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A Simulation Model to Compare Strategies for the Reduction of Health-Care–Associated Infections

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Cook County Hospital, like many hospitals in the United States and worldwide, is pursuing a strategy to combat health-care–associated infections (HAIs). In the United States, approximately two million people are infected each year and over 100,000 die. In this paper, an interdisciplinary team of researchers from Georgia Tech 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 to capture 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, and that a complex interplay between factors exists. This suggests that a systems-level approach to infection-control procedures will be required to contain health-care–associated infections.

Key words: health care; health-care–associated infections; discrete-event simulation.
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A health-care–associated infection (HAI) is defined as one in which there is no evidence of patient infection (or colonization) at the time of admission to a hospital (Emori and Gaynes 1993). The infections we consider in this study are a subset of HAIs—namely, the hospital-acquired, or nosocomial, infections. Approximately two million patients contract HAIs in the United States each year; of these, more than 100,000 die (McCaughey 2005). Dealing with these infections costs more than $30 billion per year, and hospitals bear most of this cost because no recognized treatments for these infections exist. The problem has become increasingly complicated because of the emergence of resistant pathogens (Hughes and Tenover 1997). In addition, there is evidence that the liberal use of antibiotics is causing evolving resistance in pathogens (Davey et al. 2006).

The US government is considering regulating infection control; however, as of now, various states have taken the lead (Weinstein et al. 2005). For example, the Pennsylvania Health Care Cost Containment Council (PHC4) provides online reports on HAIs (http://www.phc4.org). Although the concept that report cards on hospital infection rates could be helpful has been slow to win acceptance, several other states are considering it (Weinstein et al. 2005). In addition, the Centers for Medicare and Medicaid Services (CMS) announced new rules for hospital inpatient cost reimbursement in response to a provision of the Deficit Reduction Act of 2005, which required hospitals to begin reporting secondary diagnoses that are present on admission, as of October 1, 2007 (Centers for Medicare and Medicaid Services (CMS) 2006). Under the new rule, diagnostic-related payments to hospitals would be reduced or not provided for certain hospital-acquired conditions.

Hospitals in the United States have a financial and legal incentive to conceal HAIs, making it especially difficult to monitor the problem (Haley et al. 1987). In addition, the HAI risk factors vary depending on patient characteristics, ailments, local frequencies of pathogens, and infection controls. Thus, the research performed is typically on very specific types of HAIs (Safdar and Maki 2002, Burger et al. 2006). Moreover, patients have varying risks for developing HAIs (Floret et al. 2006). Hence, even if the problem is potentially solvable, it is also complex and requires 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 example, 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 combined 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). In this paper, we compare the costs, benefits, efficacy, and efficiency of various strategies for HAI reduction, including screening and isolation.

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

Literature Review

The literature on HAIs is extensive, spanning both medical and economics journals, and includes various approaches. We draw on the health and economics literature that focuses on pathogens and treatments.

Public Health and Medical Literature

We can classify HAIs by pathogen or by type of infection. The major infection types are bloodstream infections (BSI), surgical-site infections (SSI), pneumonia, urinary-tract infections, and other, a catchall category (Emori and Gaynes 1993). Catheters particularly contribute to BSI; however, they are manageable. One study found that mean rates of catheter-related BSI dropped from 7.7 to 1.4 per 1,000 catheter-days because of 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, p. 239).

One approach to reducing SSI is to provide feedback to the hospitals on their performance. When Germany's Krankenhaus Infektions Surveillance System (KISS) used this approach, its relative risk was 0.54 when compared to conditions prior to installation of the measurements (Gastmeier et al. 2005). Naturally, such a system relies on a hospital's willingness to trust that its self-reported measurements will not be used against it. The efficacy of using measurements is not limited to systemwide initiatives. St. Luke's Episcopal Health System counted incidents of hospital-acquired pneumonia and was able to identify risk factors, such as the use of intra-aortic balloon pumps, renal failure, reintubation, and total intubation time. It reduced its pneumonia rate from 6.5 percent in FY96 to 2.8 percent in FY01 (Houston et al. 2003). However, they noted that keeping staff aware of and involved in the infection-control program was a "major obstacle." A larger program involving 56 hospitals decreased SSI rates from 2.3 percent to 1.7 percent over three months by applying correct antibiotics (within one hour of surgery); keeping patients at correct temperature, blood sugar, and blood-oxygen levels; and even correcting hair-removal procedures (Dellinger et al. 2005).

