Healthcare-Associated Infection and Exposure to Infected or Colonized Concurrent Roommates and Prior Bed Occupants

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ABSTRACT

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This dissertation examines factors associated with healthcare-associated infections (HAIs) in four acute care hospitals located in New York City. Specifically, this investigation focuses on the role that the physical environment plays with regard to patient-to-patient transmission.

The initial analyses describe the scope of the problem by reporting the incidence of HAIs and antimicrobial resistance over a seven-year period in the study institutions. In total, 19,052 HAIs were identified among 761,426 discharges. HAI rates fell over time within all hospitals and for all organisms and infection types included in the study, and the odds of acquiring an HAI decreased significantly over time for all organisms. Resistance levels were stable for *Enterococcus* spp., *Staphylococcus aureus, Acinetobacter baumannii,* and *Streptococcus pneumoniae*. Multidrug resistance increased for *Pseudomonas aeruginosa* and decreased for *Klebsiella pneumoniae,* though imipenem resistance among *K. pneumoniae* climbed sharply in 2011.

A systematic literature review is presented to summarize what is known and unknown about how patients' exposure to infected or colonized concurrent roommates and prior bed occupants affects their risk of developing HAIs. Eighteen articles meeting the inclusion criteria were identified. More than half reported at least one statistically significant positive association between the infection/colonization status of a roommate or previous room occupant and the development of HAIs. Only a single article identified a statistically significant negative

association. The remainder found no associations that reached statistical significance, though this may be due to the fact that they were insufficiently powered.

The dissertation concludes with a matched case-control study designed to quantify the association between having a prior bed occupant or roommate with a positive blood, respiratory, urine, or wound culture and subsequent infection with the same organism. In a multivariable analysis controlling for patient characteristics and mutually controlling for each exposure, the odds of being exposed to a prior bed occupant with the same organism were 5.83 (95% Confidence Interval [3.62, 9.39]) times greater for cases versus controls and the odds of being exposed to a roommate with the same organism were 4.82 [3.67, 6.34] times greater.

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DEDICATION

This dissertation is dedicated to my parents, who told me I could be anything I wanted to be.

What's more, they actually believed this.

CHAPTER ONE

Introduction

Healthcare-associated infections (HAIs) are endemic in healthcare institutions throughout the world and are considered to be one of the greatest safety threats to hospitalized patients.[1-3] Since the 1970s, focus on the development, implementation, and evaluation of hospital infection prevention and control programs has grown substantially.[4-5] Yet, HAIs remain a major issue, both in hospitals and long-term and sub-acute care settings.[6-8] The most recent estimates for acute care hospitals in the United States (US) indicate that approximately four percent of patients contract at least one HAI during their stay; this amounts to more than 700,000 infections each year.[9] Nearly six percent of patients who develop HAIs die as a direct or indirect result of their infections, making HAIs one of the top 10 causes of death in US hospitals.[10,11] Patients who survive HAIs endure longer recovery periods, increased exposure to surgical and other therapeutic interventions, prolonged courses of antibiotics and other medications, and loss of life quality and productivity.[12]

Beyond the morbidity and mortality suffered by individual patients with HAIs, infections in hospitals also have a broader impact on the healthcare system as a whole. Patients, hospitals and insurers must bear the financial burden of HAIs, which includes all marginal costs associated with each additional day of hospitalization, costs of therapeutic interventions necessitated by the infection, and costs of preventing the spread of infection to other patients through the use of isolation rooms, personal protective equipment (PPE) such as gowns, gloves and masks, and additional laboratory testing.[12-14] Current estimates suggest that the increased length of stay and total cost attributable to HAIs are five to ten days and $12,000-$21,000 per infection, though studies have reported a wide range of figures totaling as high as $260,000.[11,15,16] There is a strong incentive to reduce the incidence of HAIs both from a patient welfare perspective and from an economic perspective, particularly in light of new reimbursement policies that deny payment for

treating hospital-acquired complications that are thought to be preventable, including several types of infections.[17,18]

Infection transmission dynamics in healthcare environments involve a complex network of factors. The potential for pathogenic organisms to be transferred from patient to patient is dependent on the interplay between biological properties of infectious agents, behavioral practices of staff, underlying medical conditions of patients, organization of the built environment, and tools and protocols designed to interrupt transmission (**Table 1.1**).[19]

Table 1.1. Factors Influencing Infection Transmission in Healthcare Settings

Biological properties of infectious agent[20,21]	▪ Efficiency of spread through various modes of transmission, e.g., direct and indirect contact, droplet, and airborne ▪ Viability and survival time under a range of environmental conditions ▪ Susceptibility to cleaning agents and methods of mechanical removal
Behavioral practices of staff[22-25]	▪ Adherence to hand hygiene and isolation protocols ▪ Appropriate wound care, device care, and adherence to sterile technique
Underlying medical conditions of patients[9,26]	▪ Age and severity of illness ▪ Immunosuppression and use of high-risk medications ▪ Use of indwelling devices and invasive procedures
Organization of the built environment[27,28]	▪ Availability of isolation rooms ▪ Placement of sinks, bathrooms, utility rooms, and trash and linen receptacles
Tools and protocols designed to interrupt transmission[29,30]	▪ Patient isolation protocols ▪ Cleaning and sterilization procedures for patient rooms, shared equipment, public spaces, and staff areas, e.g., computer terminals and nurses stations ▪ Care bundles designed to prevent infections in patients undergoing high-risk procedures or device use

Although little is known about the relative importance of the physical environment with regard to infection transmission, there is a growing consensus that environmental contamination does contribute to the spread of HAIs.[28,31-39] There are several pathways through which susceptible patients could be exposed to pathogens in the environment. One method of exposure is direct contact. All patients have direct contact with objects in their immediate surroundings, such as their bed, bedding, bedside tables, and other equipment residing in or around the bedside.

Ambulatory patients can have direct contact with portable (e.g., chairs, tables, curtains) and fixed (e.g., walls, floors, bathrooms) surfaces within their assigned rooms and in common recreation or therapy areas. Patients could also be exposed to pathogens in the environment through indirect contact with healthcare workers, supplies, or equipment serving as vectors.[35] If pathogens become aerosolized or suspended as droplets, patients could be exposed through inhalation or contact with mucous membranes.[39]

Just as patients can be exposed to environmental pathogens via several different pathways, the environment can likewise be contaminated in a multitude of ways. All patients can contaminate their immediate bedside surroundings through direct contact. Ambulatory patients may also contaminate other areas of their assigned rooms or shared spaces through direct contact. Indirect contact mediated by healthcare workers could be another source of contamination in the environment, as hands, PPE, uniforms, supplies, and equipment are easily soiled during patient care.[40] The impact of indirect contact may be especially great since healthcare workers move throughout a unit and, in some cases, throughout one or more hospitals, thereby providing opportunities for organisms to spread to a vast environmental network.[41] The environment may also become contaminated in ways not mediated by healthcare worker interaction with patients. Methicillin-resistant *Staphylococcus aureus* (MRSA) and Norwalk virus, for example, may become suspended in the air and land on surfaces.[39,42] Spore-producing bacteria such as *Clostridium difficile* and desiccation-resistant bacteria such as MRSA can be spread via dust particles without the aid of contact with contaminated hands or equipment.[39] Cleaning supplies such as mops and buckets may also be a vehicle for spreading bacteria from one patient area to another.[39]

Given the intricacy of elements that contribute to the spread of infectious organisms in healthcare settings, isolating the effects of any one source of exposure is challenging. While previous authors have hypothesized that prior bed occupants and hospital roommates may be important sources of exposure to pathogenic organisms that cause HAIs, few have studied the risks associated with such exposures and none have done so in a comprehensive acute care hospital setting.[43] The purpose of this dissertation was to conduct a thorough evaluation of the roles that prior bed occupants and hospital roommates play in the transmission of HAIs. The results of three related studies are presented in the subsequent chapters. To understand the magnitude of the problem posed by HAIs, Chapter Two provides a descriptive analysis of the incidence of HAIs and antimicrobial resistance in four acute care hospitals over a seven-year period. Chapter Three summarizes and synthesizes the research published to date on the relationship between exposure to infected or colonized prior room occupants and roommates and subsequent colonization or infection with the same organism. Chapter Four presents the results of a case-control study designed to quantify the association between the onset of HAIs and exposure to infected or colonized prior room occupants and hospital roommates for six commonly implicated pathogens.

CHAPTER TWO

Changes in the Incidence and Antimicrobial Susceptibility of Healthcare-Associated Infections in an Urban Hospital System, 2006-2012

ABSTRACT

Although national efforts to curtail healthcare-associated infections (HAI) have proliferated, data detailing progress over time are limited. This study aims to describe changes in incidence and antimicrobial susceptibility of HAI in four New York City hospitals within the same network over seven years. Electronic data were collected retrospectively for all patient discharges between 2006 through 2012. Previously validated computerized algorithms based on National Healthcare Safety Network criteria were used to detect bloodstream infections, pneumonia, surgical site infections, and urinary tract infections with six organisms commonly associated with HAI: *Enterococcus* spp., *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae.* Antimicrobial susceptibilities were obtained from electronic laboratory records. Logistic regression was used to assess changes in odds of acquiring an HAI and odds of antimicrobial resistance over time, controlling for age, gender, severity of illness, previous hospitalizations, and admission source. In total, 19,052 HAI were identified among 761,426 discharges. HAI rates fell over time for all organisms, all infection types, and within all hospitals, and the odds of acquiring an HAI decreased significantly over time for all organisms. Resistance levels were stable for *Enterococcus* spp., *S. aureus*, *A. baumannii*, and *S. pneumoniae*. Multidrug resistance increased for *P. aeruginosa* and decreased for *K. pneumoniae*, though imipenem resistance among *K. pneumoniae* climbed sharply in 2011. This study suggests that HAI incidence rates are falling, possibly due to increased federal, state and local attention to healthcare quality and patient safety. Though we found no substantial reductions in resistance, recent national attention towards antimicrobial stewardship may precipitate a change in coming years.

BACKGROUND

Healthcare-associated infections (HAI) remain endemic in United States (US) healthcare facilities despite growing emphasis on infection prevention and control programs designed to curtail their spread.[44] The latest national data released by the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NSHN) show notable decreases for some HAI including central line-associated bloodstream infections (BSI) and certain types of surgical site infections (SSI).[8] However, national longitudinal data are available only for the selected types of HAI tracked by the NHSN, which are limited primarily to procedure- and device-associated infections. The NHSN data also reveal substantial differences across regions and states, emphasizing the importance of monitoring trends at the local level.[8]

Antimicrobial resistance among common healthcare pathogens is similarly persistent in hospitals, even with advances in stewardship efforts and transmission-based precautions for patients with drug-resistant organisms.[45-47] Multidrug-resistant phenotypes are implicated in more than 20 percent of HAI nationally, though prevalence varies considerably by region and institution.[48] The CDC's most recent comprehensive report on antimicrobial susceptibilities shows only slight changes in resistance for most organisms over the past several years, but data are likewise limited to specific types of HAI and trends are evaluated for only a short time period.[48]

In light of the need for longitudinal data at the local level, this study aims to describe changes in the epidemiology of HAI in four New York City hospitals over a seven-year period from 2006 through 2012. Specifically, this study assesses changes in incidence of HAI, prevalence of antimicrobial resistance, and patient-level factors at admission that are associated with these outcomes for six of the most common bacterial pathogens in healthcare settings.

METHODS

Sample and setting

Data were collected from four hospitals in a single academically-affiliated network located in New York, NY. The facilities included a 221-bed community hospital, a 283-bed pediatric acute care hospital, a 647-bed adult tertiary/quaternary care hospital, and a 914-bed adult and pediatric tertiary/quaternary care hospital. All discharges occurring from January 1, 2006 through December 31, 2012 were included in the analyses. Although some patients were admitted multiple times throughout the seven-year study period, the unit of analysis for this study was each patient discharge.

Data collection

All data were collected retrospectively from the network's Clinical Data Warehouse, which stores information from a variety of electronic sources shared by the four hospitals.[49] Dates of hospital admission and discharge, source of admission, and previous in-network hospitalizations were obtained from the admission-discharge-transfer (ADT) record. Complete lists of International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes associated with each admission were obtained from billing records. Time-stamped culture results and antimicrobial susceptibility patterns were obtained from clinical microbiology laboratory records. All data were linked using patients' unique medical record numbers and admission dates. The study was approved by the Institutional Review Boards of Columbia University Medical Center and Weill-Cornell Medical Center.

Definitions of infections, antimicrobial resistance, and patient characteristics

Four types of commonly occurring HAIs were included in this analysis: BSI, SSI, urinary tract infections (UTI), and pneumonia. These infections were selected because all four have

been the target of national and local HAI reduction campaigns.[5,8] Algorithms for identifying infections in the electronic data were designed in accordance with the NHSN guidelines for surveillance of HAI (**Figure 2.1**).[50] The algorithms were created and validated by an interdisciplinary team that included an infectious disease physician, and infection prevention nurse, an epidemiologist, a database manager, and an IT systems manager with expertise in hospital administrative data.[49,51,52] Dates of culture collection and hospital admission were used to determine whether infections were healthcare-associated, i.e., developed at least two days after hospital admission.

This study included HAI associated with *Staphylococcus aureus, Acinetobacter baumannii, Streptococcus pneumoniae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis* and *Enterococcus faecium*. Binary classifications of antibiotic resistance were defined for *S. aureus* (oxacillin), *S. pneumoniae* (penicillin), *A. baumannii* (ampicillin-sulbactam), and *E. faecalis* and *E. faecium* (vancomycin). For *P. aeruginosa* we assessed resistance to cefepime, gentamicin, levofloxacin, meropenem, piperacillin/tazobactam, and tobramycin. For *K. pneumoniae* we assessed resistance to cefepime, ceftriaxone, gentamicin, imipenem, levofloxacin, meropenem, piperacillin/tazobactam, tobramycin, and trimethoprim/sulfamethoxazole. Multidrug resistance for *P. aeruginosa* and *K. pneumoniae* was defined as resistance to at least three antibiotic classes among those assessed.[53] Resistance to each antibiotic was determined by the hospitals' clinical microbiology laboratories. These organisms were selected because they have exhibited long-term trends of increasing antimicrobial resistance and because they are either endemic to healthcare settings or, in the case of *S. pneumoniae,* frequently introduced into acute care environments from the community.[8,9]

Patient characteristics at admission were assessed using several measures. A weighted Charlson Comorbidity Index was created using ICD-9-CM diagnosis codes for conditions indicated as being present upon hospital admission.[54] Patients who had at least one within-network inpatient hospitalization in the previous year were identified using ADT records. In addition, ADT records were used to determine patients' admission source, defined as either healthcare (i.e., transfer from another hospital, ambulatory surgery center, skilled nursing facility, hospice center) or non-healthcare (e.g., from home). Patient age, sex, admission hospital, and admission year were also collected from the Clinical Data Warehouse.

Statistical analysis

To assess changes in HAI over time we tabulated the number of HAI occurring each year and stratified by organism and body site of infection. Percent changes in HAI incidence per 10,000 discharges between 2006 and 2012 were calculated. Multiple logistic regression was used to evaluate changes in odds of infection over time, controlling for hospital, age (continuous), sex, within-network hospitalization in the previous year, admission source, and Charlson Comorbidity Index. A separate model was constructed for each of the six organisms. Patients who had an infection in more than one body site with the same organism during a single admission were represented only once in each multivariable model. In order to evaluate whether patient characteristics associated with HAI changed throughout the study period, we also assessed interaction between year and age, sex, prior hospitalization, admission source and Charlson Comorbidity Index for each body site of infection.

To assess changes in antibiotic sensitivities over time, we tabulated the annual proportion of infections resistant to each of the antibiotics identified *a priori* for each organism. Multiple logistic regression was used to evaluate changes in the odds of resistance over time, controlling

for hospital, age, sex, within-network hospitalization in the previous year, admission source, and Charlson Comorbidity Index. Each organism was modeled separately. Patients who had an infection at more than one body site with the same organism during a single admission were represented only once in each multivariable model and were considered to have a resistant infection if at least one of the infections was caused by a resistant organism.

RESULTS

Characteristics of the 761,426 patient discharges that occurred during the study period are summarized by year in **Table 2.1**. A total of 19,052 HAI with the six organisms of interest were identified. Forty-nine percent were UTI (N=9,319), 23% were pneumonia (N=4,414), 19% were BSI (N=3,602), and 9% were SSI (N=1,717). From 2006 to 2012, incidence per 10,000 discharges fell for each type of HAI (**Figure 2.2.a**), for each of the six organisms included in this study (**Figure 2.2.b**), and within all four hospitals (**Figure 2.2.c**).

