1.2)	505 (8)	4 (0.07)	6,046	0.7 (0.3, 1.8)
Total	140 (1.4)	779 (8)	16 (0.17)	9,693	1.5 (0.9-2.5)

* All percentages are percentages of totals in the row

Table 7.4: Univariate predictors of acquisition of MRSA and C.*difficile*

Predictor	Risk Ratio (CI)	P
MRSA		
Previous MRSA positive bed occupant	2.1 (1.3, 3.3)	<0.001
Hospital RVH	0.2 (0.2, 0.3)	<0.001
Patient age > 65	1.5 (1.1, 2)	<0.01
Hospital LOS (prior to the ICU bed stay)*	1.003 (1, 1.01)	0.3
Prevalence: low	Reference	
Prevalence: medium	1.4 (0.9, 2.2)	0.13
Prevalence: high	1.7 (1.04, 2.7)	0.04
Private room (in the RVH)†	2.4 (1.4, 4)	<0.01
Post room privatization (in the MGH)‡	0.6 (0.4, 0.8)	<0.01
C.difficile		
Previous *C.difficile* positive bed occupant§	1.2 (0.6, 2.2)	0.5
Hospital RVH	0.6 (0.4, 0.7)	<0.001
Patient age > 65	1.7 (1.4, 2.3)	<0.001
Hospital LOS (prior to the ICU bed stay)	1.01 (1.004, 1.01)	<0.001
Prevalence: low	Reference	
Prevalence: medium	1.1 (0.8, 1.5)	0.7
Prevalence: high	1.6 (1.1, 2.3)	0.01
Private room (in the RVH)	1.1 (0.7, 1.6)	0.7
Patient immuno-compromised	1.9 (1.2, 3)	<0.01

* in days of hospital stay

† In the RVH there was a mixture of private and common rooms throughout the study period. At the MGH there was a change with calendar time – see pre/post room privatization.

‡ Room privatization at the MGH alone, therefore the result for the MGH alone. At the RVH this is not a significant predictor.

§ Results for the two hospitals combined diluted the signal for the study exposure (see results/discussion); for the RVH only the result is 1.8 (0.6, 2.2)

Table 7.5: Predictors of MRSA acquisition using a multivariate logistic regression model

Predictor	Adjusted Risk Ratio (CI)	P
Previous MRSA positive bed occupant	2.3 (1.2, 4.2)	<0.001
Hospital RVH	0.1 (0.1, 0.2)	<0.001
Patient age > 65	1.5 (1.1, 2)	<0.01
Prevalence: Low	reference	
Medium	2 (1.4, 3.2)	0.001
High	3.2 (2, 5.2)	<0.001
Private room in the RVH*	2.2 (1.3, 3.8)	0.005
Post room privatization (post March 2002)	0.7 (0.5, 0.9)	0.02
Previous occupant MRSA+ and post room privatization in the MGH†	0.3 (0.07, 0.7)	0.02
Previous occupant MRSA+ and post room privatization in the RVH	1 (0.2, 7.7)	1

* Interaction term with hospital. The term for the MGH is meaningless.

† Three way interaction. For a patient with MRSA+ previous occupant, at the MGH, post room privatization, the odds ratio of acquiring MRSA compared to an exposed patient at the MGH before room privatization are: exp(log(0.6858) + log(0.2446)) = exp(-0.377-1.408) = 0.168 which is the exponentiated coefficient of post room privatization and the interaction term of post privatization with the exposure and hospital. Since the MGH hospital is the reference, a term for the hospital and 2 way interactions terms do not have to be added.

95% CI: exp(-3.77-1.408 +(+/-1)*(0.15526 +0.6033)) = (0.0786, 0.358)

This is equivalent to the calculation with the exposure:

exp(0.84-0.377-1.408) =exp(log(2.32) + log(0.6858) + log(0.2446)) = exp(-0.945) = 0.3887 compared to exp(0.84) = 2.3 which is 0.3887/2.3 = 0.169

Chapter 8 Summary and Conclusions

In this dissertation, I have demonstrated how routinely collected electronic data can be extracted from hospital information systems and used to derive comprehensive information on rates of organisms and antimicrobial susceptibility, to study the effectiveness of infection control interventions, and to support the individualized assessment of the infection risk of a patient. In the first study, I focused on the steps needed to derive population level information from such data applied these steps and presented information on prevalence, rates, and time trends of bacteria and antibiotic resistance in two university hospitals in the first half of this decade. In the subsequent studies, I explored the potential of such data to inform infection control efforts by studying bacteria acquisition. The confluence of the increasing challenge imposed by hospital acquired infections (HAI), and the growing amount of data available from hospital information systems, is the reason I have chosen to focus in this dissertation on potential uses of these data for infection control.

