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Mathematical Models of Infection Prevention Programs in Hospital Settings

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MATHEMATICAL MODELS OF INFECTION PREVENTION PROGRAMS IN HOSPITAL SETTINGS

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Systems Modeling and Analysis at Virginia Commonwealth University.

by

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Hospitals play a vital role in providing for the healthcare needs of a community. Patients can develop hospital-acquired infections (HAIs) during their hospitalization due to exposure to foreign bacteria, viruses, and fungi. Infection prevention programs target and reduce HAIs, but implementing the infection prevention programs often comes with a cost. The goal of my research is to use mathematical models to quantify the impact of infection prevention programs on cases of HAIs and total healthcare costs. First, I use a Markov chain model to quantify how one infection prevention program reduces general HAIs in the hospital. Then, I calculate the impact of resistance by healthcare leaders to implement two infection prevention techniques on two HAIs in the hospital. I used ordinary differential equations to quantify the timing of initiation and termination of two infection prevention programs within a region divided into two components to understand how a community intervention and a localized intervention affect the peak number of infections in an epidemic. Finally, I

used an agent-based model to quantify the impact of one specific infection prevention program on one HAI in one ward within the hospital. Overall, my research supports implementing the specific infection prevention programs examined to reduce the burden on healthcare systems and improve patient outcomes.

CHAPTER 1

INTRODUCTION

Mathematical epidemiology focuses on modeling infectious diseases to better understand the causes, predict the spread, determine ways to control the spread and simulate how various disease prevention programs may affect the disease's impact on a community. A specific set of infections, hospital-acquired infections (HAIs), are infections that a patient develops during their stay at the hospital. Because a patient is not often admitted with an HAI, it is important to prevent HAIs with proper infection prevention programming to reduce the patient's length of stay, overall morbidity, mortality and healthcare costs. My research focuses on quantifying the potential impact of infection prevention programs on HAIs.

I employ mathematical models to fit the settings and conditions within the hospital. My process includes identifying model variables, parameters, estimating the costs of the prevention program as well as the costs of the infection, and providing conclusions targeted towards healthcare leaders to inform best practices.

Mathematical modeling allows me to perform studies on HAIs *in silico*. The experiments that I simulate often cannot be done in a clinical setting due to ethical standards of treatment. Because of this, precise parameter values are unknown and have to be estimated through simulations. The results from the mathematical models provide general trends for complicated problems. The mathematical simulations are low cost, provide quick results, are easily modifiable and have defined control and treatment groups.

HAIs affect about one in 25 hospitalized patients and are largely preventable

[Johnson et al., 2014, Magill et al., 2014, Bearman et al., 2019]. In 2001, HAIs were one of the leading causes of death in the United States [Wenzel and Edmond, 2001]. Cases of HAIs declined from 2015 until 2020 due to successful infection prevention and control policies enforced by the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network. Unfortunately, due to the COVID-19 pandemic and the subsequent stress placed on healthcare facilities, HAI incidence has increased since the pandemic began in late 2019 [Weiner-Lastinger et al., 2022]. This highlights the importance of maintaining the effectiveness of HAI prevention practices even when public health emergencies arise [Weiner-Lastinger et al., 2022].

Revelas [2012] broadly defines HAIs to be infections "acquired in the hospital or healthcare service unit that first appear 48 hours or more after hospital admission or within 30 days after discharge of patient care". Some HAIs include "catheter-associated urinary tract infections, central line-associated bloodstream infections, surgical site infections, ventilator-associated pneumonia, hospital-acquired pneumonia, and *Clostridioides difficile* infections" [Monegro et al., 2017]. The CDC provides context for the morbidity of HAIs in the United States in Table 1.

Major Site of Infection	**Estimated Number**
Pneumonia	157,500
Gastrointestinal Illness	123,100
Urinary Tract Infections	93,300
Primary Bloodstream Infections	71,900
Surgical site infections from any inpatient surgery	157,500
Other types of infections	118,500
Estimated total number of infections in hospitals	**721,800**

Table 1 : HAI Estimates Occurring in US Acute Care Hospitals, 2011 [Centers for Disease Control and Prevention, 2018]

HAIs are most frequently caused by viruses, bacteria and fungal pathogens. Mon-

itoring and treating HAIs has become increasingly more difficult because patients are being discharged from the hospital sooner than ever due to medical and technological advances [Collins, 2011]. HAIs also continue to challenge healthcare systems due to increasing bacterial and antibiotic resistance [Revelas, 2012].

The World Health Organization suggests that HAIs continue to plague even the most advanced hospitals. This is due to the fact that medical devices and patient wounds provide access for external bacteria to enter the patient's body. Also, drug-resistant bacteria make it difficult for patients to be treated under traditional preventative practices [Serra-Burriel et al., 2020].

Mortality rates, length of patient stay in the hospital and cost are much higher for patients with HAIs than patients without HAIs [Glance et al., 2011]. Further, the total cost of the hospital stay is about "2.6 to 6 times higher in patients with HAI compared with patients without HAIs" [Glance et al., 2011], and they cost about $45,000 on average [Dancer, 2014].

HAIs are largely preventable when effective infection prevention strategies are sustainably implemented and followed at high compliance levels [Bearman et al., 2019]. These prevention strategies often include improving catheter insertion techniques, following contact precautions, monitoring hand hygiene, disinfecting caps for IV lines and bathing patients, especially near the site of device insertion. These often prevent and reduce HAIs from developing or worsening [Bearman et al., 2018, Climo et al., 2013]. Healthcare institutions need to have effective leadership and access to information on infection control practices in order to sustain best practices [Bearman et al., 2019].

In summary, prior research indicates that HAIs are a burden to healthcare systems and infection intervention strategies can prevent HAIs from developing. In the following chapters I develop and utilize mathematical models to quantify the impact

of infection prevention strategies on yearly HAIs and the associated costs. Providing estimations on the number of cases of HAIs and potential savings related to the timing and effectiveness of implementing the program allows healthcare leaders to make decisions on whether or not the infection prevention program should be incorporated into their standard practices.

In Chapter 2, I first examine how CHG bathing, an infection intervention program, affects general HAIs. This was done using a Markov chain model examining different levels of compliance in CHG bathing, and then measuring the effects on the number of HAIs and associated costs. I also examine the effects of the delay in implementing infection prevention strategies that can occur at the administrative level of a hospital. Here, I employ a Markov chain model to quantify implementing CHG bathing at 10% incremental compliances, and examine how the delay in starting CHG bathing and using a standardized central line bundle kit affects cases of central-line bloodstream infections (CLABSI) and catheter-associated urinary tract infections (CAUTI). I also look at costs associated with treating HAIs and implementing these programs.

In Chapter 3, I quantify the interplay of implementation and termination of different infection prevention strategies during a pandemic. The research was inspired by the beginning of the COVID-19 pandemic when healthcare workers did not have enough personal protective equipment (PPE) to adequately keep them safe from the transmission of the virus in addition to social distancing being introduced and enforced in the community. I used a Susceptible-Infected-Recovered (SIR) Model, which is a system of ordinary differential equations, to model the dynamics of the two infection prevention techniques and how they affect the timing and the size of the peak number of infections during the outbreak.

In Chapter 4, I simulate implementing a specific infection intervention program

in efforts to reduce the incidence of *Clostridiodes difficile* infections (CDIs) in only the Bone Marrow Transplant (BMT) unit within a hospital. I use an agent-based model (ABM) to quantify how testing a patient for *Clostridiodes difficile* (*C. diff*) before the patient is admitted to the BMT Unit affects the number of cases of CDI. The process of testing a patient for *C. diff* before admission is called active detection and isolation (ADI). I quantify the impact of implementing ADI on the number of community-acquired and hospital-acquired cases of CDI. I also calculate the costs associated with implementing ADI, and compare it to the cost of not using ADI as an infection prevention practice.

CHAPTER 2

CHLORHEXIDINE GLUCONATE BATHING AND A STANDARDIZED CENTRAL LINE BUNDLE KIT

2.1 Background

As medical technology has advanced, the use of invasive devices within hospitals has increased. These invasive devices prolong life but offer foreign entities access to the body [Kollef et al., 2021]. The use of vascular catheters, such as central vein, arterial and pulmonary artery catheters can result in a patient developing central line-associated blood stream infections (CLABSIs). Urinary catheters, such as urethral, supracubic and percutaneous nephrostomy catheters can cause a patient to develop catheter-associated urinary tract infections (CAUTIs) [Kollef et al., 2021]. Patients may also acquire an HAI from being immunocompromised, receiving prophylactic antibiotics and being exposed to pathogens in the hospital environment [Kollef et al., 2021].

Prevention strategies are effective in reducing HAIs in hospital units [Glance et al., 2011]. In an effort to reduce HAIs, studies have been conducted to determine the effectiveness with bathing patients with an antimicrobial solution, chlorhexidine gluconate (CHG) [Frost et al., 2016, Rupp et al., 2012]. CHG is a strong antiseptic because it affects the membrane structure of bacteria, yeasts and viruses [Donskey and Deshpande, 2016]. Chlorhexidine also is known for having residual antiseptic effects hours after application, which also makes it favorable in clinical applications [Donskey and Deshpande, 2016].

To quantify the number of infections that can be prevented by CHG bathing,

Climo et al. [2013] and Amirov et al. [2017] conducted clinical studies to estimate the impact of CHG bathing on the reduction of HAIs compared to the use of soap and water. Bathing patients with CHG washcloths in prior studies showed that patients often had adverse skin reactions, but the study by Climo et al. [2013] showed that patients rarely had adverse skin reactions. Amirov et al. [2017] focused on determining the effect of CHG bathing in hospital units where patients stayed for months and years rather than days. They also concluded the CHG bathing reduces the incidence of HAIs.

In a meta-analysis study, Frost et al. [2016] estimated the reduction of HAI risk with daily CHG CLABSI, vancomycin-resistant Enterococcus (VRE), CAUTI, Methicillin-resistant Staphylococcus aureus (MRSA), ventilator-associated pnuemonia (VAP), and CDI. They reported a 56% decreased risk of CLABSI, 37% decreased risk for VRE, 7% decreased risk of CAUTI, 36% decreased risk of MRSA bacteraemia, 18% decreased risk of VAP, and a 7% decreased risk of CDI with daily CHG bathing. In addition, Huang et al. [2016] conducted a meta-analysis study on CHG data and reported a 32% decreased risk of acquiring CAUTI.

Another method of improving patient outcomes with central lines is using a standardized central line bundle kit. This kit includes all of the materials needed to insert a central line, including the supplies to clean the patient with CHG, in addition to the educational material for healthcare workers to reference in order to maximize the success of the insertion [McMullan et al., 2013]. The alternative is that a healthcare professional would gather the supplies themselves and remember the process of inserting a central line [Fenik et al., 2013].

The use of a standardized central line bundle kit is one infection prevention program that has proven to reduce CLABSIs [McMullan et al., 2013, Lee et al., 2018]. The wards of the hospital with the lowest central line kit utilization had the highest

rate of CLABSI, and the ward with the highest utilization of the kit had the lowest rate of CLABSI. Fenik et al. [2013] found that healthcare workers spent less time and wasted fewer materials with the bundled kit than if they obtained the materials together themselves. Upon implementation of the standardized central line bundle kit, McMullan et al. [2013] saw a 59% decrease in CLABSI cases over a five-year period. Allen et al. [2014] also reported a decrease in CLABSIs from 2.72 per 1,000 catheter-days before the intervention to 0.40 per 1,000 over the 37 months following intervention when the standardized kit was incorporated into the care of patients within the ICUs of Fletcher Allen Hospital in Vermont.

CLABSIs and CAUTIs are largely preventable with proper education and maintenance of the patient's device under the care of the patient's healthcare team [MacEwan et al.]. According to Magill et al. [2014], 4% of all hospitalized patients had at least one HAI at the time of their research. In the same study, CAUTIs accounted for 12.9% of all HAIs and CLABSIs accounted for 9.9% of all HAIs [Magill et al., 2014]. However, research by Agency for Healthcare Research and Quality [2019] supports CAUTI (32%) and CLABSI (14%) accounting for 46% of all HAIs.

Although CHG bathing and implementing a standardized central line bundle kit have clinical research support to improve patient outcomes, successful prevention practices are not always put into practice. New practices or improvement of current practices may be rejected by "active resistors", individuals in healthcare leadership positions who can stop initiatives before they start, and by "organizational constipators", healthcare leaders who slow the implementation of a new practice. The ideas may be rejected because infection prevention initiatives may directly contradict mandates given to other divisions, such as reducing supply costs per patient days. Resistance can create unnecessary delays that have large ramifications for patient outcomes as well as the health system's overall fiscal health.

The goal of this chapter is to quantify the costs and predict the number of preventable HAIs associated with the quality and timing of two infection prevention programs. More specifically, I examine how the compliance level of CHG bathing affects annual rates of HAIs and their costs. Additionally, I calculated the number of preventable CLABSI and CAUTI cases and their associated costs when the standardized central line bundle kit and CHG bathing are not immediately put into the routine practice of caring for patients with urinary catheters, central lines, when healthcare leaders delay implementing these prevention practices.

2.2 Mathematical Modeling with Markov Chains, HAIs Prevented and Money Saved

Here, the objective is to track a patient's status throughout their stay in the hospital to keep track of a patient's infection status, whether or not they receive the infection intervention program, and whether they are being admitted or discharged. I note that the timing of events during their stay influence a patient's probability of developing an infection. A Markov chain model was used because infections are probabilistic in nature. So, the outcome for an individual patient is only determined by these probabilities that they received a device, or acquired an infection.

2.2.1 Markov Chain Modeling the Reduction of HAIs with CHG Bathing

A Markov chain model is a mathematical modeling technique consisting of various compartments and the probabilities of transitioning into another compartment. The compartments are chained together with directed pathways where one compartment can transition into another compartment as seen in Figure 1. The current state of the system depends on the conditional probability that an event occurred at the previous time step. I use a discrete Markov chain model where each time step is a single day.

The model incorporates the classes of patients and the daily probabilities that a patient was bathed, discharged or infected. In Figure 1, patient compartments or states are depicted by black boxes and the transitions between the compartments are denoted by the colored arrows. N_j $(j = 0, 1, 2)$ are patients who have not been CHG bathed or become infected. P_j $(j = 0, 1, 2, 3)$ are patients who received a CHG bath j days ago. Patients who have an HAI are in P_I.

The CHG bathing bathing compliance is the daily probability that a patient will receive a CHG bath, and is represented by the blue arrows. When a patient received a CHG bath, they transition into the P_0 class, meaning that the patient just received a CHG bath. The red arrows are the probabilities of being discharged. When a patient is discharged, a new patient is admitted into N_0. The likelihood of getting an HAI is denoted by the yellow arrows.

When a patient gets an HAI, they move into the P_I class where they remain for the rest of their stay. Finally, if a patient is not bathed, discharged, or infected with an HAI on a given day, the patient moves to the next state in the diagram as denoted by the green arrows.

The green arrows transition patients into the $j + 1$ state from where they were previously, except for patients in terminal states of N_2 and P_3. Without receiving a CHG bath, getting an HAI or being discharged, patients in N_2 transition into P_3 and patients in P_3 remain in P_3. This is because a patient's microbiome regenerates after 72 hours, or three days, of injury (such as invasive surgery or an accident) [Howard et al., 2017]. So, a patient who was admitted to the hospital two days ago and a patient who received a CHG bath three days ago both have regenerated microbiomes. However, the probability of getting an HAI is lower for patients in P_3 than for patients in N_2, since they have residual CHG on their skin, which continues to kill bacteria.

The state of the system, $A(t)$, is given by

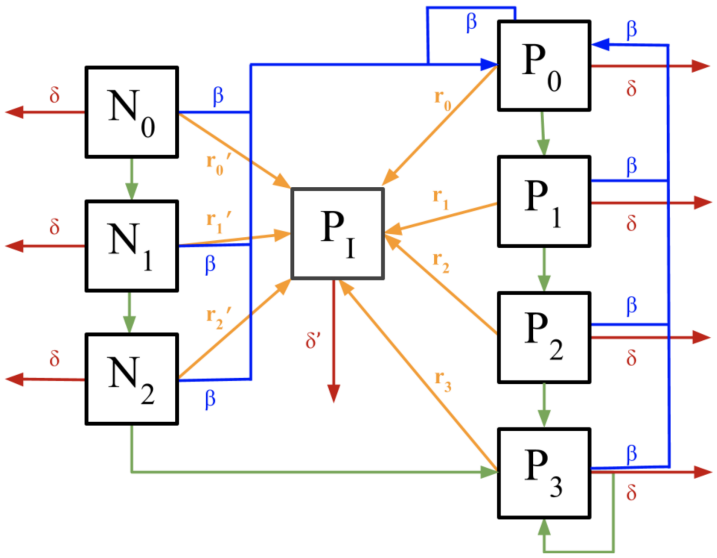

Figure 1 : Markov chain model schematic with all possible patient states and arrows denoting possible transitions between states.

$A(t) = \begin{bmatrix} N_0(t) & N_1(t) & N_2(t) & P_0(t) & P_1(t) & P_2(t) & P_3(t) & P_I(t) \end{bmatrix}^T$. To determine the distribution of patients on day $t+1$, I use

$$A(t+1) = [B][I][D]A(t),$$

where D, I and B are transition matrices that represent the probabilities of being discharged, infected, and bathed for all patient states, respectively. D, the discharge

matrix, is defined by

$$\begin{bmatrix} 1 & \delta & \delta & \delta & \delta & \delta & \delta & \delta' \\ 0 & 1-\delta & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1-\delta & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1-\delta & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1-\delta & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1-\delta & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1-\delta & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1-\delta' \end{bmatrix} \tag{2.1}$$

. I, the infection matrix, is defined by

$$\begin{bmatrix} 1-r'_0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1-r'_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1-r'_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1-r_0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1-r_1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1-r_2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1-r_3 & 0 \\ r'_0 & r'_1 & r'_2 & r_0 & r_1 & r_2 & r_3 & 1 \end{bmatrix} \tag{2.2}$$

. B, the CHG bathing matrix, is defined by

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1-\beta & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1-\beta & 0 & 0 & 0 & 0 & 0 & 0 \\ \beta & \beta & \beta & \beta & \beta & \beta & \beta & 0 \\ 0 & 0 & 0 & 1-\beta & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1-\beta & 0 & 0 & 0 \\ 0 & 0 & 1-\beta & 0 & 0 & 1-\beta & 1-\beta & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix}. \tag{2.3}$$

δ is the discharge rate for $N_0, N_1, N_2, P_0, P_1, P_2, P_3$ and δ' is discharge rate for P_I, which was assumed to be lower due to the HAI. r_i and r_i' are the infection rates. Specifically, $r_i = (1 - \frac{(3-i)\alpha}{3})r$ for $i = 0, 1, 2, 3$ and $r_i' = \eta r_i$ for $i = 0, 1, 2$, $\eta \in [0, 1]$, where α is the CHG bathing effectiveness and η is a newly admitted patient's resistance to infection with their unaltered microbiome. β is the CHG bathing compliance rate.

The costs associated with giving patients CHG baths are calculated based upon the number of patient baths given, and is calculated by tracking the number of patients who entered P_0 at every time step. The number of HAIs are calculated by counting all of the patients who entered P_I. The total cost calculation include costs related to bathing materials and the costs associated with HAIs.

2.2.2 Potential Annual Savings and Prevented HAIs

To quantify the impact of incorporating CHG bathing as an infection prevention practice, the transition rates in Table 2 are estimated from two years of data from Virginia Commonwealth University (VCU) Medical Center in Richmond, VA. This

data includes the average observed incidence rate of 1.025 cases per 1,000 patient days for CLABSI, CAUTI, and CDI in 2017 and 2018 [Bearman et al., 2018]. VCU Medical Center recorded an average total of 318 CAUTIs, CLABSIs and CDIs between 2017 and 2018.