Which pathogens are most troubling at any point in time changes as bacteria migrate and develop resistance, and as technology provides both new avenues for microbes to attack and new tools, methods, and pharmaceuticals to combat various agents of infection. Currently, the major problem pathogens in the United States are methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE) (Edwards et al. 2007).

Although *Staphylococcus aureus* is a widespread bacterium, the most prevalent problem involves primarily methicillin-resistant strains. MRSA has been estimated to increase patient length of stay (LOS) by 50 percent and the cost of hospitalization by 100 percent when compared to the susceptible strain, methicillin-susceptible *Staphylococcus aureus* (MSSA) (Lodise and McKinnon 2005). MRSA tends to remain in hospitals that have been infected, and carriers may harbor this bacterium for more than three years (Sanford et al. 1994). Asymptomatic carriers could contribute significantly to the spread of MRSA; thus, this argues in favor of screening (Vonberg et al. 2006). However, others have found 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 of these results are consistent with the argument that health-care workers (HCWs) spread the bacterium; the number of manipulations does appear to increase its spread (Dziekan et al. 2000).

VRE, on the other hand, has only become a significant problem 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 in a manner similar to MRSA, VRE cross-colonization occurs easily, and colonization may persist for some time (Bonten et al. 1996).

In addition to the VREs and MRSAs, there are several other major pathogens, and an even larger group of so-called zoonotic diseases, including hantavirus, anthrax, and hemorrhagic fevers, such as Ebola, plague, and rabies (Weber and Rutala 2001). Because pathogens follow cycles and modeling can easily become intractable with too-fine a structure, we will not discuss individual microbes in detail. It is important for models to include risk factors that are common to HAIs, such as LOS, hand hygiene, and colonization among HCWs (Trick et al. 2001). In addition, it is important to include resistance to antibiotics and biocides (Cookson 2005).

There are two major categories of research in the control of HAIs: surveillance and avoidance. Surveillance techniques observe and report on a hospital's record, whereas avoidance techniques help to hinder infection. In our simulation study, we focus on screening and hand hygiene as different approaches to avoiding HAIs.

Surveillance. Surveillance can be done either at the hospital level or the system level (i.e., the all-patient level). It can be passive, such as inspecting patients or records, or active, which might involve culturing samples from asymptomatic patients and HCWs. The United States does not have a nationwide surveillance system; however, as of 2005, six states had systems in place (Becker 2005) and 39 were considering 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, whereas those that fail to report an HAI risk fines of $1,000 per day. Hospitals report their various rates of infection (i.e., performance compared to a standard or mean) because absolute numbers of incidents are very poor measures of how well they are doing. They should be able to trust that their reports will not be used against them. It is also important that we consider risk-adjusted patients to ensure that hospitals cannot "improve" their performance by cherry-picking cases (Weinstein et al. 2005), because immune-compromised patients such as the elderly or prematurely born infants require much more care to avoid infection than healthy adults do.

Screening. It is difficult to know when to classify an infection as health-care–associated. If a hospital takes an active approach to screening all patients and HCWs, it must take cultures to test for different pathogens. In one study in Israel, a country in which MRSA is endemic, such an approach reduced the cases of bacteremia in half (Shitrit et al. 2006), whereas a US 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; 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 that isolation had 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; i.e., the economic evaluation was sufficiently limited that it could not be generalized (Cooper et al. 2003). Similarly, a survey of German hospitals found that isolation did help control MRSA (Gastmeier et al. 2004). From a system-design perspective, isolation could primarily benefit the entire health-care system, whereas hand washing could be most beneficial to individual patients.

Hand Hygiene. Hand hygiene is sufficiently important that the Centers for Disease Control and Prevention (CDC) has written guidelines for its adherence (Boyce and Pittet 2002). These guidelines recommend washing visibly dirty hands, and using alcohol-based hand rubs and gloves in certain cases. Rates of adherence to hand-hygiene guidelines are typically less than 50 percent (Vernon et al. 2003); thus, measures to improve compliance could have a significant impact. Lai et al. (2006) found that gels were no better than traditional hand-hygiene methods; in addition, an increase in the number of sinks, which supposedly reduce the inconvenience of hand washing, had no significant impact on compliance (Vernon et al. 2003). These suggest that alcohol-based hand rubs are a better choice. An alternative might be to use gloves, which has similar efficacy but is cheaper and easier to comply with than hand washing (Trick et al. 2004). Weinstein (2001) has noted that improved hand hygiene will also reduce the need for antibiotics and retard the evolution of resistant strains of pathogens.