In the first manuscript I presented the information available in typical laboratory information systems, and summarized the prevalence of different organisms, and the antimicrobial susceptibility of selected bacteria. Time trends over six years of selected multi-drug resistant organisms and time trends of susceptibility to antimicrobials were also presented. These data had to be extracted from hospital information systems, and processed in order to enable aggregation of data to the population level. The process of building the database used in this research, from extracting the raw data, processing, linking, grouping, and developing definitions, is described at the data description section of this dissertation. The challenges involved in translating individual data, which were not collected as part of a planned study, into representative population-level data suitable for surveillance are discussed in the first manuscript.

Prevalence information from all available Microbiology results, representing both isolates from infected and colonized patients, was chosen as the best available proxy for the true bacterial exposure faced by a patient during a hospitalization. The likely large representation of clinical infections among the positive isolates due to testing procedures is discussed in the first and second manuscripts. The results of analyses using data from

hospital information systems are sensitive to the exclusion criteria used applied to isolates. I used the exclusion criteria adopted by the CDC-NNIS surveillance system (22), which was designed to monitor the prevalence of different types of infections by body sites. The method recommended by the National Committee for Clinical Laboratory Standards (NCCLS) for reporting antimicrobial susceptibility test data for identifying and excluding duplicate isolates for reporting antimicrobial resistance patterns (88) was used for reporting susceptibility results. The NCCLS method is an accepted standard that does not over-represent resistant strains due to repeat testing. The resulting trends, even if not directly comparable to results that are derived with different methodology, are internally consistent over time, and describe well the *C.difficile* epidemic and the rise in MRSA cases the hospitals experienced. The subsequent manuscripts rely on the calculated prevalence of bacteria by hospital ward (and specifically for the ICU), as a representation of the bacterial colonization pressure a patient is exposed to at the ward level.

In both manuscripts 2 & 3, the measured outcome was bacterial acquisition by patients. The first positive test result of a patient for a type of bacteria, derived from electronic data, proved to be a sensitive measure of bacterial transmission. Many factors that are independent of acquisition of a bacteria influence the chance that an exposed patient will develop an infection. Such factors include the patient's age and general health status, co-morbidities, procedures performed, and medication taken. Commonly, studies of transmission rely on infections rates as the outcome, but the factors that influence infection following transmission tend to dilute any measured association, and this measurement error makes it difficult to assess transmission by studying infection rates. Reducing bacterial transmission is an important target of infection control efforts.

The second manuscript describes a study of the impact of a physical intervention: the re-opening of the MGH ICU in a new location with all private rooms, on bacterial acquisition rates. The availability of data on all organisms allowed me to consider in this analysis all potentially exogenous bacteria. The availability of data from the RVH, the modeling approach that adjusted for background time trends and other factors allowed for a comprehensive demonstration of the effect of the intervention on bacterial acquisition.

Following the intervention, the rate of acquisition of bacteria and yeast decreased by more than half. The adjusted rate of acquisition of C.*difficile*, VRE, and MRSA combined decreased by 54% (95% CI: 29%-70%). Twelve common and likely exogenous organisms and exogenous/endogenous organisms had a reduction in acquisition rate following the intervention; for six of them, this reduction was statistically significant. No effect was observed on the acquisition rate of Coagulase-negative Staphylococcus, the most common endogenous organism, for which no change would be expected. The adjusted rate ratio of the average length of stay in the ICU was 10% (0%-20%) lower following the intervention. The observed decrease in ICU LOS is consistent with knowledge that infections in ICU patients increase the average ICU and hospital LOS (7). Acquisition is on the causal pathway to LOS, but there are many other important factors affecting LOS. Acquisition as a more direct outcome than LOS was influenced more strongly by the intervention. In addition, the results of the sensitivity analysis of exclusion of post-ICU cases, suggest that the benefit from reduced acquisition will continue to be observed after a patient is discharged from the ICU. Although this study provided some evidence that the LOS decreased following the intervention, the data are noisy and could also be consistent with a small temporal trend. A larger study is needed in order to measure with adequate precision the effect of such an intervention on LOS.