Table 2.2 displays results of the multivariable regression analyses modeling the association between advancing year and odds of HAI. For each organism there was a statistically significant decrease in the odds of HAI over time, controlling for hospital and patient characteristics. Patients with a healthcare admission source were significantly more likely to develop an HAI with all organisms except *S. pneumoniae*, for which a positive but not statistically significant association was found. Within-network hospitalization in the previous year significantly increased the odds of developing an HAI with all organisms except *S. pneumoniae*, for which a statistically significant negative association was found. Advancing age and greater severity of illness were significantly associated with development of HAI for all organisms. Male patients were significantly more likely to develop an HAI with *S. aureus, P.*

aeruginosa, *S. pneumoniae* and *A. baumannii*, while female patients were significantly more likely to develop an HAI with *K. pneumoniae* and *E. faecalis/E. faecium*.

As shown in **Figures 2.3.a** and **2.3.b**, the impact of admission source and within-network hospitalization in the previous year decreased significantly over time, with the association between HAI and previous hospitalization decreasing steadily throughout the study period and the association between HAI and admission source decreasing steadily through 2010 and then rising again. Statistically significant interaction with year was not identified for any other factor.

The annual proportion of HAI caused by antibiotic-resistant organisms is presented in **Table 2.3**. The multivariable logistic regression analyses show no appreciable change in levels of antibiotic resistance for any organism except *P. aeruginosa*, for which multidrug resistance increased significantly over the study period and *K. pneumoniae*, for which multidrug resistance decreased significantly (**Table 2.4**). There was a small but statistically significant decrease in oxacillin resistance among *S. aureus* isolates. Resistance to all tested antibiotics increased for *P. aeruginosa* (**Figure 2.4.a**). For *K. pneumoniae*, resistance decreased slightly for some antibiotics but increased sharply for carbapenem, rising from an average of 17 percent in 2006-2010 to 46 percent in 2011 (**Figure 2.4.b**).

Patients with a healthcare admission source were significantly more likely to develop a resistant infection for all organisms except *S. pneumoniae* and *A. baumannii*. Resistance was significantly associated with within-network hospitalization in the previous year for *K. pneumoniae*, *S. aureus*, and *E. faecalis/E. faecium*. Odds of resistance were significantly higher for males among those infected with *K. pneumoniae* and *S. pneumoniae* and significantly higher for females among those infected with *E. faecalis/E. faecium*. There was a small but significant positive association between severity of illness and resistance among *S. pneumoniae* and *E.*

faecalis/E. faecium infections. Advancing age was associated with resistance among *S. aureus* infections, while younger age was associated with resistance among *P. aeruginosa* infections.

DISCUSSION

Using data from four hospitals in a major metropolitan center, we observed persistent and statistically significant declines in the incidence of healthcare-associated BSI, SSI, UTI, and pneumonia between 2006 and 2012. The reductions in BSI, SSI, and pneumonia paralleled trends tracked at the national level for selected conditions including central line-associated BSI, BSI with MRSA, ventilator-associated infections, and SSI following common orthopedic, cardiac, gastrointestinal, and gynecological procedures.[8,55-57] Though US rates of catheter-associated UTI climbed in 2009-2012, our study sites continued to experience annual reductions of total UTI.[8,55]

The reduced incidence of HAI across the study institutions is noteworthy, particularly in light of changes to the patient population, which occurred in tandem. Though severity of illness remained stable over the course of the study, the proportion of patients admitted from other healthcare facilities and who had been hospitalized in-network within the previous year increased considerably, rising from 23 to 45 percent and from 10 to 17 percent, respectively. Patients who have had prolonged contact with the healthcare system tend to be more vulnerable to infection and more likely to enter the hospital already having been colonized with common healthcare-associated pathogens.[58] Yet, the observed reductions in HAI were robust despite the demographic shift to include a higher burden of these patients. In fact, the results of the interaction models indicate that rates of HAI were falling even more among patients who had previous healthcare exposures compared with other patients, suggesting that the overall decline

in HAI may be due, in part, to a reduced risk among this subset. Improved screening procedures for patients admitted from healthcare sources or with known history of hospitalization may have contributed to falling HAI rates, possibly because a higher proportion of infections that were present upon hospital admission would have been diagnosed within the first 48 hours and therefore not counted as HAI, or because interventions such as decolonization were effective at preventing HAI.[59] Similarly, the slight decrease in *S. pneumoniae* may be due to faster diagnosis and appropriate classification as non-HAI, since these infections are more likely to be acquired in the community. Changes in infection prevention practices at the study institutions such as hand hygiene improvement and implementation of a central line care bundle may have contributed to declining infection rates overall, though it is difficult to evaluate the impact of specific policies since they varied across settings and throughout the course of the study.

In addition to risk differences between patients with and without previous healthcare contact, we also identified risk differences based on gender. That male patients had higher odds of developing HAI caused by *S. aureus, P. aeruginosa, S. pneumoniae* and *A. baumannii* while female patients had higher odds of *K. pneumoniae* and *E. faecalis/E. faecium* may be related to the types of infections that these organisms are most likely to cause. For example, *S. aureus* is a common cause of BSI, which are more common in male patients, and *E. faecalis/E. faecium* have emerged as common causes of UTI, which are more common in female patients.[60-62] The fact that female patients were more likely to have a vancomycin-resistant strain of *E. faecalis/E. faecium* may be the result of previous antibiotic treatment for recurring UTI.[63] *S. pneumoniae* has been reported to occur more frequently among men, possibly due to higher rates of smoking and underlying conditions such as chronic heart and lung diseases.[64] Previous antibiotic

treatment for *S. pneumoniae* and other causes of pneumonia may explain why resistance was higher among men.[65]

While the incidence of HAI was greatly reduced, little progress was made with regard to reducing antimicrobial resistance. The strongest trend occurred among *P. aeruginosa*, for which aminoglycoside, carbapenem, cephalosporin, fluoroquinolone, and beta-lactamase inhibitor resistance increased. The proportion of multidrug-resistant *P. aeruginosa* isolates increased from less than one percent in 2006 to over 10 percent in 2012, and statewide data suggest that this upward trajectory has continued in recent years.[66] For *K. pneumoniae* we observed moderate decreases in resistance to aminoglycoside, cephalosporin, fluoroquinolone, and sulfonamide antibiotics as well as increased beta-lactamase activity, though resistance to carbapenems more than doubled in 2011 following an outbreak of carbapenem-resistant *K. pneumoniae*. It is likely that this outbreak contributed to the overall rise in *K. pneumoniae* infections that occurred in 2011 after several years of steadily falling rates. The considerable uptick in carbapenem resistance is reflective of a national epidemic of *K. pneumoniae* carbapenemase, which first appeared in New York City in the early 2000s.[67,68] Still, the percent of *K. pneumoniae* isolates that were multidrug-resistant was lower than statewide reports of 25 percent and decreased throughout the study period.[66] This discrepancy may be due to differences in the definition of multidrug resistance and the specific drugs for which antimicrobial activity was assessed. Similar to trends reported at the state and national levels, methicillin resistance among *S. aureus* remained relatively stable after 2007, following precipitous declines in the previous decade.[45,48,66,69,70] Consistent with data available from the CDC, no meaningful changes in vancomycin resistance among *Enterococcus* spp. occurred in the study facilities during the observed time frame.[48,66]

This study was conducted during a period of heightened attention toward HAI prevention.[44] The application of evidence-based practices and bundles coupled with the adoption of new reimbursement policies that reframed many healthcare-associated conditions as preventable events likely played a role in reducing HAI.[71,72] However, since many changes to infection prevention practice have been introduced during the last decade, it is not feasible to isolate the effects of any single initiative. Moreover, it is unlikely that any one factor was solely responsible for the reduction.[73] Analogous broad efforts towards reducing antimicrobial resistance among healthcare-associated pathogens were also introduced during this timeframe. Antimicrobial stewardship programs may have had some effect with regard to halting the upward trends in resistance for many organisms; nonetheless, data suggest that they have not yet had much impact with regard to lessening the burden of resistance at the state or national level.[48,60,74] The evidence of such impact is likely to require longer periods of time than other practices associated with prevention of HAI.

One of the major strengths of this analysis is its application of a consistent methodology for identifying HAI over time. Unlike other sources of longitudinal data, the electronic algorithms used to define infections in this study were not sensitive to changes in case definitions, infection prevention personnel training, or financial and regulatory incentives that may have altered reporting practices.[75] Still, the gold standard for diagnosis of an infection is clinician adjudication after full chart review, and disadvantages to using electronic data sources have been identified.[76] The SSI algorithm was designed to include only infections associated with NHSN operative procedures, so infections resulting from other procedures were not identified. Previous studies have reported low sensitivity for some of the ICD-9-CM codes used to create the Charlson Comorbidity Index, though specificity is generally high.[77] Data on

previous out-of-network hospitalizations were not available, and it is possible that some within-network hospitalizations were not captured due to erroneous assignment of new medical record numbers to patients who were readmitted within one year. This type of misclassification, however, could only lessen the magnitude of the observed association between previous admission and odds of HAI. As the quality and availability of electronic patient data improves, the validity of some data elements may have changed over time, though we are not aware of any specific changes to the way data were collected or recorded that would have affected the study variables.

In addition to issues of data quality, there are also some limitations to our statistical analyses. We were unable to account for previous use of antibiotics, which is a known risk factor for resistance and may also confound the associations between infection and prior hospitalization or admission from a healthcare source, since patients with previous healthcare contact may be more likely to have taken antibiotics.[78] In addition, the multivariable model predicting antimicrobial resistance for *S. pneumoniae* was not adequately powered to detect differences over time. The low incidence of healthcare-associated *S. pneumoniae* throughout the study suggests that nosocomial transmission of this pathogen remains relatively rare.

Overall, this study provides strong support for the observation that the incidence of HAI is falling and that the reduction in HAI is not limited to device- and procedure-associated infections. Although we were unable to measure the impact of any specific policy or practice changes due to the overlapping nature of their implementation, the reduction may be the result of increased federal and state attention to healthcare quality and patient safety. Accordingly, although we have yet to observe substantial reductions in antimicrobial resistance, the recent

uptick in national attention towards antimicrobial monitoring and stewardship may precipitate a change in coming years.

Table 2.1. Characteristics of hospitalized patients by year

Year	2006	2007	2008	2009	2010	2011	2012
N	104,645	106,783	105,177	109,631	112,656	112,122	110,412
% (no.) admitted to each hospital							
Community	13.1 (13,668)	12.6 (13,476)	12.7 (13,376)	11.7 (12,803)	11.6 (13,072)	11.2 (12,557)	11.1 (12,225)
Pediatric acute care	15.8 (16,507)	17.1 (18,281)	18.0 (18,959)	15.2 (16,694)	14.6 (16,487)	14.5 (16,260)	14.9 (16,405)
Adult tertiary/quaternary care	31.9 (33,355)	31.7 (33,839)	31.4 (33,054)	31.9 (35,005)	32.2 (36,283)	31.7 (35,579)	31.3 (34,608)
Adult/pediatric tertiary/quaternary care	39.3 (41,115)	38.6 (41,187)	37.8 (39,788)	41.2 (45,129)	41.6 (46,814)	42.6 (47,726)	42.7 (47,174)
% (no.) admitted from healthcare source*	9.6 (10,044)	10.5 (11,228)	10.7 (11,287)	17.3 (18,983)	16.7 (18,798)	17.5 (19,653)	16.6 (18,270)
% (no.) hospitalized within previous year**	22.6 (23,658)	32.4 (34,601)	37.2 (39,069)	40.2 (44,054)	43.3 (48,772)	44.4 (49,747)	45.1 (49,800)
Mean (standard deviation) Charlson Comorbidity Index	1.4 (2.75)	1.6 (2.95)	1.6 (2.93)	1.6 (2.99)	1.7 (3.08)	1.8 (3.30)	1.8 (3.36)
Mean (standard deviation) age in years	44.5 (27.82)	44.3 (27.89)	44.4 (27.99)	44.6 (28.11)	44.8 (28.11)	45.5 (28.3)	45.4 (28.46)
% (no.) male sex	44.9 (46,989)	44.5 (47,511)	44.2 (46,473)	44.4 (48,717)	44.3 (49,930)	44.5 (49,939)	44.4 (48,989)

*Admission from another hospital, ambulatory surgery center, skilled nursing facility, or hospice center.

**Within-network hospitalizations only.

Table 2.2. Relationship between advancing year and odds of healthcare-associated infection at four New York City hospitals, 2006-2012

Organism	*Enterococcus faecalis, Enterococcus faecium*	*Staphylococcus aureus*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*	*Streptococcus pneumoniae*
N	6,301	4,399	4,116	2,758	688	195
Year (continuous, 2006-2012)	0.86 [0.85,0.87]	0.89 [0.88,0.90]	0.89 [0.87,0.90]	0.90 [0.88,0.92]	0.88 [0.85,0.92]	0.85 [0.79,0.92]
Hospital*						
Community	0.44 [0.40,0.48]	0.59 [0.52,0.66]	0.55 [0.49,0.63]	0.49 [0.42,0.56]	0.76 [0.56,1.02]	0.82 [0.49,1.36]
Pediatric acute care	0.57 [0.51,0.65]	0.70 [0.61,0.79]	1.01 [0.86,1.17]	0.85 [0.71,1.02]	0.78 [0.54,1.13]	0.60 [0.32,1.13]
Adult/pediatric tertiary/quaternary care	0.54 [0.51,0.57]	0.80 [0.75,0.86]	1.27 [1.20,1.36]	0.80 [0.74,0.87]	1.37 [1.15,1.61]	0.94 [0.69,1.30]
Healthcare admission source**	2.08 [1.96,2.21]	1.91 [1.78,2.05]	1.88 [1.75,2.02]	2.23 [2.05,2.43]	2.63 [2.23,3.10]	1.39 [0.96,2.00]
Hospitalized within previous year***	1.75 [1.66,1.85]	1.47 [1.39,1.57]	1.49 [1.40,1.59]	1.64 [1.52,1.78]	1.39 [1.19,1.63]	0.68 [0.50,0.93]
Charlson Comorbidity Index (continuous)	1.08 [1.075,1.085]	1.08 [1.07,1.09]	1.08 [1.07,1.09]	1.06 [1.05,1.07]	1.08 [1.07,1.09]	1.08 [1.05,1.11]
Age in years (continuous)	1.017 [1.016,1.018]	1.009 [1.007,1.010]	1.021 [1.019,1.022]	1.022 [1.020,1.024]	1.01 [1.007,1.014]	1.006 [1.00,1.01]
Male sex	0.87 [0.83,0.91]	1.57 [1.48,1.67]	0.81 [0.77,0.87]	1.11 [1.03,1.20]	1.42 [1.23,1.65]	1.84 [1.37,2.46]

Notes: Results of logistic regression analyses controlling for hospital and patient characteristics. Data are odds ratios (95% confidence intervals). N for each organism is less than the total incidence for each organism because some patients had infections with the same organism in multiple body sites.