The estimated average reduction in the probability of acquiring an HAI due to CHG bathing, $\alpha = 32\%$, was based on the reductions of risk of HAIs in Frost et al. [2016] and Huang et al. [2016]. r is calculated with a baseline compliance rate of 60% and the effect of CHG bathing on the reduction of incidence of CLABSI, CAUTI, and CDI [Frost et al., 2016, Huang et al., 2016]. The baseline compliance rate of 60% is estimated to be the average compliance rate of CHG bathing followed at VCU Medical Center.

In order to calculate the costs of implementing CHG bathing, K. Gurney from VCU Medical Center prices one CHG bath to cost \$5.71 (personal communication, October 18, 2018). Patients who do not receive a CHG bath on a given day were assumed to receive a bath with non-CHG wipes, which costs \$1.16 per bath, as priced by K. Gurney (personal communication, October 18, 2018). Each specific HAI has an individual cost to the hospital. On average, I assume an HAI costs the hospital \$45,000 as presented by Dancer [2014].

The simulations were run in MATLAB for 100 days before calculating the results for 365 days at steady state with 850 patients in the hospital. The time step was one day. Costs were calculated using \$5.71 for one CHG bath on one patient, \$1.16 for a non-CHG bath for one patient and \$45,000 if a patient got an HAI. If a patient did not receive a CHG bath, then they received a non-CHG bath. The number of daily CHG baths, non-CHG baths and HAIs were tracked over one year and the costs were totaled for each 10% CHG bathing compliance rate.

The results show the impact of increasing the CHG bathing compliance on the

Parameter	**Symbol**	**Value**
Daily probability of infection	r	0.00134 (32% effectiveness)
CHG bathing effectiveness	α	0.32 HAIs per day
Unaltered microbiome resistance	η	0.95 per day
Discharge rate for all classes except P_I	δ	0.2 patients per day
Discharge rate for P_I	δ'	0.1 patients per day

Table 2 : Parameter values used in the Markov chain model simulations with CHG bathing compliance is increased in 10% increments.

number of HAIs and the amount of healthcare costs saved. In Figure 2, every 10% increase in CHG bathing compliance results in about 10 HAIs prevented. Additionally, Figure 3 shows that every 10% increase in CHG bathing compliance would result in about $450,000 saved per year.

Assuming 90% is an attainable compliance rate to reach, increasing the CHG bathing compliance from 60% to 90% incurs an additional cost of $106,291.65 spent on CHG bathing wipes. However, at 32% reduction in HAI incidence, increasing the compliance rate from 60% to 90% results in 20 averted infections and $815,301.75 saved cost. Further, based on the HAI mortality rate of 15%-25%, approximately 5 lives will be saved [O'Horo et al., 2012].

2.2.3 Markov Chain Modeling and the Timing of Implementing Infection Prevention Programs

Unfortunately, it is not always straightforward to change hospital practices. Active resistors and organizational constipators are individuals in leadership positions who block change, delay adoption of best practices, and inhibit new prevention protocols from being implemented in hospital systems. A strategy to overcome active

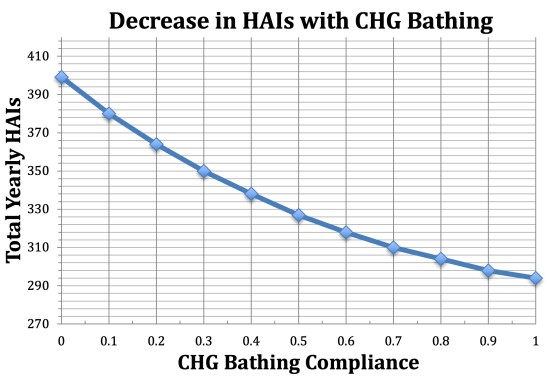

Figure 2 : The decrease in yearly HAIs at 32% reduction in incidence due to CHG bathing with an increase in CHG bathing compliance.

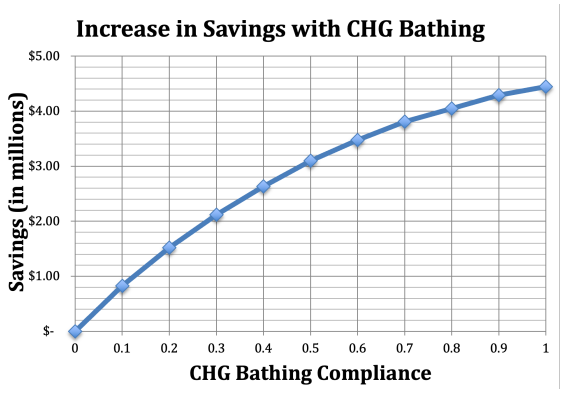

Figure 3 : The increase of overall savings with a 32% reduction in incidence due to CHG bathing by increasing CHG bathing compliance from 0%.

resistors is to present data and scientific evidence supporting a new practice over the current practice.

To quantify the impact of active resistors and organizational constipators, the Markov chain model is expanded to focus on the delay of implementation of CHG bathing and the use of the standardized central line bundle kit, and examine this delayed effect on CLABSIs and CAUTIs. Patient compartments are modified to include patients with urinary Foley catheters (foleys), central lines, both and neither devices. CHG bathing reduces incidence of CLABSI and CAUTI because of its antimicrobial properties that fight harmful bacteria [Donskey and Deshpande, 2016]. The standardized central line bundle kit reduces incidence of CLABSI because it provides everything that a healthcare worker needs in order to successfully and sanitarily insert a central line [McMullan et al., 2013, Lee et al., 2018].

In this model, there are different patient types: newly admitted patients without a central line or foley, N, patients without a central line or foley and are not newly admitted, O, patients with a central line and have not received a new central line

with the standardized kit in i days ($i = 0, 1, 2, 3$), C_i, patients with a foley and have not had a CHG bath in i days ($i = 0, 1, 2, 3$), F_i, and patients with both a central line and a foley and have not received wither a new central line or a CHG bath in i days ($i = 0, 1, 2, 3$), T_i. It is assumed that the effectiveness of the intervention program decreases each day until $i = 3$, when the altered microbiome regenerates [Howard et al., 2017]. If a patient receives a device during their hospital stay, then they move to the $i = 0$ subclass. Patients with central lines may acquire CLABSI, and patients with foleys may acquire CAUTI. U, B and I patient classes have CAUTI, CLABSI or both CAUTI and CLABSI respectively. Patient compartments are denoted by the black boxes in Figure 4.

Patients with CLABSI or CAUTI may develop a secondary infection of the other type. Patients may also acquire both infections within the same day. Additional infections beyond acquiring CAUTI and CLABSI are not considered. If a patient acquires an infection, their transition is denoted by the red arrows in Figure 4. If a patient does not acquire a new infection or utilize a new intervention, then the patient moves to the $i + 1$ version of the same class, as they did in the general HAI Markov chain model. If the patient has an infection or is within the circulating class, O, the patient stays within their class as indicated in Figure 4 by the purple arrows. If a patient is discharged, as indicated by the green arrows, then a new patient is admitted into N. If a patient gets a device, then they move into C, T or F as indicated by the gold arrows.

The distribution of patients in each class at each time step, t (number of days), is given by the state vector

$$X(t) = [N(t), O(t), C_0(t), C_1(t), C_2(t), C_3(t), F_0(t), F_1(t), F_2(t), F_3(t), ... \\ T_0(t), T_1(t), T_2(t), T_3(t), B(t), U(t), I(t)].$$

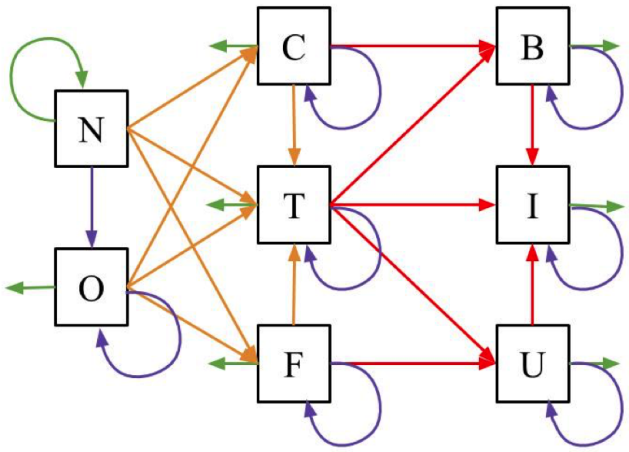

Figure 4 : A flow diagram of the model. The gold arrows, ρ_p, indicate a patient getting a device. The red arrows, r, show patients acquiring an infection. The green arrows, δ_w, are patients being discharged. The purple arrows are the patients' progression through the diagram if the patient does not receive any actions.

The distribution of patients on day $t+1$ is defined by the state vector $X(t+1) = [B^*][I^*][P^*][D^*]X(t)$, where B^*, I^*, P^*, and D^* are transition matrices. In particular B^* represents patients receiving a CHG bath or obtaining a new standardized central line kit. I^* represents the probability of patients getting an infection. P^* represents the probability of getting a central line or foley, and D^* is the transition matrix for being discharged.

The patient's average length of stay, $\frac{1}{\delta_w}$, differs for each class w. The daily probability of getting an intervention p, ρ_p, is calculated using, $\rho_p = 1 - (1 - K)^{\delta_w}$, where K represents the percentage of hospitalized patients with intervention p. It is assumed that getting a catheter and getting a central line are independent events.

The infection rate, r, is calculated with a baseline compliance rate of 60% CHG bathing and with the pre- and post-intervention values of the standardized kit. The reduction of incidence of CAUTI and CLABSI due to CHG bathing is represented by η. The reduction of CLABSI due to the standardized kit is represented by κ. The

equation for r for those with central lines or both devices is $r_i = (1 - \frac{(3-i)\eta\kappa}{3})r$ for $(i = 0, 1, 2, 3)$. The equation for r for patients with catheters is $r_i = (1 - \frac{(3-i)\eta}{3})r$ for $(i = 0, 1, 2, 3)$. Chlorhexidine's antimicrobial agents can last on the skin for up to 48 hours and it is assumed that the effectiveness of the CHG reduced the longer it has been on the skin, which is why the infection rate increases with each day since the patient received a CHG bath or since the patient was first admitted [Ilango et al., 2013, Donskey and Deshpande, 2016].

2.2.4 Number of CLABSIs, CAUTIs and Total Cost Due to Delaying Best Practices

Overall, I calculate the impact of active resistors and organizational constipators on yearly CLABSIs and CAUTIs by looking at the changes to annual number of HAIs and associated costs. In the Markov chain model, I estimate the values for r_i, r_k, η, κ and r (see Table 3 for values) by running simulations to mimic data from VCU Medical Center before both interventions. The parameters η and κ were estimated based upon the reduction of incidence of the infection prevention programs on CLABSI and CAUTI. Prior to the standardized central line bundle kit and CHG bathing interventions, there were 80 CLABSI and 39 CAUTI infections annually at VCU Medical Center. The probability of a patient developing CAUTI was 0.1257 per 1000 patient days and 0.2579 per 1000 patient days for CLABSI. The simulations were run in MATLAB R2018b with time steps of one day. The results are based on simulations run for 100 days to reach steady state and then calculated for 365 days with 850 patients.

The Markov chain model simulations were run with parameter values associated with patients with central lines and foleys. The specific values from literature used to calculate δ_w and ρ_p are presented in Table 3, which also contains the calculation

for the infection rates, r.

Monetizing the impact of the delay of infection prevention programs on CLABSIs and CAUTIs includes costs related to CHG bathing materials for CAUTI, the standardized central line bundle kit for CLABSI, and the costs associated with HAIs. The costs used in this project are different from the previous project because they were updated at the time of completing the project. In this study, the updated cost for one CHG bath costs $8.47 (US dollars). Patients that do not receive a CHG bath on a given day were assumed to receive a bath with non-CHG wipes that cost $2.47 per bath. The non-centralized central line bundle costs $0.04 more due to the compilation of necessary supplies needed to insert a central line compared to the standardized central line bundle kit. On average, I assumed that a CAUTI infection costed $13,793 [Agency for Healthcare Research and Quality, 2017] and a CLABSI infection costed $70,696 [Agency for Healthcare Research and Quality, 2013]. The total cost calculation includes the number of CHG baths given, the number of non-CHG baths given, the number of standardized central line bundle kits used and the costs associated with getting CAUTI and CLABSI over one year.

Implementation of CHG bathing and the standardized central line bundle kit, and the associated costs, are simulated to be initiated in increments of six-month delays, and compared to no implementation over 5 years. Simulations were run for the desired delay amount without either infection prevention program, then once the time delay was reached, the programs were implemented hospital-wide at 100% compliance. Overall, as the delay in implementation for the infection intervention programs increases, the number of HAIs increases as seen in Figure 5, and the associated savings in healthcare costs by implementation decreases seen in Figures 6 and 7. When a linear trend line is fit to the results, every six-month delay in improvement of CHG bathing compliance results in about 11 preventable CAUTIs and an additional

Parameter	**Parameter Symbol**	**Parameter Value**	**Source**
Discharge rate for patients with central lines	δ_{CL}	0.0556	[Dube et al., 2020]
Discharge rate for patients with CAUTI	δ_{CAUTI}	0.0556	[Al-Hazmi, 2015]
Discharge rate for patients with central lines and catheters	δ_{both}	0.0556	[Dube et al., 2020]
Discharge rate for patients with CLABSI	δ_{CLABSI}	0.0417	[Dube et al., 2020]
Discharge rate for patients with catheters	δ_{CATH}	0.1	[Al-Hazmi, 2015]
Discharge rate for all other patients in the hospital	δ_{Other}	0.2	[Baek et al., 2018]
Probability of getting a central line	ρ_{CL}	0.01232	[Chopra et al., 2014]
Probability of getting a catheter	ρ_{CATH}	0.01270	[Carrouget et al., 2017]
Probability of getting both a central line and a catheter	ρ_{Both}	$1.565*10^{-4}$	[Chopra et al., 2014] [Carrouget et al., 2017]
Actual infection rate for those who have received a central line or both devices in i days	r_i	$(1-\frac{(3-i)(\eta+\kappa)}{3})r_*$	Estimated based upon data
Actual infection rate for those who have received a catheter k days ago	r_k	$(1-\frac{(3-i)\kappa}{3})r_\#$	Estimated based upon data
Reduction of incidence of CAUTI and CLABSI due to CHG bathing	η	0.11	Estimated based upon data
Reduction of CLABSI due to the standardized kit	κ	0.49	Estimated based upon data
Base infection rate for patients with central lines or both devices	r_*	$4.5*10^{-9}$	Estimated based upon data
Base infection rate for patients with catheters	$r_\#$	$1.15*10^{-10}$	Estimated based upon data

Table 3 : Parameter values used in the Markov chain model simulations to quantify the impact of resistors and constipators on CLABSIs and CAUTIs.

cost of $11,000. Every six-month delay in implementing the standardized central line bundle kit results in about 10 CLABSIs and an additional $715,000 in costs.

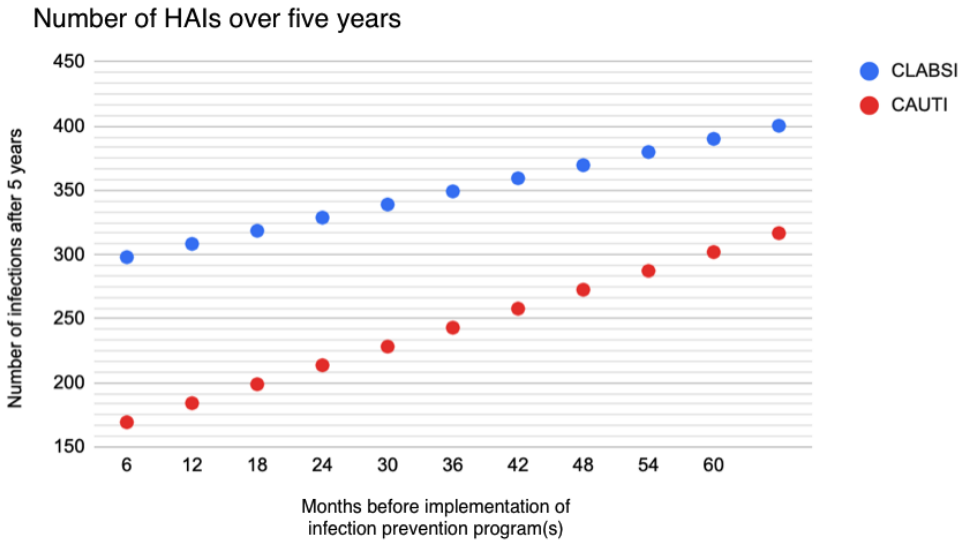

Figure 5 : Number of infections over five years when the infection prevention program is delayed by x months. The number of CAUTIs over five years is represented by the red data points, and the number of CLABSIs over five years is represented by the blue data points.

2.3 Conclusions

Delaying implementation of infection prevention initiatives leads to increased HAIs and total associated healthcare costs. If more expensive intervention strategies reduce infections, such as with CHG bathing, the strategies may end up saving healthcare costs. When the standardized central line bundle kit and CHG bathing are immediately implemented, healthcare systems comparable to VCU Medical Center can prevent approximately 200 HAIs. Each monthly delay led to decreases in total associated healthcare savings. There were less overall savings for CAUTI infections due to the $6.00 difference with the implementation of CHG compared to a $0.04 difference for the standardized central line bundle kit. Also, the healthcare costs dealing

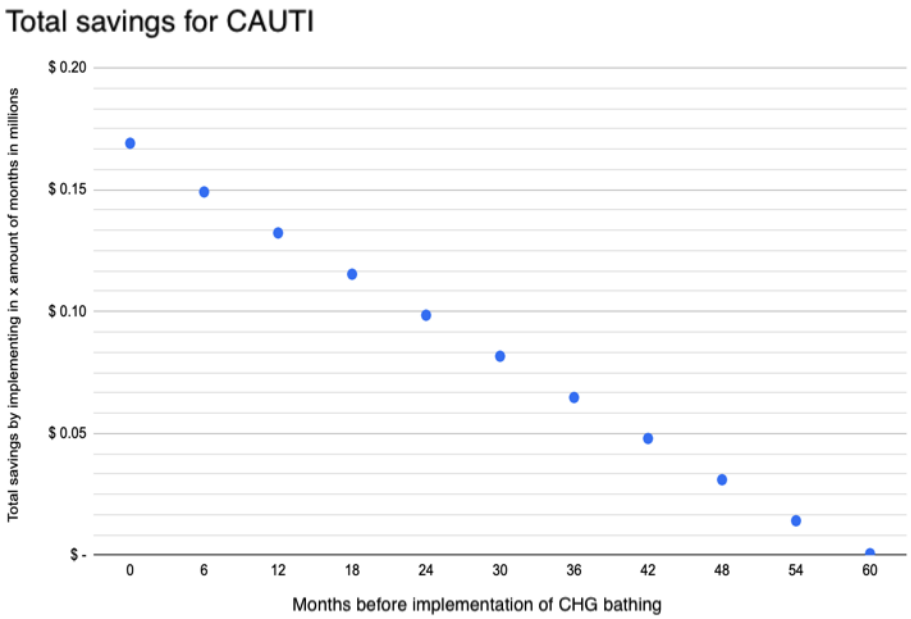

Figure 6 : Amount of savings over five years when the use of CHG bathing is delayed by x months. As the number of months to implement the infection prevention programs increases, the potential cost savings decreases.

with a CAUTI were less than for CLABSI.

