A Simulation Model to Compare Strategies for the Reduction of Healthcare-Associated Infections

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Cook County Hospital, like many hospitals in the U.S. and worldwide, is pursuing a developing strategy to combat healthcare-associated infections (HAIs). Annually, the human toll in the U.S. is approximately two million infected, of which over 100,000 die. An interdisciplinary team of researchers from Georgia Tech, the CDC, and Cook County Hospital, with backgrounds in engineering, economics and medicine, analyze the flow of pathogens. We combine infection rates and cost data to build a discrete event simulation model for the purpose of capturing the complex relationships between hand-hygiene, isolation, demand, and costs. We find that both hand-hygiene and isolation policies have a significant impact on rates of infection, with a complex interplay between factors. This suggests a systems-level approach to infection-control procedures will be required to contain healthcare-associated infections.

Key words: Healthcare, Healthcare-Associated Infections, Discrete Event Simulation.

1. Introduction

A healthcare-associated infection (HAI) is defined as one where there is no evidence that the patient was infected (or colonized) at the time of admission (Emori and Gaynes 1993). The infections we consider in this study are a subset of HAI, namely the hospital acquired, or nosocomial, infections. Roughly two million patients contract HAIs each year in the United States alone, of which more than 100,000 die (McCaughey 2005). Dealing with these infections costs more than thirty billion dollars per year, most of which must be borne by hospitals, since they are not part of any recognized treatment. The problem is becoming increasingly complicated, due to the emergence of resistant pathogens (Hughes and Tenover 1997). In addition, there is evidence that the liberal use of antibiotics is resulting in evolving resistance in pathogens (Davey et al. 2002).

The federal government is considering regulating infection control, but as of now, various states have taken the lead (Weinstein et al. 2005). For example, the Pennsylvania Health Care Cost Containment Council (PHC4) now reports on HAIs online (www.phc4.org). The idea that report cards on hospitals infection rates may help has been slow to win acceptance, but is being considered by a number of other states (Weinstein et al. 2005). In addition, the Centers for Medicare and Medicaid Services (CMS) recently announced new rules for hospital inpatient cost reimbursement in response to a provision of the Deficit Reduction Act of 2005, which requires hospitals to begin reporting secondary diagnoses that are present on admission by October 1, 2007 (Centers for Medicare & Medicaid Services (CMS) 2005). Under the new rule, diagnostic related payments to hospitals would be reduced or not provided for certain hospital-acquired conditions.

In the U.S. health system, where hospitals have a financial and legal incentive to conceal HAIs, it has been especially difficult to monitor the problem (Haley et al. 1987). In addition, the risk factors change depending on patient characteristics, ailments, local frequencies of pathogens, and
infection controls. This leads to research on very specific types of HAIs (Safdar and Maki 2002, Burger et al. 2006). Different types of patients also have different risks for developing HAIs (Floret et al. 2006). Hence even if the problem is significant and potentially solvable, it is also complex and in need of some level of aggregation.

We therefore seek to address the following research questions:

- Does the system of infections in a hospital behave as a set of independent problems, or do the relationships between parts change depending on the state of the system? For instance, does greater compliance with hand-hygiene measures reduce costs?
- What are the relative merits of isolation versus hand-hygiene?
- How do infection control measures impact hospitals costs?

To address these questions, we combine data from Cook County Hospital (Roberts et al. 2003) with parameter estimates from the literature to build a simulation model of HAIs in an intensive care unit (ICU). We compare the costs, benefits, efficacy, and efficiency of various strategies for HAI reduction including screening and isolation.

The paper is organized as follows. We first provide an overview of the literature that provides the basis for our study. We describe our research design, and how it relates to the literature. Then we discuss the data used in the model, followed by the simulation model. After describing the different experiments based on the model, we assess the economic impact of different approaches to infection control. Finally, we give preliminary recommendations for policy, along with an overview of proposed future research.

2. Literature Review
The literature on HAIs is very large, spanning both medical and economics journals, and with varied approaches. We will draw on the health and economics literature, in which pathogens and treatments are the focus.

2.1. Public Health and Medical Literature
HAIs can be classified by pathogen or by what is infected. The major types of infections are surgical site infections (SSI), pneumonia, bloodstream infections (BSI), urinary tract infections (UTI) and a catch-all class of Other (Emori and Gaynes 1993). Catheters in particular contribute to BSI, but these may be managed, as one study found mean rates of catheter related BSI dropped from 7.7 to 1.4 per 1000 catheter-days due to an intervention (Pronovost et al. 2006). A recent review estimated that “up to 1/3 of all HAIs may be prevented by adequate cleaning of equipment” (Schabrun and Chipchase 2006).