* Reference: adult tertiary/quaternary care

**Admission from another hospital, ambulatory surgery center, skilled nursing facility, or hospice center.

***Within-network hospitalizations only.

Table 2.3. Changes over time in the proportion of healthcare-associated infections resistant to antibiotics, 2006-2012

	2006	2007	2008	2009	2010	2011	2012	% change in proportion of resistant infections, 2006 to 2012
Enterococcus faecalis and Enterococcus faecium (N=6,476)	483/1,120 (43)	529/1,178 (45)	361/927 (39)	406/975 (42)	425/897 (47)	322/763 (42)	279/616 (45)	+ 5%
Staphylococcus aureus (N=4,553)	346/735 (47)	395/810 (49)	282/647 (44)	296/679 (44)	295/624 (47)	241/572 (42)	192/486 (40)	− 15%
Klebsiella pneumoniae (N=4,237)	69/735 (9)	118/782 (15)	85/633 (13)	29/477 (6)	30/431 (7)	37/570 (7)	43/609 (7)	− 22%
Pseudomonas aeruginosa (N=2,859)	3/435 (1)	7/426 (2)	11/479 (2)	35/430 (8)	42/417 (10)	34/361 (9)	33/311 (11)	+ 1,000%
Acinetobacter baumannii (N=731)	34/109 (31)	69/144 (48)	69/125 (55)	38/95 (40)	32/81 (40)	40/93 (43)	24/84 (29)	− 6%
Streptococcus pneumoniae (N=196)	15/40 (38)	21/43 (49)	19/39 (49)	2/15 (13)	0/12 (0)	10/23 (43)	9/24 (38)	0%
Total (N=19,052)	950/3,174 (30)	1,139/3,383 (34)	827/2,850 (29)	779/2,671 (29)	824/2,462 (33)	684/2,382 (29)	580/2,130 (27)	− 10%

Data are no. resistant isolates/no. total isolates (% resistant). Antimicrobial resistance was defined as resistance to: oxacillin for *Staphylococcus aureus;* penicillin for *Streptococcus pneumoniae;* ampicillin-sulbactam for *Acinetobacter baumannii;* vancomycin for *Enterococcus faecalis* and *Enterococcus faecium;* and ≥3 antibiotic classes for *Pseudomonas aeruginosa* and *Klebsiella pneumoniae.*

Table 2.4. Relationship between advancing year and odds of antimicrobial resistance for patients with healthcare-associated infections at four New York City hospitals, 2006-2012

Organism	*Enterococcus faecalis, Enterococcus faecium*	*Staphylococcus aureus*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*	*Streptococcus pneumoniae*
N (%) resistant	2,716 (43.1)	1,964 (44.7)	404 (9.8)	165 (5.6)	276 (40.1)	75 (38.5)
Year (continuous, 2006-2012)	0.98 [0.95,1.01]	0.94 [0.91,0.97]	0.86 [0.82,0.91]	1.45 [1.32,1.59]	0.95 [0.88,1.03]	0.86 [0.73,1.01]
Hospital*						
Community	0.61 [0.49,0.76]	1.30 [1.03,1.65]	0.63 [0.42,0.95]	0.48 [0.20,1.13]	0.98 [0.52,1.85]	0.88 [0.28,2.76]
Pediatric acute care	0.40 [0.29,0.55]	1.34 [0.98,1.83]	0.17 [0.09,0.34]	0.34 [0.16,0.74]	0.11 [0.03,0.50]	0.67 [0.16,2.78]
Adult/pediatric tertiary/quaternary care	2.77 [2.46,3.11]	1.00 [0.87,1.14]	0.37 [0.29,0.47]	0.78 [0.55,1.12]	2.01 [1.42,2.84]	0.74 [0.36,1.53]
Healthcare admission source**	1.36 [1.21,1.54]	1.28 [1.10,1.48]	1.98 [1.58,2.49]	1.47 [1.04,2.08]	1.05 [0.74,1.49]	2.26 [0.97,5.27]
Hospitalized within previous year***	1.46 [1.31,1.63]	1.62 [1.42,1.84]	1.59 [1.28,1.98]	1.18 [0.84,1.66]	0.82 [0.59,1.14]	1.40 [0.70,2.79]
Charlson Comorbidity Index (continuous)	1.04 [1.03,1.05]	1.01 [1.00,1.03]	1.00 [0.98,1.03]	0.98 [0.94,1.03]	1.00 [0.96,1.04]	1.12 [1.03,1.21]
Age in years (continuous)	1.002 [0.999,1.005]	1.017 [1.014,1.020]	0.99 [0.98,1.00]	0.98 [0.97,0.99]	1.00 [0.99,1.01]	0.99 [0.97,1.00]
Male sex	0.84 [0.75,0.93]	0.99 [0.87,1.13]	1.26 [1.02,1.56]	1.08 [0.78,1.49]	1.25 [0.91,1.73]	2.14 [1.11,4.14]

Notes: Results of logistic regression analyses controlling for hospital and patient characteristics. Data are odds ratios (95% confidence intervals). Antimicrobial resistance was defined as resistance to: oxacillin for *Staphylococcus aureus;* penicillin for *Streptococcus pneumoniae;* ampicillin-sulbactam for *Acinetobacter baumannii;* vancomycin for *Enterococcus faecalis* and *Enterococcus faecium;* and ≥3 antibiotic classes for *Pseudomonas aeruginosa* and *Klebsiella pneumoniae.*

* Reference: adult tertiary/quaternary care

**Admission from another hospital, ambulatory surgery center, skilled nursing facility, or hospice center.

***Within-network hospitalizations only

Figure 2.1. Algorithms for identifying four types of infections using electronically available data from laboratory records and International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes. Definitions are based on the Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN) guidelines for surveillance of HAIs.[49,50]

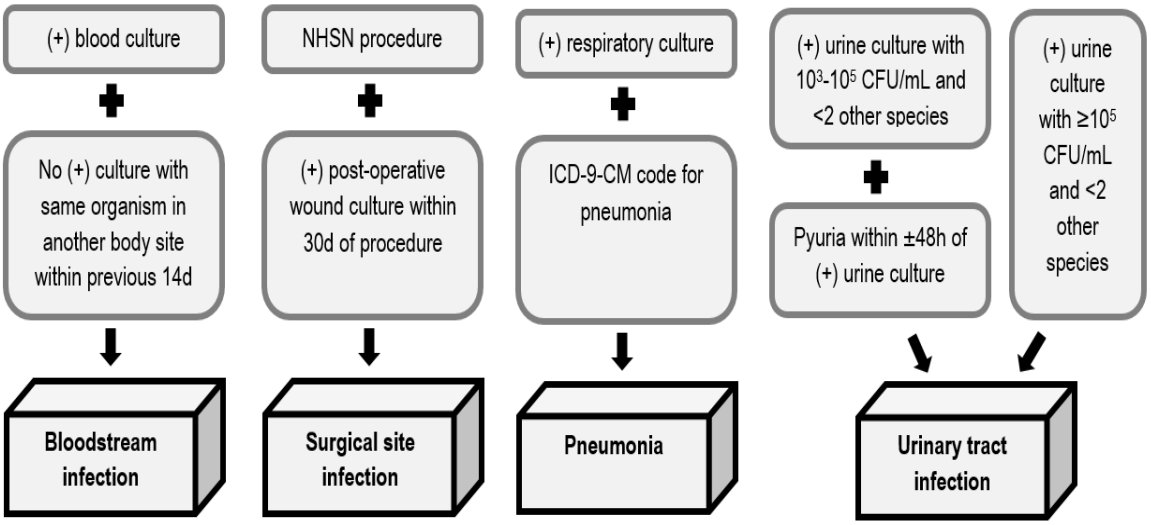


Figure 2.2.a. Annual incidence of healthcare-associated infections per 10,000 admissions in four New York City hospitals by body site, 2006-2012. The percent decrease in infection rate between 2006 and 2012 is displayed for each infection type.

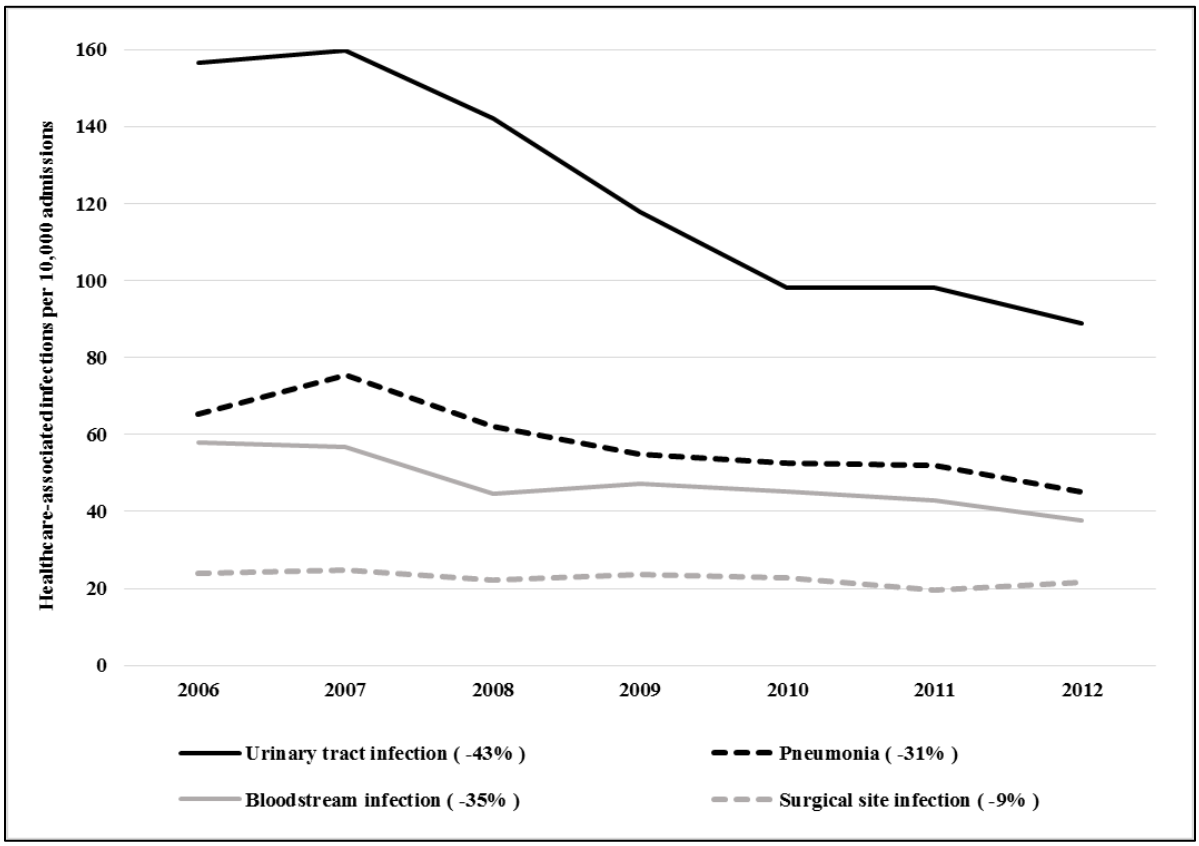


Figure 2.2.b. Annual incidence of healthcare-associated infections per 10,000 admissions in four New York City hospitals by organism, 2006-2012. The percent decrease in infection rate between 2006 and 2012 is displayed for each organism.

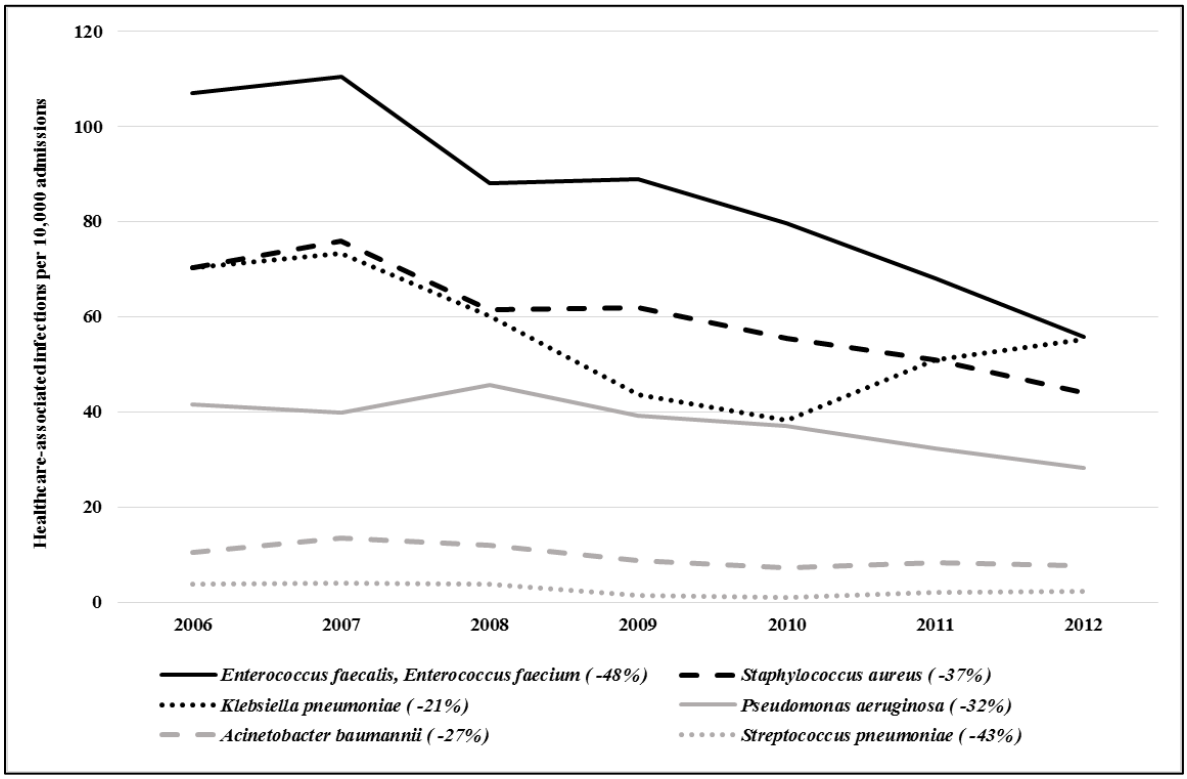


Figure 2.2.c. Annual incidence of healthcare-associated infections per 10,000 admissions in four New York City hospitals by hospital, 2006-2012. The percent decrease in infection rate between 2006 and 2012 is displayed for each hospital.

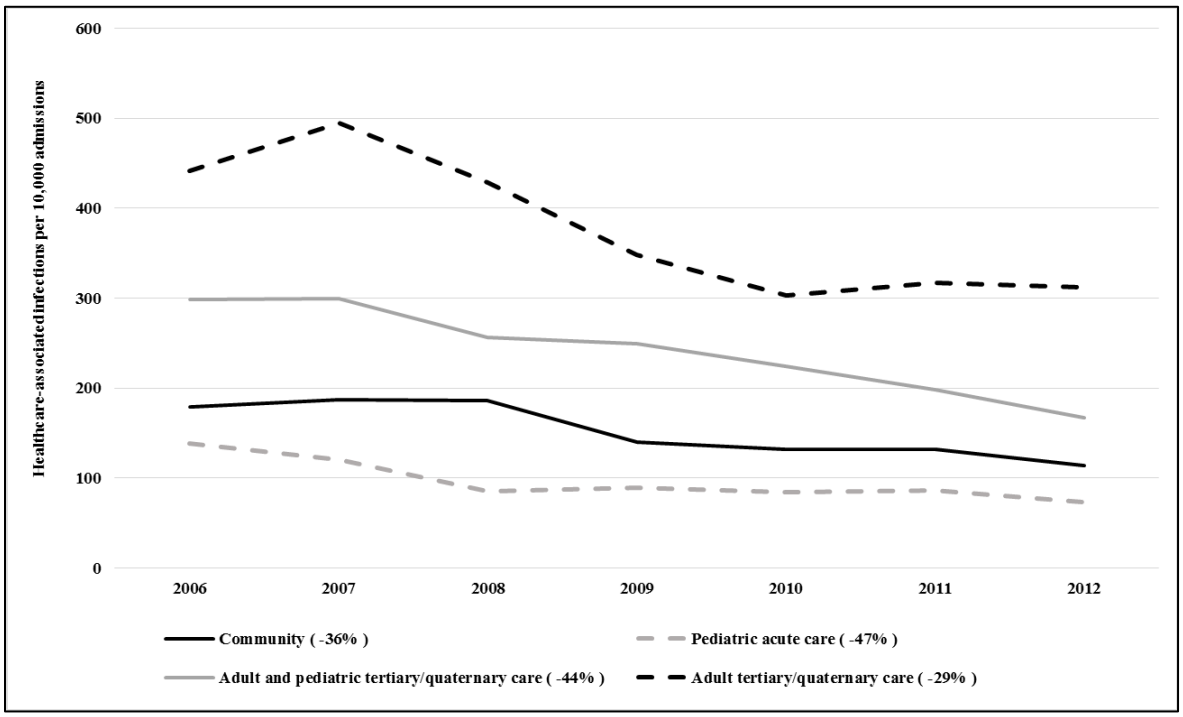


Figure 2.3.a. Changes in association between admission source and healthcare-associated infection over time. Significant interaction between year and admission source in multiple logistic regression models controlling for hospital, in-network hospitalization in previous year, Charlson Comorbidity Index, age, and gender ($p<0.001$).