The role of active resistors and organizational constipators in implementing CHG bathing and the standardized central line bundle kit had a dramatic impact on healthcare costs and patient outcomes. The model was limited by the assumptions, such as not including educational and monitoring costs or considering varying levels of compliance, but allowed for predictions and quantitative analysis of immediate or delay in implementation of CHG bathing and the standardized central line bundle kit.

Using Markov chain modeling to simulate the impact of CHG bathing and the standardized central line bundle kit allowed me to estimate results that would have been otherwise unethical to perform in a clinical setting. Additionally, performing all of the simulations as clinical studies would have taken years to complete, and would have required researchers to make sure that other infection intervention programs

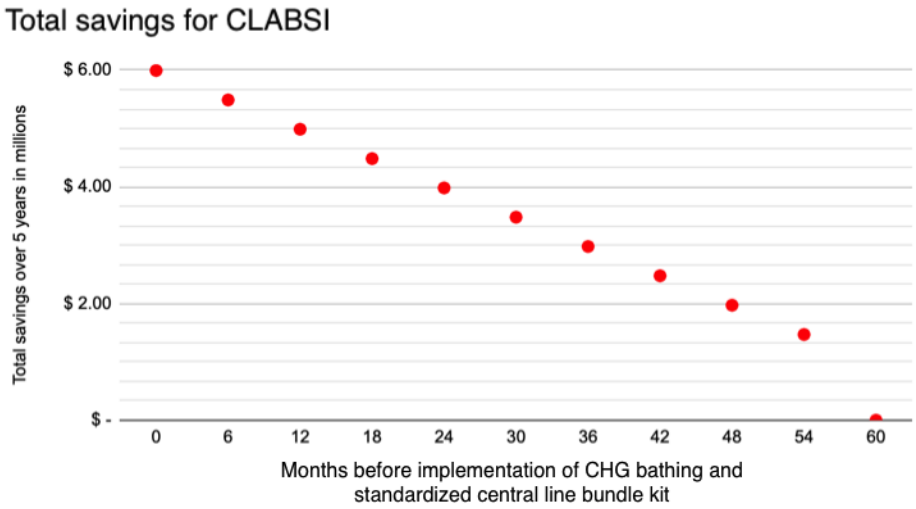

Figure 7 : Amount of savings over five years when the use of CHG bathing and the standardized central line bundle kit is delayed by x months. As the number of months to implement the infection prevention programs increases, the potential cost savings decreases.

were not introduced during the study period. The mathematical simulations allowed for the programs to be isolated without confounding variables affecting the results.

With only a few extra dollars spent on each patient, thousands of dollars can be saved over the span of years. Also, applying the standardized central line bundle kit and/or CHG bathing to any patient reduces the risk of developing HAIs, which reduces the amount of time that a patient spends in the hospital. Reducing a patient's length of stay allows the hospital to see more patients and reduce healthcare costs.

CHAPTER 3

FLATTENING THE CURVE

3.1 Introduction

Highly contagious diseases require public health officials to develop and enforce prevention programs within communities to reduce the burden that these diseases have. Some highly contagious diseases include norovirus (stomach flu), influenza, meningitis, hand, foot and mouth disease, pertussis (whooping cough), sexually transmitted infections, Methicillin-resistant staphylococcus aureus (MRSA), tuberculosis and severe acute respiratory syndrome coronavirus 2 (COVID-19). Some prevention programs are not resource intensive, such as encouraging people to wash their hands and to stay home if they are feeling sick. Other programs, such as vaccines, require extensive research and supplies in order for the programs to be effective in preventing transmission.

During outbreaks of highly virulent diseases, various intervention strategies may be implemented to reduce disease spread and "flatten the infection curve." Flattening the curve allows for smaller peaks of infections, that are often delayed. This is critical for the success of healthcare services. Not only do these strategies allow for more time to prepare for the influx of patients, but caring for a smaller number of patients at one time prevents healthcare providers and systems from being overwhelmed.

Consider a population broken up into two components: a smaller subset of the community where an intervention strategy is lost, and large city or small country where an intervention strategy is implemented. Examples of the smaller subset are schools, religious centers, healthcare facilities, nursing homes, jails or homeless shel-

ters.

For example, schools could be considered to be a small subset of a community. Schools may lose a mask mandate that required the faculty and the students to wear a protective mask during the day. Alternatively, schools may also lose adequate air circulation or the air quality might be reduced if proper circulation systems cannot be afforded or if the school has to close windows during the winter. The remainder of the community, the larger subset, may have to follow a mask mandate when they are outside of their homes or be required to social distance (maintain at least six feet apart from other people).

In the example of a community with a large religious organization as the smaller subset, the religious center may also act as a school, a shelter or a meeting place. The religious center may lose its ability to keep safe distance between people during large events or if there was an increased need to shelter people. Then, in the remainder of the community, the larger subset, a vaccine could be introduced.

My research considers the case of dividing the community into hospitals and the general population in application to studying a future highly virulent strain of COVID-19. COVID-19 is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [WHO, 2020]. Common symptoms are respiratory infections, fever and dry cough [WHO, 2020]. Patients usually develop symptoms within twelve days [Lauer et al., 2020]. The virus is contracted from other infectious individuals from direct contact with mouth or nose droplets [WHO, 2020], and from a person touching an infected object or surface [Lauer et al., 2020].

One COVID-19 prevention program is social distancing. Social distancing involves maintaining a minimum of six feet between people and is recommended to help stop the spread of the virus. It is not resource-intensive and is effective in reducing the spread of COVID-19 [Nanotkar et al., 2020]. Caley et al. [2008] showed that

social distancing was effective during the Spanish Influenza of 1918. Approximately 260 per 100,000 lives were likely saved as a result of social distancing [Caley et al., 2008]. Social distancing is critical in preventing infections when there exist asymptomatic carriers within a community [Whitehead and Feibel, 2020, Wilder-Smith and Freedman, 2020].

Another infection prevention program that reduces the transmission of many infections is the use of personal protective equipment (PPE). The Occupational Safety and Health Administration recommends that all healthcare workers protect themselves with PPE when interacting with infectious patients. PPE are any pieces of equipment worn in order to reduce injury or illness due to hazards in the workplace [OSHA, 2020]. In the specific case of studying COVID-19, goggles or face shields, facemasks and gloves are all recommended by the CDC as PPE to prevent the transmission of the virus [Centers for Disease Control and Prevention, 2020]. Contact precautions or airborne precautions (depending on the patient) and eye protection should all be utilized to prevent the spread of the virus [OSHA, 2020], as well as standard precautions like washing hands. The demand for PPE increases as COVID-19 becomes more prevalent.

This research focuses on the timing of initiation and termination of social distancing in the general community and PPE use in hospitals, and how these affect the total number of COVID-19 cases. Previous studies reported combinations of disease control methods are most effective in reducing the transmission of COVID-19 [Patiño-Lugo et al., 2020, Nussbaumer-Streit et al., 2020]. Additionally, assuming early control of the epidemic, I considered the results of removing social distancing restrictions. Overall, I analyzed the impact of these intervention strategies on the total number of infections on a scale of a small country.

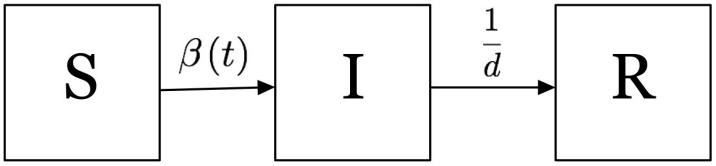

Figure 8 : SIR model diagram with transition rates $\beta(t)$ and $\frac{1}{d}$.

3.2 Mathematical Modeling

The focus on this study is to examine the effect of the removal and start of intervention strategies. In particular the implementation of social distancing on the general public, and the loss of PPE in healthcare facilities. To accomplish this, I use a simple Susceptible-Infected-Recovered (SIR) model with a time-dependent infection rate, $\beta(t)$. The model to calculate the total number of COVID-19 cases is given by,

$$\begin{aligned} \frac{dS}{dt} &= -\beta(t)SI \\ \frac{dI}{dt} &= \beta(t)SI - \tfrac{1}{d}I \\ \frac{dR}{dt} &= \tfrac{1}{d}I, \end{aligned} \tag{3.1}$$

where d represents the length of time individuals remain infectious.

The infection rate, $\beta(t)$, is defined to be

$$\beta(t) = \beta_1(t)H + \beta_2(t)(1 - H), \tag{3.2}$$

where H is the weighted proportion of the infection rate parameter that is due to the infections within the hospital. β_1 and β_2 are defined as

$$\beta_1(t) = \begin{cases} \beta_h E_h, & t \leq T_h \\ \beta_h, & t > T_h \end{cases}, \tag{3.3}$$

and

$$\beta_2(t) = \begin{cases} \beta_s, & t \leq T_s \\ \beta_s E_s, & t > T_s \end{cases}, \tag{3.4}$$

where β_h and β_s are the base infection rates in the hospital setting and outside hospitals, respectively. E_h is the effectiveness of PPE in hospitals, and E_s is the effectiveness of social distancing in preventing the spread of the disease. T_h is when hospitals run out of effective PPE. T_s is the initiation time of social distancing.

The proportion of infections due to hospital transmission varies by community. This proportion is likely to be much smaller in countries with efficient and properly staffed healthcare systems than in countries where that is not the case, and the hospital or healthcare facilities could be the main hub of transmission. The effectiveness of PPE, E_h, may vary with the quality of PPE as well as with proper or repeated use. The effectiveness of social distancing, E_s, is likely to vary dramatically between and within communities based on how seriously the local population follows recommended or mandated mitigation strategies. The values of E_h and E_s were varied.

Figures 9 and 10 give examples of the infection parameter $\beta_1(t)$, $\beta_2(t)$, and β when social distancing starts on day 45 and 105 ($T_s = 45,\ 105$), respectively, and hospitals run out of PPE on day 100 ($T_h = 100$). In this example, the weighted proportion of the infection rate parameter that is due to the infections within the hospital, H, is 15%. In Figure 9 initially β is large since there is no social distancing, and then decreases, once social distancing starts. After β drops, due to the start of social distancing, it rises again after the hospitals run out of PPE.

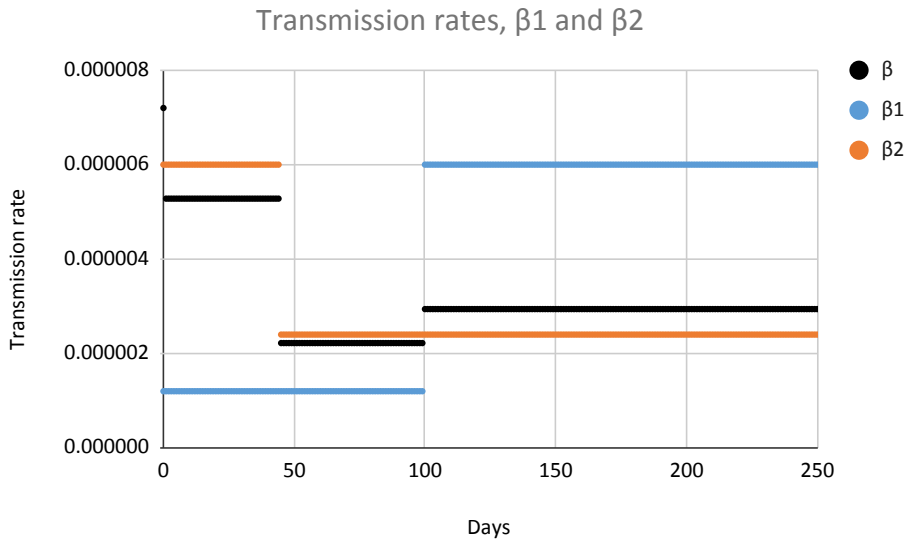

Figure 9 : Social distancing begins at 45 days with modest effectiveness level and PPE are lost at 100 days.

3.3 Results

To examine the effects of these intervention strategies, the simulations are divided into three categories of effectiveness of social distancing: high (75%, $E_s = 0.25$), moderate (60%, $E_s = 0.4$) and modest (40%, $E_s = 0.6$). Social distancing is simulated to be initiated at different points in time, T_s, after 45, 60, 75, 90 and 105 days of the initial outbreak. These initiation times are chosen based on the peak number of infectious individual occurred around 100 days. I assume the effectiveness of PPE was 80% ($E_h = 0.2$). To explore the loss of PPE, I consider the cases where there is an early loss of PPE at 50 days ($T_h = 50$), and a loss near the peak of the number of infectious individuals at 100 days ($T_h = 100$). It is assumed that once PPE run out, supplies are not replenished to any significant degree within the time frame of the simulations. I also assume for convenience that $\beta_s = \beta_h$.

The initial conditions are $S(0) = 4,500,000$, $I(0) = 2$, $R(0) = 0$ to simulate two cases being introduced into a small country in an outbreak situation. To solve the

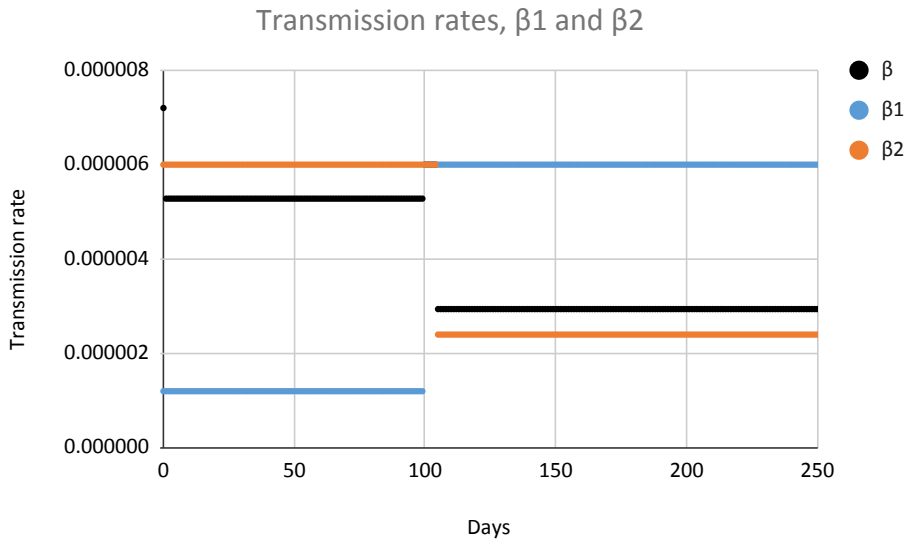

Figure 10 : Social distancing begins at 105 days with modest effectiveness level and PPE are lost at 100 days.

system of ODEs, the equations were discretized in Microsoft Excel with time steps of one day and Forward Euler's Method was applied. The system of ODEs was also solved in MATLAB using `ode15s`. The simulations are run for 530 days to capture the dynamics over the course of a year and a half.

Parameters are chosen to exhibit a peak in the infectious class occurring around 100 days without using any intervention strategies. I also assume that individuals would be infectious for two weeks, and that infections occur between close proximity between individuals. It is possible that a disease like COVID-19 may be transmitted through contact with surfaces, though I assume that social distancing and the use of proper PPE will dramatically reduce the spread through close proximal vicinity including transfer through surfaces.

The spread of COVID-19 is complex in many respects. Many individuals are asymptomatic [Whitehead and Feibel, 2020]. Spread can occur between individuals in close proximity through the air, or through contact to surfaces where the virus can

remain over time [WHO, 2020]. Due to many factors including the inability to conduct widespread testing, it is difficult to estimate infection rates. Additionally, rates found in the literature vary over a wide range of values [Mandal et al., 2020, Zhang et al., 2020, Roda et al., 2020, Cherniha et al., 2020]. Roda et al. [2020] specifically mentioned that modeling parameters and results vary because of the uncertainty of when the outbreak began, the complexities in defining who is infected with COVID-19, and the wide range in the case-infection ratio [Roda et al., 2020]. In retrospect, patients did not contract COVID-19 from healthcare facilities at high rates during the initial outbreak of COVID-19 [Pryor et al., 2022]. Due to this, I consider a future virulent strain of COVID-19.

3.3.1 Highly effective social distancing

Individuals need to obtain food and other goods, and at times medical care, which makes social distancing impossible to achieve at extremely high percentages. In this situation I assume highly effective social distancing reduces the infection parameter by 75%. Figure 11 shows that postponing social distancing results in a dramatic increase in the peak number of infections. Starting social distancing before day 75 results in a peak of approximately 225,000 infections, whereas after 75 days, peaks of 1,000,000 infections or more occur. Delays in peaks allow for healthcare agencies both time to prepare and with lower peaks the ability to better handle the patient load.

Comparing β in Figure 9 and 10, it is clear what the effect of a delayed social distancing from initiating on day 45 in the former and on day 105 in the latter has on the transmission rate. The former situation has a lower overall β between day 45 and 105. This decrease in β during this time results in the delay in the peak infections seen in Figure 11. In general initiating social distancing 15 days earlier results in a

delay in the peak by almost 100 days, unless social distancing starts near 100 days in which the peak occurs early.

Similar results are seen in Figure 12 where the overall percentage of people who become infected rises well above 50% when social distancing starts after day 75. This quickly becomes over 90% of the population having been infected in most cases where social distancing is started after 90 days. Also seen in Figure 12 is the importance of hospital protocols and PPEs where there is high hospital transmission. In the case with low transmission and early social distancing, as seen by the red and blue curves in Figure 12, the epidemic can be controlled to very low levels when social distancing begins before 70 days. Starting social distancing later, such at 100 days, abates the effect of hospital transmission since eventually each situation eventually reaches the same effective β.

Figure 12 shows the effects of losing PPE. For low hospital transmission the percent eventually infected drops 3% to 10% for a given day of initiation of social distancing. In the high hospital transmission case the percent can drop nearly 20% in some instances. However, when initiation starts early or very late there is nearly no difference between the early loss of PPE on day 50, or when PPE are lost near the peak of the infection on day 100.

3.3.2 Moderately effective social distancing

In the case with moderately effective social distancing, with a reduction of 60% in the infection parameter ($E_s = 0.4$), I see in some cases more than twice the size in infection peaks than in the highly effective case, see Figure 13. This decrease in the effectiveness results in the peaks with early social distancing range from 550,000 to 600,000 individuals, whereas the with late social distancing the peaks are again over 1,000,000. Overall this is a significant rise in the peak number of cases with this drop

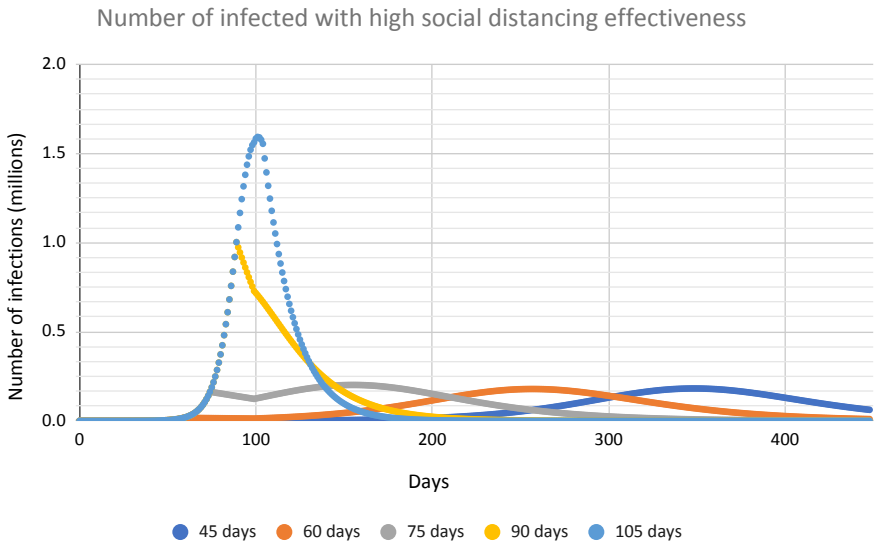

Figure 11 : The social distancing effectiveness is 75%, hospital transmission is 15% and the hospital runs out of PPEs at 100 days.