Economics

The framework for general economic analysis of health-care (Scott et al. 2001), and the problem of HAIs specifically, has been discussed in several papers. The economics of HAIs are especially challenging because of measurement difficulties and the uncertainties associated with cost allocation and quantification (Roberts and Scott 2003; Roberts et al. 1999; Graves 2004; Graves et al. 2007a, b). Research has estimated that fixed costs represent 84 percent of hospital costs (Roberts et al. 1999, Graves 2004). This leads to questions about how to assess both these costs and the benefits that infection-control programs and regulations provide. McCaughey (2005) provides a useful summary of the financial and human cost of hospital-acquired infections. A white paper of the Association for Professionals in Infection Control and Epidemiology (APIC) also provides an overview of the financial impact for hospitals, emphasizing that because of the increase in LOS from HAI, hospitals that are close to capacity should also look at the opportunity cost (Murphy et al. 2007). Because 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 economic analysis should only include marginal costs, if the study is done from the perspective of hospitals (Graves et al. 2007b). They also make the argument that quality-adjusted life years (QALY) should be used to measure the benefits of infection control. Clearly, extra mortality is also a relevant cost (Yalçın 2003), although the hospital does not bear this cost.

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, and to develop insights that can help establish effective policies.

Data

The data we use in this work are based on the Chicago Antimicrobial Resistance Project (CARP) study (Roberts et al. 2003) conducted at Cook County Hospital in Chicago, Illinois. The data set includes records of the hospitalization of 1,254 patients, with information on the patient's age, whether the patient died during the hospitalization, whether the patient had surgery, the time spent in the ICU, or whether the patient had a confirmed or suspected HAI in his or her urinary tract, bloodstream, surgical site, lungs, or elsewhere. We also have LOS data, two severity-of-illness scores, and various costs. Rebecca Roberts, a coauthor of this paper, constructed them carefully using actual hospital outlays and procedures; they 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.

We are limiting this study to ICUs; therefore, we first reduce our data set to the 212 patients who were in the ICU. Of these, 33 died and 70 developed a confirmed HAI (as CDC guidelines define an HAI); an additional 20 lacked one indicator and are therefore counted as suspected of having an HAI. Because of overlap, the

	ICU		With HAI		No HAI	
	LOS	Cost ($)	LOS	Cost ($)	LOS	Cost ($)
Mean	15.73	38,072.54	23.65	59,711.30	10.43	23,589.91
Standard deviation	15.10	38,610.31	19.16	49,996.29	8.16	17,398.89
Count	212		85		127	

Table 1: The table data show summary statistics for the ICU.

total number of patients classified as having any HAI is 85, or approximately 40 percent (Table 1).

A t-test for differences in means gives p-values of 0.000 for LOS and total cost; thus, this confirms 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, and model the LOS using a probability of discharge, which we estimate using maximum likelihood means for a geometric distribution of length of stay (LOS), for both those infected and those not infected: $\hat{\theta} = N/\sum_{i=1}^{N} \mathrm{LOS}_i$. This gives $\hat{\theta}_{\mathrm{NoHAI}} = 0.095291$ and $\hat{\theta}_{\mathrm{HAI}} = 0.04289$. 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 2)

$$EstTotalCost = 3{,}028.81 + 445.9 * \mathrm{HAILOS} + 1{,}944.2 * \mathrm{LOS}, \quad (1)$$

where $\mathrm{HAILOS} = \mathrm{AnyHAI} * \mathrm{LOS}$, i.e., an interaction effect to increase the average daily cost once infected. This gives $R^2 = 0.88$ after we remove one outlier. In Table 2, we provide the results from a linear regression of total cost on LOS and an interaction term of HAI and LOS. In combination, the two predictors account for approximately 88 percent of the variation in total cost; both terms have a statistically significant impact.

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

Summary output					
Regression statistics					
Multiple R					0.939
R square					0.8819
Adjusted R square					0.8807
Standard error					13,301.08
Observations					211
ANOVA					
	df	SS	MS	F	Significance F
Regression	2	2.75E+11	1.37E+11	776.46	3.32E−97
Residual	208	3.68E+10	1.77E+08		
Total	210	3.12E+11			
	Coefficients	Standard error	t Stat	p-value	
Intercept	3,028.81	1,477	2.050559	0.041564	
HAILOS	445.9	113.0168	3.945	0.000109	
LOS	1,944.186	125.4174	15.50172	1.55E−36	

Table 2: Total cost regressing total cost on LOS and HAILOS gave the Excel output reported above.