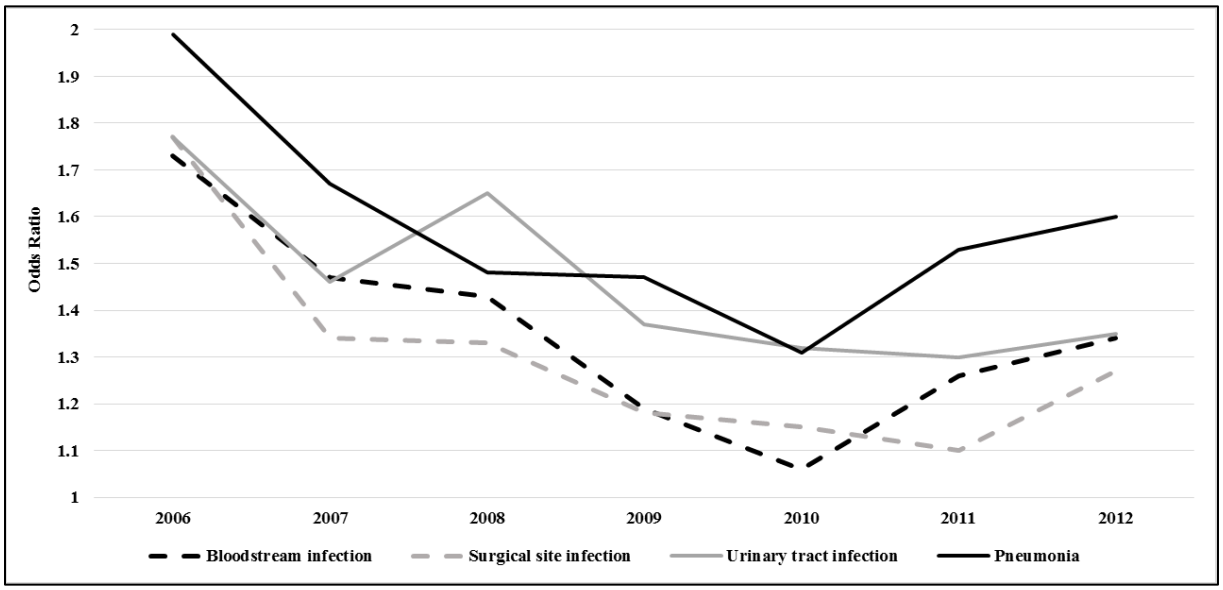


Figure 2.3.b. Changes in association between prior in-network hospitalization and healthcare-associated infection over time. Significant interaction between year and prior in-network hospitalization in multiple logistic regression models controlling for hospital, admission source, Charlson Comorbidity Index, age, and gender ($p<0.001$).

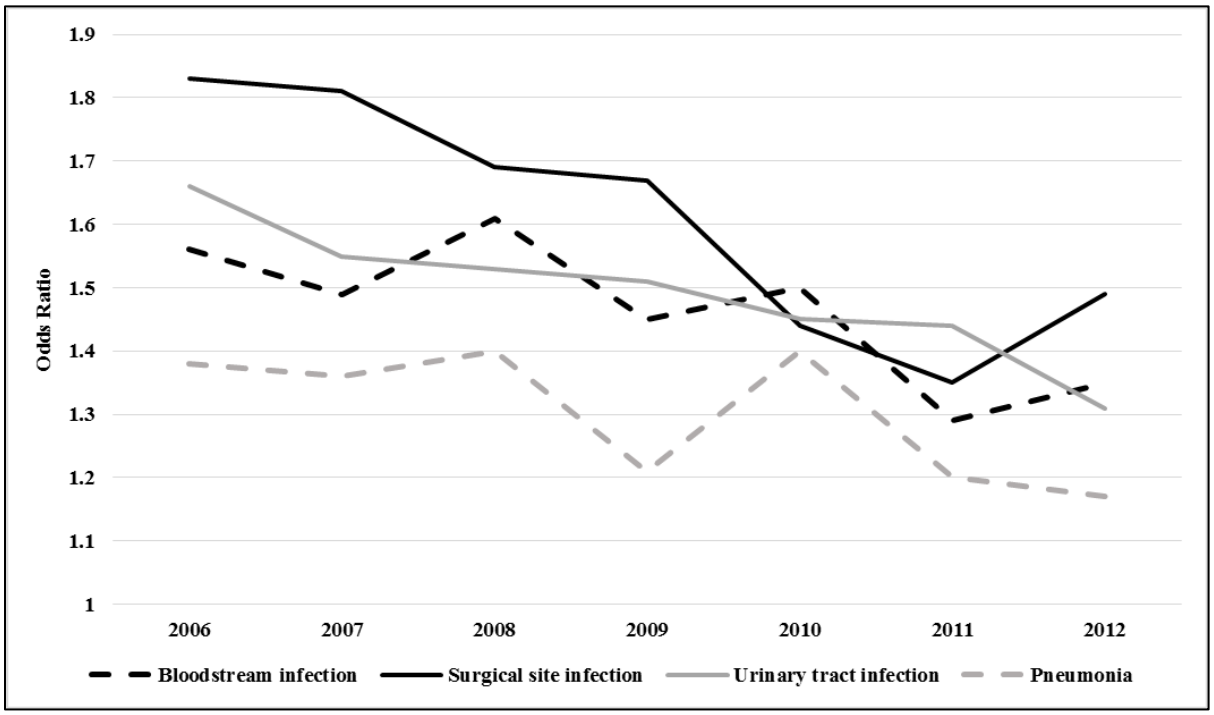


Figure 2.4.a. Proportion of *Pseudomonas aeruginosa* infections resistant to antibiotics in four New York City hospitals, 2006-2012. The percent change in the proportion of resistant isolates between 2006 and 2012 is displayed for each antibiotic.

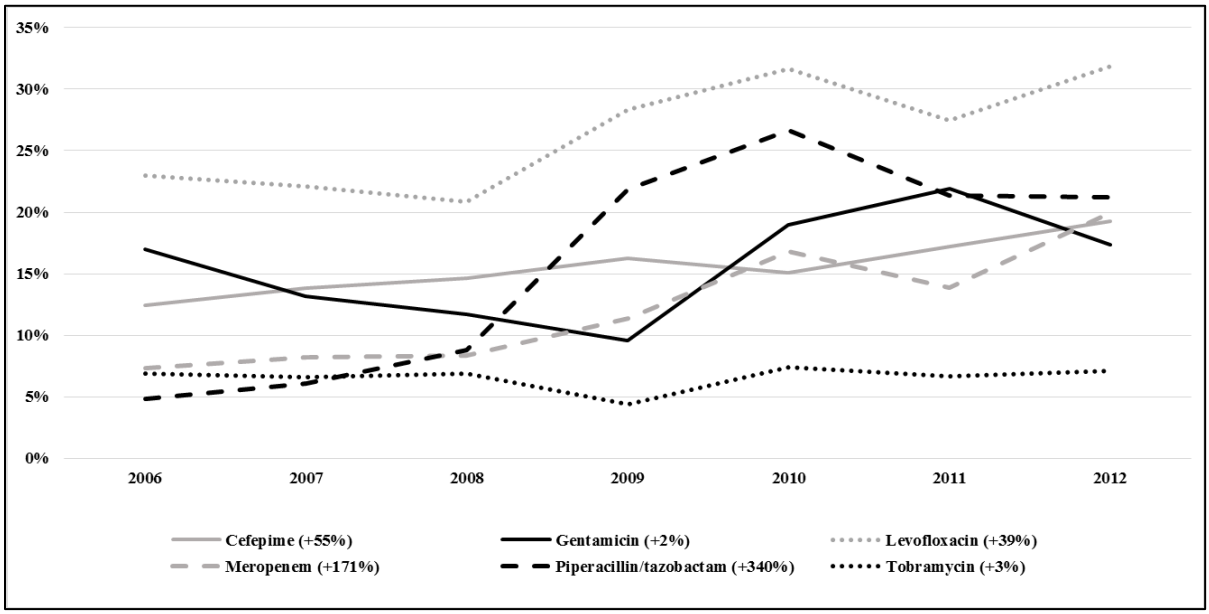
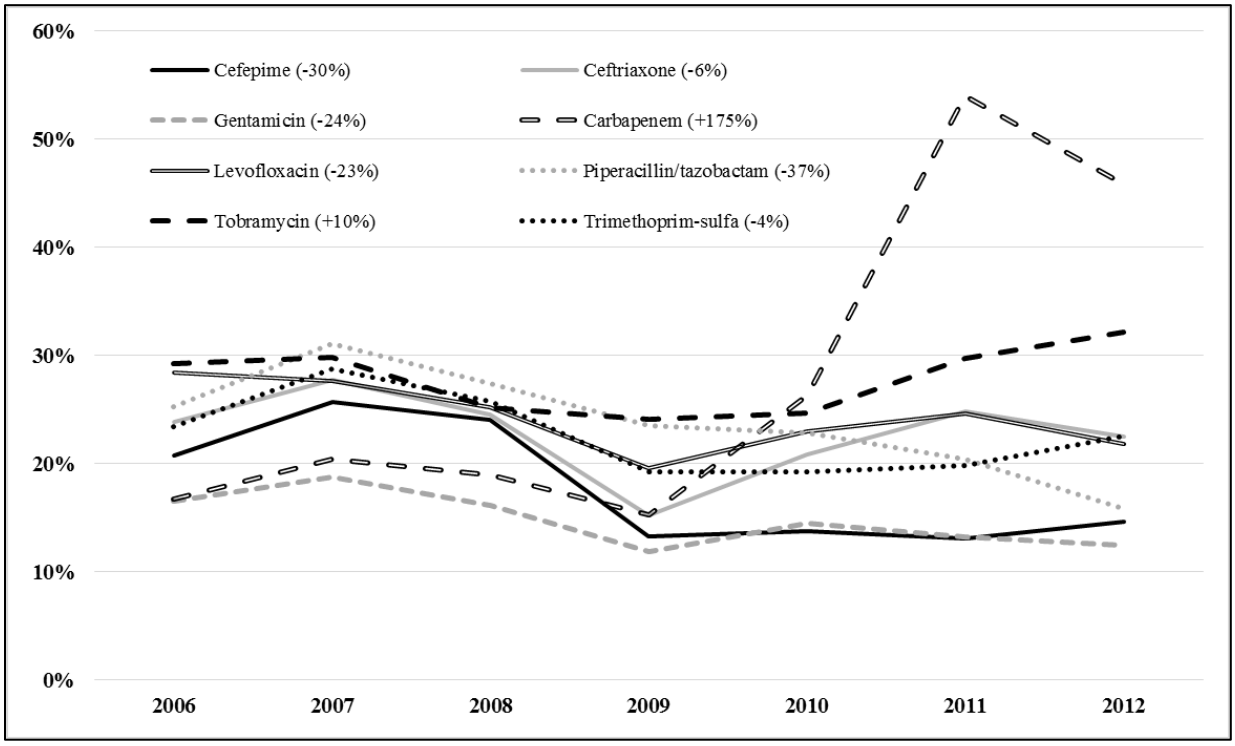


Figure 2.4.b. Proportion of *Klebsiella pneumoniae* infections resistant to antibiotics in four New York City hospitals, 2006-2012. The percent change in the proportion of resistant isolates between 2006 and 2012 is displayed for each antibiotic or class. Isolates were considered carbapenem resistant if they were resistant to meropenem, imipenem, or both.



CHAPTER THREE

Systematic Review of Literature Describing Transmission of Healthcare-associated Infections from Roommates and Prior Room Occupants

ABSTRACT

Pathogens that cause healthcare-associated infections (HAI) are known to survive on surfaces and equipment in healthcare environments despite routine cleaning. As a result, the infection status of prior room occupants and roommates may play a role in HAI transmission. This systematic review summarizes the literature evaluating the association between patients' exposure to infected/colonized hospital roommates or prior room occupants and their risk of infection/colonization with the same organism. A PubMed search for English articles published in 1990-2014 yielded 330 studies which were screened by three reviewers. Eighteen articles met our inclusion criteria. Multiple studies reported positive associations between infection and exposure to roommates with influenza and group A *Streptococcus*, but no associations were found for *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Cryptosporidium parvum*, or *Pseudomonas cepacia*; findings were mixed for vancomycin-resistant enterococci (VRE). Positive associations were found between infection/colonization and exposure to rooms previously occupied by patients with *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, but no associations were found for resistant Gram-negative organisms; findings were mixed for *C. difficile*, MRSA, and VRE. Although the majority of studies suggest a link between exposure to infected/colonized roommates and prior room occupants, methodological improvements such as increasing statistical power and conducting universal screening for colonization would provide more definitive evidence needed to establish causality.

INTRODUCTION

Despite decades of infection prevention research and quality improvement initiatives, healthcare-associated infections (HAI) remain common adverse events in hospitals and long-term care facilities.[4] Over 700,000 HAIs occur annually in the United States alone, leading to death in six percent of cases and costing the healthcare system 28-45 billion U.S. dollars each year.[9,10,12] Recently there has been renewed interest in understanding the role of the physical environment in the spread of HAIs.[31,32] Countless studies have reported that pathogenic organisms can survive on a variety of fomites in healthcare settings including those at the patient bedside (e.g., mattresses, linens, pillows, bedframes, bedrails), inside patient bathrooms (e.g., toilets, floors, soap dispensers) and on medical instruments (e.g., blood pressure cuffs, suctioning systems).[40,79-85] Moreover, the effectiveness of cleaning regimens has been called into question as a number of studies have reported that pathogens remain on hospital surfaces even after they have been disinfected in accordance with recommended protocols.[86-89] Pathogens that survive on fomites can subsequently be transferred from contaminated surfaces to patients through direct contact, indirect contact via the hands and gloves of healthcare workers, or by aerosolization of surface particles.[40,82,90-92]

Patients hospitalized with infections frequently contaminate their surrounding environments with pathogenic organisms; therefore, roommates and previous room occupants may serve as potential sources of exposure to other patients.[20,40] Yet our understanding of how such exposures contribute to a patient's overall risk of infection remains limited, and the effects of these exposures may be dependent on a variety of factors unique to each organism species, such as their robustness to atmospheric conditions, susceptibility to cleaning agents, and virulence. Therefore, the aim of this study was to systematically review the literature describing

organism transmission from concurrent roommates or previous room occupants in healthcare settings.

METHODS

Inclusion Criteria

This systematic literature review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[93]

Search Strategy

The literature search was conducted in February 2015. All databases indexed within PubMed were searched using the following combination of keyword and Medical Subject Heading (MeSH) search terms linked with Boolean operators: {[MeSH (Patients' Rooms)] AND [MeSH (Infection Control Practitioners) OR MeSH (Infection Control) OR MeSH (Cross Infection) OR MeSH (Infection) OR MeSH (Wound Infection) OR MeSH (Surgical Wound Infection) OR Keyword (Infection)]} OR {Keyword (Prior Room Occupant*)} OR {Keyword (Roommate) AND [Keyword (Transmission) OR Keyword (Infection*) OR Keyword (Outbreak*)]}. The search was limited to articles published in English from January 1, 1990 through December 31, 2014.

Article Selection, Review and Quality Scoring

Three reviewers independently assessed each article at all stages of the review and quality scoring processes. Discrepancies between reviewers were discussed as a group until a consensus was reached. First, reviewers screened the titles and abstracts of all articles and eliminated those that were not relevant to the aims of the review. The remaining articles underwent full text review to determine whether they met the following inclusion criteria: (1)

compared infection and/or colonization rates between patients known to be exposed to infectious roommates and/or prior room occupants and patients not known to be exposed; (2) were conducted in an acute or long-term healthcare setting; and (3) were original research studies. Articles meeting the inclusion criteria were scored according to a modified 20-item version of the *Checklist for Measuring Study Quality* developed by Downs and Black (**Table 3.1**).[94] Some measures were not applicable to all articles; these items were removed from the score denominator and not assessed for studies in which they were not relevant. Final scores were converted to percentages.

RESULTS

Eighteen articles meeting the inclusion criteria were identified (**Figure 3.1**). Ten articles investigated the effects of exposure to infected or colonized roommates,[95-104] six investigated the effects of exposure to infected or colonized prior room occupants,[105-110] and two investigated both exposures.[111,112]

Study designs and definitions of exposures and outcomes

The articles in this review represent a range of observational and interventional designs including retrospective and prospective cohort studies (n=11),[96,98-102,105,108-110,112] case-control studies (n=4),[95,97,103,104] and quasi-experimental studies (n=3).[106,107,111] The studies varied considerably in their definitions of exposure and outcome measures. Among studies that examined exposure to roommates with non-viral pathogens, four (44%) defined the exposure as having a roommate with a clinical infection[95-97,112] and five (56%) defined the exposure as having a roommate who was either infected or colonized.[101-104,111] Among studies that examined exposure to previous room occupants, there was variation both in the determination of whether a

previous occupant was infectious and in the timeframe during which they occupied the room. Four studies (50%) defined the exposure as a previous occupant who was infected or colonized,[105,108,109,111] two studies (25%)—both of *Clostridium difficile*—defined the exposure as a previous occupant with a history of infection,[110,111] and two studies (25%) did not specify.[106,107]

With regard to timing of the exposure, most of the studies implied that only the occupant immediately prior to the study subject was included, although only three articles stated this explicitly.[105,107,110] One study also analyzed exposure to any infectious patient who had occupied the same room within the previous two week period.[107] Finally, there was notable variation in the definition of study outcomes. Half of the articles used an outcome measure of clinical infection[95,96,97-100,102,110,112] while the other half used an outcome measure of infection or colonization.[101,103-109,111] Methods of case detection ranged from universal screening to sampling based on clinical indication.