Another approach to reducing SSI is to provide feedback to the hospitals on their performance. This approach in Germany’s KISS system (Krankenhaus Infektions Surveillance System), led to a relative risk of 0.54 as compared to conditions prior to installation of the outcome measures (Gastmeier et al. 2005). Naturally, such a system relies on the hospitals to trust that their self-reported measures will not be used against them. The efficacy of outcome measures is not limited to system-wide initiatives. St. Luke’s Episcopal Health System counted incidents of hospital-acquired pneumonia, and were able to identify risk factors such as the use of intra-aortic balloon pumps, renal failure, re-intubation, and total intubation time, and reduce the rate of pneumonia from 6.5% in FY96 to 2.8% in FY01 (Houston et al. 2003). However, they noted that a “major obstacle” was to keep staff aware and involved in the infection control program. A larger program involving 56 hospitals decreased SSI rates from 2.3% to 1.7% over three months by applying correct antibiotics (within one hour of surgery), keeping the patient at correct temperature, blood sugar and blood-oxygen, and even correct hair removal (Dellinger et al. 2005).
Which pathogens are most troubling at any one time changes as bacteria migrate and develop resistance, and as technology provides both new avenues for microbes to attack, as well as new tools, methods, and pharmaceuticals to combat various agents of infection. Currently, the main problem pathogens in the U.S. are Methicillin-resistant Staphylococcus aureus (MRSA) and Vancomycin-Resistant Enterococcus (VRE) (Edwards et al. 2007).

Although Staphylococcus aureus is a widespread bacterium, the current problem is primarily with Methicillin-resistant strains. MRSA has been estimated to increase length-of-stay (LOS) by 50% and the cost of hospitalization by 100%, when compared to the susceptible strain, MSSA (Lodise and McKinnon 2005). MRSA tends to stay in hospitals that have been infected, and carriers may harbor MRSA for more than three years (Sanford et al. 1994). Asymptomatic carriers may contribute a great deal to the spread of MRSA, which argues in favor of screening (Vonberg et al. 2006). However, others find that isolating MRSA patients either alone or in cohorts does little to reduce the risk of cross-infection (Cepeda et al. 2005). Of course, both those results are compatible with the argument that health-care workers spread the bacterium; the number of manipulations does appear to increase the spread (Dziekan et al. 2000).

VRE, on the other hand, has become a significant problem only since 1990 (Trick et al. 1999, Bonten et al. 1996). Just as with other HAIs, VRE leads to greater LOS and cost (Suntharam et al. 2002), and similar to MRSA, VRE cross-colonization is easy, and colonization may persist for some time (Bonten et al. 1996).

In addition to the VREs and MRSAs, there are a number of other major pathogens, and an even larger group of so-called zoonotic diseases (e.g. hantavirus, anthrax, hemorrhagic fevers such as Ebola, plague and rabies) (Weber and Rutala 2001). Since pathogens follow cycles and modeling can easily become intractable with too fine a structure, we will not go into more detail on individual microbes. It is important to retain risk factors that are common to HAIs, such as LOS, hand hygiene, and colonization among health-care workers (HCW) (Trick et al. 2001). In addition, it is important to include resistance to antibiotics and biocides (Cookson 2005).

2.1.1. Medical Treatments

There are two major lines of research in the control of HAI: surveillance and avoidance. Surveillance techniques observe and report on the record of the hospital, while avoidance techniques help to hinder infection. In our simulation model, we focus on screening and hand-hygiene, as different approaches to avoiding HAIs.

**Surveillance** This may be done either at the level of the hospital or of all patients, i.e. the system. In addition, surveillance may be passive, inspecting patients or records, or active, which involves culturing samples from asymptomatic patients and health care workers (HCW). There is no nationwide surveillance system in the U.S., but six states had systems in 2005 (Becker 2005), and 39 have considered legislation (Weinstein et al. 2005). Although it is not clear that all HAIs are being reported, hospitals that do report their performance are not penalized, while those that fail to report risk $1000 dollar per day fines. In addition to the importance of trust that their reports will not be used against them, it is important to take into account risk-adjusted patients, so that hospitals cannot ”improve” their performance by cherry-picking cases (Weinstein et al. 2005).

**Screening** It is difficult to know when to classify an infection as healthcare-associated. If an active approach to screening all patients and HCW is applied, cultures must be taken to test for different pathogens. In one study in Israel, a country where MRSA is endemic, such an approach cut the cases of bacteremia in half (Shitrit et al. 2006), while a U.S. study found a cost-effective reduction in the incidence of MRSA (Clancy et al. 2006).