Simulation

We use discrete-event simulation to model the process by which pathogens, patients, and visitors enter an ICU, interact with HCWs and each other, infect, become infected and cured of both primary disease and 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 this period, the pathogen could spread from an asymptomatic patient, HCW, or visitor.

We incorporate the various pieces described above to try to answer 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 must do 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) and the CARP data to provide ICU rates of HAI in a US hospital, as well as total cost data.

The ICU has 10 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

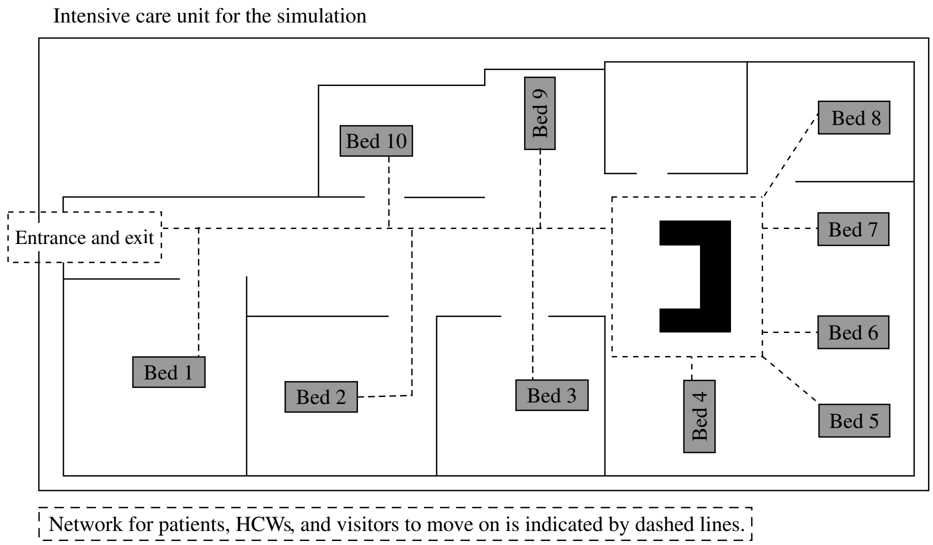

Figure 1: This schematic provides an overview of the ICU from the model.

visitors all move on a network between an entrance (and exit), and individual and cohort rooms (Figure 1).

We alter the base model to allow for screening and isolation using two scenarios:

1. We add an additional isolation ward.
2. We carve an isolation ward out of the available space, and model hand-hygiene efficacy (HHE) and compliance using 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. This parameter represents both the probability of cleansing hands and the success of the effort, because there is nothing to be gained from including failed attempts at hand hygiene in the simulation model.

We focus on the dynamic aspects of the movement of pathogens and thus limit ourselves to one generic pathogen. Although this is a simplification, it is reasonable because of the level of aggregation that we utilize. Specifically, we do not include surgeries, intravenous devices, or different pharmaceutical products, which we would require to benefit from differentiated pathogens. In the following section, we describe the base model and each scenario.

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. To keep some measure of control within the model, only the locations transfer the pathogens; however, we adjust the parameters to force the infection rates in the simulation to mimic those seen in the data (Table 3).

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

- Locations: We allocated 10 beds and 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: Entities are patients and visitors; both can be colonized with susceptible or resistant pathogens. However, our assumption is that only patients arrive with actual infections.
- Path networks: Patients, visitors, nurses, and doctors move on a network of paths between locations (Figure 1). Although we have a geographical model of the ICU, we do not allow the simulation to use all the possible locations; this would require processing time but would not add useful results.
- Resources: Doctors and nurses are resources; they can be colonized. However, we assume that infected HCWs stay away from the ICU (Bergogne-Berezin 1999, Sethi 1974). Colonized individuals can then spread the pathogen to other locations.