Findings of studies examining exposure to infected or colonized roommates

The twelve articles investigating effects of exposure to infected or colonized roommates are described in **Table 3.2.a** and their findings are summarized in **Figure 3.2.a**. Five studies evaluated bacterial pathogens that are transmitted via contact.[101,103,104,111,112] No significant associations between roommate exposure and infection with methicillin-resistant *Staphylococcus aureus* (MRSA), *C. difficile*, or *Pseudomonas cepacia* were identified.[101,103,112] Results for vancomycin resistant enterococci (VRE) were inconsistent, with Bass, *et al.*[111] reporting a statistically significant positive association (hazard ratio [HR]: 18.8, 95% confidence interval: [5.4-66.2]) and Shorman, *et al.*[104] reporting a statistically significant negative association (odds ratio [OR]: 0.04 [0.004 -0.4]).

Three studies conducted in long-term care settings examined group A *Streptococcus*, which is transmitted via contact and droplet routes.[95,97,102] All three found significant positive associations between roommate exposure and infection, with odds ratios (ORs) ranging from 2.0 [1.1-5.1] to 15.3 [2.5-110.9] (point estimate not reported by Auerbach, *et al.*[95]).

Three studies examined exposure to roommates infected with viral pathogens.[98-100] Two studies of influenza conducted within the same long-term care facility found significantly elevated risks of infection among those with infected roommates (relative risk (RR): 3.1 [1.6-5.8] for influenza A and RR: 2.6 [1.2–5.6] for influenza B).[98,99] One study evaluated transmission of hepatitis C, a viral bloodborne pathogen, in a liver transplant ward of an acute care hospital and found significantly increased odds of infection after sharing a room with an infected patient (OR: 12.0 [1.4-103.0]).[100] One parasitic pathogen spread via fecal-oral contact, *Cryptosporidium parvum*, was evaluated in an acute care Human Immunodeficiency Virus (HIV) ward and no association was found.[96]

Findings of studies examining exposure to rooms previously occupied by infected or colonized patients

The eight articles investigating the effects of exposure to rooms previously occupied by infected or colonized patients are described in **Table 3.2.b.** and their findings are summarized in **Figure 3.2.b**. All of the articles studied bacterial pathogens spread through contact transmission in acute care hospitals, with all but two[111,112] taking place in intensive care units (ICUs). Nsier, *et al.*,[109] found that exposure to rooms previously occupied by patients with *Acinetobacter baumannii* and *Pseudomonas aeruginosa* resulted in significantly higher odds of infection or colonization (OR: 4.2 [2.0-8.8] and OR: 2.3 [1.2-4.3], respectively), while the two studies that examined extended spectrum beta-lactamase-producing gram negative organisms found no

association.[105,109] Effects of exposure to rooms previously occupied by patients with *C. difficile*, MRSA, and VRE were examined by at least two studies each. For each of these organisms, significant positive associations were reported by one article (*C. difficile*, HR: 2.4 [1.2 - 4.5];[40] MRSA, OR: 1.4 (p=0.04);[106] VRE, HR: 3.8 [2.0-7.4][107]), with the remainder of articles reporting no significant associations.[108,111,112]

Quality of included articles

Quality scores ranged from 50 to 95%, with the majority of articles scoring at or above 80% (median=83%, mean=82%). **Table 3.1** provides a summary of scores for each item. All of the articles had clearly stated aims, adequate descriptions of study populations, appropriate control groups, and acceptable reporting of results. However, many of the studies did not appropriately control for confounding (50%, n=9), address differential follow-up between exposed and unexposed patients (33%, n=6), or use acceptable statistical methods (17%, n=3). In addition, some articles did not include sufficient or precise definitions of the exposures (17%, n=3) or outcomes (6%, n=1) under investigation. Notably, none of the articles reported a sample size calculation indicating adequate power to detect differences between patients exposed versus unexposed to infected/colonized roommates or prior room occupants.

DISCUSSION

More than half of the articles identified in this systematic literature review reported at least one statistically significant positive association between the infection/colonization status of a roommate or previous room occupant and the development of HAIs.[95,97-100,102,106,107,109-111] Only a single article identified a statistically significant negative association.[104] The remainder found no associations that reached statistical significance, though this may be due to the fact that

they were insufficiently powered; none of the articles reviewed included a statement indicating that statistical power was adequate for the analyses presented. Another factor which may have contributed to findings of no association is that many studies included patients who were either infected or colonized as potential sources of exposure. Patients with symptomatic infections may shed greater amounts of infectious body fluids to surrounding fomites compared with patients who are asymptomatically colonized.[113] Therefore, if a causal association does indeed exist, including both infected and colonized patients as potential sources of exposure may have driven findings toward the null, since exposure to colonized roommates and prior room occupants could present less risk to patients. Heterogeneity of the exposure may have also arisen from variation in the infection or colonization site of a roommate or prior room occupant. In a study of patients with MRSA, environmental contamination was more prevalent on fomites surrounding patients with positive wound or urine cultures compared with patients who had positive blood or sputum cultures.[40]

The studies we reviewed revealed consistent findings for some pathogens (influenza, group A *Streptococcus*) and inconsistent findings for others (VRE, MRSA, *C. difficile*). For endemic healthcare pathogens such as VRE, MRSA, and *C. difficile*, it may be difficult to isolate the effects of roommates and previous room occupants since the exposure and outcome are common and may originate from multiple sources.[47] On the contrary, pathogens such as influenza and group A *Streptococcus* are more commonly associated with outbreak scenarios, making it easier to single out the effects of particular exposures.[114] Other factors which may have contributed to inconsistent findings across studies are variations in how exposures and outcomes were defined and operationalized (e.g., differences in case definitions, case finding methods, and timing of exposure).

While the inconsistency of findings for some of the organisms could be due to artifact, there may nevertheless be real differences in the effects of roommate and prior room occupant exposure based on biological characteristics of the infecting species. Microorganisms vary in their abilities to produce spores and survive changes to atmospheric temperature and moisture conditions.[39] In addition, some organisms favor specific sites of colonization or infection that may produce greater shedding of infectious material and higher potential for environmental contamination.[39] For example, a study of multidrug resistant pathogens found that environmental contamination was more common surrounding patients with gram-positive versus gram-negative infections.[20] Furthermore, organism species differ in their resiliency to withstand cleaning agents and methods.[115,116]

The preponderance of evidence presented in this review suggests that there is a link between exposure to infected or colonized roommates and previous room occupants and the risk of HAIs. These findings present a number of practice and policy implications. First, the fact that patient rooms may serve as a reservoir for pathogens deposited by roommates and previous occupants highlights the importance of proper hand hygiene, not just for staff but for competent patients and their visitors as well.[117] To underscore this point, a molecular typing study demonstrated that 12% of patients who became newly colonized with MRSA while in the ICU acquired a strain that most probably came from contamination in their immediate environment.[84] Second, these results emphasize the need for improved cleaning and disinfection of patient rooms, both during patients' hospital stays and upon their discharge. For patients with known infection or colonization, targeted daily and terminal cleaning procedures that are tailored to specific organisms may reduce environmental contamination and infection rates.[118] Enhancement of routine cleaning measures should not be limited to the rooms of patients with known infection

or colonization, however, since patients may contaminate their environments during incubation periods before infections are detected or when colonization is not detected through active surveillance.

There were some limitations to this systematic review. It is possible that some studies that would have met the inclusion criteria were not identified, and that some studies are missing from the literature due to publication bias. Our restriction to articles published in English may have also excluded some relevant papers. Lastly, while a major strength of this study is its coverage of two and a half decades of literature, changes in the epidemiology of HAIs, infection control policies and procedures, and study methodology over time may have introduced some variability to the studies we reviewed.

Notwithstanding these limitations, it is notable that the studies reporting significant findings were conducted across a range of institutions in several different countries across multiple decades. Presumably, the diverse study facilities employed a variety of cleaning products, methods, and infection control policies. Despite possible variations in practice, exposure to roommates and prior room occupants may have played a role in infection outcomes.

Table 3.1. Assessment of study quality

	Yes	No	Cannot determine	Not applicable
1. Is the hypothesis/aim/objective of the study clearly described? Population, intervention or exposure, and outcome included? Yes=1; No=0. *Note: Score may be based on study's main aim.*	18 (100%)	0	0	0
2. Are the main outcomes to be measured clearly described in the introduction or methods section? Enough information provided to replicate study? Yes=1; No=0.	17 (94%)	1 (6%)	0	0
3. Are the characteristics of the patients included in the study clearly described? General patient population and inclusion/exclusion criteria described? Yes=1; No=0. *Note: Descriptive statistics not required.*	18 (100%)	0	0	0
4. Is exposure of interest clearly described? Enough information provided to replicate study? Yes=1; No=0. *Note: Score based on exposure of interest (i.e., prior room occupant and/or roommate infection status).*	15 (83%)	3 (17%)	0	0
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described? Most clinically relevant characteristics described=2; Only a few general patient characteristics described=1; No characteristics described=0.	Most described: 13 (72%) Few described: 3 (17%)	0	0	0
6. Are the main findings of the study clearly described? Results presented for all proposed analyses and outcome measures? Yes=1; No=0.	18 (100%)	0	0	0
7. Does the study provide estimates of the random variability in the data for the main outcomes? Confidence intervals, p-values, or other measures of standard error included? Yes=1; No=0. *Note: Score based on analyses for roommate and/or prior room occupant exposures.*	18 (100%)	0	0	0
8. Have the characteristics of patients lost to follow-up been described? If loss to follow-up is implied, are patients described or compared to those who participated? Yes=1; No=0. *Note: If loss to follow-up not mentioned by authors, item scored as "not applicable" and removed from denominator.*	2 (11%)	0	0	16 (89%)
9. Have actual probability values been reported for the main outcomes except where p< 0.001? Yes=1; No=0.	18 (100%)	0	0	0
10. Were patients selected in a way that is representative of the source population the authors identified in the inclusion/exclusion criteria? All patients identified in source population included=1; Certain patients included in source population systematically excluded (e.g., patients who died, were transferred, refused participation, etc.)=0. *Note: Zero was scored if authors did not provide enough information to determine representativeness.*	16 (89%)	0	2 (11%)	0
11. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? Facility similar to other institutions of the same type? Yes=1; No=0. *Note: Zero was scored if authors did not provide enough information to determine representativeness.*	17 (94%)	0	1 (6%)	0
12. If any of the results of the study were based on "data dredging", was this made clear? All sub-group analyses described in methods section or noted as post-hoc analyses=1; Unplanned sub-group analyses presented and not noted as post-hoc=0. *Note: If study included no sub-group analyses, item scored as "not applicable" and removed from denominator.*	0	0	2 (11%)	16 (89%)

13. Do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? If follow-up is differential between groups, was this controlled for in the design or analysis? Yes=1; No=0. *Note: If follow-up is same for all patients, item scored as "not applicable" and removed from denominator.*	8 (44%)	6 (33%)	0	4 (22%)
14. Were the statistical tests used to assess the main outcomes appropriate? Statistical tests minimally appropriate for the data and research questions? Yes=1; No=0.	15 (83%)	3 (17%)	0	0
15. Were the main outcome measures used valid and reliable? Systematic, repeatable methods of case finding and appropriate lab definitions used? Yes=1; No=0. *Note: Zero was scored if authors did not provide enough information to assess outcome measures.*	16 (89%)	1 (6%)	0	1 (6%)
16. Were the patients in different intervention groups or cases and controls recruited from the same population? Yes=1; No=0.	18 (100%)	0	0	0
17. Were study subjects in different intervention groups or cases and controls recruited over the same period of time? Yes=1; No=0.	18 (100%)	0	0	0
18. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? Key confounders included in multivariable models? Yes=1; No=0. *Note: Score based on exposure of interest (i.e., prior room occupant and/or roommate infection status).*	9 (50%)	6 (33%)	3 (17%)	0
19. Were losses of patients to follow-up taken into account? If loss to follow-up is reported, is an appropriate statistical method used to account for this? Yes=1; No=0. *Note: If no loss to follow-up is reported, item scored as "not applicable" and removed from denominator. Zero was scored if authors did not provide enough information to assess loss to follow-up.*	1 (6%)	1 (6%)	16 (89%)	0
20. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%? Power calculation included and adequate power reported=1; Power calculation included and inadequate power reported or no power calculation mentioned=0. *Note: Score based on exposure of interest (i.e., prior room occupant and/or roommate infection status). Zero was scored if authors did not provide enough information to assess power.*	0	4 (22%)	14 (78%)	0

Adapted from the 1998 *Checklist for Measuring Study Quality* published by Downs and Black.[24]

Table 3.2.a. Summary and quality assessment of studies reporting associations between healthcare-associated infection and exposure to infected or colonized roommates

Author, Year, Quality	Study period	Setting	Design	Subjects	N	Outcome	Exposure	Analysis	Results
Auerbach, et al., 1992 Score: 83%	Aug 1989 – Feb 1990	50-bed nursing home, North Carolina	Outbreak investigation and case control	All residents who underwent diagnostic testing for GAS, excluding those who died from causes other than GAS	37 roommate pairs	Symptomatic or asymptomatic GAS infection detected via culture or serology	Roommate w/ symptomatic or asymptomatic GAS infection	2-tailed Fisher's exact test	26 pairs concordant uninfected, 6 concordant infected, 5 pairs discordant p=0.0009
Bass, et al., 2013 Score: 83%	Mar 2010 – Oct 2010	34-bed hematology-oncology ward in 427-bed tertiary care teaching hospital, Melbourne, Australia	Quasi-experimental	All pts w/ neg VRE rectal swab upon admission and no known history of VRE	439 pts	Incident VRE colonization detected by rectal surveillance culture	Roommate w/ VRE infection or colonization	Cox proportional hazard adjusted for prior bed occupant status and study intervention phase	HR: 18.8 [5.4-66.2]
Bruce, et al., 2000 Score: 50%	Aug 1994 – Oct 1996	Special Immunity Service ward for HIV-positive patients, Grady Memorial Hospital	Retrospective cohort	Exposed: All roommates of pts w/ *Cryptosporidium* stool sample and no prior history; Unexposed: Roommates of pts w/o *Cryptosporidium* matched by nearest CD4 count and hospitalization date	74 pts (37 exposed, 37 not exposed)	Incident Cryptosporidiosis	Roommate w/ Cryptosporidiosis	Unadjusted RR	RR undefined (1 case in unexposed roommates, 0 cases in exposed roommates)
Chang, et al., 2000 Score: 94%	Mar 1987 – Aug 1987	305-bed community hospital, Baltimore, Maryland	Retrospective cohort	All pts w/ LOS >48hrs	2,859 pts	Incident *C. difficile* diarrhea >48hrs after admission and within 15d of discharge	Roommate w/ *C. difficile* diarrhea	Unadjusted RR	RR: 2.7 [0.6-7.0]
Deutscher, et al., 2011	Oct 2007 – Feb 2008	57-bed long-term acute care hospital, New Mexico	Case control	Cases: All pts w/ incident GAS infection >48 hours after admission; Controls: Randomly	50 residents (11 cases, 39 controls)	Incident GAS infection >48 hours after admission	Roommate w/ GAS infection or colonization	Logistic regression adjusted for age, sex, BMI, death, admission to special care unit, LOS >4wks, admission from home, *C.*	OR: 15.3 [2.5-110.9]