**Isolation** If carriers and those with infection can be isolated, either privately or in cohorts, then such quarantine might control outbreaks. For individual patients, each test costs approximately $30, and comprehensive screening is estimated to cost $300 (Donohue 2007). Isolating MRSA-colonized patients is given credit for working in the Netherlands, Denmark and Finland (Farr 2006b,a). However, a study in the UK found no effect (Cepeda et al. 2005). Two reviews of the
literature found some support for isolation in response to MRSA (Cooper et al. 2004), but no robust economic evaluation (Cooper et al. 2005). Similarly, a survey of German hospitals found that isolation did help control MRSA (Gastmeier et al. 2004). From a system-design perspective, it seems that isolation may primarily benefit the entire health-care system, while hand-washing may be most important for individual patients.

**Hand Hygiene** The issue of hand hygiene is sufficiently important for the Centers for Disease Control and Prevention (CDC) to provide a Morbidity and Mortality Weekly Report (MMWR) guideline (Boyce and Pittet 2002). In short, these recommend washing visibly dirty hands, and otherwise using alcohol-based hand rubs, as well as gloves in certain cases. Rates of adherence to hand-hygiene guidelines are typically less than 50% (Vernon et al. 2003), so measures to improve compliance may have a significant impact. Although Lai et al. (2006) found that gels were no better than traditional methods, the fact that an increase in the number of sinks, and therefore a reduction in the inconvenience in hand-washing, had no significant impact on compliance (Vernon et al. 2003), suggests that alcohol gels are a better choice. An alternative may be to use gloves, which has similar efficacy, but is cheaper and easier to comply with than hand-washing (Trick et al. 2004). It has been noted that improved hand-hygiene will have a secondary positive impact, in reducing the need for antibiotics and retarding the evolution of resistant strains of pathogens (Weinstein 2001).

### 2.2. Economics

The framework for general economic analysis of health care (Scott et al. 2001), and to the problem of HAIs specifically, has been discussed in several papers. The economics of HAIs are especially challenging due to measurement difficulties and the uncertainties associated with cost-allocation and quantifying (Roberts and Scott 2003, Roberts et al. 1999, Graves 2004, Graves et al. 2007a). Research has estimated fixed costs to represent 84% of hospital costs (Roberts et al. 1999, Graves 2004), which leads to questions of how to assess such costs, as well as the benefits from infection control programs and regulations. McCaughey (2005) provides a useful summary of the financial and human cost of hospital acquired infections. A briefing for the Association for Professionals in Infection Control and Epidemiology (APIC) also provided an overview of the financial impact for hospitals, emphasizing that due to the increase in LOS from HAI, the opportunity cost should also be counted, for hospitals running close to capacity (Murphy et al. 2007). Since HAIs extend the stay of patients in hospitals, but do not usually require additional surgeries or alternative treatment, several studies indicate that hospital acquired infections primarily have the effect of increasing LOS (Beyersmann et al. 2006, Graves et al. 2007b). This has led to the argument that only marginal costs should be included, as long as the perspective is the hospitals (Graves et al. 2007a). Graves et al. (2007b) also makes the argument that quality-adjusted life-years (QALY) should be employed to measure the benefits of infection control. Clearly, extra mortality is also a relevant cost (Yalcin 2003), although this cost is not borne by the hospital.

The literature on HAIs is primarily based on specific transfers and pathogens, without consideration for the complex interactions within a hospital setting. Our focus is on the dynamics of the system as a whole. The contribution of this paper then is to develop insights from HAIs in a hospital setting, accounting for the relatively complex set of interactions, to develop insights that can help establish effective policies.

### 3. Data

The data we use in in this work are based on the CARP study (Roberts et al. 2003), conducted at Cook County Hospital located in Chicago, Illinois. In the overall data-set we have records for the hospitalization of 1,254 patients, with information on the patients' age, whether or not they died during hospitalization, if they had surgeries, spent any time in the ICU, and had a
confirmed or suspected HAI in their urinary tract, blood-stream, surgical site, lungs, or elsewhere. We further have available the LOS, two severity of illness scores (the Apache III and the Charlson), in addition to various costs. These have been carefully constructed through actual hospital outlays and procedures, and include fixed charges for admittance ($635.33) and treatment in the emergency department ($250.45). Variable costs include a charge for the LOS, charges for procedures done at the bedside (i.e. without an operating room), charges for use of an operating room, and charges for blood, pharmaceutical, and radiological laboratory tests.

Since we are limiting this study to ICU’s, we first reduce our data-set to the 212 patients who were in the ICU. Of these, 33 died, 70 developed a confirmed HAI based on the CDC guidelines, and a further 20 lacked one indicator, and so are counted as suspected of having an HAI. Due to overlap, the total number patients classified as having any HAI is 85, or approximately 40% (see Table 1). A t-test for differences in means gives p-values of 0.000 for LOS and total cost, confirming that the difference in means between patients with and without HAI is statistically significant.