Parameter	Value	Comment
mArrivalRate	1	Parameter governing the rate of patient arrival.
mVisitorMultiplier	3	Visitors arrive at a rate of three times the number of patients.
mColonProp	0.2	Proportion colonized in the community.
mComResistProp	0.3	Proportion of those colonized in the community carrying a resistant strain.
mTreatmentTime	0.04	Approximate number of days between visits from HCWs.
mHandHygEffic	0.8	Efficacy of hand hygiene, considered as a combination of probability of washing or using gel, with probability that pathogen is removed.
mLocToHCWColRate	0.5	Probability per treatment incidence of transfer from location to HCW.
mLocToHCWColRate	0.5	Probability per treatment incidence of transfer from location to HCW.
mHCWtoPatientColRate	0.5	Probability per treatment incidence of transfer from HCW to patient.
mHCWtoLocColRate	0.7	Probability per treatment incidence of transfer from HCW to location.
mLocToPatientColRate	0.8	Probability per treatment incidence of transfer from location to patient.
mPatientToHCWColRate	0.4	Probability per treatment incidence of transfer from patient to HCW.
mPatientToLocColRate	0.9	Probability per treatment incidence of transfer from patient to location.
mColToInfRate	0.3	Probability per treatment incidence a colonized patient develops an infection.
mDisinfectLoc	0.1	Probability per treatment incidence a colonized location is disinfected.
mCureSProb	0.4	Probability per treatment incidence a susceptible infection is cured.
mCureRProb	0.1	Probability per treatment incidence a resistant infection is cured.
mHealthyExitProb	0.06	Probability per treatment incidence of exit if patient is healthy.
mInfSExitProb	0.02	Probability per treatment incidence of exit if patient has a susceptible infection.
mInfRExitProb	0.01	Probability per treatment incidence of exit if patient has a resistant infection.

Table 3: The base model was populated with the parameters shown in the table.

• Processing: Entities are processed when they move from one location to another and while they remain at a given location. Visitors bring pathogens from outside the hospital and can pass them along to the locations visited. Patients are treated by the health-care workers, and because 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 simulate the data from Cook County Hospital (see "Path networks" above). When a patient exits, a cleanup of the location is performed if the patient was infected; this limits the colonization. The exit process also captures data, such as the LOS and the infections that the patient caught, and calculates the total cost for that patient.

• Arrivals: Arrivals, which represent the rate at which patients and visitors arrive at the entrance, 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 numbers of patients entered and discharged, infections, colonizations, lengths of stay, and the state of occupancy in the ICU.

• Parameters: Parameters are given constant values within each simulation run; for example, they might represent the probabilities of colonization, infection, or cure.

In Table 4, we define the parameters we used in the models.

Validity of the Base Model

Because a simulation model is necessarily a simplification, its internal validity is limited, and its external validity depends on how well changes are reflected in the model and in reality. Only the base model can be fitted to the data, unless the system itself is available for experimentation. For ethical and other reasons, this is infeasible in our case. In addition, traditional statistical hypothesis tests are often misleading because a

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

Table 4: The parameter and variable definitions used in the models are presented above.

null hypothesis that the model fits could be rejected by performing sufficient simulation runs. Therefore, the data set provides a starting point for tuning the base model, and because we took many parameters from the literature, we adjust these constants to have output that approximates the sample means in the data from Cook County Hospital. In particular, we adjusted the hand-hygiene efficacy and the probabilities of transmission to equate the average length of stay and average total cost.

Scenario with Area Reserved for Isolation

In this scenario, we remove three beds next to the entrance (beds 8, 9, and 10) from the base model and create an isolation ward. Patients are screened; then, they go to the isolation ward or the usual entrance. This significantly lowers capacity; however, it provides a scenario that is directly comparable to the base model because no more room is devoted to the ICU.

Scenario with Additional Isolation Ward

In this scenario, we add a separate isolation ward to the base model. This increases capacity because valuable beds are no longer used for decolonization purposes. We recognize that this solution might be somewhat unrealistic, because patients with a need to be in an ICU would also require intensive care in any isolation facility; however, it allows for another direct comparison with the base model.

Analysis

We seek to understand the interplay between HHE, isolation, arrival rates, and costs on the dynamic flow of HAIs. Therefore, we simulate different scenarios of isolation: none (Base), an isolation ward carved out of the main ICU (Carve-out), and an isolation ward added to the ICU (Plus-Screen). We use high, medium, and low levels for the HHE and arrival rate (Arr) parameters. Following a warm-up period of 10 days for each scenario, we replicated the simulations 50 times for 100 days. Tables 5, 6, and 7 display the parameter values, calculated means, and standard deviations. Total costs and lengths of stay remain in line with results from the CARP data set.

Higher overall infection rates increase costs, reduce capacity, and increase lengths of stay. However, 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. Although there is no reason to assume linearity, we emphasize this point because previous statistical models used to assess the cost impact of HAIs have been linear and uncoupled from LOS (Graves et al. 2007a, b).

Note that as the patients' interarrival time decreases (e.g., $\text{Arr} = 0.1$ rather than $\text{Arr} = 1.0$), the proportion of time that the ICU is full increases. Only when there is a significantly lower patient inflow does the ICU have spare capacity. In addition, a significant increase in volume occurs only at the highest level of HHE.