Score: 89%				selected pts w/o GAS symptoms or cultures				*difficile*, diabetes, CHF, hypertension, PVD, chronic renal failure/dialysis, malignancy, ventilator, cellulitis, nonsurgical wound, neg pressure	
Drinka, et al., 2003 Score: 72%	1993 – 2000	Wisconsin Veterans Home, a 635-bed skilled nursing facility	Retrospective cohort	All residents	3,294 resident-seasons	Culture confirmed influenza A infection	Roommate w/ pos influenza A culture	Unadjusted RR comparing exposed to positive roommate vs. single room	RR: 3.1 [1.6-5.8]
Drinka, et al., 2005 Score: 76%	1992 – 1993 season	Wisconsin Veterans Home, a 635-bed skilled nursing facility	Retrospective cohort	All residents	489 resident-seasons	Culture confirmed influenza B infection	Roommate w/ pos influenza B culture	Unadjusted RR comparing exposed to positive roommate vs. single room	RR: 2.6 [1.2–5.6]
Forns, et al., 2005 Score: 80%	Aug 2000 – Oct 2002	3-ward liver unit in tertiary care center	Prospective cohort	All pts w/ neg anti-HCV screen upon ward admission	1,301 pts	Incident HCV infection assessed 6 months post-discharge	Roommate w/ HCV infection	Unadjusted OR	OR: 12.0 [1.4-103.0]
Furuno, et al., 2011 Score: 95%	Mar 2005 – Sept 2008	120-bed Baltimore Rehabilitation & Extended Care Center, 150-bed Perry Point VA Medical Center, 180-bed University Specialty Hospital, Maryland	Prospective cohort	All residents w/o history of MRSA colonization, ≥1 neg MRSA screen from anterior nares or skin breakdown at enrollment, LOS >7 days, and ≥1 follow-up culture	Resident care: 286; Rehab care:157	Incident MRSA colonization in anterior nares or site of skin breakdown	Roommate w/ MRSA colonization	Residential care: Cox proportional hazard adjusted for antibiotic therapy and bedbound status; Rehabilitation care: Cox proportional hazard HR adjusted for bedbound status and limited mobility status	Residential care HR: 1.4 [0.5-3.9]; Rehabilitation care HR: 0.5 [0.1-2.2]
Greene, et al., 2005 Score: 78%	Jan 2001 – Dec 2001	120-bed long-term care facility, Georgia	Retrospective cohort	All residents	125 residents	GAS infection or colonization	Roommate w/ GAS colonization or infection	Unadjusted and Mantel-Haenszel RR (variables included in multivariable not described)	Adjusted RR: 2.0 [1.1-5.1]; Unadjusted RR: 2.1 [1.1-4.0]

Pegues, et al., 1994 Score: 72%	Aug 1989 – Sept 1989	Saint Christopher's Hospital for Children, a 350-bed pediatric referral center, Philadelphia, PA	Case control	Cases: CF pts w/ initial isolation of *P. cepacia* from respiratory secretions; Controls: randomly selected CF pts w/ neg *P. cepacia* sputum cultures	28 pts (14 cases, 14 controls)	Pos *P. cepacea* culture in pts hospitalized ≥1 time between last neg and first pos culture	Roommate w/ pos *P. cepacea* culture	Unadjusted OR	OR: 12.5 [0.6-607.0]
Shorman, et al., 2013 Score: 76%	Feb 2006 – Mar 2010	Tertiary care referral hospital, Damman, Saudi Arabia	Case control	Cases: pts w/ pos surveillance or clinical VRE cultures; Controls: randomly selected pts w/ neg clinical or surveillance VRE cultures	90 pts (30 cases, 60 controls)	VRE colonization or infection	Roommate with VRE infection or colonization	Unadjusted OR	OR: 0.04 [0.004 -0.4]

BMI, body mass index; C. difficile, Clostridium difficile; CF, cystic fibrosis; *CHF, congestive heart failure;* GAS, Group A *Streptococcus*; HCV, hepatitis C virus*; HR, hazard ratio; LOS, length of stay;* MRSA, methicillin-resistant *Staphylococcus aureus*; *OR, odds ratio; P. cepacia, Pseudomonas cepacia; PVD, peripheral vascular disease; RR, relative risk;* VRE, vancomycin-resistant enterococci.

Table 3.2.b. Summary and quality assessment of studies reporting associations between healthcare-associated infection and exposure to infected or colonized prior room occupants

Author, Year, Quality	Study period	Setting	Design	Subjects	N	Outcome	Exposure	Analysis	Results
Ajao, et al., 2013 Score: 94%	Sept 2001 – Jun 2009	Medical & surgical ICUs in University of Maryland Medical Center	Retrospective cohort	All pts ≥18yrs w/o ESBL at hospital admission, neg ESBL screen at ICU admission, and ICU stay ≥48hrs	9,371 admissions (7,651 unique pts)	Acquisition of ESBL-producing pathogen during ICU stay detected via clinical or surveillance culture	Immediate prior room occupant w/ pos clinical or surveillance ESBL culture	Logistic regression adjusted for colonization pressure, renal disease, anti-MRSA and anti-pseudomonal beta lactam therapies	Unadjusted OR: 1.9 [1.3-2.7]; Adjusted OR: 1.4 [0.9-2.1]
Bass, et al., 2013 Score: 83%	Mar 2010 – Oct 2010	34-bed Hematology/ oncology ward in 427-bed tertiary care teaching hospital, Melbourne, Australia	Quasi-experimental	All patients w/ neg VRE rectal swab upon admission and no known history of VRE	439 pts	Incident VRE colonization detected by rectal surveillance culture	Prior bed occupant w/ VRE colonization or infection	Cox proportional hazard adjusted for roommate status and study intervention phase	HR: 0.4 [0.1-1.2]
Chang, et al., 2000 Score: 94%	Mar 1987 – Aug 1987	305-bed community hospital, Baltimore, Maryland	Retrospective cohort	All pts w/ LOS >48hrs	2,859 pts	Incident *C. difficile* diarrhea >48hrs after admission and within 15d of discharge	Prior room occupant with *C. difficile* or roommate with prior *C. difficile* infection who is no longer symptomatic	Unadjusted RR	RR: 1.2 [0.3-3.4]
Datta, et al., 2011 Score: 78%	Sept 2003 – Apr 2005 & Sept 2006 – Apr 2008	ICUs in 750-bed academic medical center	Quasi-experimental	All pts w/ neg MRSA and/or VRE screening culture prior to ICU admission	MRSA: 16,345 pts (7,629 baseline, 8,716 post); VRE: 16,630 pts (7,806 baseline, 8,824 post)	Incident MRSA or VRE acquisition	Prior room occupant	GLM adjusted for age, sex, pre-ICU LOS, prior occupant LOS, duration of room vacancy, clustering by ward, diabetes, end-stage renal and liver diseases, malignancies, immunocompromised status	MRSA: baseline OR: 1.4 (p=0.04), post OR: 1.1 (p=0.66); VRE: baseline OR: 1.4 (p=0.02), post OR: 1.4 (p=0.04)

Drees, et al., 2008 Score: 94%	Feb 2002 – Mar 2003	Medical & surgical ICUs, Tufts New England Medical Center, Boston, MA	Prospective interventional crossover	All pts in ICU ≥48hrs w/ neg VRE screens within first 48 hours of ICU admission and no known history of VRE	638 pts.	Acquisition of VRE during ICU stay detected via surveillance culture	Prior room occupant (immediate and within previous 2 weeks)	HR adjusting for average colonization pressure and mean antibiotics per day	Immediate prior occupant HR: 3.8 [2.0-7.4]; Prior occupant within 2 weeks HR: 2.7 [1.4-5.3]
Huang, et al., 2006 Score: 94%	Sept 2003 – Apr 2005	8 adult ICUs, Brigham and Women's Hospital, Boston, MA	Retrospective cohort	All pts w/o pos MRSA or VRE surveillance cultures within 2 days of ICU admission	MRSA: 7,629 pts; VRE: 7,806 pts	Acquisition of MRSA or VRE	Prior room occupant with MRSA or VRE colonization or infection	GLM accounting for clustering within ICUs and controlling for age, sex, LOS before ICU admission, prior occupant LOS, duration of room vacancy before occupancy, diabetes, end-stage renal and liver diseases, non-cancer immunocompromised state, and malignancies	MRSA OR:1.4 [1.0-1.8]; VRE OR: 1.4 [1.0-1.9]
Nseir, et al., 2011 Score: 89%	Dec 2006 – Dec 2007	30-bed medical/ surgical ICU	Prospective cohort	All pts in ICU >48 hours w/ neg MDR GNB screen at admission	511 pts	Acquisition of *P. aeruginosa* resistant to ceftazidime or imipenem, *A. baumannii*, or ESBL-producing GNB	Prior room occupant w/ pos MDR GNB screening or diagnostic culture	Logistic regression: MDR *P. aeruginosa* model adjusted for age, SAPS II, LOD, inter-unit transfer, LOS prior to ICU, prior antibiotics, room occupancy rate, central venous, arterial, and urinary catheters, tracheostomy, sedation, % of days in the ICU with amoxicillin-clavulanate acid, piperacillin-tazobactam, fourth-generation cephalosporins, carbapenems, fluoroquinolones, aminoglycosides, mechanical ventilation, and LOS in ICU; *A. baumannii* model adjusted for SAPS II, LOD, admission type, prior antibiotics, colonization pressure, central venous, arterial and, urinary catheters, sedation, percentage of days in ICU with piperacillin-tazobactam, fourth-generation cephalosporins, and fluoroquinolones	MDR *P. aeruginosa* OR: 2.3 [1.2-4.3]; *A. baumannii* OR: 4.2 [2.0-8.8]; ESBL-producing GNB OR: 1.5 [0.6-3.5] (multivariable results not reported)

Shaughnessy, et al., 2011 Score: 94%	Jan 2005 – Jun 2006	20-bed ICU in 809-bed tertiary care hospital	Retrospective cohort	All pts w/o *C. difficile* diagnosis in previous 3 months	1,770 patients	Incident *C. difficile* infection >48hrs after ICU admission and within 30 days of ICU discharge	Immediate prior room occupant w/ history of positive *C. difficile* toxin results within 30 days prior to current occupant's ICU admission	Adjusted hazard ratio controlling for age, APACHE II, proton pump inhibitor, and exposure to antibiotics	HR: 2.4 [1.2 - 4.5]

A. baumannii, *Acinetobacter baumannii*; APACHE II, acute physiology and chronic health evaluation II; *C. difficile*, *Clostridium difficile;* ESBL, extended spectrum beta-lactamase-producing organism; *GLM*, *generalized linear mixed model; GNB*, Gram negative bacteria; ICU, intensive care unit; LOD, logistic organ dysfunction score; LOS, length of stay; MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; *P. aeruginosa*, *Pseudomonas aeruginosa*; *RR, relative risk;* SAPS II, simplified acute physiology score II; VRE, vancomycin-resistant enterococci.

Figure 3.1. Identification, screening, eligibility, and inclusion of articles according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Three hundred and thirty articles were identified via the database search and no additional records were identified from other sources. No duplicates were identified.

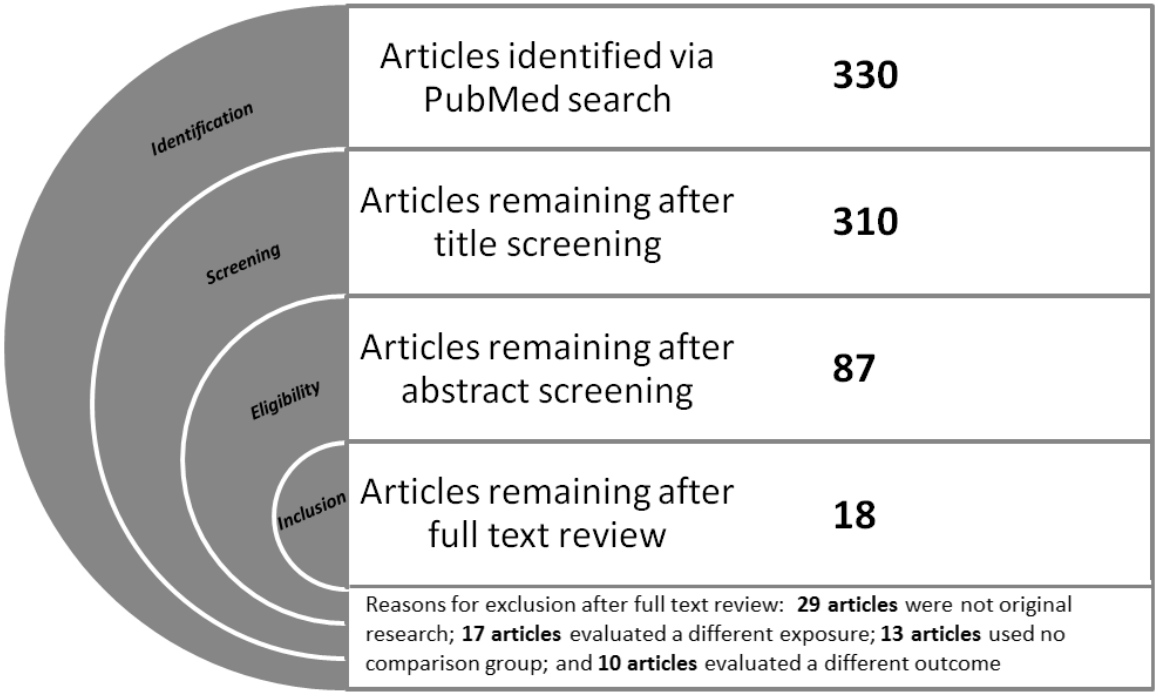


Figure 3.2.a. Findings of studies investigating the association between healthcare-associated infection or colonization and exposure to infected or colonized roommates. Studies reporting significant positive associations are represented in black circles and studies reporting significant negative associations are represented in white circles. Studies which did not find statistically significant associations are represented in gray circles.

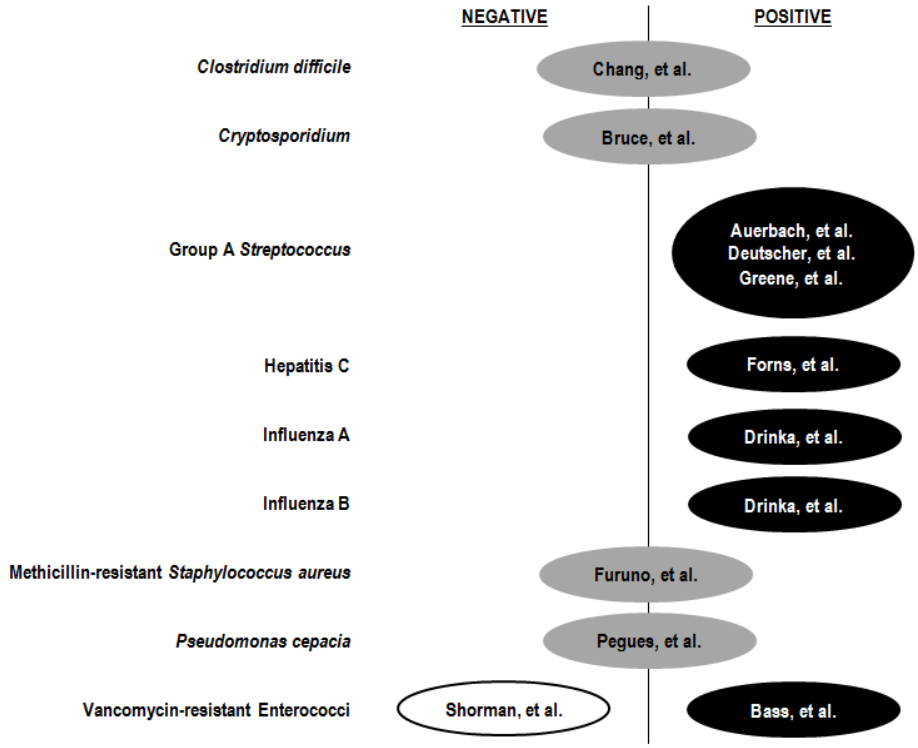
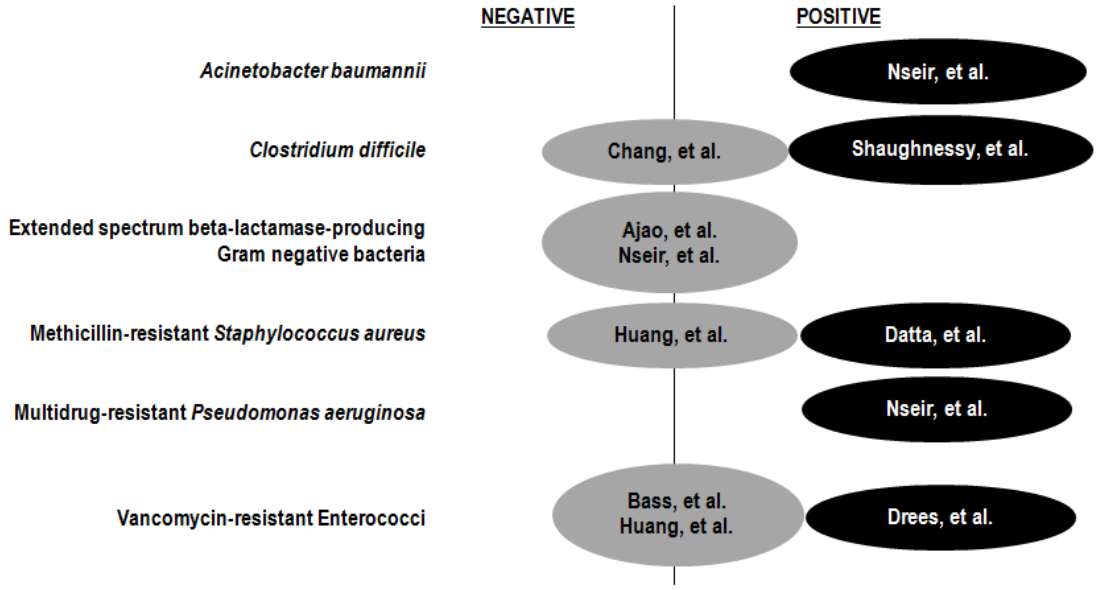


Figure 3.2.b. Findings of studies investigating the association between healthcare-associated infection or colonization and exposure to infected or colonized prior room occupants. Studies reporting significant positive associations are represented in black circles. Studies which did not find statistically significant associations are represented in gray circles. No studies reported a significant negative association.