We use the data to provide parameter estimates and a method to assign costs. The LOS is modeled through a probability of discharge, which we estimate using maximum likelihood means for a geometric distribution of length of stay (LOS): $\hat{\theta} = N / \sum_{i=1}^{N} LOS_i$ for both those infected, and those not infected. This gives $\hat{\theta}_{NoHAI} = 0.095291$ and $\hat{\theta}_{HAI} = 0.042289$. These are adjusted slightly, to make the LOS for infected and uninfected patients conform with the CARP patients.

Finally, upon patient exit, costs are assessed using the CARP data. After running several regressions, the best parsimonious fit for total costs is (see Table 8):

$$\hat{TotalCost} = 3028.81 + 445.9 * HAILOS + 1944.2 * LOS$$

Here $HAILOS = AnyHAI * LOS$, i.e. an interaction effect to increase the average daily cost once infected. This gives an $R^2 = 0.88$, after we remove one outlier.

The total costs we use since we do not have what the patients incur for specific categories such as pharmacological costs. However, the CARP data gives us valuable validation through both the average LOS and the average total cost incurred.

This aggregate approach ignores the types of HAI, the demographics, and the breakdown of costs into LOS, consults, drugs, diagnostics, etc. However, since we are focused on the effect of HAI on overall costs, we use the total costs attributed to the patients.

4. Simulation
Discrete event simulation is used to model the process by which pathogens, patients and visitors enter an ICU, interact with HCW and each other, infect, become infected and cured of both primary disease and their additional infections, and finally are discharged and assigned costs. Note that those who carry an infection agent are colonized, and that there is an incubation period between colonization and infection, during which the pathogen may spread from an asymptomatic patient, HCW, or visitor.

We incorporate the various pieces described above to shed light on the research questions, in particular the complex interactions between the various parts of the infection process. We simulate
rather than pursue a closed-form approach, because the large number of interacting factors means
we must trade precision for greater realism. This approach allows us to include all the various
factors mentioned above, which we need to address the research questions.

We incorporate location, patient demographics, and variable bed-occupancy into the simulation.
We construct a base model using an ICU (Cepeda et al. 2005), along with the CARP data to
provide ICU rates of HAI in a U.S. hospital, as well as total cost data.

The ICU has ten rooms, in which two doctors and four nurses provide transportation for the
pathogens. The HCWs mix in random groups of one doctor and two nurses, and spread the
pathogens between patient locations and HCWs. These HCWs, patients and visitors all move on
a network between an entrance (and exit), and individual and cohort rooms (see Figure 1).

We alter the base model to allow for screening and isolation in two formats:
1. An additional isolation ward is added.
2. An isolation ward is carved out of the available space.

Hand-hygiene efficacy (HHE) and compliance is modeled through the assumption that there is
a hand-hygiene station in every patient room, and that HCWs attempt to cleanse their hands,
with a positive probability of success. We use an efficacy parameter to quantify the probability
of removing any colonization, and represent both the probability of cleansing hands, and that the
effort is successful.

We focus on the dynamic aspects of the movement of pathogens, and so limit ourselves to one
generic pathogen. Although this is a simplification, it is reasonable due to the level of aggregation
we utilize. Specifically, we do not include surgeries, intravenous devices, different pharmaceutical
products, which we would require in order to benefit from differentiated pathogens. In the following we describe each of the models and report on the results.

4.1. Base Model
The base model takes the ICU as given, but allows both patients and visitors to bring colonizations of resistant and susceptible pathogens into the locale. The health care workers then probabilistically spread the pathogen to different locations. In order to keep some measure of control with the model, only the locations transfer the pathogens, but we adjust the parameters to force the infection rates in the simulation to mimic those seen in the data (See Table 2).

Using MedModel (Harrell and Field 2001) structures, the discrete event simulation is formulated using the following elements:

- **Locations:** Ten beds, along with visitor stations for each bed; one entrance for patients, and another for visitors. The locations capture the transmission of pathogens by passing along colonizations.
- **Entities:** Patients and visitors. Both can be colonized with susceptible or resistant pathogens, but only patients are assumed to arrive with actual infections.
- **Path networks:** The movement of the patients, visitors, nurses and doctors are constrained to a network between locations (see 1). Although we have a geographical model of the ICU, we do not allow the simulation to use all the possible locations, as that would draw processing time, without adding useful results.
- **Resources:** Doctors and nurses. These can be colonized, but infected HCWs are assumed to stay away from the ICU (Bergogne-Berezin 1999, Sethi 1974). Colonized individuals can then spread the pathogen to other locations.
- **Processing:** Entities are processed when they move from one location to another, and while they remain at a given location.
  1. Visitors bring pathogens from the outside, and can pass those along to the locations visited.
  2. Patients are treated by the health care workers, and since this is an ICU, the patients are seen frequently. The simulation process selects one doctor and two nurses at random for each patient care event. Each visit provides an opportunity for pathogens to move between the HCW, locations, and patients. In addition, a patient can stochastically develop or be cured of an infection, and also has a probability of discharge. As mentioned above, this probability falls substantially when the patient is infected, but not from a colonization. The probabilities were selected to imitate the data from Cook County Hospital (see 3).
  3. Upon a patient’s exit there is a cleanup of the location if the patient was infected, in order to limit the colonization. The exit process also captures data, such as the LOS, which infections had been caught, and calculates the total cost for that patient.
- **Arrivals:** The rate at which patients and visitors arrive at the entrance. Arrivals are modeled using exponential distributions.
- **Variables:** Global variables track the incidence of colonization for HCWs, locations, patients and visitors. In addition, global variables count various items of interest, such as the number of the different types of patients entered and discharged, infections and colonizations, lengths of stay, and the state of occupancy in the ICU.
- **Parameters:** Are given constant values within each simulation run, representing the probabilities of colonization, infection, cure, etc.

4.2. Model with Area Reserved for Isolation
In this model, we remove three beds next to the entrance (beds 8, 9 and 10) from the base model, and turn these into an isolation ward. Patients are first screened, then go to the isolation ward or the regular entrance. This significantly lowers capacity, but provides a model directly comparable to the base model, as no more room is devoted to the ICU.
Table 2  Base Model Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>mArrivalRate</td>
<td>1</td>
<td>Parameter governing the rate of patient arrival.</td>
</tr>
<tr>
<td>mVisitorMultiplier</td>
<td>3</td>
<td>Visitors arrive at a rate of three times the number of patients.</td>
</tr>
<tr>
<td>mColonProp</td>
<td>0.2</td>
<td>Proportion colonized in the community.</td>
</tr>
<tr>
<td>mComResistProp</td>
<td>0.3</td>
<td>Proportion of those colonized in the community carrying a resistant strain.</td>
</tr>
<tr>
<td>mTreatmentTime</td>
<td>0.04</td>
<td>Approximate number of days between visits from HCWs.</td>
</tr>
<tr>
<td>mHandHygEffic</td>
<td>.8</td>
<td>Efficacy of hand-hygiene, considered as a combination of probability of washing or using gel, with probability that pathogen is removed.</td>
</tr>
<tr>
<td>mLocToHCWCosRate</td>
<td>.5</td>
<td>Probability per treatment incidence of transfer from location to HCW.</td>
</tr>
<tr>
<td>mHCWtoPatientCosRate</td>
<td>.5</td>
<td>Probability per treatment incidence of transfer from HCW to patient.</td>
</tr>
<tr>
<td>mHCWtoLocCosRate</td>
<td>.7</td>
<td>Probability per treatment incidence of transfer from HCW to location.</td>
</tr>
<tr>
<td>mLocToPatientCosRate</td>
<td>.8</td>
<td>Probability per treatment incidence of transfer from location to patient.</td>
</tr>
<tr>
<td>mPatientToHCWCosRate</td>
<td>.4</td>
<td>Probability per treatment incidence of transfer from patient to HCW.</td>
</tr>
<tr>
<td>mPatientToLocCosRate</td>
<td>.9</td>
<td>Probability per treatment incidence of transfer from patient to location.</td>
</tr>
<tr>
<td>mColToInfRate</td>
<td>.3</td>
<td>Probability per treatment incidence a colonized patient develops an infection.</td>
</tr>
<tr>
<td>mDisinfectLoc</td>
<td>.1</td>
<td>Probability per treatment incidence a colonized location is disinfected.</td>
</tr>
<tr>
<td>mCureSProb</td>
<td>.4</td>
<td>Probability per treatment incidence a susceptible infection is cured.</td>
</tr>
<tr>
<td>mCureRProb</td>
<td>.1</td>
<td>Probability per treatment incidence a resistant infection is cured.</td>
</tr>
<tr>
<td>mHealthyExitProb</td>
<td>.06</td>
<td>Probability per treatment incidence of exit if patient is healthy.</td>
</tr>
<tr>
<td>mInfSExitProb</td>
<td>.02</td>
<td>Probability per treatment incidence of exit if patient has a susceptible infection.</td>
</tr>
<tr>
<td>mInfRExitProb</td>
<td>.01</td>
<td>Probability per treatment incidence of exit if patient has a resistant infection.</td>
</tr>
</tbody>
</table>

4.3. Model with Additional Isolation Ward
In this model we add a separate isolation ward to the base model. This increases capacity, since valuable beds are no longer used for de-colonization purpose. We recognize that this solution may be somewhat unrealistic, as patients with a need to be in an ICU would also require intensive care in any isolation facility, but it allows for another direct comparison with the base model.