Screening also has an impact on capacity. When we add an additional screen to the base model, there is a slight increase in the patient throughput. Because we do not allow for patient healing during isolation, this estimate is conservative, solely because of the decrease in HAIs. When the isolation room is taken from space formerly devoted to 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.

Arr	HHE	Number of discharged patients	Number discharged with HAI	Number discharged without HAI	Avg. LOS of patients with HAI	Avg. LOS for patients without HAI	Avg. total cost with HAI	Avg. total cost—No HAI	ICU full
0.1	0.4	39.46	37.76	1.7	23.71	1.43	59,706.72	5,201.85	1
0.1	0.6	46.74	43.8	2.94	21.31	1.55	53,965.47	5,738.28	1
0.1	0.8	102.48	78.34	24.14	12.45	3.72	32,785.01	10,259.30	0.99
0.25	0.4	40.14	38.48	1.66	22.84	1.42	57,622.88	4,814.78	0.99
0.25	0.6	47.2	44.44	2.76	21.1	1.47	53,464.89	5,159.56	0.99
0.25	0.8	106.34	74.86	31.48	12.36	3.96	32,565.22	10,721.27	0.94
0.5	0.4	40.46	37.96	2.5	21.87	1.19	55,288.03	4,680.92	0.97
0.5	0.6	47.72	43.82	3.9	20.4	1.73	51,792.26	5,905.90	0.95
0.5	0.8	100.94	64.42	36.52	12.44	4.66	32,756.32	12,085.96	0.78
1	0.4	38.86	35.62	3.24	21.13	1.78	53,538.45	5,888.04	0.82
1	0.6	45.4	40.2	5.2	19.49	2.25	49,606.30	7,092.66	0.76
1	0.8	87.46	39.46	48	12.29	5.05	32,411.16	12,844.22	0.28

Table 5: The output of sample means from the base model gave the sample means shown above.

Arr	HHE	Number of discharged patients	Number discharged with HAI	Number discharged without HAI	Avg. LOS of patients with HAI	Avg. LOS for patients without HAI	Avg. total cost with HAI	Avg. total cost—No HAI	ICU full
0.1	0.4	43.08	40.16	2.92	25.16	1.87	63,174.05	6,169.10	1
0.1	0.6	49.1	44.46	4.64	23.32	3.05	58,761.50	8,829.71	1
0.1	0.8	103.76	77.06	26.7	14.18	5.01	36,925.70	12,765.78	1
0.25	0.4	46.84	43.6	3.24	22.91	2.44	57,793.02	7,404.14	1
0.25	0.6	53.26	48.12	5.14	21.27	2.58	53,863.11	7,914.37	1
0.25	0.8	105.7	70.74	34.96	14.07	5.5	36,654.79	13,714.98	0.99
0.5	0.4	51.8	46.68	5.12	20.59	2.26	52,231.42	7,061.51	0.98
0.5	0.6	53.84	48.14	5.7	20.58	2.7	52,214.10	8,153.28	0.97
0.5	0.8	107.5	61.12	46.38	13.46	5.58	35,208.61	13,879.55	0.88
1	0.4	50.8	44.94	5.86	18.41	2.59	47,042.37	8,064.89	0.79
1	0.6	60.76	49.44	11.32	16.62	3.16	42,748.23	9,175.49	0.69
1	0.8	93.08	32.78	60.3	12.57	6.03	33,074.01	14,759.42	0.3

Table 6: The scenario with an additional isolation ward gave the sample means reported above.

Arr	HHE	Number of discharged patients	Number discharged with HAI	Number discharged without HAI	Avg. LOS of patients with HAI	Avg. LOS for patients without HAI	Avg. total cost with HAI	Avg. total cost—No HAI	ICU full
0.1	0.4	30.02	27.6	2.42	27.53	2.48	68,832.41	7,676.66	1
0.1	0.6	34.94	31.64	3.3	24.63	3.41	61,905.13	9,354.25	1
0.1	0.8	76.26	56.14	20.12	14.59	5.82	37,906.77	14,346.53	1
0.25	0.4	31.54	27.82	3.72	26.82	2.57	67,129.00	7,604.63	1
0.25	0.6	35.88	31.78	4.1	23.99	3.52	60,377.19	9,624.01	1
0.25	0.8	79.38	50.14	29.24	14.45	6.41	37,563.15	15,486.66	1
0.5	0.4	35.08	30.62	4.46	23	3.28	57,990.86	9,035.83	0.99
0.5	0.6	38.9	33.9	5	21.87	3.86	55,292.43	10,297.95	0.99
0.5	0.8	79.16	43.7	35.46	13.94	6.82	36,355.71	16,294.40	0.95
1	0.4	39.16	34.6	4.56	19.66	3	50,024.59	8,738.02	0.91
1	0.6	42.88	35.94	6.94	18.97	3.56	48,364.56	9,890.36	0.88
1	0.8	77.38	30.32	47.06	13.26	6.3	34,730.30	15,266.53	0.67

Table 7: The output from the scenario with an isolation ward carved out from the ICU gave the sample means shown above.