CHAPTER FOUR

Case Control Study of the Association between Exposure to Roommates or Prior Bed Occupants with Positive Bacterial Cultures and Subsequent Infection with the Same Organism

ABSTRACT

Patients who are infected or colonized by pathogenic bacteria are known to contaminate surfaces and equipment in hospital rooms, yet little is understood about the risk this poses to subsequent bed occupants or concurrent roommates. The objective of this matched case-control study was to quantify the association between having a prior bed occupant or roommate with a positive blood, respiratory, urine, or wound culture and subsequent infection with the same organism. The study was conducted in four New York City hospitals: a 221-bed community hospital, a 283-bed pediatric acute care hospital, a 647-bed adult tertiary/quaternary care hospital, and a 914-bed pediatric and adult tertiary/quaternary care hospital. Cases included all inpatients discharged January 1, 2006 through December 31, 2012 who developed a healthcare-associated infection (HAI) with *Staphylococcus aureus, Acinetobacter baumannii, Streptococcus pneumoniae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis*, or *Enterococcus faecium*. Controls were uninfected patients matched by fiscal quarter, hospital and length of stay. For each bed a case occupied during the 3-5 day period prior to infection, all microbiology results for (1) the patient who occupied the bed immediately prior to the case and (2) all assigned roommates were collected. The same process was applied for controls, with the matched case's day of infection serving as the reference point. HAIs were identified using standardized national surveillance definitions applied to electronic health records. A total of 10,289 HAIs were identified among 761,426 admissions. In a multivariable analysis controlling for patient characteristics and mutually controlling for each exposure, odds of being exposed to a prior bed occupant with the same organism were 5.83 (95% Confidence Interval [3.62, 9.39]) times greater for cases versus controls and the odds of being exposed to a roommate with the same organism were 4.82 [3.67, 6.34] times greater. HAIs are common, costly, debilitating and

deadly. The results of this study indicate that some HAIs may be preventable through the use of enhanced terminal cleaning procedures or products and intermittent cleaning protocols designed to break the chain of transmission between hospital roommates.

INTRODUCTION

Over 700,000 healthcare-associated infections (HAIs) occur in US hospitals each year.[10] These infections—considered to be largely preventable—accrue $28-45 billion annually in excess healthcare costs and are fatal in nearly 6 percent of cases.[9,12,119] Efforts to improve quality of care while reducing costs have made HAI prevention a national priority and sparked a surge of innovative measures aimed at curtailing their spread.[18,120] Many of these interventions have specifically targeted high-risk patients with protocols for the care and maintenance of indwelling devices, with measurable but varied success.[121]

Meanwhile, a growing body of evidence demonstrating widespread contamination of hospital rooms and equipment has led to increasing concern about the risks posed to patients by current cleanliness standards and practices.[38] A deluge of new products are being developed and marketed to hospitals for the purpose of improving environmental disinfection, with particular attention paid to routine cleaning for patients with multidrug-resistant organisms and terminal cleaning after discharge.[122] However, very few studies have examined whether there is a link between contamination in patient rooms and risk of infection. Given the constraints of financial and human resources for infection prevention and control, it is important to quantify the potential impact of enhanced environmental cleanliness. Our study addressed this question by evaluating whether there is an association between HAIs and exposure to infected or colonized hospital roommates or prior room occupants using seven years of data from four inpatient acute care hospitals.

METHODS

Sample and Setting

This study was conducted in four inpatient hospitals located in New York City. The hospitals, all part of the same healthcare network, included a community hospital (221 beds), a pediatric acute care hospital (283 beds), an adult tertiary/quaternary care hospital (647 beds), and a pediatric and adult tertiary/quaternary care hospital (914 beds). All patients discharged during the period of January 1, 2006 through December 31, 2012 were eligible for inclusion.

Data Collection

All study data were collected retrospectively. Data were sourced from multiple electronic systems used for clinical documentation and administrative purposes throughout the hospital network and linked using unique medical record numbers and dates of admission and discharge.[49] Demographic information and patient characteristics were sourced from administrative data and included age, sex, risk of mortality as measured by the Charlson Comorbidity Index,[54] and specific comorbid conditions including malignancies, renal failure, and diabetes. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes were used to create the Charlson Comorbidity Index and identify comorbid conditions. Patients' room and bed assignments for each day of hospitalization were collected from the admission-discharge-transfer system. Culture results and antimicrobial susceptibility data including date and site of culture collection were obtained from clinical microbiology records.

Study Design

A matched case-control design was used to evaluate the association between having a prior bed occupant or roommate with a positive blood, respiratory, urine, or wound culture and subsequent infection with the same organism and comparable antibiotic sensitivity profile. Cases included all patients who developed a hospital-acquired bloodstream infection (BSI), urinary

tract infection (UTI), surgical site infection (SSI), or pneumonia with one of the following organisms: oxacillin-sensitive *Staphylococcus aureus,* oxacillin-resistant *S. aureus,* ampicillin-sulbactam-sensitive *Acinetobacter baumannii,* ampicillin-sulbactam-resistant *A. baumannii,* penicillin-sensitive *Streptococcus pneumonia,* penicillin-resistant *S. pneumonia,* levofloxacin-sensitive *Pseudomonas aeruginosa,* levofloxacin-resistant *P. aeruginosa,* imipenem-sensitive *Klebsiella pneumoniae,* imipenem-resistant *Klebsiella pneumoniae,* vancomycin-sensitive *Enterococcus faecalis* and *E. faecium* and vancomycin-resistant *E. faecalis* and *E. faecium*. HAIs were detected via electronic algorithms analogous to the Centers for Disease Control and Prevention National Healthcare Safety Network surveillance definitions (**Figure 2.1**).[49,50] The included infection types were selected due to their high incidence in healthcare settings and because they have been specifically targeted by national and local HAI reduction campaigns.[5,8] Organisms were selected due to their high prevalence in healthcare settings and concerning trend towards increasing antimicrobial resistance.[8,9]

Controls were matched to cases in a 1:1 ratio and were randomly selected from all patients who: (1) never had a positive culture with the organism under investigation during their hospitalization; (2) were admitted during the same fiscal quarter as the case; (3) were admitted to the same hospital as the case; (4) had a length of stay at least as long as the case's length of stay prior to infection.

Exposure to prior bed occupant

All beds that each case occupied during the 3-5 day period prior to infection were identified using a computerized algorithm. For each of these beds, a second algorithm was applied to identify the patient who occupied the bed immediately prior to the case. A third algorithm was used to search the clinical microbiology data to determine whether or not any of

the previous occupants had a positive culture with the organism of interest at any point prior to being discharged from the bed they occupied prior to the case. The same process was applied for controls, with the matched case's day of infection serving as the reference point. For example, if the matched case had an infection on day 10, we looked back 3-5 days from day 10 of the control's hospital stay.

Exposure to hospital roommate

All rooms that each case occupied during the 3-5 day period prior to infection were identified using a computerized algorithm. For each of these rooms, a second algorithm was applied to identify any other patients assigned on the same date(s) as the case. A third algorithm was used to search the clinical microbiology data to determine whether or not any of the roommates had a positive culture with the organism of interest at any point prior to sharing a room with the case. The same process was applied for controls, with the matched case's day of infection serving as the reference point.

Data Analysis

Bivariate comparisons between cases and controls with respect to exposure to infected or colonized prior room occupants, exposure to infected or colonized roommates, age, Charlson Comorbidity Index, sex, presence of malignancies, renal failure, and diabetes mellitus were conducted within each organism category using chi-square tests for independence, Fisher's exact tests, or two-sample t-tests, as appropriate. The total numbers and proportions of cases and controls exposed to infected or colonized prior room occupants and roommates were tabulated to determine crude odds ratios (OR) and 95% confidence intervals (CI). Multivariable logistic regression analysis was performed to calculate adjusted odds ratios mutually controlling for both of the exposures, patient characteristics, and comorbidities.

To determine with greater certainty whether a prior occupant or roommate was the source of exposure, we compared isolates for a sample of exposed case-roommate and case-prior occupant pairs. Since molecular typing of isolates was not available, we compared antimicrobial susceptibilities based on available antimicrobial susceptibility data. *K. pneumoniae* was selected for this sub-analysis due to the range of antibiotics tested for this organism in the study institutions. The tested antibiotics included cefepime, ceftriaxone, gentamicin, imipenem, levofloxacin, meropenem, piperacillin-tazobactam, tobramycin, and trimethoprim.

RESULTS

Patient admissions across the four facilities totaled 761,426 during the study period. There were 10,289 HAIs identified and eligible controls were available for 10,033 (97.5%). **Table 4.1** displays bivariate comparisons between cases and controls with respect to demographic characteristics, comorbid conditions, and exposure to infected or colonized roommates and prior bed occupants by organism. A total of 136 cases were exposed to a prior bed occupant with the same organism compared with 20 controls (crude OR [95% CI]: 6.88 [4.30, 11.01]). A total of 309 cases were exposed to a roommate with the same organism compared with 64 controls (crude OR [95% CI]: 4.95 [3.78, 6.49]). Fewer than two percent of cases were exposed to a previous bed occupant with the same organism and fewer than four percent were exposed to roommates with the same organism (**Figure 4.1**). In the multivariable analysis controlling for patient characteristics and mutually controlling for each exposure, the odds of being exposed to a prior bed occupant with the same organism were 5.83 [3.62, 9.39] times greater for cases versus controls and the odds of being exposed to a roommate with the same organism were 4.82 [3.67, 6.34] times greater (**Table 4.2**).

In the *K. pneumoniae* sub-analysis comparing antibiotic sensitivity of case isolates with roommate isolates, antimicrobial susceptibility data were available for 38 of 43 exposed case-roommate pairs. Of those, 22 pairs (58%) had identical susceptibility profiles. Notably, among the remaining 16 pairs, most (n=11, 69%) displayed additional antibiotic resistance in the case isolate, leaving open the possibility that resistance was acquired during the roommate's course of treatment and the more resistant isolate was passed on to the case. The unadjusted OR [95% CI] was 1.6 [0.80, 3.10] after limiting the cases to pairs with identical susceptibility profiles and 2.02 [1.06, 3.84] when limiting the cases to pairs with identical susceptibility profiles or additional resistance in the case. For prior room occupant pairs, susceptibility data were available for 20 of 27 pairs and of those, 11 (55%) had identical susceptibility profiles. Among the remaining nine pairs, six (67%) displayed additional antibiotic resistance in the case isolate. The unadjusted OR [95% CI] was 5.5 [1.22, 24.98] after limiting the cases to pairs with identical susceptibility profiles and 8.58 [1.98, 37.17] when limiting the cases to pairs with identical susceptibility profiles or additional resistance in the case.

DISCUSSION

The long campaign towards improving patient safety and reducing preventable deaths in hospitals has had many successes.[123,124] Still, too many Americans continue to die unnecessarily from infections they contract while in the hospital.[119] The need to focus on prevention is evermore acute with the proliferation of multidrug resistant organisms and increasingly limited options for successful treatment.[124]

The good news is that we now have strong evidence that interventions designed to improve environmental cleanliness do make a difference. Indeed, the first multicenter

randomized controlled trial to determine the efficacy of enhanced terminal cleaning procedures for patients with multidrug resistant organisms was recently published. This study of nine hospitals showed a statistically significant decrease in organism acquisition when targeted cleaning methods—particularly ultraviolet light technology—were incorporated into the standard cleaning protocol, adding only four extra minutes to the total cleaning time.[126]

As the largest study to quantify the association between HAIs and exposure to infected or colonized previous bed occupants and roommates, encompassing data from all inpatient units in four acute care hospitals and surveying exposure to six different organisms, our analysis serves to illustrate how many infections might be prevented by implementing enhanced cleaning measures. Previous studies have reported mixed findings due to wide variations in sample size, study quality, design, patient population, and definitions of exposures and outcomes, though the majority did find statistically significant relationships between at least one of their exposures and outcomes of interest.[127] Our findings revealed robust and statistically significant associations, with exposure to an infected or colonized prior bed occupant conferring a nearly six-fold increase in the odds of infection, and exposure to an infected or colonized roommate conferring a nearly five-fold increase. It is possible that these results actually underestimate the true association, since by limiting the look-back period to the most likely period of exposure—three to five days prior to infection—we only captured a portion of roommates and prior room occupants who could have been sources of exposure.[50]

The primary limitation of this study was the unavailability of molecular typing, which made it impossible to determine with certainty whether a case acquired a pathogen genetically identical to that of the roommate or prior occupant presumed to be the source of exposure. Nonetheless our conclusion that there is a true chain of transmission from prior bed occupants

and roommates remains plausible for two reasons. First, we performed a sub-analysis to assess whether or not isolates were phenotypically similar with regard to their susceptibility to a variety of antibiotic agents and still found statistically significant associations between prior bed occupant or roommate exposure and the development of HAIs. Furthermore, in the majority of cases where antibiotic sensitivity did differ, resistance was more prevalent among the cases than among the prior occupants or roommates presumed sources of exposure. This supports the possibility that resistance was acquired during the roommate or prior occupant's antibiotic therapy, and the resistant organism was passed to the case. Second, the epidemiological association we identified remained sizeable and highly significant even after controlling for a number of potential confounders. It is possible that the association could be due to an unknown confounder that we were unable to identify or measure in this retrospective study. For example, if certain rooms were reserved for the highest risk patients, patients assigned to such rooms could have both a higher risk of exposure due to their room placement as well as a higher risk of infection due to their condition upon admission to the unit. This is especially true for single rooms, which are frequently used for isolation and thus may have greater bioburden. Indeed, there were some statistically significant differences between cases and controls at baseline with regard to the comorbid conditions that affect infection risk. However, the associations remained robust in the multivariable model controlling for these variables, suggesting that confounding by factors related to patient severity of illness was minimal, if present at all. Lastly, though all in-network culture results prior to room assignment were known, it is possible that some roommate pairs were cohorted based on reports of colonization or infection from other institutions at the time of admission.

The human and financial costs associated with HAIs are unacceptably high and may continue to grow along with antimicrobial resistance and the shortage of novel therapies on the immediate horizon.[125] In light of mounting evidence that (1) patients harboring pathogens do contaminate their hospital rooms,[128] (2) current standards for cleaning and disinfection are not sufficient for decontamination,[129] and (3) exposure to contaminated rooms confers a five- to six-fold increase in odds of infection, hospitals must take action by adopting proven methods for reducing environmental contamination.