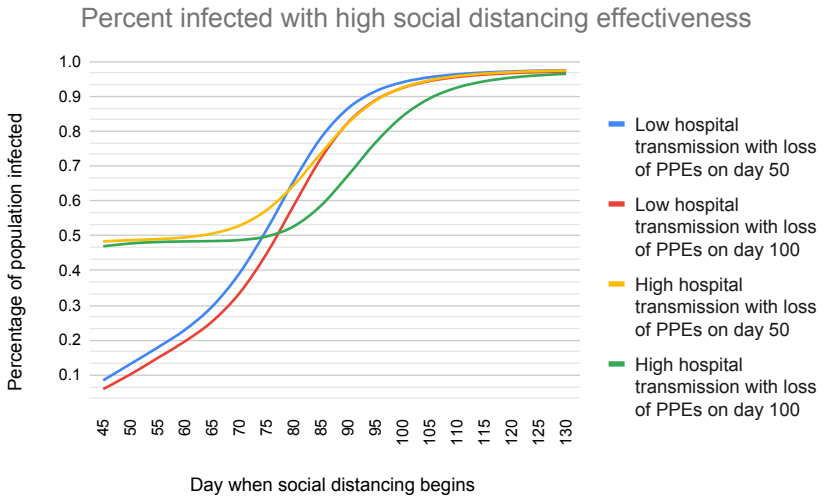

Figure 12 : The percentage of the total population infected when social distancing has a high effectiveness level.

in effectiveness.

There are still delays in the peak with early initiation of social distancing, though the delays are noticeably shorter. In the highly effective case the peaks occurred around 340, 250, and 150 days for social distancing initiation occurring on day 45, 60 and 75, respectively. In the moderately effective scenario the peaks occur approximately on days 200, 170 and 140. Overall these peaks are delayed by approximately a month for implementing 15 days earlier. This is around a third of the delay in the highly effective case.

In Figure 14, around day 85, there is an increase in the percentage of the population infected eventually by the virus. However in this case, due to the effectiveness of social distancing, the benefits to the overall percentage of infected are reduced where a majority of the population will eventually become infected. The effect of low and high hospital transmission are relatively small.

The effect of losing PPE is evident in Figure 14 where under low hospital transmission a reduction of 3% to 5% is typical depending on the day of initiation of social distancing. In the case of high hospital transmission the percent reduction may range as large as 13%, though again there is little effect whether initiation occurs early or late.

Modest effective social distancing

For modest effective social distancing, 40% effective ($E_s = 0.6$), the overall effect are unsurprisingly relatively small. In Figure 15 the number of infections at the peak are at or above 1,000,000 individuals. It is interesting to observe that there is a small increase in the peak number of infections with an earlier delay in initiation of social distancing. The cause of the increase in the size of the peak is due to the higher infection rate that occurs after day 100, and the fact that on day 100 there is a larger

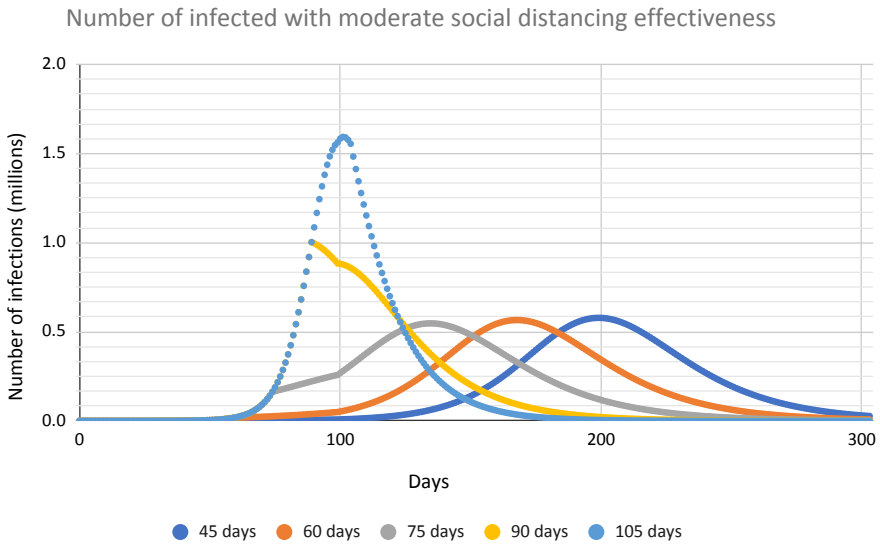

Figure 13 : The social distancing effectiveness is 60%, hospital transmission is 15% and the hospital runs out of PPEs at 100 days.

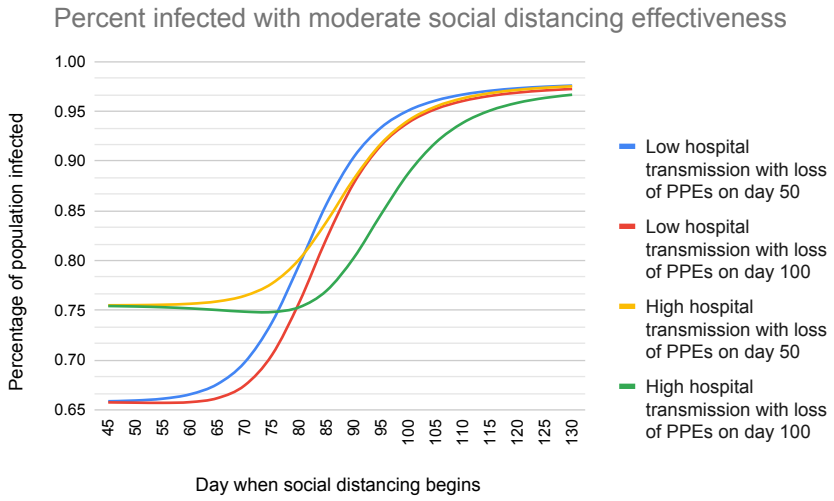

Figure 14 : The percentage of the total population infected when social distancing is moderately effective.

susceptible population for the situations with earlier initiation, see Figure 15.

The delay in peak infectious individuals exhibited here is on the order of about 10 days for each 15 day increment of earlier initiation of social distancing. This delay can be important in order to prepare, though the with large scale of the peaks of infectious individuals the benefits are small compared to the cases of moderate and high effectiveness.

In Figure 16 nearly the entire population acquires the infection. The effect of high and low hospital transmission and when the low of PPE occur is relatively small when compared to the entire population, though the trends are similar to the other cases. There is a dip in the percentage of infected with the delay in loss of PPE on day 100, this is again due to the higher infection rate on a large susceptible population.

3.3.3 Impact of terminating social distancing

Finally, I examine the situation where social distancing is terminated after being initiated. In particular, I consider the case where social distancing starts on day 45 and then is terminated on days 150, 200, 250, and 300. The results are seen in Figure 17.

In each case of termination, a relatively large peak soon follows the termination. Without termination the peak is a little over 200,000, though the peak grows to over 1.5 million with early termination after 150 days, and to near 700,000 for the late termination on day 300. Each additional delay of 50 days does have noticeable drop in the peak as well as a delay in the timing of the peak.

Figure 18 shows that the earlier that social distancing is terminated, the higher the percentage of the population is infected when social distancing begins at day 45. There are modest differences in the low and high hospital transmission cases. This does show that ending social distancing before day 300 results in about 90% of

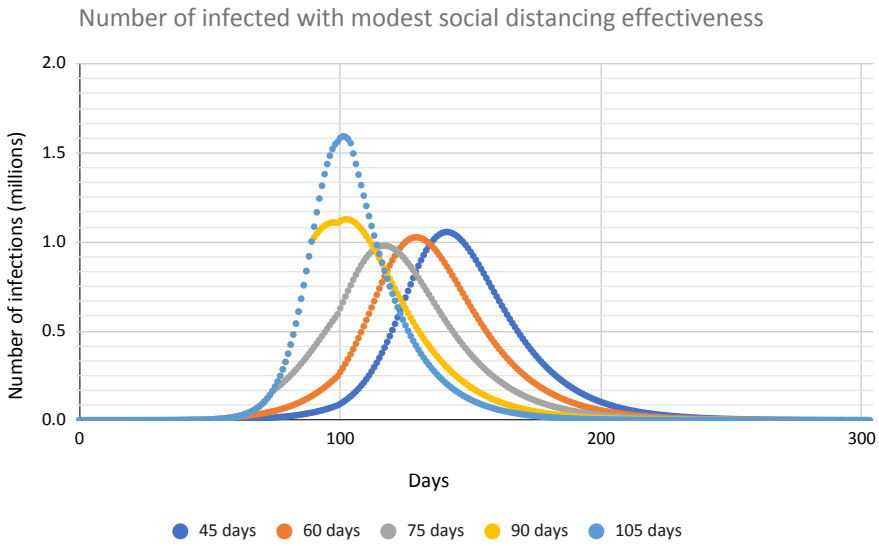

Figure 15 : The social distancing effectiveness is 40%, hospital transmission is 15% and the hospital runs out of PPEs at 100 days.

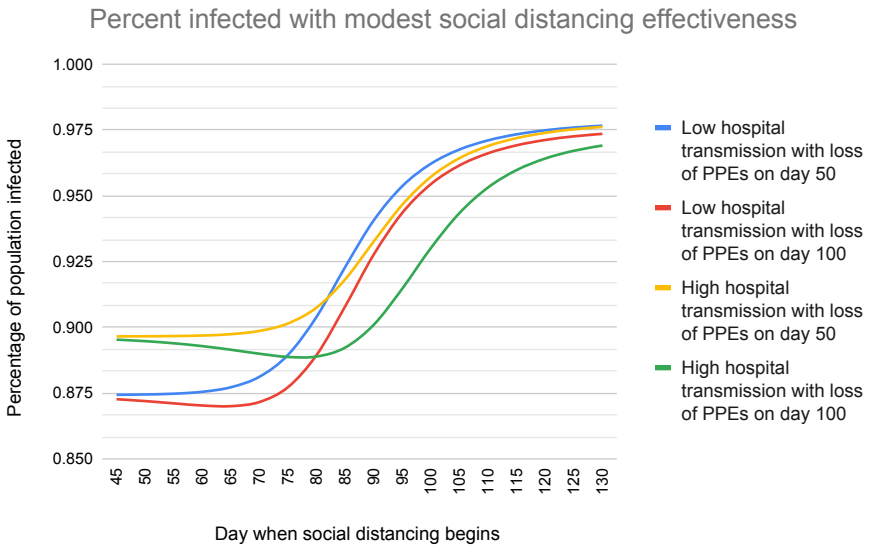

Figure 16 : The percentage of the population when social distancing has a modest effectiveness level.

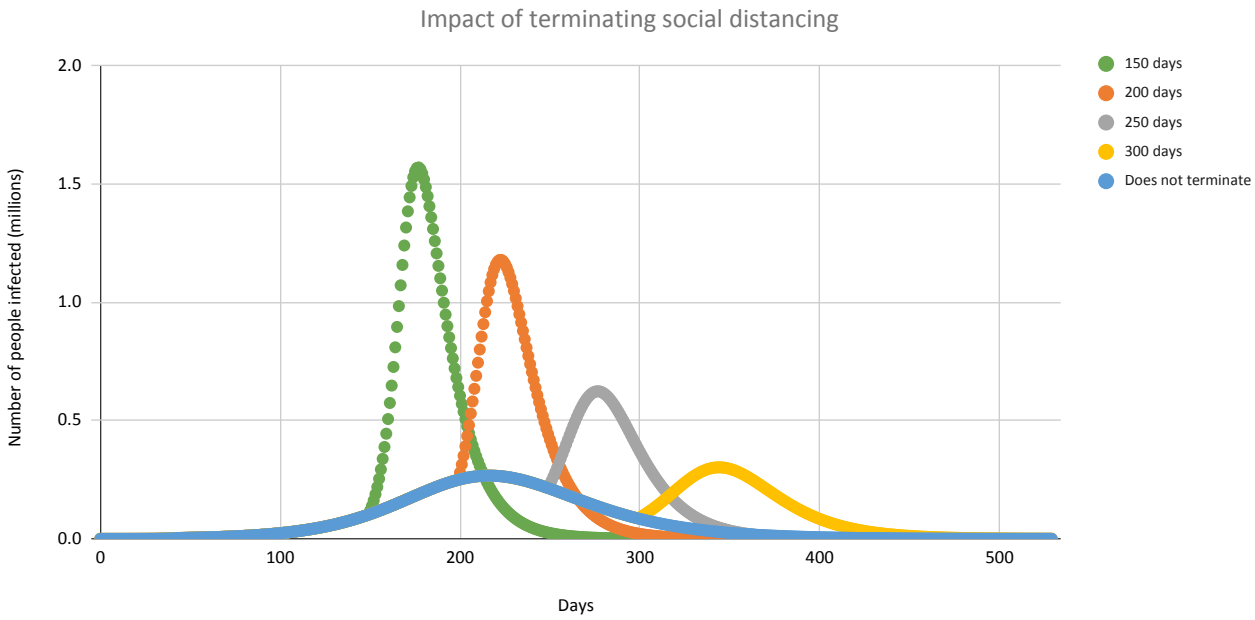

Figure 17 : The social distancing effectiveness is 60%, hospital transmission is 15% and the hospital does not run out of PPEs.

the population acquiring the virus, whereas waiting an additional 150 days results in about 55% of the population getting infected.

3.4 Conclusions

I developed an SIR model with a time-dependent infection parameter that focuses on the intervention strategies, social distancing and PPE use within hospitals. My simulations examine a regional population of 4.5 million. Due to change from initiation and termination of social distancing as well as hospitals running out of PPE, there is dramatic variation in when the peak number of infectious individuals occur and the size of this peak.

My model is unique because it analyzes the interaction between starting one infection prevention program and the loss of another. The example that I chose to model is beginning social distancing and losing adequate PPE supplies in an outbreak

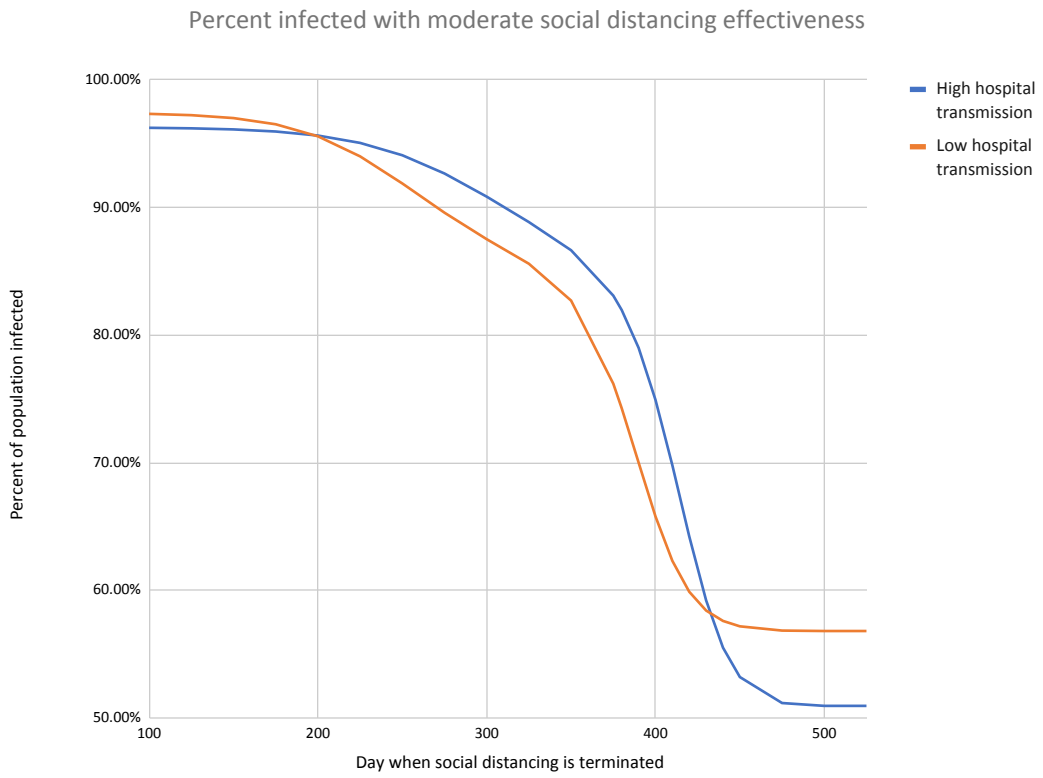

Figure 18 : This represents the percent of the population eventually infected under moderately effective social distancing beginning on day 45 and being terminated. PPEs are assumed to be plentiful.

of a virulent strain of COVID-19. The model uses average values for nationwide estimates. I also do not include other factors such as contract tracing and vaccination.

It is clear of the importance of healthcare facilities having sufficient equipment to reduce the transmission of the disease within the facilities. However, it is also important that the effectiveness of social distancing is critical in reducing the number of infections. Public education of social distancing is vital to save lives and to not burden the health system within each community.

3.5 Discussion

This research example considers a future strain of COVID-19. At the beginning of the COVID-19 pandemic in 2019, many parameters related to transmission of the virus were unknown since historical data related to COVID-19 did not exist [Petropoulos and Makridakis, 2020]. Also, at the time of the research, I made educated inferences that disease transmission within the country due to hospitalizations may be 5%, 10% or 15% in the most severe situations. As I know now, hospital-acquired COVID-19 accounts for about 0.10% of total COVID-19 cases [Pryor et al., 2020].

Instead of applying the model to a country divided by hospitals and the rest of the community, hospitals could be replaced by a congregate setting where transmission is high. The initiation and termination of social distancing may still be governed by the region, but other settings may set their own regulations by extending social distancing. The implementation of social distancing may also be delayed if facilities have to rearrange their space and residents, if possible. The effectiveness of social distancing in the community would not be different than with the hospital example. However, social distancing can be challenging in congregate settings by limitations of the physical space.

PPE in nursing homes, jails, homeless shelters and schools would include face

masks, face shields, gloves and perhaps disinfectants. The timing of the loss of PPE for staff and residents would still impact the transmission of a disease or infection through the space, but it would also impact the willingness of staff to show up for work and/or perform their job at high quality due to safety concerns. In the hospital setting, the effectiveness of PPE would be mostly driven by the availability of new supplies since healthcare workers are trained on proper use of PPE. In the congregate settings, the effectiveness would be mostly determined by the education around PPE use and by the enforcement of correct use.

Overall, I found that the infection prevention program on the larger subset of the country has the largest impact on the number of cases of the disease or infection. There is a large variation in simulation results when the effectiveness and initiation of the community infection prevention program varies and when the smaller subset loses an infection prevention program. It is clear of the importance of the smaller subset having the infection prevention program in place. However, it is also important that the effectiveness of the community infection prevention program is critical in reducing the number of infections. An ineffective community program has little effect on the spread of the disease within the population.

CHAPTER 4

CLOSTRIDIOIDES DIFFICILE AND ACTIVE DETECTION AND ISOLATION

4.1 Introduction

Clostridioides difficile (*C. diff*) is an anaerobic bacterium that produces spores and toxins which lead to diarrhea and colitis. Many healthy people live with *C. diff* bacteria in their gut as a part of their natural microbiome. However, when the gut is disturbed, the *C. diff* bacteria can produce harmful toxins and cause a *Clostridioides difficile* infection (CDI). Symptoms of CDI include severe watery diarrhea, fever, stomach tenderness, loss of appetite and nausea [Centers for Disease Control and Prevention, 2021]. CDIs are one of the most common healthcare-associated infections in the United States [Lee et al., 2021]. The CDC report that there are nearly half a million infections in the United States per year [Centers for Disease Control and Prevention, 2021]. One report from 2021 estimates that *C. diff* infections nearly quadruple hospitalization costs [Spanos, 2021]. It is also estimated that the cost of treating CDI is $1.5 billion annually in the United States [Zimlichman et al., 2013].