5. Analysis
We seek to understand the interplay between hand-hygiene (HHE), isolation, arrival rates and costs on the dynamic flow of HAIs. We therefore simulate different scenarios of isolation, namely, none...
Figure 2: Average Total Cost v. HHE in Patients without HAI

We observe that higher overall infection rates increase costs, reduce capacity, and increase lengths-of-stay. However, we note that the relationships do not appear to be linear, and are sometimes surprising when we focus solely on subsets of patients, e.g., those who did not catch an HAI. The apparently nonlinear relationships include the relationship between the number of discharged patients (total, with and without HAI) versus HHE, LOS and average cost versus HHE, and the proportion of time the ICU is full versus HHE. There is no reason to assume linearity, but we emphasize this point because previous statistical models used to assess the impact of HAIs on costs have been linear, and in fact uncoupled from LOS (Graves et al. 2007b).

Another capacity related effect is due to the physical locations of the screens. When we add an additional screen to the base model, there is a slight increase in the patient throughput. Since we
Table 3  Parameter and Variable Definitions

<table>
<thead>
<tr>
<th>Name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arr</td>
<td>The mean interarrival time of patients.</td>
</tr>
<tr>
<td>HHE</td>
<td>Hand-hygiene efficacy parameter.</td>
</tr>
<tr>
<td>vDischargedPatients</td>
<td>The number of patients discharged.</td>
</tr>
<tr>
<td>vNumDischargedHAI</td>
<td>The number of patients discharged that had an HAI.</td>
</tr>
<tr>
<td>vNumDischargedNoHAI</td>
<td>The number of patients discharged that never had an HAI.</td>
</tr>
<tr>
<td>vAvgLOSwithHAI</td>
<td>The average length of stay of patients discharged that had an HAI.</td>
</tr>
<tr>
<td>vAvgLOSnoHAI</td>
<td>The average length of stay of patients discharged that never had an HAI.</td>
</tr>
<tr>
<td>vAvgTCwithHAI</td>
<td>The average total cost of patients discharged that had an HAI.</td>
</tr>
<tr>
<td>vAvgTCnoHAI</td>
<td>The average total cost of patients discharged that never had an HAI.</td>
</tr>
<tr>
<td>vICUfull</td>
<td>The average proportion of time the ICU was full.</td>
</tr>
</tbody>
</table>

Table 4  Output from Base Model

<table>
<thead>
<tr>
<th>Arr</th>
<th>HHE</th>
<th>Statistic</th>
<th></th>
<th>Number Discharged Patients</th>
<th>Number Discharged with HAI</th>
<th>Number Discharged Without HAI</th>
<th>Avg LOS of patients with HAI</th>
<th>Avg LOS of patients without HAI</th>
<th>Avg TC with HAI</th>
<th>Avg TC no HAI</th>
<th>ICUfull</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>0.4</td>
<td>Mean</td>
<td>39.46</td>
<td>37.76</td>
<td>1.70</td>
<td>23.71</td>
<td>1.43</td>
<td>59706.72</td>
<td>5201.85</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>0.4</td>
<td>SE</td>
<td>0.98</td>
<td>0.99</td>
<td>0.22</td>
<td>0.49</td>
<td>0.21</td>
<td>1172.03</td>
<td>518.45</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>0.6</td>
<td>Mean</td>
<td>46.74</td>
<td>43.80</td>
<td>2.94</td>
<td>21.31</td>
<td>1.55</td>
<td>53965.47</td>
<td>5738.28</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>0.6</td>
<td>SE</td>
<td>1.04</td>
<td>0.90</td>
<td>0.34</td>
<td>0.43</td>
<td>0.17</td>
<td>1016.22</td>
<td>398.88</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>0.8</td>
<td>Mean</td>
<td>102.48</td>
<td>78.34</td>
<td>24.14</td>
<td>12.45</td>
<td>3.72</td>
<td>32785.01</td>
<td>10259.30</td>
<td>0.99</td>
<td></td>
</tr>
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do not allow for patient healing during isolation, this estimate is conservative, and solely due to the decrease in HAIs. When the screen is carved out of the ICU, however, capacity and throughput drop significantly, in line with expectations. The effects are mirrored for those with and without HAIs. However, the number discharged who ever had an HAI does not drop significantly when the isolation room is added. Instead, the additional throughput is comprised of patients who do not contract HAIs. We note here that visitors are not screened, and bring in a steady stream of pathogens from the community.
In order to assess the numerical effects of the different parameter values, we average across the different scenarios (Table 7). We cautiously interpret these results, and note that a standard
deviation is meaningless due to the fact that these are arbitrarily selected parameter-settings. Nevertheless, we do observe that the effect of changes in HHE is monotonic for each variable.