Table 4.1. Bivariate comparisons between cases and controls with respect to demographic characteristics, comorbid conditions, and exposure to infected or colonized roommates and prior bed occupants

	Sensitive isolates			Resistant isolates		
	Cases	**Controls**	**P-value**	**Cases**	**Controls**	**P-value**
Acinetobacter baumannii	**N=258**	**N=258**		**N=214**	**N=214**	
Infected or colonized prior occupant	3 (1.1)	0 (0)	0.25	6 (2.8)	0 (0)	0.01
Infected or colonized roommate	3 (1.1)	0 (0)	0.25	16 (7.5)	1 (0.5)	<0.001
Age	54.6 (25.6)	54.2 (25.8)	0.84	46.6 (30.3)	47.5 (30.8)	0.74
Charlson Comorbidity Index	5.9 (5.2)	4.9 (4.8)	0.02	3.7 (5.5)	3.7 (4.1)	0.97
Female	113 (43.8)	126 (48.8)	0.25	116 (54.2)	116 (54.2)	1.00
Malignancies	51 (19.8)	30 (11.6)	0.01	20 (9.4)	27 (12.6)	0.28
Renal failure	93 (36.1)	59 (22.9)	0.001	24 (11.2)	18 (8.4)	0.33
Diabetes mellitus	61 (23.6)	53 (20.5)	0.40	36 (16.8)	37 (17.3)	0.90
Enterococci	**N=1,259**	**N=1,259**		**N=1,238**	**N=1,238**	
Infected or colonized prior occupant	13 (1.0)	2 (0.2)	0.004	28 (2.3)	2 (0.2)	<0.001
Infected or colonized roommate	32 (2.5)	3 (0.2)	<0.001	25 (2.0)	5 (0.4)	<0.001
Age	54.5 (25.3)	52.9 (26.3)	0.10	60.0 (19.1)	56.6 (24.1)	<0.001
Charlson Comorbidity Index	5.7 (6.0)	4.9 (5.2)	<0.001	6.7 (4.4)	5.3 (5.6)	<0.001
Female	559 (44.4)	523 (41.5)	0.15	579 (46.8)	570 (46.0)	0.72
Malignancies	264 (20.1)	210 (16.7)	0.006	417 (33.7)	191 (15.4)	<0.001
Renal failure	343 (27.2)	258 (20.5)	<0.001	457 (36.9)	310 (25.0)	<0.001
Diabetes mellitus	313 (24.9)	259 (20.6)	0.01	296 (23.9)	285 (23.0)	0.60
Klebsiella pneumoniae	**N=1,091**	**N=1,091**		**N=629**	**N=629**	
Infected or colonized prior occupant	20 (1.8)	1 (0.1)	<0.001	7 (1.1)	1 (0.2)	0.07
Infected or colonized roommate	36 (3.3)	11 (1.0)	<0.001	7 (1.1)	3 (0.5)	0.34
Age	55.8 (25.4)	52.1 (27.1)	0.001	57.4 (22.9)	55.1 (25.2)	0.09
Charlson Comorbidity Index	6.4 (5.4)	4.4 (4.0)	0.001	6.6 (5.0)	5.0 (5.2)	<0.001
Female	508 (46.6)	501 (45.9)	0.76	292 (46.4)	283 (45.0)	0.61
Malignancies	340 (31.2)	143 (13.1)	<0.001	151 (24.0)	88 (14.0)	<0.001
Renal failure	324 (29.7)	214 (19.6)	<0.001	228 (36.3)	136 (21.6)	<0.001
Diabetes mellitus	234 (21.5)	216 (19.8)	0.34	165 (26.2)	135 (21.5)	0.047
Pseudomonas aeruginosa	**N=1,027**	**N=1,027**		**N=500**	**N=500**	
Infected or colonized prior occupant	11 (1.1)	0 (0)	<0.001	1 (0.2)	0 (0)	0.999
Infected or colonized roommate	51 (5.0)	6 (0.6)	<0.001	11 (2.2)	1 (0.2)	0.006
Age	57.6 (25.1)	53.7 (25.4)	<0.001	58.9 (22.8)	57.4 (23.2)	0.33
Charlson Comorbidity Index	6.1 (4.7)	4.8 (4.7)	<0.001	5.6 (4.1)	5.2 (4.5)	0.10
Female	474 (46.2)	462 (54.0)	0.60	236 (47.2)	232 (46.4)	0.80
Malignancies	219 (21.3)	144 (14.0)	<0.001	76 (15.2)	62 (12.4)	0.20
Renal failure	277 (27.0)	221 (21.5)	0.004	157 (31.4)	109 (21.8)	<0.001
Diabetes mellitus	244 (23.8)	200 (19.5)	0.02	138 (27.6)	123 (24.6)	0.28
Staphylococcus aureus	**N=2,008**	**N=2,008**		**N=1,632**	**N=1,632**	
Infected or colonized prior occupant	21 (1.1)	9 (0.5)	0.03	26 (1.6)	5 (3.5)	<0.001
Infected or colonized roommate	81 (4.0)	25 (1.3)	<0.001	46 (2.8)	9 (0.6)	<0.001
Age	50.8 (25.8)	52.0 (26.6)	0.15	60.5 (22.4)	56.1 (24.3)	<0.001
Charlson Comorbidity Index	5.3 (4.9)	4.5 (4.4)	<0.001	6.6 (4.5)	4.9 (4.5)	<0.001

Female	824 (41.0)	873 (43.5)	0.12	678 (41.5)	731 (44.8)	0.06
Malignancies	335 (16.7)	223 (11.1)	<0.001	309 (18.9)	207 (12.7)	<0.001
Renal failure	475 (23.7)	394 (19.6)	0.002	564 (34.6)	351 (21.5)	<0.001
Diabetes mellitus	443 (22.1)	445 (22.2)	0.94	459 (28.1)	361 (22.1)	<0.001
Streptococcus pneumoniae	**N=107**	**N=107**		**N=70**	**N=70**	
Infected or colonized prior occupant	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A
Infected or colonized roommate	0 (0)	0 (0)	N/A	1 (1.4)	0 (0)	0.999
Age	55.6 (23.4)	56.7 (26.6)	0.75	49.9 (23.2)	50.2 (28.4)	0.94
Charlson Comorbidity Index	4.8 (4.1)	5.6 (4.5)	0.27	5.8 (5.6)	3.9 (3.6)	0.02
Female	44 (41.1)	44 (44.1)	1.00	20 (28.6)	29 (41.4)	0.11
Malignancies	17 (15.9)	13 (12.2)	0.43	13 (18.6)	0 (0)	<0.001
Renal failure	26 (24.3)	26 (24.3)	1.00	14 (20.0)	12 (17.1)	0.66
Diabetes mellitus	19 (17.8)	18 (16.8)	0.86	15 (21.4)	12 (17.1)	0.52

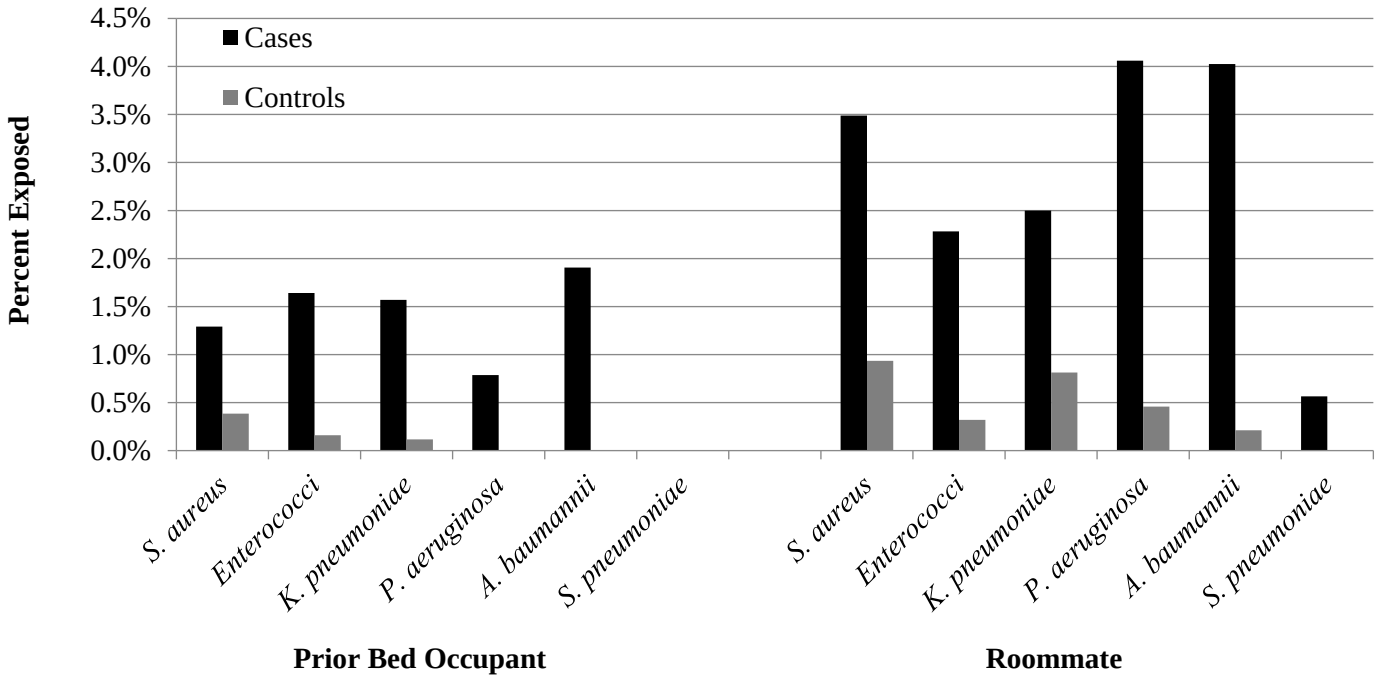
Categorical variables are frequency (percent) with bivariate comparisons conducted using chi-square test for independence or Fisher's exact test. Continuous variables are mean (standard deviation) with bivariate comparisons conducted using two-sample t-test.

Table 4.2. Association between exposure to infected or colonized prior bed occupants and roommates

Exposure	Odds Ratio [95% Confidence Interval]
Exposure to infected or colonized prior occupant	5.83 [3.62, 9.39]
Exposure to infected or colonized roommate	4.82 [3.67, 6.34]
Age in years	1.00 [0.999, 1.001]
Charlson Comorbidity Index	1.04 [1.03, 1.05]
Female	1.00 [0.95, 1.06]
Malignancies	1.61 [1.48, 1.76]
Renal failure	1.50 [1.40, 1.60]
Diabetes mellitus	1.03 [0.96, 1.11]

Results of multivariable logistic regression analysis.

Figure 4.1. Percent exposed to infected prior bed occupants and roommates in controls versus cases of healthcare-associated infection with *Staphylococcus aureus, Acinetobacter baumannii, Streptococcus pneumoniae, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis* and *Enterococcus faecium* exposed to prior bed occupants and roommates infected or colonized with the same organism.



CHAPTER FIVE

Conclusion

The aim of this dissertation was to describe the extent to which healthcare-associated infections (HAIs) continue to plague acute care hospitals and to evaluate the role of prior bed occupants and concurrent hospital roommates in infection transmission. In pursuit of this aim, three related studies were conducted. The first was a seven-year retrospective cohort study examining changes in the incidence and antimicrobial susceptibility of HAIs in four New York City acute care hospitals. The second was a systematic review of the literature on organism transmission from hospital roommates and prior room occupants. The third was a case-control study in the same four hospitals examining the association between exposure to roommates or prior bed occupants with positive bacterial cultures and subsequent infection with the same organism.

The descriptive analysis in Chapter Two revealed several important trends. First, levels of antimicrobial resistance remained consistent throughout the study period for all organisms with the exception of *P. aeruginosa*, for which resistance increased, and *K. pneumoniae*, for which resistance decreased. The relatively steady rates of resistance occurred in the setting of local and national efforts aimed at halting or reducing the proliferation of resistance genes in common healthcare-associated pathogens. The fact that resistance rates were largely unchanged suggests that such efforts may have had some impact on slowing their growth.

Another significant finding from this analysis is that patients admitted from other healthcare facilities and those who had been previously admitted to one of the study hospitals were more likely to have antibiotic resistant versus sensitive infections. This result is not surprising due to the fact that such patients have greater exposure to drug-resistant organisms and to antibiotics. Nevertheless, it is troubling because the proportion of patients with previous exposure to the healthcare system increased throughout the study period—a trend that has been

observed nationally. This result highlights the importance of reducing environmental contamination through enhanced cleaning methods, since an increasing number of patients may harbor drug-resistant organisms as a result of repeated hospitalizations and stays in long-term or sub-acute care facilities.

Chapter Two also revealed that the overall incidence of HAIs dropped significantly from 2006 to 2012. Since patient comorbidities and host factors have remained stable over time, this suggests that some infection prevention strategies have been effective. Like many organizations across the United States, the Department of Infection Prevention and Control at the study hospitals instituted a number of new initiatives aimed at curbing infection rates, including central line care bundles, policies for the expedient removal of urinary catheters, hand hygiene monitoring, universal contact precautions, universal and targeted screening for multidrug-resistant organisms, revised cleaning procedures and products, and countless other efforts. The number of concurrent changes, the unit-specific implementation of some programs, and the brevity of some policies makes it impossible to retrospectively attribute HAI reductions to any one specific initiative. Given the heterogeneous etiology of HAIs and the multitude of points along the transmission pathway at which the chain can be broken, it is likely that each of these initiatives played some role in preventing a small portion of infections. The unfortunate reality is that given the complexity of this issue, optimal infection prevention will undoubtedly involve a combination of many strategies, each targeting different points in the infection transmission pathway. The fact that HAI incidence remained high at 19.3 per 1,000 admissions at the end of the study period, after reductions had already occurred, indicates a need for further advances in infection prevention practice.

In this dissertation, the focus was on the patient room as a pathogen reservoir. Chapter Three summarizes a review of the existing literature regarding the risk posed to patients by infected or colonized previous room occupants and roommates. Although findings were mixed, the majority of previously published articles reported a statistically significant positive association while only one identified a statistically significant negative association. Insufficient power was a common theme throughout the studies, which may explain why many failed to detect any association between exposure to prior occupants or roommates and organism acquisition.

Chapter Four describes the largest and most comprehensive study to date of the association between exposures to infected or colonized previous room occupants or roommates and subsequent infection with the same organism. In addition to overcoming the insufficient power faced by previous studies and including a wider range of bacterial species, this study also focused specifically on the outcome of infection, as opposed to organism acquisition, which includes both colonization and infection. This allowed for a more precise estimation of the real impact that exposure to infected or colonized roommates and previous bed occupants can have on patients and hospitals in terms of actual HAIs. In this seven-year case-control study of 761,426 admissions across four acute care hospitals, exposure to an infected or colonized prior bed occupant conferred a nearly six-fold increase in the odds of infection and exposure to an infected or colonized roommate conferred a nearly five-fold increase.

Overall, the proportion of cases exposed to infected or colonized prior bed occupants and roommates were relatively low at about two percent and four percent, respectively. Still, it is important to keep in mind that the prior room occupant exposure defined in this study likely represents only a portion of possible exposures. Since organisms can survive on surfaces for

long periods of time, sources of exposure could include patients who were discharged from a room days, weeks, or months earlier. Similarly, incubation periods vary, meaning that roommates from one or two weeks prior to infection could be sources of exposure.

Taken together, these findings lend support to the hypothesis that the environment plays a significant role in the transmission of HAIs within the hospital setting. The data suggest that patient-to-patient transmission does occur indirectly with the hospital room serving as a mediator and reservoir for pathogens. The results of this dissertation have important practical implications for infection prevention and control. For one, the "foam in, foam out" hand hygiene paradigm whereby healthcare workers are encouraged to perform hand hygiene upon entry and exit to each room may need to be revisited, since contamination inside patient rooms likely includes a host of potential pathogens left behind by previous room occupants or spread around by current roommates, which can be picked up by healthcare workers' hands or gloves and brought directly to the patient. For another, a review of current policies and procedures for routine cleaning in shared hospital rooms and terminal cleaning at discharge is warranted. The evidence from this study suggests that although costly, effective interventions for room disinfection like ultraviolet light may be lifesaving. Hospitals needing to make a business case to justify the investment in enhanced room cleaning should carefully weigh the expense of these measures against the costs of treating preventable HAIs.

Public health relevance

In addition to the high fatality rates attributable to infections with multidrug-resistant bacteria, patients with difficult-to-treat infections can suffer serious morbidity, including amputations and multi-organ failure.[10] However, the risks associated with pathogenic bacteria in the hospital environment are not limited to hospitalized patients, and reducing cross transmission

of HAIs has important public health implications both within and beyond the hospital setting. Advances in patient care along with cost containment pressures have led to shorter hospital stays and more outpatient treatment, accelerating the opportunity for organisms that were once confined to hospitals to proliferate in the community.[130,131] Higher rates of HAI transmission result in an increased need for antimicrobial prescriptions, which can negatively affect selection pressures inside healthcare facilities and in the environment more generally, potentially leading to further antimicrobial resistance.[132] Furthermore, the connection between bacterial contamination in hospitals and the community is not limited to patients. Public water supplies, for example, may be at risk of contamination with antibiotic-resistant pathogens from hospital waste water.[133] The many points of interface between hospital and community underscore the public health importance of minimizing microbial contamination in healthcare settings through enhanced cleaning procedures.

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