Cases of CDI can be classified upon their origin: community-acquired or hospital-acquired (hospital-onset). If a patient develops symptoms of CDI within 48 hours of admission and their last hospital discharge was at least 12 weeks ago, then their case is classified as being community-acquired CDI. However, if a patient has been in the hospital for more than 48 hours, then the CDI case is considered to be hospital-acquired [Ofori et al., 2018]. A patient may have acquired CDI from the community through outpatient healthcare institutions, receiving antibiotics through the outpa-

tient healthcare institution or ingesting contaminated food or water [Ofori et al., 2018].

Immune-compromised individuals, elderly people and patients prescribed antibiotics are more susceptible to getting CDI than the general population [Lee et al., 2021]. Immune-compromised individuals lack the ability to fight off harmful bacteria, such as toxic *C. diff* spores. Elderly people are more susceptible to CDI due to frequent healthcare visits and physiological changes to their gut [Jump, 2013]. Antibiotics alter the patient's microbiome, which can trigger otherwise unproblematic *C. diff* to produce toxins. In particular, patients in the Bone Marrow Transplant (BMT) unit are prone to CDI since they are immune-compromised and are prescribed antibiotics during their treatment [Barker et al., 2018].

C. diff is transmitted when asymptomatically colonized, which I will refer to as just colonized, and infectious patients shed *C. diff* spores into the environment and the spores enter a susceptible patient's body through the mouth [Mayo Clinic Staff, 2022, Gilboa et al., 2020]. If the patient has three or more loose stools within 24 hours, the patient is tested for toxigenic *C. diff* to confirm that the patient has CDI and not another diarrhea-causing condition [Lee et al., 2021]. When the patient is symptomatic and tested, they are placed under contact precautions. Contact precautions include hand washing with soap and water, wearing gloves and gowns, requiring patients to stay in an isolated room, and sanitizing the room and equipment with sporicidal disinfectants [Widmer et al., 2017, Doll et al., 2019].

Instead of only testing patients with symptoms, one can implement active detection and isolation (ADI) where patients are initially tested before entering the hospital to determine whether they are colonized by *C. diff* [Thompson, 2018]. When a patient tests positive for *C. diff* bacteria upon admission, that patient is placed under contact precautions and is immediately isolated for the remainder of their stay at the

hospital [Cho et al., 2018].

ADI is not always implemented due to costs and being more resource-intensive than traditional techniques of testing a patient only when they are symptomatic [Madden et al., 2018, Weinstein et al., 2007]. Examples of the additional resources needed for ADI are tests, rooms for isolating patients, healthcare workers to administer the test and protective equipment for healthcare workers. Resistance towards not implementing ADI also includes feedback from patients about increased isolation, depression, anxiety, prolonging the patient's length of stay, and increased wait time in emergency departments [Weinstein et al., 2007].

Overall though, ADI has shown to reduce the incidence of CDI [Weinstein et al., 2007, Longtin et al., 2016, Lanzas and Dubberke, 2014, Cho et al., 2018, Barker et al., 2018]. Particularly vulnerable wards in the hospital, such as the BMT Unit, could benefit from ADI [Barker et al., 2018]. The goal of my research is to use mathematical modeling to describe how ADI decreases CDIs and to quantify the costs associated with ADI compared to testing patients when they show symptoms of CDI in the BMT Unit.

4.2 Mathematical Model

Because patients acquire *C. diff* indirectly by ingesting *C. diff* spores from the environment, the mathematical modeling technique used for implementing ADI in the BMT Unit must also incorporate patient interactions with a contaminated environment. Due to the small number of patients in the BMT unit of the hospital, I utilized an agent-based model (ABM) to simulate the interactions between the patients and the environment. ABM is a simulation technique incorporating agents and an environment. The agents are autonomous and they can interact with other agents and/or the environment. In my example, the agents only interact with the environment. The

agents' actions in the simulations are governed by rules.

I use an ABM to model patients staying the BMT unit to study the transmission of *C. diff* within the unit. In the model, the agents are patients that exhibit independent behavior from other agents. The environment is the BMT unit and healthcare workers. The environment's level of contamination is determined by the spores shed by colonized and infectious patients. When a patient is discharged, I assume that the patient's room is disinfected and another patient is admitted into the room. So, the level of *C. diff* contamination within the environment decreases when a patient is discharged.

Although the patients do not directly interact with one another, the indirect patient contributions to the contamination of the environment causes *C. diff* to spread. Patients in the BMT unit are at high risk for CDI because of long hospitalizations, high antibiotic use and because chemotherapy negatively impacts a patient's intestinal health [Barker et al., 2018].

I implement two agent-based models, ADI-model and non-ADI model, to measure the outcomes of implementing ADI on the transmission of *C. diff*. The two models consider the practice of testing only symptomatic patients, non-ADI model, depicted by Figure 19, and the process of ADI of patients, ADI-model, depicted by Figure 20.

The ABM has two main components: the environment and the agents. First, the environment, $P(t)$, estimates the amount of contamination in the environment and $\Omega(t)$ is the proportion of environment that is contaminated with *C. diff* spores. $P(t)$ is defined as:

$$P(t+1) = \max(0, 0.4P(t) + \sum \alpha_i T_i(t)),$$

where $i \in \{C_A, C_H, C_N, C_S, I_N, I_S, R, D\}$, $\alpha_i \in \{-1, 0, 1, 2\}$, and T_i is the number of spores shed by class i.

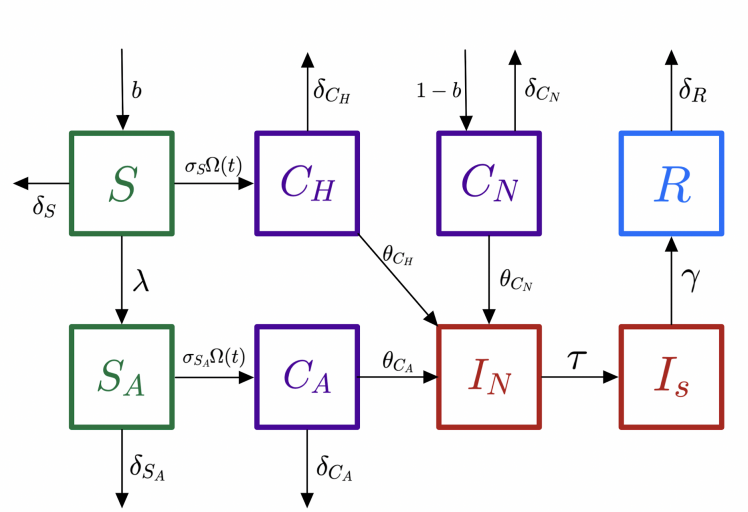

Figure 19 : Model diagram for non-ADI model with patient states susceptible, S, susceptible on antibiotics, S_A, asymptomatic colonization by environment, C_H, asymptomatic colonization by antibiotics, C_A, admitted with asymptomatic colonization, C_N, infectious, not-screened yet, I_N, infectious, screened, I_S, and recovered, R. The arrows indicate a probability of transitioning to the next class.

The contribution of patients shedding spores is quantified by α_* where $*$ denotes the particular class, or state, of the patient. The maximum of zero and the summation was taken to maintain a non-negative level of *C. diff* spores in the environment. A positive α_* value indicated that the class added spores to the environment and a negative value removed spores from the environment. Spores are eliminated when a patient is discharged.

$\Omega(t)$ utilizes the total contribution of infectious spores by colonized and infected patients and is scaled by η and ψ. η influences the threshold point where the environment is at 50% contamination. ψ determines how quickly the environment becomes toxic to patients. $\Omega(t)$ is defined as:

$$\Omega(t+1) = \frac{\psi P(t)}{\eta + \psi P(t)}.$$

The second component of my ABM is the set of patients in the BMT Unit.

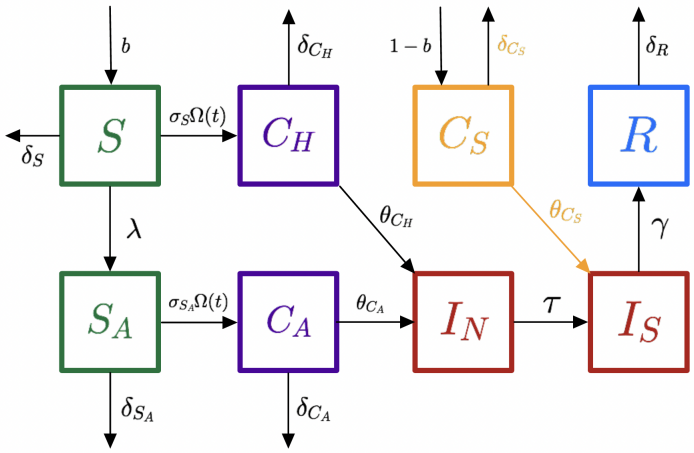

Figure 20 : Model diagram for ADI-model when ADI is implemented. The differences between non-ADI model and ADI-model are highlighted in gold.

Patients can be in one of eight different compartments on any given day. As seen in Figure 19, for non-ADI model, patients can either be admitted into S, if they are not colonized, or C_N, if they are. I assume that the general population is colonized at a rate of $(1-b)$. From S, a patient can be prescribed antibiotics and move into the S_A class, or they can become colonized from exposure with a contaminated environment (transmitted via surfaces and healthcare workers) and transition into the C_H class. Every patient can be discharged from class κ, $\kappa \in \{S, S_A, C_H, C_A, C_N, R\}$, at a rate of δ_κ, unless they are infectious. Patients are transitioned from susceptible to colonized at the rate $\sigma_z\Omega(t)$, $z \in \{S, S_A\}$.

From S_A, if a patient becomes colonized, the patient moves into C_A. Any colonized patient, C_A, C_H, C_N, can develop CDI and transition into I_N. Patients in I_N have not yet been placed under contact precautions. Once a patient is in I_N, they can only transition into the I_S class. While a patient is being treated for CDI in I_S, they stay in I_S with additional contact precautions. When they recover, they move to R. Once a patient is in R, they remain there until they are discharged.

Incorporating ADI alters one patient compartment and one transition between compartments in the model. With ADI implemented, before patients are admitted, they are tested for colonization of *C. diff* bacteria and are immediately placed under contact precautions in C_S if they test positive. Otherwise, if they are not colonized, they are placed in S, seen in Figure 20.

The goal of the research is to determine how ADI reduces cases of CDI, and to track hospital-acquired and community-acquired infections. Patients that transition from either C_H to I_N or C_A to I_N count as hospital-acquired CDIs. The number of community-acquired cases of CDI is calculated by counting the number of new patients entering I_N from C_N in non-ADI model. In ADI-model, the number of community-acquired cases was calculated by adding all of the patients who transition from C_S to I_S.

The other research goal is to quantify the cost of implementing ADI and compare it to the cost of testing patients only when they are symptomatic. In non-ADI model, any time a patient entered I_N, a test was taken and accounted for. In ADI-model, all admitted patients were tested in addition to any patient who entered I_N from $\{C_H, C_A\}$ or I_S from C_S. Other costs to consider are the costs of contact precautions and disinfecting patient rooms. Contact precautions were implemented for patients in I_S in non-ADI model and for patients in both C_S and I_S in ADI-model. In addition to disinfecting rooms occupied by patients in I_S, ADI-model assumes full environmental cleaning of rooms occupied by patients in C_S as well.

4.3 Results

4.3.1 Simulation Results

In order to quantify the impact of implementing ADI in the BMT unit, I assume the unit to always be at full capacity of 21 patients. Patients have an average stay of six weeks. Simulations were run in MATLAB R2021a for one year before making calculations to avoid transients. Results are based on the averages of 100 - 10 year simulations.

The parameters used in the simulations are shown in Table 4. Huang et al. [2016] estimated that about 20% of patients are already colonized with *C. diff* upon admission, so the remaining 80%, b, are assumed to be admitted into S. In the BMT Unit, patients are prescribed antibiotics due to being immune-compromised [BeTheMatch.org, 2022]. These patients typically receive antibiotics within the first six days of their hospital stay, so the daily probability of being prescribed antibiotics is $\lambda = 1/6$. If a patient develops CDI, a 10-day course of antibiotics is typically used to treat the infection, so $\gamma = 1/10$ is the daily rate of recovery from CDI [Leffler and Lamont, 2015].

The remaining parameters are estimated based upon CDI data from the BMT unit within VCU Medical Center from February 2014 until December 2019 (77 months) before ADI. The data are visualized in Figure 21. The data has a yearly average of 25.29 infections and a yearly standard deviation of 4.19 infections.

The averages taken over 100 simulations with my estimated parameters in non-ADI model agree with the real data as confirmed by a two-sample t-test under 99% confidence. After the simulations were run, a random sample of 77 months was taken by using the datasample method in MATLAB R2021a. An F-test was conducted at 99% confidence to test if the variances between the simulated data and the real data

were the same. The null hypothesis that the variances were the same was not rejected, so a two-sample t-test could be conducted. A t-test looks at overall variability in the simulated data and compares it to the overall variability in the real data.

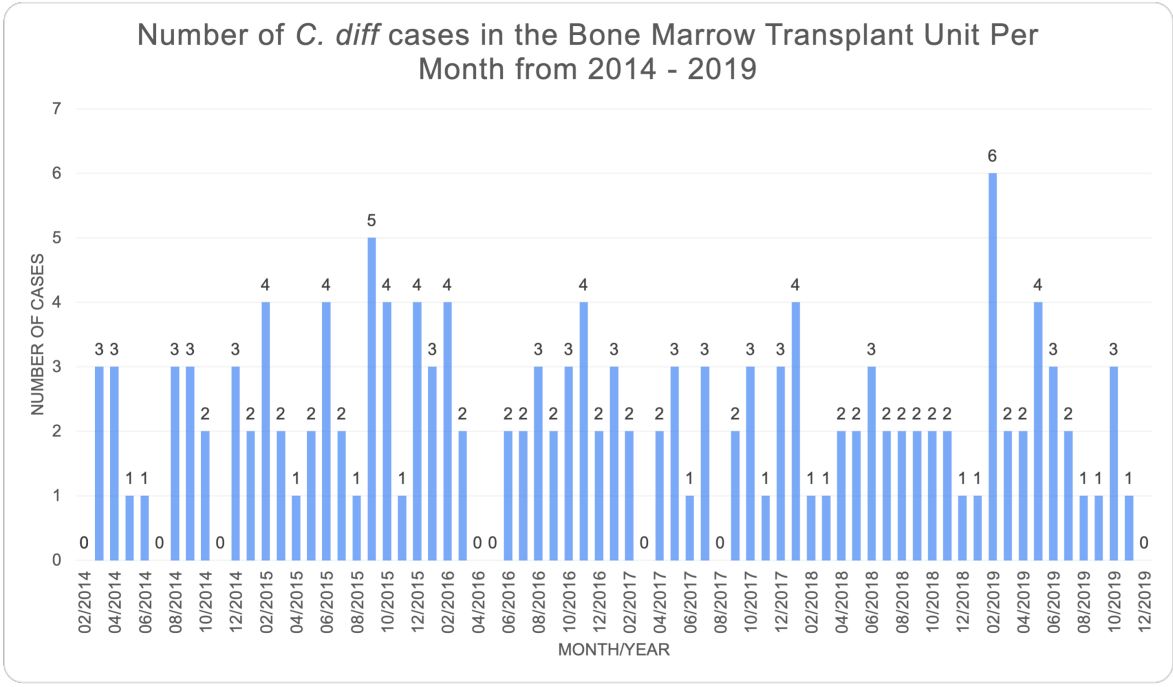

Figure 21 : Monthly *C. diff* data from VCU Medical Center BMT unit from February 2014 - December 2019.

When ADI is implemented, there is an estimated 23% decrease in the total number of infections between non-ADI model and ADI-model in Table 5. The number of community-acquired infections does not change because 20% of patients are assumed to be colonized with *C. diff* from the community in both models. This results in an overall reduction in 6.42 CDIs per year, which is a 84.38% reduction in hospital-acquired cases. The reduction in cases of CDI from ADI-model compared to the data are statistically significantly different under 99% confidence in a two-sample t-test.

Unfortunately, community-acquired infections are inevitable since about 20% of the population is already colonized with *C. diff* [Hung et al., 2015]. However, as expected, implementing ADI reduces the number of hospital-acquired infections due

Parameter symbol	Parameter description	Parameter value	Source
α_{I_N}	Contribution of spores by patients in the I_N state	2	Estimated
b	Proportion of patients admitted as susceptible	0.800	[Hung et al., 2015]
η	Environment coefficient	1000	Estimated
ψ	Environment impact scalar	6	Estimated
γ	Rate of recovery	0.100	[Leffler and Lamont, 2015]
λ	Rate of antibiotic prescription	0.167	[BeTheMatch.org, 2022]
σ_S	Rate of susceptible patients becoming colonized with *C. diff* from the environment	0.010	Estimated
σ_{S_A}	Rate of susceptible patients on antibiotics becoming colonized with *C. diff*	0.050	Estimated
θ_{C_A}	Rate of colonized patients on antibiotics becoming symptomatic	0.017	Estimated
θ_{C_H}	Rate of colonized patients from the environment becoming symptomatic	0.100	Estimated
θ_{C_N}	Rate of admitted colonized patients becoming symptomatic in non-ADI model	0.017	Estimated
θ_{C_S}	Rate of admitted colonized patients becoming symptomatic in ADI-model	0.017	Estimated

Table 4 : Parameter values used in the simulations. Estimated parameters come from data from the BMT Unit at VCU Medical Center from February 2014 - December 2019.

to contact precautions placed on colonized patients and the contribution of spores to the environment is reduced. When the environment is less contaminated, patients are less likely to acquire *C. diff*.

For all cases of CDI, according to research conducted by Barker et al. [2020], the excess hospital cost attributable to a new case of CDI is $13,779.31. Table 5 shows that the average of 25.29 infections per year results in $348,478.75 spent on treating patients with CDI. Non-ADI model had an average of 25.60 infections per

	Data	non-ADI model	ADI-model
Percent of infections that are community-acquired	69.00%	70.31%	93.84%
Percent of infections that are hospital-acquired	31.00%	29.69%	6.16%
Average number of community-acquired infections per year	17.25	17.98	17.99
Average number of hospital-acquired infections per year	7.75	7.62	1.19
Average number of infections per year	25.29	25.60	19.18
Number of tests per year	–	25.60	195.46
Number of additional patients placed under contact precautions per year	–	–	17
Number of additional rooms to disinfect upon discharge	–	–	17
Cost of infections per year	$348,478.75	$352,750.34	$264,287.17
Cost of tests per year	–	$200.19	$1,329.40
Cost of additional contact precautions per year	–	–	$1,845.35
Cost of additional terminal cleaning per year	–	–	$9,616.73
Total cost per year	–	$352,950.53	$277,277.75

Table 5 : Results from ABM simulations over ten years with 100 simulations.

year which results in $352,750.34 spent on treating patients with CDI. When the number of infections are reduced to an average of 19.18 in ADI-model, the total cost for treating patients with CDI decreases to $264,287.17. This results in $88,463.17 saved by preventing CDI with ADI.

ADI reduces CDIs, but does require more resources than not implementing ADI. Additional costs associated with ADI include the cost of testing a patient, $7.82, implementing contact precautions, $108.55, and thoroughly disinfecting any room that contained a colonized or infectious patient $565.69 [Barker et al., 2020].