This study demonstrated the potential benefit of single rooms in reducing the transmission of infections in ICU settings. The older ICU had a small number of sinks, which were not easily accessible. The new ICU environment might have resulted in improved infection control practices, as it is hypothesized that single rooms facilitate more frequent hand washing by health care workers and are also easier to clean (59;60). Single rooms also reduce the number of patient transfers between rooms. Further research is needed to determine the mechanisms through which transmission is reduced. Better knowledge of the routes of transmission could assist in the development of improved infection control policies.

In the third study in this dissertation, I explored how data from hospital information systems could be used to derive individualized estimates of exposure, in addition to hospital and ward-level estimates of exposure, according to the exact location of a patient over time in the ICU. Specifically, I assessed the risk of a patient acquiring MRSA or

C.*difficile* from a previous bed occupant who was positive for these bacteria. Only one previous study has examined the potential risk from a previous bed occupant and found an increased risk of MRSA in current room occupants following a previous room occupant positive for MRSA (85). However this study did not adjust for the prevalence of bacteria on the unit. If the prevalence is not constant during the entire study period, it may lead to an overestimation of the risk. The previous study also did not address the potential bias due to selective room assignment. No previous study has assessed the risk of C.*difficile* acquisition from a previous bed occupant.

I found that patients at the RVH who were admitted to an ICU bed previously occupied by an MRSA or C.*difficile* positive patient were at increased risk to acquire these bacteria. The adjusted risk ratio of exposed vs. unexposed patients to acquire MRSA, accounting for potential confounders was 2.3 (1.2, 4.2). The risk was higher during bed stays in non-private rooms. At the MGH, the risk for exposed patients was elevated only before the intervention that transformed the ICU to all private rooms. In both hospitals, private rooms protected patients from an increased risk of infection due to a previous occupant. The attributable risk fractions in the exposed were high (62% for MRSA in the RVH), but low (6.5% for MRSA in the RVH and statistically non-significant) in the population. This risk from previous bed occupant helps to explain the route of transmission for a small number of cases, because the frequency of exposure in the population was low. However, the rising prevalence of MRSA could result in an increase in the number of patients exposed, and an increase in transmission via this mechanism.

MRSA and C.*difficile* are considered 'environmental' bacteria. Residual contamination with these pathogens can remain in a room after a patient has transferred, and in some cases after standard cleaning procedures were applied. This residual contamination can place other patients at risk. The findings of this study suggest that environmental contamination was present after patients were transferred, and that this contamination placed patients at increased risk of MRSA and C.*difficile*. The results also suggest that following the transition of the ICU at the MGH to all private rooms, cleaning in the new ICU environment between patients was sufficient to interrupt this route of transmission. The new ICU may have facilitated better infection control practices and was probably easier to clean.

The results of the third study explain some portion of the improvement in the rates of bacterial acquisition that followed the room privatization at the MGH. However, the frequency of the exposure was low for both MRSA and C.*difficile*, as was reflected in the low attributable fractions in the population. Therefore, the third study isolated one component of the reduction in bacteria transmission that followed the intervention, but this component was likely responsible for a small fraction of the improvement that was measured. There were other routes of transmission that were affected by the intervention, and more research is needed to understand the mechanisms that led to the reduction in bacterial acquisition. There is probably variability among different departments in the relative importance of different routes of transmission. A similar approach to that used in the third study could be used to identify problem areas and help target infection control efforts wherever similar data from hospital information systems are available. It could also assist in assessing the individualized exposure of a patient, and therefore the risk to a given patient of acquiring a specific type of bacteria.

With enormous investment in Canada (15) and the US (14) to support wide scale implementation of clinical information systems, electronic data in hospitals are certain to become more abundant and more accessible. In addition to increased accessibility to data, the data collected are likely to become more comprehensive, including genetic typing data in electronic form, and far more detailed data on the movement of hospital equipment and staff, and these data have the potential to improve the effectiveness of infection control. Through the studies that comprise this dissertation, I have demonstrated a few applications of data from hospital information systems to research on HAI. There are many other potential applications of these data, from the development of individualized empirical antimicrobial treatment algorithms for patients, to the examination of components of infection control policies such as the frequency and timing of MRSA and VRE screening. With accessible data, such investigations could be routinely applied as a component of comprehensive infection prevention and control efforts.

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