Scenario	HHE	Number of discharged patients	Number of discharged patients with HAI	Number of discharged patients without HAI	Average LOS with HAI	Avg. LOS without HAI	Avg. total cost with HAI	Avg. total cost without HAI	Proportion of time the ICU is full
Base	0.4	39.7	37.5	2.3	22.4	1.5	56,539.00	5,146.40	0.95
Base	0.6	46.8	43.1	3.7	20.6	1.8	52,207.20	5,974.10	0.93
Base	0.8	99.3	64.3	35	12.4	4.3	32,629.40	11,477.70	0.75
AddIsol	0.4	60.7	51.3	9.4	21.4	3.1	54,163.60	8,792.20	1
AddIsol	0.6	66.2	53.4	12.7	19.1	3.3	48,740.90	9,211.00	0.99
AddIsol	0.8	78	47.1	31	15.3	4.3	39,518.30	11,469.80	0.67
CarveOut	0.4	43.2	35.8	7.4	23.4	3.6	58,943.30	9,745.50	1
CarveOut	0.6	47.3	36.6	10.7	20.8	4.3	52,805.90	11,111.10	1
CarveOut	0.8	59.6	36.1	23.5	16.5	4.9	42,368.80	12,547.30	0.85

Table 8: Changes in hand-hygiene efficacy gave average effects across scenarios as reported above.

The hospital is not immune to infections from the community because visitors are not screened.

To assess the numerical effects of the different parameter values, we average across the different scenarios (Table 8).

We cautiously interpret these results and note that a standard deviation is meaningless because these are arbitrarily selected parameter settings. Nevertheless, we do observe that the effect of changes in HHE is nearly monotonic for each variable. The only two exceptions to this statement are for high HHE in the two changed circumstances of an added isolation unit, or a carved-out isolation unit. In both, the number of patients discharged with HAIs falls slightly for the highest HHE, a result that is consistent with the much larger increase in discharged patients who never contracted an HAI.

Therefore, an increase in HHE is a clear benefit, although for some parameter values it would seem to lead to more absolute numbers of HAI. This increase is more than balanced by the increase in patient volume. As an example, note that in Table 6, with Arr set to 0.1, the volume of patients increases from 43.08, through 49.10, to 103.78 as HHE increases from 0.4, through 0.6, to 0.8. However, although the absolute number of patients with HAI increases, the percentage of patients without HAI grows with the increase in HHE, from 6.8 percent, through 9.5 percent, to 25.7 percent, respectively.

This counterintuitive result is not surprising in light of the overall increase in volume; however, it would suggest that an effort to decrease the absolute number of patients who contract HAIs through increased efficacy of hand hygiene would simply not work. Although there would be a benefit, it would have the effect of greater throughput, rather than fewer patients with HAI. This result suggests that isolated measures of success in controlling infections might be misleading, and a systemwide 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; therefore, the effect comes from the dynamics of the model. This 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 patient not having caught an HAI. When HHE increases, more patients who would otherwise have caught an HAI are treated until discharge without being infected, although their hospital stays might be lengthy. In other words, when infections are rampant, it is a rare patient who is lucky enough, and recovers swiftly enough, to avoid an infection. Only those few patients are counted among the group discharged without contracting an HAI; thus, 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. This explains why the same relationship holds for the average total cost per patient. At present, because the CARP data allocate cost, true variable costs have not been calculated. However, because using marginal costs 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, because we do not have these figures. The major impact appears to be on capacity and revenue; therefore, we must base our conclusions on increased service to patients. However, because our simulation period is 100 days, we note that the average increase in patients served over the full year is 192.3, whereas the percentage of time the ICU is full declines from 95 percent to 82 percent.

Discussion

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

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

The effects of better compliance with hand-hygiene infection control are 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. Because variable costs comprise less than one-fifth of a hospital's costs (Roberts et al. 1999, Graves 2004), average per-patient costs could decline if a successful infection-control program is implemented. However, overall costs will increase because of the program itself; in addition, because of 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.