As seen in Table 5, increasing the number of tests from 25.60 without ADI to

195.46 results in about 170 additional tests. One-hundred seventy additional tests (170 * $7.82) costs $1,329.40. Implementing contact precautions on an additional 17 patients ($108.55 * 17), those patients who were colonized upon admission in ADI-model, costs $1,845.35. Then, disinfecting the 17 additional rooms ($565.69 * 17) of the C_S patients costs $9,616.73.

Although ADI requires these additional costs, these costs do not outweigh the costs of treating cases of CDI. Seven preventable cases of CDI by not implementing ADI costs $96,455.17 ($13,779.31 * 7) based on costs from Barker et al. [2020]. The costs of treating CDI and the costs of ADI resources are combined at the bottom of Table 5. Comparing ADI-model to non-ADI model, I see that ADI can save about $83,663.69 per year.

4.3.2 Parameter Sensitivity Analysis

I explore implementing ADI by adjusting the values of the parameters to determine how the results are sensitive to each of the parameters. This allows one to understand which parameters within the model are most significant in influencing the number of yearly infections. Here, each parameter was doubled and cut in half. The outcomes of the number of yearly community-acquired CDIs, hospital-acquired CDIs, average number of yearly CDIs and number of tests used per year were calculated after adjusting the parameters. These results are shown in Table 6 for non-ADI model and in Table 7 for ADI-model.

The parameters chosen are those that could potentially be monitored or modified with medical and scientific advancements. For instance, σ_S and σ_{S_A} could be monitored if it was known exactly how and when a patient became colonized with additional testing. ψ could be altered by the effectiveness of disinfecting patient rooms. Being able to predict how quickly a patient who is colonized upon admission became

non-ADI model	# of Comm. Infs Per Year	# of Hosp. Infs Per Year	Mean # of Yearly Infs	# Tests Per Year
σ_S				
$= 0.01$	17.98	7.62	25.60	25.60
$= 0.02$	17.95	7.90	25.85	25.85
$= 0.005$	17.98	7.46	25.44	25.44
σ_{S_A}				
$= 0.05$	17.98	7.62	25.60	25.60
$= 0.1$	17.80	16.36	34.15	34.15
$= 0.025$	18.16	3.76	21.92	21.92
ψ				
$= 6$	17.98	7.62	25.60	25.60
$= 12$	17.81	15.85	33.66	33.66
$= 3$	17.75	3.61	21.36	21.36
θ_{C_N}				
$= 0.02$	17.98	7.62	25.60	25.60
$= 0.04$	26.75	7.64	34.38	34.38
$= 0.01$	10.55	7.62	18.17	18.17
γ				
$= 0.1$	17.98	7.62	25.60	25.60
$= 0.2$	18.06	7.47	25.53	25.53
$= 0.05$	17.59	8.08	25.67	25.67

Table 6 : Parameter sensitivity results for non-ADI model, when ADI is not implemented.

symptomatic, θ_{C_N} and θ_{C_S}, would influence the urgency of preventative practices to be used on these patients. The strength of the antibiotics used to treat CDI would impact how quickly a patient recovered, which is γ in both models.

By manipulating the parameters, I found that both models are sensitive to σ_{S_A}, the rate at which susceptible patients on antibiotics become colonized, but neither model is sensitive to σ_S. In Table 6, doubling σ_{S_A} more than doubles the number of yearly hospital-acquired infections per year and cutting σ_{S_A} in half reduces yearly hospital-acquired cases by more than 50%. The results for the parameter sensitivity analysis for ADI-model in Table 7 show a similar reaction towards hospital-acquired CDIs to altering σ_{S_A}.

Because all BMT patients receive antibiotics as a part of their treatment, increas-

ADI-model	# of Comm. Infs Per Year	# of Hosp. Infs Per Year	Mean # of Yearly Infs	# Tests Per Year
σ_S				
$= 0.01$	17.99	1.19	19.18	195.46
$= 0.02$	18.00	1.16	19.19	195.46
$= 0.005$	17.79	1.17	18.96	195.35
σ_{S_A}				
$= 0.05$	17.99	1.19	19.18	195.46
$= 0.1$	17.84	2.43	20.26	196.50
$= 0.025$	17.51	0.61	18.11	194.57
ψ				
$= 6$	17.99	1.19	19.18	195.46
$= 12$	18.07	1.18	19.25	195.57
$= 3$	18.06	1.12	19.17	195.51
θ_{C_S}				
$= 0.02$	17.99	1.19	19.18	195.46
$= 0.04$	26.62	1.17	27.79	204.01
$= 0.01$	10.61	1.20	11.81	188.41
γ				
$= 0.1$	17.99	1.19	19.18	195.46
$= 0.2$	17.99	1.18	19.17	196.20
$= 0.05$	17.58	1.23	18.81	192.75

Table 7 : Parameter sensitivity analysis for ADI-model, when ADI is implemented.

ing the rate that those patients become colonized and ultimately symptomatic would increase the number of yearly infections. Similarly, reducing the rate of colonization would allow patients to avoid getting *C. diff* before they are discharged. The models are not reactive to σ_S because patients rarely transition from S to C_H.

In Table 6, I see that non-ADI model is sensitive to ψ. When ψ is doubled, the number of hospital-acquired infections per year more than doubles. When ψ is reduced by half, the number of hospital-acquired infections is reduced by about 53%. Because the environment is less controlled in non-ADI model, since colonized patients are unknown and therefore shed spores into the environment. This impacts the environment and increases the rate of susceptible patients becoming colonized that could increase the number of hospital-acquired *C. diff* cases. ADI-model is less

effected by the environment because there are fewer unknown colonized patients and therefore fewer spores contaminating the environment.

In Table 7, I see that ADI-model is not sensitive to ψ since increased awareness of who is colonized with *C. diff* reduces the amount of spores that contaminate the environment. ψ scales the effect of the environment, but with only 6% of patients getting CDI due to the contaminated environment in ADI-model, doubling or halving the value does not impact many patients.

Both models are also sensitive to θ_{C_N} and θ_{C_S}, the rates of patients who are colonized upon admission become symptomatic. Tables 6 and 7 both show that yearly community-acquired cases of CDI are doubled when θ_{C_N} and θ_{C_S} are respectively doubled. When θ_{C_N} and θ_{C_S} are reduced by half, the number of community-acquired infections are reduced by about 39%.

θ_{C_N} and θ_{C_S} are significant parameters because they represent the movement of patients into the symptomatic infected class. Decreasing the rate of this transition would allow patients to stay within the colonized class until they are discharged. ADI identifies colonized patients initially and institutes preventative measures to decrease the spores from spreading into the environment. Otherwise colonized patients that are not immediately isolated can contribute more spores to the environment consequently causing more infections to susceptible patients.

Both models are not sensitive to γ since γ affects recovery of CDI, which does not play a large role in transmission of *C. diff*. While γ affects the amount of spores contributed into the environment by patients waiting to recover from CDI, the additional days spent in I_S are not enough days for a patient to make a significant contribution of spores into the environment to impact yearly infections.

4.4 Discussion

Utilizing an ABM with eight patient states allows me to quantify the impact of implementing ADI in the BMT unit on the number of cases of CDI and to generate a data set statistically similar to the data provided by VCU Medical Center. The data have a yearly average of 25.29 infections and a yearly standard deviation of 4.19 infections. Upon implementing ADI, I found a 25% reduction, on average, in total cases of CDI per year. Additionally, there is an 84.38% decrease in hospital-acquired cases alone.

Modeling patients in the BMT unit is challenging due to the varying underlying conditions that the patients are in, the variable, long length of stays and the high rate of antibiotic prescription [Barker et al., 2018]. Cases of CDI may occur in outbreaks due to a contaminated environment or may be isolated cases from those that are colonized.

ADI reduces hospital-acquired cases of CDI due to the reduction of spore shedding by infectious patients through the implementation of contact precautions on all known cases of colonization and active infection. However, while ADI identifies community-acquired colonizations, it cannot prevent community-acquired colonizations from being admitted into the BMT unit.

My results are in agreement with other studies of implementing ADI in the BMT unit showing that ADI could reduce hospital-acquired cases of CDI. My results showed a 84.38% decrease in hospital-acquired cases of CDI when ADI was implemented. Barker et al. [2018] showed an 82.93% reduction, and Lanzas and Dubberke [2014] showed a 25% reduction in hospital-acquired cases of CDI with ADI. Lanzas and Dubberke [2014] studied six medicine wards within a hospital with two strains of *C. diff*. The data in the study showed that 58% of CDI cases were hospital-acquired.

After using an ABM to model ADI, the mean number of hospital-acquired CDI cases were reduced by 25% [Lanzas and Dubberke, 2014]. Because the study was set in less vulnerable wards within the hospital, it is less likely that the patients would develop CDI.

Barker et al. [2018] studied the impact of ADI on CDI cases specifically in the BMT unit at a hospital in Madison, Wisconsin. Pre-intervention and post-intervention data show that 10.3% of BMT patients were tested for *C. diff* upon admission before screening was implemented and increased to 74.5% upon implementation [Barker et al., 2018]. There was a 82.93% decrease in hospital-acquired cases of CDI within the study.

The parameter sensitivity analysis provides insight on which parameters are most important to focus on to prevent or lower the chance of patients getting CDI. Both models, with and without ADI, are sensitive to σ_{S_A}, the rate at which susceptible patients on antibiotics become colonized, and θ_{C_N} and θ_{C_S}, the rates of patients who are colonized upon admission become symptomatic. Healthcare providers should monitor patients who are prescribed antibiotics by potentially testing those patients for *C. diff* bacteria and toxins. Furthermore, knowing which patients are admitted with *C. diff* would allow for proper contact precautions and careful antibiotic prescription to occur to prevent the asymptomatic colonization from becoming an active and symptomatic infection. It is also important to note that results are not sensitive in terms of the parameters estimating the effects of the environment under ADI since the colonized patients are better controlled, unlike in the non-ADI situation. This implies that awareness of which patients are colonized upon admission ultimately reduces the environment's impacts on other patients.

The basic structure of my model could allow for more questions about preventing cases of CDI from occurring by altering different parameters, such as the testing

accuracy. In this study I did not consider the effect of testing accuracy of CDI. I assumed that testing of CDI and colonization is 100% accurate. If this was not the case, then patient transitions would be more complicated as well as the resulting dynamics.

Overall, the ABM allowed me to track the status of patients in the BMT unit in order to track patients developing CDI, with and without ADI in place. I were also able to break down the cases of CDI into hospital-acquired and community-acquired to quantify the impact of ADI on the reduction of hospital-acquired cases specifically. Given the high cost of a case of CDI and the relatively low cost of a PCR test, my study also supports the implementation of ADI from a cost savings perspective.

CHAPTER 5

CONCLUSIONS AND DISCUSSION

I have presented multiple different mathematical models that simulate the effects of different intervention strategies in order to limit the cases of hospital-acquired infections. In each of these different models, I quantified the subsequent impact on yearly cases of HAIs and estimated the resulting costs. This research supports implementing the particular intervention strategies examined within each model where the cost of implementing the infection prevention programs outweigh the cost of treating HAIs. Reducing HAIs allows hospitals to decrease the amount of resources and time necessary for treating each individual patient, which has positive consequences for healthcare costs and for the patient's experience during their hospitalization.

A variety of mathematical modeling techniques were used in my research. The studies that I conducted incorporated a combination of infection prevention techniques. Each problem also presented unique set of assumptions, focused on a specific set of HAIs, and required me to track and emphasize different components of the model. Developing mathematical models to quantify the impact of infection prevention programs is challenging because the parameters required for the simulations have to be estimated. Clinical studies cannot be ethically performed for the research problems proposed, so precise parameters are not available.

Chapter 2 supports early action of using CHG bathing to prevent HAIs, and encourages healthcare leaders to enforce high levels of CHG bathing compliance hospital-wide. I also saw that immediate full implementation of the standardized central line bundle kit and CHG bathing resulted in more CLABSIs and CAUTIs prevented and

more savings than when the implementation of these programs were delayed.

In Chapter 3, I simulated the loss of one infection intervention practice and the start of another. The results predict how the interplay of the two strategies affects the community as a whole. I found that the effectiveness of the infection prevention program used on the entire community has the largest impact on the size and timing of the peak number of infections during an outbreak.

Finally, in Chapter 4, I modeled the reduction in hospital-acquired cases of CDI when ADI was implemented on patients in the BMT Unit. While community-acquired cases were not reduced, they were identified with ADI and therefore the amount of spores being contributed to the environment was reduced. Because the environment was less contaminated, hospital-acquired cases of CDI decreased when ADI was implemented. The parameter sensitivity analysis allowed me to identify transitions between patient states that had the greatest impact on yearly cases of CDI. I found that the rate of patients on antibiotics becoming colonized with *C. diff* and patients who are colonized becoming symptomatic have a significant impact on cases of CDI.

Even with today's medical advancements, HAIs continue to increase the mortality and morbidity of hospitalizations as antibiotic-resistant organisms become more prevalent. HAIs are preventable through the implementation of infection prevention programs. Overall, effective compliance and early initiation of infection prevention programs can reduce the burden of HAIs on healthcare systems and improve patient outcomes.

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Appendix A

ABBREVIATIONS

ABM	Agent-based model
ADI	Active Detection and Isolation
BMT	Bone Marrow Transplant
CAUTI	Catheter-associated urinary tract infection
CDC	Centers for Disease Control and Prevention
CDI	*Clostridiodes difficile* infection
CHG	Chlorhexidine gluconate
CLABSI	Central line-associated bloodstream infection
HAI	Hospital-acquired infection
PPE	Personal protective equipment
VCU	Virginia Commonwealth University

Appendix B

MATLAB CODE– CHG BATHING ONLY

```
infectionsTable = ["Uniform discharge rate" "discharge  ...
   PI" "Daily probability of infection" "CHG Bathing  ...
   compliance" "Number of yearly infections" "N0 at  ...
   equi" "N1 at equi" "N2 at equi" "P0 at equi" "P1 at  ...
   equi" "P2 at equi" "P3 at equi" "PI at equi" "total  ...
   number of patients"];
betaValues = [0 .10 .20 .30 .40 .50 .60 .70 .80 .90 1.00];
ΔValues = [1/14 1/12 1/10 1/9 1/8 1/7 1/6 1/5 1/4 1/3 1/2];

%28% effectiveness
rValues = [0.000345];

%71% effectiveness
%rValues = [0.000665];

for d=1:length(ΔValues)
    for r=1:length(rValues)
        for b=1:length(betaValues)
            infections = [];
            ΔN0 = ΔValues(d); %discharge rates
            ΔN1 = ΔN0;
            ΔN2 = ΔN0;
            ΔP0 = ΔN0;
            ΔP1 = ΔN0;
            ΔP2 = ΔN0;
            ΔP3 = ΔN0;
            ΔPI = 1/10;

%            28% effectiveness
            r3 = rValues(r); %infection rates
            r2 = (1-.0933333)*rValues(r);
            r1 = (1-.1866666)*rValues(r);
            r0 = (1-.28)*rValues(r);
            r0prime = 0.95*r0;
            r1prime = 0.95*r1;
            r2prime = 0.95*r2;


%             71% effectiveness
```

```
%             r3 = rValues(r); %infection rates
%             r2 = (1-.236666667)*rValues(r);
%             r1 = (1-.473333333)*rValues(r);
%             r0 = (1-.71)*rValues(r);
%             r0prime = 0.95*r0;
%             r1prime = 0.95*r1;
%             r2prime = 0.95*r2;

            beta0=betaValues(b); %each of the bathing  ...
               rates for the iterations are set here
            beta1=betaValues(b);
            beta2=betaValues(b);
            beta3=betaValues(b);

            t = 365; %number of days the simulation was run

%             N0 = 125;  %number of patients in each class
%             N1 = 50;
%             N2 = 25;
%             P0 = 150;
%             P1 = 150;
%             P2 = 150;
%             P3 = 150;
%             PI=50;
              N0 = 0;
              N1 = 850;
              N2 = 0;
              P0 = 0;
              P1 = 0;
              P2 = 0;
              P3 = 0;
              PI = 0;


            totalPop = N0 + N1 + N2 + P0 + P1 + P2 + P3  ...
               + PI;

            % % ----- discharge matrix -----
            dischargeMatrix = zeros(8,8); %setting up  ...
               the discharge matrix

            dischargeMatrix(1,1) = 1;
            dischargeMatrix(1,2) = ΔN1;
            dischargeMatrix(1,3) = ΔN2;
            dischargeMatrix(1,4) = ΔP0;
            dischargeMatrix(1,5) = ΔP1;
            dischargeMatrix(1,6) = ΔP2;
            dischargeMatrix(1,7) = ΔP3;
            dischargeMatrix(1,8) = ΔPI;

            dischargeMatrix(2,2) = 1 - ΔN1;
```

```
dischargeMatrix(3,3) = 1 - ΔN2;
dischargeMatrix(4,4) = 1 - ΔP0;
dischargeMatrix(5,5) = 1 - ΔP1;
dischargeMatrix(6,6) = 1 - ΔP2;
dischargeMatrix(7,7) = 1 - ΔP3;
dischargeMatrix(8,8) = 1 - ΔPI;

% % ----- infection matrix -----
infectMatrix = zeros(8,8); %setting up the  ...
   infection matrix

infectMatrix(1,1) = 1 - r0prime;
infectMatrix(2,2) = 1 - r1prime;
infectMatrix(3,3) = 1 - r2prime;
infectMatrix(4,4) = 1 - r0;
infectMatrix(5,5) = 1 - r1;
infectMatrix(6,6) = 1 - r2;
infectMatrix(7,7) = 1 - r3;
infectMatrix(8,8) = 1;

infectMatrix(8,1) = r0prime;
infectMatrix(8,2) = r1prime;
infectMatrix(8,3) = r2prime;
infectMatrix(8,4) = r0;
infectMatrix(8,5) = r1;
infectMatrix(8,6) = r2;
infectMatrix(8,7) = r3;

% % ----- bathing matrix -----
batheMatrix = zeros(8,8); %setting up the  ...
   bathing matrix

batheMatrix(2,1) = 1 - beta0; %then entered  ...
   into the matrix
batheMatrix(3,2) = 1 - beta1; %the code is  ...
   set up this way to accomodate
batheMatrix(7,3) = 1 - beta2; %for when I  ...
   want the bathing rate to be
batheMatrix(5,4) = 1 - beta0; %a random  ...
   number from a normal distribution
batheMatrix(6,5) = 1 - beta1;
batheMatrix(7,6) = 1 - beta2;
batheMatrix(7,7) = 1 - beta3;
batheMatrix(8,8) = 1;

batheMatrix(4,1) = beta0;
batheMatrix(4,2) = beta1;
batheMatrix(4,3) = beta2;
batheMatrix(4,4) = beta0;
batheMatrix(4,5) = beta1;
batheMatrix(4,6) = beta2;
```

```
batheMatrix(4,7) = beta3;


% % ----- patient matrix -----
patientMatrix = zeros(8,1); %setting up the  ...
   patient matrix
patientMatrix(1,1)=N0;
patientMatrix(2,1)=N1;
patientMatrix(3,1)=N2;
patientMatrix(4,1)=P0;
patientMatrix(5,1)=P1;
patientMatrix(6,1)=P2;
patientMatrix(7,1)=P3;
patientMatrix(8,1)=PI;

newPatients0 =[];
newPatients1 = [];
newPatients2 = [];
patients0 = [];
patients1 = [];
patients2 = [];
patients3=[];
patientsInfected = [];
application1 = dischargeMatrix*infectMatrix;
application2 = application1*batheMatrix;


for i = 1:465
    patientMatrix = application2*patientMatrix;
    newPatients0 =  ...
       [newPatients0;patientMatrix(1,1)];
    newPatients1 =  ...
       [newPatients1;patientMatrix(2,1)];
    newPatients2 = [newPatients2;  ...
      patientMatrix(3,1)];
    patients0 = [patients0;patientMatrix(4,1)];
    patients1 = [patients1;patientMatrix(5,1)];
    patients2 = [patients2;patientMatrix(6,1)];
    patients3 = [patients3;patientMatrix(7,1)];
    patientsInfected =  ...
       [patientsInfected;patientMatrix(8,1)];

end
ceil(patientMatrix);
newInfectionsMatrix = [];

for m=1:465 %calculating new infections
    newInfections = r0prime*newPatients0(m)  ...
       + r1prime*newPatients1(m) +  ...
       r2prime*newPatients2(m)+  ...
       r0*patients0(m) + r1*patients1(m) +  ...
```

```
                    r2*patients2(m) + r3*patients3(m);
                 newInfectionsMatrix =  ...
                    [newInfectionsMatrix; newInfections];
              end

              newInfectionsMatrix2 = [];
              for j=100:465 %only looking at new  ...
                 infections beyond one hundred days of  ...
                 the simulation
                  newInfections2 =  ...
                     r0prime*newPatients0(j) +  ...
                     r1prime*newPatients1(j) +  ...
                     r2prime*newPatients2(j)+  ...
                     r0*patients0(j) + r1*patients1(j) +  ...
                     r2*patients2(j) + r3*patients3(j);
                  newInfectionsMatrix2 =  ...
                     [newInfectionsMatrix2; newInfections2];
              end

              sum(newInfectionsMatrix2);
              infections =  ...
                 [infections;sum(newInfectionsMatrix2)];

              ev = 465;
              infectionVector = [▵Values(d) ▵PI  ...
                 rValues(r) betaValues(b)  ...
                 mean(infections) newPatients0(ev)  ...
                 newPatients1(ev) newPatients2(ev)  ...
                 patients0(ev) patients1(ev)  ...
                 patients2(ev) patients3(ev)  ...
                 patientsInfected(ev)  ...
                 sum(newPatients0(ev)+newPatients1(ev)+newPatients2(ev)
              +patients0(ev)+patients1(ev)+  ...
                 patients2(ev)+patients3(ev)+patientsInfected(ev))];

              infectionsTable = [infectionsTable;  ...
                 infectionVector];
        end
     end
end
```