It appears clear that an increase in HHE is an unmitigated benefit. However, it is of interest to note that under our specifications, and with low arrival rates, an increase in HHE increases overall throughput, while the absolute number of patients who ever contract HAIs remains roughly constant. This counterintuitive result is not surprising in light of the overall increase in volume, but would suggest that an effort to decrease the absolute number of patients who contract HAI’s through increased efficacy of hand-hygiene, would simply not work. There would be a benefit, but this would have the effect of greater throughput, rather than fewer patients with HAI. This result suggests that isolated measures of success in controlling infections may be misleading, and a system-wide perspective is needed.

The most counterintuitive results are arguably that higher efficacy in hand-hygiene leads to longer lengths of stay, and higher costs, for patients who never contract an HAI. We assume no additional costs for the increased HHE, so the effect comes from the dynamics of the model. We also note that the relationship holds across all the scenarios. The key to understanding this result is to bear in mind that the mean LOS is conditional on the event that the patient did not catch an HAI. When HHE increases, more patients that would otherwise have gotten an HAI are treated until discharge without being infected, even though it may take longer. Said another way, when infections are rampant, it is a rare patient who is lucky enough, and recovers swiftly enough, to avoid an infection. Only those swift patients are counted among the group that were discharged without contracting an HAI, so they must have a short average LOS. Conversely, LOS falls for those who did contract an HAI, because with better cleanliness, they are less likely to catch another infection.

Returning to cost, we note that LOS is the primary driver, which explains why the same relationship holds for the average total cost per patient. We do note that the CARP data as presently utilized uses an allocated mechanism, so true variable costs have not been calculated. However, since doing so would increase the benefit from freeing up capacity, the approach currently utilized underestimates the impact of HAIs on cost. We cannot compare the change in costs for the added isolation ward, nor from carving out such a ward, as we do not have these figures. Since the main effect appears to be on capacity and revenue, we must base our conclusions on increased service to patients. However, since our simulation period is 100 days, we note that the average increase in patients served over the full year is 192.3, while the percentage of time the ICU is full declines from 95% to 82%.

6. Discussion

On the basis of these simulation models, we can draw several useful observations.

Observation 1: Both hand-hygiene and isolation policies have a strong impact on rates of HAIs, capacity, and costs.

The effects of better compliance with hand-hygiene infection control is different when capacity is tight, versus when there is slack in the system. This is intuitive for any change that increases or decreases the average throughput of the hospital. Since variable costs comprise less than a fifth of
a hospital cost (Roberts et al. 1999, Graves 2004), average per-patient costs may decline with a successful infection-control program. However, overall costs will increase due to the program itself, and due to the shift in patients that do or do not acquire HAI, it is not clear that per-patient average costs will decrease for every class of patient.

Observation 2: Hand-hygiene and isolation policies interact, so that the relative merits of the two approaches change for each scenario.

We are not surprised to find that drastically reducing capacity by carving out an isolation ward left the ICU full much more often than under the base model or the model with an added isolation ward (see tables 4, 5, 6). Although costs were generally higher when we added isolation policies, we had to expect that, since we merely added this feature. In order to draw a strong conclusion, we would have to compare the added cost from isolation to the cost of hand-hygiene campaigns, and this data was not available. Since hand-hygiene is often poor, but may be improved through inexpensive alcohol-gels, while ICU isolation wards require significant capital expenditure, the small difference in results between isolation-ward models and the base models suggests the benefits to cost ratio is greater for hand-hygiene improvements. The burden of proof, therefore, must lie with those recommending isolation wards over hand-hygiene.

Observation 3: The relationships between arrival rates (i.e. demand), physical structure, hand-hygiene efficacy, and length of stay are complex, and unlikely to be adequately modeled with a single linear equation. Therefore, the infection control problem does not decompose into a set of independent problems.

The non-linear nature of the system we simulate is difficult to model in closed-form, which means that any linear approximation will only be valid for a limited interval of parameter values. As an example, this means that if compliance with hand-hygiene regulations is increased from 30% to 50%, a linear model to predict performance changes may be invalid. A simulation that incorporates such non-linear relationships remains usable.

Observation 4: When increasing HHE, the change in the dynamic system is too complex to model with a linear approximation.

For example, based on our simulation, we would predict that the average length of stay, as well as average total cost per patient, for patients who do not contract an infection, would increase with greater HHE. Further, greater HHE would not lead to a lower absolute number of patients who contract an HAI. We suggest that these results are not intuitive at first glance, yet perfectly reasonable upon reflection. Such insight into a service system is valuable in analyzing different approaches to improving infection control.