The isolation policies impact the number of HAI patients, as well as the overall volume, much less than HHE does, for the parameter values that we examine. Given that costs associated with improved HHE are low, e.g., adding alcohol-gel dispensers, while new capacity is very expensive, it seems clear that HHE is a more promising lever to reduce HAI. One caveat: The difficulty in changing habits of infection-control compliance should not be underestimated.

Observation 2. Hand-hygiene and isolation policies interact such 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 scenario with an added isolation ward (Tables 5–7). Although costs were generally higher when we added isolation policies, we expected that because we merely added this feature. To draw a strong conclusion, we would have to compare the added cost from isolation to the cost of hand-hygiene campaigns—data that were not available. Because hand hygiene is often poor but could be improved by using inexpensive alcohol gels, whereas ICU isolation wards require significant capital expenditure, the small difference in results between isolation-ward scenarios and the base model suggests that 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 methods.

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 using a single linear equation. Therefore, the infection-control problem does not decompose into a set of independent problems.

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

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

For example, based on our simulation, we would predict that the average length of stay, and average total cost per patient, for patients who do not contract an infection would increase with greater HHE. Additionally, greater HHE would not lead to a lower absolute number of patients who contract an HAI. We suggest that these results are not intuitive; however, upon reflection, they are perfectly reasonable. 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 perspective is sufficient because the environment remains a reservoir for pathogens that 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 multihospital simulation would require linked levels of pathogens throughout a given region.

Contribution to the Literature

Our model, which we based on actual data, adds to the set of studies that applies 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 $15,000 to the treatment of the average patient, largely because of extended hospital 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, their approach 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 that 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).

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 might be allocated for specific events in a simulation. This will add veracity; however, given the very high proportion of hospital costs that are fixed, it is unlikely that it will 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. To examine the underlying factors driving compliance with infection-control procedures, we are currently working with multiple hospitals in the Atlanta area to construct a survey instrument.

Finally, this study is meant to be only a first step in evaluating the costs and benefits of different types of regulations the US Congress could enact. The CDC is required to evaluate such regulations, and this was the initial impetus to the model. Therefore, we seek to build models for different types of hospitals before we use these submodels as input into a nationwide study of HAIs and regulation. Currently, four hospitals are cooperating with us by providing information and data—two from Children's Hospital of Atlanta, Athens Regional Hospital, and Cook County Hospital, the original source of data.

The final outcome of this research is intended as guidance for how different sets of national regulations would impact HAIs, rates, costs, and benefits. Because everything outside the hospital functions as a reservoir for infections, we expect that a systemwide approach will be required to fully control resistant pathogens.

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Ibrar Ahmad, Research Associate, Department of Emergency Medicine, Research Division, John H. Stroger, Jr. Hospital of Cook County, 1900 West Polk Street, 10th Floor, Chicago, Illinois 60612-9985, writes: "I am writing this letter to verify that the Healthcare Associated Infection Simulation Model developed by Dr. Reidar Hagtvedt, Dr. Paul M. Griffin, Dr. Pınar Keskinocak, Dr. R. Douglas Scott II, and Dr. Rebecca R. Roberts has been used at our hospital. Further, the model was useful and has caused us to develop two more infection control interventions that we will study in the next few months.

"First, we enhanced our opportunities for following good hand hygiene by placing over 20 additional alcohol-based hand gel dispensers in our emergency department. Next, we placed student observers throughout the hospital to observe staff hand hygiene compliance. The preliminary results for both of these interventions were improved hand hygiene.

"Our next planned study is to perform microbiological cultures of patient care environments in the emergency department. Whenever a pathogen is cultured, that microenvironment will receive special enhanced housekeeping cleaning. In addition, we will use our electronic medical record system to track patients who were treated in that space before special cleaning. We will compare their incidence of subsequent infection compared to those treated in non-contaminated spaces.

"To address the compliance factors described in the simulation model, we have written a research plan for engaging our patients and their families in this effort. We already post hand hygiene reminder signs and conduct annual training. However, it appears that busy staff mimbers rapidly become habituated to these static interventions. Staff are busy because they are caring for sick patients. Therefore, we will enlist the help of patients and their families in the compliance reminder effort. Signs will be posted for patients/families urging them to remind their staff members to please clean their hands before treating them. Cards will be handed out to all registered patients urging them to remind their staff to follow hand hygiene guidelines. We are in the process of developing catchy slogans for this campaign to avoid any social offense.

"We plan to compile our results from these interventions and use the data to re-specify and further improve the simulation model."