Appendix C

MATLAB CODE – RESISTORS AND CONSTIPATORS

```
clear all

betaStar = 1.0;


▵CL = 1/18; %average LOS for patient with central line:  ...
   18 days  ...
   (https://academic.oup.com/intqhc/article/29/1/63/2660332)
▵Cath = 1/10; %average LOS for patient with catheter:  ...
   10 days  ...
   (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378875/)
▵CLinf = 1/24; %average LOS for patient with CLABSI: 24  ...
   days  ...
   (https://academic.oup.com/intqhc/article/29/1/63/2660332)
▵Cathinf = 1/18; %average LOS for patient with CAUTI:  ...
   18 days  ...
   (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378875/)
▵Other = 1/5; %average LOS for patient in hospital  ...
   without device

%getCL = 0.2;  ...
   %https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4997807/
%getCath = 0.12;  ...
   %https://www.ncbi.nlm.nih.gov/pubmed/28392431
getCL = 0.0123203;
getCath = 0.012702;
getCLandCath = getCL*getCath;

eta1 = 0.59;
eta2 = 0.5;
eta3 = 0.55;

kappa1 = 0.3;
kappa2 = 0.3;

%CLABSI has a 56% reduction with CHG bathing
% Need to also include further reduction with  ...
   standardized kit
% estimating impact to be an additional 10%
r03 = 0.000405;
```

```
r02 = (1- (eta1 +kappa1)*(1/3))*r03;
r01 = (1- (eta1 + kappa1)*(2/3))*r03;
r00 = (1- (eta1 + kappa1))*r03;
%CAUTI has a 32% reduction with CHG bathing
r13 = 0.03;
r12 = (1- (eta2 /3))*r13;
r11 = (1 - (eta2 *(2/3))) * r13;
r10 = (1 - eta2)* r13;
%I am going to assume a 44% reduction if you have both
% Need to also include further reduction with  ...
   standardized kit
% estimating further impact to be 10%
r23 = (r03+r13)/3;
r22 = (1 - (eta3+kappa2)/3)*r23;
r21 = (1 - 2*(eta3+kappa2)/3) * r23;
r20 = (1 - (eta3+kappa2))*r23;

r03prime = r23;
r02prime = (1 - (eta3+kappa2)/3)*r03prime;
r01prime = (1 - 2*(eta3+kappa2)/3)*r03prime;
r00prime = (1 - (eta3+kappa2))*r03prime;

r13prime = r23;
r12prime = (1 - (eta3+kappa2)/3)*r13prime;
r11prime = (1 - 2*(eta3+kappa2)/3)*r03prime;
r10prime = (1 - (eta3+kappa2))*r03prime;

rI0 = r23;
rI1 = r23;



years = 5; %years interested in computing to
daysInYear = 365;
daysInMonth = 30.4;
currentComp = 0.6; %current CHG bathing compliance
desiredComp = 0.9; %desired CHG bathing compliance



monthIncrementTest = [0 3 6 9 12 15 18 21 24 27 30 33  ...
   36 39 42 45 48 51 54 57 60];

%monthIncrementTest = [0 3 6 9 12 15 18 21 24 27 30 33  ...
   36 39 42 45 48 51 54]; %comment out (1)

%monthIncrementTest = [0 3 6 9 12 15 18 21 24 27 30 33  ...
   36 39 42 45 48]; %comment out (1)-(2)

%monthIncrementTest = [0 3 6 9 12 15 18 21 24 27 30 33  ...
   36 39 42];
```

```
%comment out (1)-(3)

%monthIncrementTest = [0 3 6 9 12 15 18 21 24 27 30 33  ...
   36]; %comment
%out (1)-(4)

%monthIncrementTest = [0 3 6 9 12 15 18 21 24 27 30];  ...
   %comment out (1)-(5)

%monthIncrementTest = [0 3 6 9 12 15 18 21 24];  ...
   %comment out (1)-(6)

%monthIncrementTest = [0 3 6 9 12 15 18]; %comment out  ...
   (1)-(7)

%monthIncrementTest = [0 3 6 9 12]; %comment out (1)-(8)

%monthIncrementTest = [0 3 6]; %comment out (1)-(9)
% monthIncrementTest = [0];


timeStep = ceil(daysInMonth*monthIncrementTest);
inc = (desiredComp -  ...
   currentComp)/(length(monthIncrementTest)-1);

ss = 300;
t = years*daysInYear + ss ; %total time

%betaChoices = [0 0.225 .45 .675 .90];
beta=[];
betaInc=[currentComp:inc:desiredComp];

for i=1:t
     if (i≥1) && (i<timeStep(2))
         beta(1,i)=betaInc(1,1);
     elseif (i≥timeStep(2))&& (i<timeStep(3))
         beta(1,i) = betaInc(1,2);
    elseif (i≥timeStep(3))&& (i<timeStep(4))  %(9)
        beta(1,i) = betaInc(1,3);
    elseif (i≥timeStep(4))&& (i<timeStep(5))  %(9)
        beta(1,i) = betaInc(1,4);
    elseif (i≥timeStep(5))&& (i<timeStep(6))  %(8)
        beta(1,i) = betaInc(1,5);
    elseif (i≥timeStep(6))&& (i<timeStep(7)) %(8)
        beta(1,i) = betaInc(1,6);
    elseif (i≥timeStep(7))&& (i<timeStep(8))  %(7)
        beta(1,i) = betaInc(1,7);
    elseif (i≥timeStep(8)) && (i<timeStep(9) )%(7)
        beta(1,i) = betaInc(1,8);
    elseif (i≥timeStep(9))&& (i<timeStep(10)) %(6)
        beta(1,i) = betaInc(1,9);
```

```
    elseif (i≥timeStep(10))&& (i<timeStep(11)) %(6)
        beta(1,i) = betaInc(1,10);
    elseif (i≥timeStep(11))&& (i<timeStep(12)) %(5)
        beta(1,i) = betaInc(1,11);
    elseif (i≥timeStep(12))&& (i<timeStep(13)) %(5)
        beta(1,i) = betaInc(1,12);
    elseif (i≥timeStep(13))&& (i<timeStep(14)) %(4)
        beta(1,i) = betaInc(1,13);
    elseif (i≥timeStep(14))&& (i<timeStep(15)) %(4)
        beta(1,i) = betaInc(1,14);
    elseif (i≥timeStep(15))&& (i<timeStep(16)) %(3)
        beta(1,i) = betaInc(1,15);
    elseif (i≥timeStep(16))&& (i<timeStep(17)) %(3)
        beta(1,i) = betaInc(1,16);
    elseif (i≥timeStep(17))&& (i<timeStep(18)) %(2)
        beta(1,i) = betaInc(1,17);
    elseif (i≥timeStep(18))&& (i<timeStep(19)) %(2)
        beta(1,i) = betaInc(1,18);
    elseif (i≥timeStep(19))&& (i<timeStep(20))  %(1)
        beta(1,i) = betaInc(1,19);
    elseif (i≥timeStep(20))&& (i<timeStep(21)) %(1)
        beta(1,i) = betaInc(1,20);
     else
        beta(i) = 0.9;
    end
end

% for i=1:t
%     if i≥ 0 && i<365+ss
%         beta(1,i) = betaChoices(1);
%     elseif i≥365+ss && i<730+ss
%         beta(1,i) = betaChoices(2);
%     elseif i≥ 730+ss && i< 1095+ss
%         beta(1,i) = betaChoices(3);
%     elseif i≥1095+ss && i< 1460+ss
%         beta(1,i) = betaChoices(4);
%     else
%         beta(1,i) = betaChoices(5);
%     end
% end


plot(beta)

newPatients = [];
circPatients = [];
clPatients0 = [];
clPatients1 = [];
clPatients2 = [];
clPatients3 = [];
cathPatients0 = [];
```

```
cathPatients1 = [];
cathPatients2 = [];
cathPatients3 = [];
bothPatients0 = [];
bothPatients1 = [];
bothPatients2 = [];
bothPatients3 = [];
infPatients0 = [];
infPatients1 = [];
infPatients2 = [];
infPatients00 = [];
infPatients11 = [];

N = 100;
O = 0;
P00 = 100;
P01 = 0;
P02  = 0;
P03  = 0;
P10  = 400;
P11 = 0;
P12 = 0;
P13 =0;
P20 = 250;
P21 = 0;
P22 =0;
P23 = 0;
I0 = 0;
I1 =0;
I2 = 0;
I00 = 0;
I11 = 0;

totalPop = N + O + P00 + P01 + P02 + P03 + P10 + P11 +  ...
   P12 + ...
    P13 + P20 + P21 + P22 + P23 + I0 + I1 + I2 + I00 + I11;

dischargeMatrix = zeros(19,19);
deviceMatrix = zeros(19,19);
batheMatrix = zeros(19,19);
infectMatrix = zeros(19,19);
kitMatrix = zeros(19,19);

patientMatrix = zeros(19,1); %setting up the patient matrix
patientMatrix(1,1)=N;
patientMatrix(2,1)=O;
patientMatrix(3,1)=P00;
patientMatrix(4,1)=P01;
patientMatrix(5,1)=P02;
patientMatrix(6,1)=P03;
patientMatrix(7,1)=P10;
```

```
patientMatrix(8,1)=P11;
patientMatrix(9,1)=P12;
patientMatrix(10,1)=P13;
patientMatrix(11,1)=P20;
patientMatrix(12,1)=P21;
patientMatrix(13,1)=P22;
patientMatrix(14,1)=P23;
patientMatrix(15,1)=I0;
patientMatrix(16,1)=I1;
patientMatrix(17,1)=I2;
patientMatrix(18,1) = I00;
patientMatrix(19,1) = I11;


for b=1:length(beta)
    for w=1:length(betaStar)
        bothinfections = [];
        CAUTIinfections = [];
        CLABSIinfections = [];




        %probability of getting device
        pN0 = getCL;
        pN1 = getCath;
        pN2 = getCLandCath;
        pO0 = getCL;
        pO1 = getCath;
        pO2 = getCLandCath;
        pO3 = getCLandCath;
        p00 = getCLandCath;
        p01 = getCLandCath;
        p02 = getCLandCath;
        p03 = getCLandCath;
        p10 = getCLandCath;
        p11 = getCLandCath;
        p12 = getCLandCath;
        p13 = getCLandCath;

        t = years*daysInYear + ss ; %number of days the  ...
           simulation was run

        %initial distribution of patients
        N = 100;
        O = 0;
        P00 = 100;
        P01 = 0;
        P02  = 0;
        P03  = 0;
```

```
P10  = 400;
P11 = 0;
P12 = 0;
P13 =0;
P20 = 250;
P21 = 0;
P22 =0;
P23 = 0;
I0 = 0;
I1 =0;
I2 = 0;
I00 = 0;
I11 = 0;

%t = 730+300;

totalPop = N + O + P00 + P01 + P02 + P03 + P10  ...
   + P11 + P12 + ...
    P13 + P20 + P21 + P22 + P23 + I0 + I1 + I2  ...
       + I00 + I11;

% % ----- discharge matrix -----
%setting up the discharge matrix

dischargeMatrix(1,1) = 1;
dischargeMatrix(1,2) = ΔOther;
dischargeMatrix(1,3) = ΔCL;
dischargeMatrix(1,4) = ΔCL;
dischargeMatrix(1,5) = ΔCL;
dischargeMatrix(1,6) = ΔCL;
dischargeMatrix(1,7) = ΔCath;
dischargeMatrix(1,8) = ΔCath;
dischargeMatrix(1,9) = ΔCath;
dischargeMatrix(1,10) = ΔCath;
dischargeMatrix(1,11) = ΔCL;
dischargeMatrix(1,12) = ΔCL;
dischargeMatrix(1,13) = ΔCL;
dischargeMatrix(1,14) = ΔCL;
dischargeMatrix(1,15) = ΔCLinf;
dischargeMatrix(1,16) = ΔCathinf;
dischargeMatrix(1,17) = ΔCLinf;
dischargeMatrix(1,18) = ΔCLinf;
dischargeMatrix(1,19) = ΔCLinf;


dischargeMatrix(2,2) = 1 - ΔOther;
dischargeMatrix(3,3) = 1 - ΔCL;
dischargeMatrix(4,4) = 1 - ΔCL;
dischargeMatrix(5,5) = 1 - ΔCL;
dischargeMatrix(6,6) = 1 - ΔCL;
dischargeMatrix(7,7) = 1 - ΔCath;
```

```
dischargeMatrix(8,8) = 1 - ΔCath;
dischargeMatrix(9,9) = 1 - ΔCath;
dischargeMatrix(10,10) = 1 - ΔCath;
dischargeMatrix(11,11) = 1 - ΔCL;
dischargeMatrix(12,12) = 1 - ΔCL;
dischargeMatrix(13,13) = 1 - ΔCL;
dischargeMatrix(14,14) = 1 - ΔCL;
dischargeMatrix(15,15) = 1 - ΔCLinf;
dischargeMatrix(16,16) = 1 - ΔCathinf;
dischargeMatrix(17,17) = 1 - ΔCLinf;
dischargeMatrix(18,18) = 1 - ΔCLinf;
dischargeMatrix(19,19) = 1-ΔCLinf;

% % ----- infection matrix -----


infectMatrix(1,1) = 1;
infectMatrix(2,2) = 1;

infectMatrix(3,3) = 1 ;
infectMatrix(4,4) = 1 ;
infectMatrix(5,5) = 1 - r02;
infectMatrix(6,6) = 1 - r03;
infectMatrix(7,7) = 1 ;
infectMatrix(8,8) = 1 ;
infectMatrix(9,9) = 1  ;
infectMatrix(10,10) = 1 - r13 ;
infectMatrix(11,11) = 1 - r20 - r00prime -  ...
   r10prime ;
infectMatrix(12,12) = 1 - r21 - r01prime -  ...
   r11prime ;
infectMatrix(13,13) = 1 - r22 - r02prime -  ...
   r12prime ;
infectMatrix(14,14) = 1 - r23 - r03prime -  ...
   r13prime ;
infectMatrix(15,15) = 1;
infectMatrix(16,16) = 1;
infectMatrix(17,17) = 1;
infectMatrix(18,18) = 1 - rI0;
infectMatrix(19,19) = 1- rI1;


infectMatrix(15,3) = 0;
infectMatrix(15,4) = 0;
infectMatrix(15,5) = r02;
infectMatrix(15,6) = r03;

infectMatrix(16,7) = 0;
infectMatrix(16,8) = 0;
infectMatrix(16,9) = 0;
infectMatrix(16,10) = r13;
```

```
infectMatrix(15,11) = r00prime;
infectMatrix(16,11) = r10prime;
infectMatrix(17,11) = r20;

infectMatrix(15,12) = r01prime;
infectMatrix(16,12) = r11prime;
infectMatrix(17,12) = r21;

infectMatrix(15,13) = r02prime;
infectMatrix(16,13) = r12prime;
infectMatrix(17,13) = r22;

infectMatrix(15,14) = r03prime;
infectMatrix(16,14) = r13prime;
infectMatrix(17,14) = r23;

infectMatrix(17,18) = rI0;
infectMatrix(17,19) = rI1;


% % ----- bathing matrix -----


batheMatrix(2,1) = 1;
batheMatrix(3,2) = 1;

batheMatrix(3,3) = beta(b);
batheMatrix(4,3) = 1- beta(b);

batheMatrix(3,4) = beta(b);
batheMatrix(5,4) = 1-beta(b);

batheMatrix(3,5) = beta(b);
batheMatrix(6,5) = 1- beta(b);

batheMatrix(3,6) = beta(b);
batheMatrix(6,6) = 1-beta(b);

batheMatrix(7,7) = beta(b);
batheMatrix(8,7) = 1-beta(b);

batheMatrix(7,8) = beta(b);
batheMatrix(9,8) = 1-beta(b);

batheMatrix(7,9) = beta(b);
batheMatrix(10,9) = 1-beta(b);

batheMatrix(7,10) = beta(b);
```

```
batheMatrix(10,10) = 1 - beta(b);

batheMatrix(11,11) = beta(b);
batheMatrix(12,11) = 1-beta(b);

batheMatrix(11,12) = beta(b);
batheMatrix(13,12) = 1- beta(b);

batheMatrix(11,13) = beta(b);
batheMatrix(14,13) = 1-beta(b);

batheMatrix(11,14) = beta(b);
batheMatrix(14,14) = 1 - beta(b);

batheMatrix(15,15) = 1;
batheMatrix(16,16) = 1;
batheMatrix(17,17) = 1;
batheMatrix(18,18) = 1;
batheMatrix(19,19) = 1;

% % ----- device matrix ------

deviceMatrix(1,1) = 1 - pN0 - pN1 - pN2;
deviceMatrix(2,2) = 1 - pO0 - pO1 - pO2;
deviceMatrix(3,1) = pN0;
deviceMatrix(3,2) = pO0;
deviceMatrix(3,3) = 1-p00;
deviceMatrix(4,4) = 1- p01;
deviceMatrix(5,5) = 1- p02;
deviceMatrix(6,6) = 1- p03;
deviceMatrix(7,7) = 1 - p10;
deviceMatrix(8,8) = 1 - p11;
deviceMatrix(9,9) = 1 - p12;
deviceMatrix(10,10) = 1 - p13;
deviceMatrix(7,1) = pN1;
deviceMatrix(7,2) = pO1;
deviceMatrix(11,1) = pN2;
deviceMatrix(11,2) = pO2;
deviceMatrix(11,3) = p00;
deviceMatrix(11,4) = p01;
deviceMatrix(11,5) = p02;
deviceMatrix(11,6) = p03;
deviceMatrix(11,7) = p10;
deviceMatrix(11,8) = p11;
deviceMatrix(11,9) = p12;
deviceMatrix(11,10) = p13;
deviceMatrix(11,11) = 1;
deviceMatrix(12,12) = 1;
deviceMatrix(13,13) = 1;
deviceMatrix(14,14) = 1;
deviceMatrix(15,15) = 1;
```

```
        deviceMatrix(16,16) =1;
        deviceMatrix(17,17) =1;
        deviceMatrix(18,18) = 1;
        deviceMatrix(19,19)=1;

         % % ----- central line standardized kit matrix  ...
            ------
  %setting up standardized kit matrix

    kitMatrix(1,1) = 1;
    kitMatrix(2,2) = 1;


    kitMatrix(3,3) = betaStar(w);
    kitMatrix(4,3) = 1- betaStar(w);

    kitMatrix(3,4) = betaStar(w);
    kitMatrix(5,4) = 1-betaStar(w);

    kitMatrix(3,5) = betaStar(w);
    kitMatrix(6,5) = 1- betaStar(w);

    kitMatrix(3,6) = betaStar(w);
    kitMatrix(6,6) = 1-betaStar(w);

    kitMatrix(7,7) = 1;
    kitMatrix(8,8) = 1;
    kitMatrix(9,9) = 1;
    kitMatrix(10,10) = 1;

    kitMatrix(11,11) = betaStar(w);
    kitMatrix(12,11) = 1-betaStar(w);

    kitMatrix(11,12) = betaStar(w);
    kitMatrix(13,12) = 1- betaStar(w);

    kitMatrix(11,13) = betaStar(w);
    kitMatrix(14,13) = 1-betaStar(w);

    kitMatrix(11,14) = betaStar(w);
    kitMatrix(14,14) = 1 - betaStar(w);

    kitMatrix(15,15) = 1;
    kitMatrix(16,16) = 1;
    kitMatrix(17,17) = 1;
    kitMatrix(18,18) = 1;
    kitMatrix(19,19) = 1;
%

     application1 =infectMatrix*deviceMatrix;
     application2 = application1*batheMatrix;
```

```
        application3 = application2*kitMatrix;
        application4 = application3*dischargeMatrix;

        patientMatrix = application4*patientMatrix;

        newPatients(b,1) = patientMatrix(1,1);
        circPatients(b,1) = patientMatrix(2,1);
        clPatients0(b,1) = patientMatrix(3,1);
        clPatients1(b,1) = patientMatrix(4,1);
        clPatients2(b,1) = patientMatrix(5,1);
        clPatients3(b,1) = patientMatrix(6,1);
        cathPatients0(b,1) = patientMatrix(7,1);
        cathPatients1(b,1) = patientMatrix(8,1);
        cathPatients2(b,1) = patientMatrix(9,1);
        cathPatients3(b,1) = patientMatrix(10,1);
        bothPatients0(b,1) = patientMatrix(11,1);
        bothPatients1(b,1) =  patientMatrix(12,1);
        bothPatients2(b,1) = patientMatrix(13,1);
        bothPatients3(b,1) = patientMatrix(14,1);
        infPatients0(b,1) = patientMatrix(15,1);
        infPatients1(b,1) =  patientMatrix(16,1);
        infPatients2(b,1) = patientMatrix(17,1);
        infPatients00(b,1) =  patientMatrix(18,1);
        infPatients11(b,1) =  patientMatrix(19,1);

        ceil(patientMatrix); %rounding patient values up

    end
end



newCAUTIInfectionsMatrix6Months = [];
newCAUTIInfectionsMatrix12Months = [];
newCAUTIInfectionsMatrix18Months = [];
newCAUTIInfectionsMatrix24Months = [];
newCAUTIInfectionsMatrix30Months = [];
newCAUTIInfectionsMatrix36Months = [];
newCAUTIInfectionsMatrix42Months = [];
newCAUTIInfectionsMatrix48Months = [];
newCAUTIInfectionsMatrix54Months = [];
newCAUTIInfectionsMatrix60Months = [];
newCAUTIInfectionsMatrix=[];


newCLABSIInfectionsMatrix6Months = [];
newCLABSIInfectionsMatrix12Months = [];
newCLABSIInfectionsMatrix18Months = [];
newCLABSIInfectionsMatrix24Months = [];
newCLABSIInfectionsMatrix30Months = [];
```

```
newCLABSIInfectionsMatrix36Months = [];
newCLABSIInfectionsMatrix42Months = [];
newCLABSIInfectionsMatrix48Months = [];
newCLABSIInfectionsMatrix54Months = [];
newCLABSIInfectionsMatrix60Months = [];
newCLABSIInfectionsMatrix=[];

newBothInfectionsMatrix6Months = [];
newBothInfectionsMatrix12Months = [];
newBothInfectionsMatrix18Months = [];
newBothInfectionsMatrix24Months = [];
newBothInfectionsMatrix30Months = [];
newBothInfectionsMatrix36Months = [];
newBothInfectionsMatrix42Months = [];
newBothInfectionsMatrix48Months = [];
newBothInfectionsMatrix54Months = [];
newBothInfectionsMatrix60Months = [];
newBothInfectionsMatrix=[];



sixMonths = ceil(30.4*6)+ss; %calculating new infections
for p=(sixMonths - ss):sixMonths
    newBothinfections6Months =   ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections6Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections6Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections6Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections6Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections6Months;
end
sixMonSumCLABSI = sum(newCLABSIMatrix(ss:sixMonths))
sixMonSumCAUTI = sum(newCAUTIMatrix(ss:sixMonths))
sixMonSumBoth = sum(newBothMatrix(ss:sixMonths))
```

```
twelveMonths = 365+ss;
for p=sixMonths+1:twelveMonths
    newBothinfections12Months =   ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections12Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections12Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections12Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections12Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections12Months;

end
twelveMonSumCLABSI = sum(newCLABSIMatrix(ss:twelveMonths))
twelveMonSumCAUTI = sum(newCAUTIMatrix(ss:twelveMonths))
twelveMonSumBoth = sum(newBothMatrix(ss:twelveMonths))


eighteenMonths = ceil(30.4*18)+ss;
for p=twelveMonths+1:eighteenMonths
    newBothinfections18Months =  ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections18Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
```

```
    newCAUTIinfections18Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections18Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections18Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections18Months;
end
eighteenMonSumCLABSI =  ...
   sum(newCLABSIMatrix(ss:eighteenMonths))
eighteenMonSumCAUTI = sum(newCAUTIMatrix(ss:eighteenMonths))
eighteenMonSumBoth = sum(newBothMatrix(ss:eighteenMonths))

twentyFourMonths = ceil(30.4*24)+ss;
for p=eighteenMonths+1:twentyFourMonths
    newBothinfections24Months =   ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections24Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections24Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections24Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections24Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections24Months;
end
twentyFourMonSumCLABSI =  ...
   sum(newCLABSIMatrix(ss:twentyFourMonths))
twentyFourMonSumCAUTI =  ...
   sum(newCAUTIMatrix(ss:twentyFourMonths))
twentyFourMonSumBoth =  ...
   sum(newBothMatrix(ss:twentyFourMonths))

thirtyMonths = ceil(30.4*30)+ss;
for p=twentyFourMonths+1:thirtyMonths
    newBothinfections30Months =   ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
```

```
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections30Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections30Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections30Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections30Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections30Months;
end
thirtyMonSumCLABSI = sum(newCLABSIMatrix(ss:thirtyMonths))
thirtyMonSumCAUTI = sum(newCAUTIMatrix(ss:thirtyMonths))
thirtyMonSumBoth = sum(newBothMatrix(ss:thirtyMonths))

thirtySixMonths = ceil(30.4*36)+ss;
for p=thirtyMonths+1:thirtySixMonths
    newBothinfections36Months =  ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections36Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections36Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections36Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections36Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections36Months;
end
thirtySixMonSumCLABSI =  ...
   sum(newCLABSIMatrix(ss:thirtySixMonths))
thirtySixMonSumCAUTI =  ...
   sum(newCAUTIMatrix(ss:thirtySixMonths))
```

```
thirtySixMonSumBoth = sum(newBothMatrix(ss:thirtySixMonths))

fortyTwoMonths = ceil(30.4*42)+ss;
for p=thirtySixMonths+1:fortyTwoMonths
    newBothinfections42Months =   ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections42Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections42Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections42Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections42Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections42Months;
end
fortyTwoMonSumCLABSI =  ...
   sum(newCLABSIMatrix(ss:fortyTwoMonths))
fortyTwoMonSumCAUTI = sum(newCAUTIMatrix(ss:fortyTwoMonths))
fortyTwoMonSumBoth = sum(newBothMatrix(ss:fortyTwoMonths))

fortyEightMonths = ceil(30.4*48)+ss;
for p=fortyTwoMonths+1:fortyEightMonths
    newBothinfections48Months =  ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections48Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections48Months = cathPatients0(p)*r10 +  ...
```

```
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections48Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections48Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections48Months;
end
fortyEightMonSumCLABSI =  ...
   sum(newCLABSIMatrix(ss:fortyEightMonths))
fortyEightMonSumCAUTI =  ...
   sum(newCAUTIMatrix(ss:fortyEightMonths))
fortyEightMonSumBoth =  ...
   sum(newBothMatrix(ss:fortyEightMonths))

fiftyFourMonths = ceil(30.4*54)+ss;
for p=fortyEightMonths+1:fiftyFourMonths
    newBothinfections54Months =   ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections54Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections54Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections54Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections54Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections54Months;
end
fiftyFourMonSumCLABSI =  ...
   sum(newCLABSIMatrix(ss:fiftyFourMonths))
fiftyFourMonSumCAUTI =  ...
   sum(newCAUTIMatrix(ss:fiftyFourMonths))
fiftyFourMonSumBoth = sum(newBothMatrix(ss:fiftyFourMonths))

sixtyMonths = ceil(30.4*60)+ss;
for p=fiftyFourMonths+1:sixtyMonths
    newBothinfections60Months =   ...
       bothPatients0(p)*r00prime  +  ...
       bothPatients1(p)*r01prime ...
        + bothPatients2(p)*r02prime +  ...
           bothPatients3(p)*r03prime ...
```

```
        +  + bothPatients0(p)*r10prime  +  ...
           bothPatients1(p)*r11prime ...
        + bothPatients2(p)*r12prime +  ...
           bothPatients3(p)*r13prime ...
        + bothPatients0(p)*r20  + bothPatients1(p)*r21  ...
        + bothPatients2(p)*r22 + bothPatients3(p)*r23 +  ...
           infPatients00(p)*rI0 ...
        + infPatients11(p)*rI1;
    newCLABSIinfections60Months = clPatients0(p)*r00+  ...
       clPatients1(p)*r01+ clPatients2(p)*r02 +  ...
       clPatients3(p)*r03 ;
    newCAUTIinfections60Months = cathPatients0(p)*r10 +  ...
       cathPatients2(p)*r12 + cathPatients1(p)*r11+  ...
       cathPatients3(p)*r13  ;
    newBothMatrix(p,1) = newBothinfections60Months;
    newCLABSIMatrix(p,1) = newCLABSIinfections60Months;
    newCAUTIMatrix(p,1) = newCAUTIinfections60Months;
end
sixtyMonSumCLABSI = sum(newCLABSIMatrix(ss:sixtyMonths))
sixtyMonSumCAUTI = sum(newCAUTIMatrix(ss:sixtyMonths))
sixtyMonSumBoth = sum(newBothMatrix(ss:sixtyMonths))

oppBetaVector = 1 - beta;
numberOfBaths = 850*sum(beta);
numberOfNonCHGBaths = 850*sum(oppBetaVector);
numberOfKits = 850*(sum(bothPatients0(ss:sixtyMonths))  ...
   + sum(bothPatients1(ss:sixtyMonths)) +  ...
   sum(bothPatients2(ss:sixtyMonths))...
    + sum(bothPatients3(ss:sixtyMonths)) +  ...
       sum(clPatients0(ss:sixtyMonths)) +  ...
       sum(clPatients1(ss:sixtyMonths)) + ...
    sum(clPatients2(ss:sixtyMonths)) +  ...
       sum(clPatients3(ss:sixtyMonths)))
printVectorCLABSI = [];
printVectorCAUTI = [];
printVectorBoth = [];
printVectorCLABSI = [printVectorCLABSI; sixMonSumCLABSI  ...
   twelveMonSumCLABSI eighteenMonSumCLABSI  ...
   twentyFourMonSumCLABSI thirtyMonSumCLABSI  ...
   thirtySixMonSumCLABSI fortyTwoMonSumCLABSI  ...
   fortyEightMonSumCLABSI fiftyFourMonSumCLABSI  ...
   sixtyMonSumCLABSI];
printVectorCAUTI =  [printVectorCAUTI; sixMonSumCAUTI  ...
   twelveMonSumCAUTI eighteenMonSumCAUTI  ...
   twentyFourMonSumCAUTI thirtyMonSumCAUTI  ...
   thirtySixMonSumCAUTI fortyTwoMonSumCAUTI  ...
   fortyEightMonSumCAUTI fiftyFourMonSumCAUTI  ...
   sixtyMonSumCAUTI];
printVectorBoth = [printVectorBoth; sixMonSumBoth  ...
   twelveMonSumBoth eighteenMonSumBoth  ...
   twentyFourMonSumBoth thirtyMonSumBoth  ...
```

```
    thirtySixMonSumBoth fortyTwoMonSumBoth  ...
    fortyEightMonSumBoth fiftyFourMonSumBoth  ...
    sixtyMonSumBoth];

printVector = [printVectorBoth; printVectorCAUTI;  ...
    printVectorCLABSI];
```