Observation 5: A systemic perspective is needed to understand infection control from a global perspective.

It is unlikely that a hospital view-point is sufficient, since the environment remains a reservoir for pathogens, which arrive at hospitals through patients, visitors and health-care workers. In this simulation, we treated the level of infection in the environment as fixed, although a multi-hospital simulation would require linked levels of pathogens throughout a given region.

6.1. Contribution to the Literature

Our model was based on actual data, and adds to the set of studies applying simulation to health issues (Fone et al. 2003). Although simulations are more opaque than closed-form solutions, we gain the benefit of solving a more realistic problem using simulation, even if we cannot feasibly investigate every possible set of parameter values.

The complex and dynamic nature of the infection control problem also directly addresses the current discrepancy in cost attributed to hospital acquired infections. Roberts et al. (2003) estimated that HAIs added more than fifteen thousand dollars to the treatment of the average patient, largely through extended stays. Graves et al. (2007b) recently estimated that the costs were statistically
insignificant for most types of HAIs under study, and practically insignificant for one. However, the approach in Graves et al. (2007b) explicitly ignores the linked effect of LOS and infection, and attributes no impact to cost from HAI through more than 100 potential variables examined to account for cost. As such, it is hardly surprising that they found no residual effect; the structural link is ignored, and the indirect impact of HAI on cost through vehicles such as increased use of pharmaceuticals is severed. Our model strongly suggests that LOS and HAI are tightly linked, and HAIs have a significant impact on the use of hospital resources and attention from HCWs, all of which increase cost (and increase the probability of yet more infections).

6.2. Future Research
We are pursuing several avenues to improve the precision and robustness of our results. First, we seek to estimate the LOS and incidence of HAI simultaneously, and isolate the effect of these on cost. A simultaneous equation approach is one possible way to properly estimate the dynamic spiral described above.

Second, we are currently working on finding levels of variable costs that may be allocated for specific events in a simulation. This will add veracity, although given the very high proportion of hospital costs that are fixed, it is unlikely to alter the overall picture drastically.

Third, although the simulation approach is valuable, it does not consider the psychological responses of health-care workers. It is unclear why compliance rates for hand-hygiene regulations are as low as they are. In order to examine the underlying factors driving compliance with infection control procedures, we are constructing a survey-instrument. We are currently working with multiple hospitals in the Atlanta area.

Finally, this study is meant to be only a first step in evaluating the costs and benefits of different types of regulations the U.S. Congress may enact. The CDC is required to evaluate such regulations, and this was the initial impetus to the model. We therefore seek to build models for different types of hospitals, before using these sub-models as input into a nationwide study of HAIs and regulation. Currently, we have four hospitals: two from Children’s Hospital of Atlanta, Athens Regional Hospital, as well as the original source of data, Cook County Hospital. cooperating with us in providing information and data.

The final outcome of this line of research is meant to be guidance for how different sets of national regulations would impact HAIs, rates, costs and benefits. Since everything outside the hospital functions as a reservoir for infections, we expect a system-wide approach will be required in order to fully control resistant pathogens.

Acknowledgments
This study was partially funded through a Health Systems Initiative Grant at Georgia Institute of Technology.
OLS Output

Table 8  Excel OLS output for Total Cost regressed on LOS and HAILOS

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References


Clancy, Megan, Amy Graepler, Michael Wilson, Ivor Douglas, Jeff Johnson, Connie Savor Price. 2006. Active screening in high-risk units is an effective and cost-avoidant method to reduce the rate of methicillin-resistant staphylococcus aureus infection in the hospital. *Infection Control and Hospital Epidemiology* **27**(10) 1009–1017.


Farr, Barry M. 2006b. What to think if the results of the national institutes of health randomized trial of methicillin-resistant staphylococcus aureus and vancomycin-resistant enterococcus control measures are negative (and other advice to young epidemiologists): A review and an an revoir. *Infection Control and Hospital Epidemiology* **27**(10) 1096–1106.


Murphy, Denise, Joseph Whiting, Christopher S. Hollenbeak. 2007. Dispelling the myths: The true cost of healthcare-associated infections. *Association for Professional Infection Control & Epidemiology White Paper*.


Shitrit, Pnina, Bat-Sheva Gottesman, Michal Katzir, Avi Kilman, Yona Ben-Nissan, Michal Chowers. 2006. Active surveillance for methicillin-resistant staphylococcus aureus (mrsa) decreases the incidence of mrsa bacteremia. *Infection Control and Hospital Epidemiology* 27(10) 1004–1008.