Appendix D

MATLAB CODE – SIR MODEL

```
% SIR Model

S0 = 4500000;
I0 = 2;
R0 = 0;

p0 = [S0 I0 R0];

tspan = 0:530;

[t,p] = ode15s(@Popmodel, tspan, p0);

% Plot
S = p(:,1);
I = p(:,2);
R = p(:,3);

figure(1)
hold on
plot(t, S,'LineWidth',3);
plot(t, I,'LineWidth',3);
plot(t, R,'LineWidth',3);
legend('S','I','R')
xlabel('Time')
ylabel('Number of Individuals')
title('SIR Model')
hold off


% Function Definitions

function pdot = Popmodel(t,u)

%Parameters for SIR Model
d = 14;

S = u(1);
I = u(2);
R = u(3);
```

```
beta = transmission(t); %beta is time dependent

dS = -beta*S*I; %SIR equations
dI = beta*S*I - (1/d)*I;
dR = (1/d)*I;

pdot=[dS dI dR]';

end

function y = beta1(t)
    betah = 0.0000006; %transmission due to hospital
    Eh = 0.8; %effectiveness of PPE
    tH = 50; %time when PPE runs out
    if t≤tH
        y = betah*Eh;
    else
        y = betah;
    end

end

function y = beta2(t)
    betas = 0.00000006; %transmission due to community
    Es = 0.6; %effectiveness of social distancing
    tS = 45; %time when social distancing starts
    if t≤ tS
        y = betas;
    else
        y = betas*Es;
    end

end

function beta = transmission(t)
    h = 0.1;
    beta = beta1(t)*h + beta2(t)*(1-h);
end
```

Appendix E

MATLAB CODE – NON-ADI MODEL

```
clear

%-------------------------------------------------------------------------
%           PARAMETERS
%-------------------------------------------------------------------------
endSim = 1;
yearlyInfectionCounter(1) = 0;
testsYearly = [];
double = 2;
half = 0.5;
ad = 1;


for w=1 :endSim
    endTime = 6*365; %10*365;
    burnInYear = 1;
    adjustTime = 1*365; %run program for this long  ...
       before making calculatio;ns
    tt = endTime + adjustTime;
    newInfection = zeros(tt,1);
    hospInfection1 = zeros(tt,1);
    commInfection1 = zeros(tt,1);
    tests = 0;

    %CANNOT ADJUST - LIT VALUES
    gamma = 1/10*ad; %recovery from C.diff,
    tau = 1;
    lambda = 1/6*ad;  %likelihood of being prescribed  ...
       antibiotics
    theta1 = 1/10*ad;
    b = 0.8; % proportion of patients coming in susceptible

    %CAN ADJUST
    sigma1 = 0.01*ad;  %becoming colonized from susceptible
    sigma2 = 0.05*ad;  %becoming colonized from  ...
       susceptible on antibiotics
    theta2 = 1/60*ad; % moving from colonized in  ...
       hospital to infectious
    theta3 = 1/60*ad;
```

```
alphaCA = 1;%1.06;
alphaC = 1;%1.06;
alphaCH = 1;%1.06;
alphaIN = 2;
alphaIS = 1;%1.03;
alphaR = 1; %1.015;
alphaD = 1;% 1.1;
alpha = 1;
enCo = 1000/ad;
enviroBoost = 6;


%-------------------------------------------------------------------
%           INITIALIZING PATIENT STATES & ENVIRONMENT
%-------------------------------------------------------------------

% S = 1, SA = 2, % Ca = 3, C = 4, IN = 5, IS = 6, R  ...
   = 7, CH = 8

p1 = 1;
p2 = 1;
p3 = 1;
p4 = 1;
p5 = 1;
p6 = 1;
p7 = 1;
p8 = 1;
p9 = 1;
p10 = 1;
p11 = 1;
p12 = 1;
p13 = 1;
p14 = 1;
p15 = 1;
p16 = 2;
p17 = 2;
p18 = 2;
p19 = 2;
p20 = 2;
p21 = 2;


vector = [p1; p2; p3; p4; p5; p6; p7; p8; p9; p10;  ...
   p11; p12; p13; p14; p15; p16; p17; p18; p19;  ...
   p20; p21];
vectorNames = {'p1'; 'p2'; 'p3'; 'p4'; 'p5'; 'p6';  ...
   'p7'; 'p8'; 'p9'; 'p10'; 'p11'; 'p12'; 'p13';  ...
   'p14'; 'p15'; 'p16'; 'p17'; 'p18'; 'p19'; 'p20';  ...
   'p21'};
P(1) = 0;
```

```
probPath(1) = 0;

array = zeros(length(vector) , endTime, 4);
array(:,1,1) = vector;
numPatients = size(vector);

initialLOS = [randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1); randi([0,42],1)];
array(:,1,2) = initialLOS;

 %tests = zeros(numPatients(1),tt);
%-------------------------------------------------------------------
%           BIG LOOP ITERATING THROUGH PATIENTS ON  ...
   INSIDE (i)
%           AND DAY SIMULATION ON THE OUTSIDE (j)
%-------------------------------------------------------------------

for j=2:(tt)

    for i=1:numPatients %want to iterate this over  ...
       entire vector except for environment

        %-----------------------------------------------------------
        %           SETTING UP RANDOM NUMBERS TO BE  ...
           USED BELOW
        %-----------------------------------------------------------

        r0 = rand();
        r1 = rand();
        r2 = rand();
        r3 = rand();
        r4 = rand();
        r5 = rand();
        r6 = rand();
        r7 = rand();
        r8 = rand();

        %-----------------------------------------------------------
        %           ADDING TO THE LOS
        %-----------------------------------------------------------

        array(i,j,2) = array(i,j-1,2) + 1;
```

```
%-------------------------------------------------------------
%           PATIENT TRANSITION STATEMENTS
%-------------------------------------------------------------
if array(i,j-1,1) == 0
    %array(i,j,2)  = 0;
    if r0 ≥ 0.2
        array(i,j,1) = 1;
    else
        array(i,j,1) = 4;
    end

elseif array(i,j-1,1) == 1 %patient is in S
    if r1≥0 && r1 < lambda
        array(i,j,1) = 2;
     elseif r1 ≥ lambda && r1 < lambda +  ...
        sigma1*probPath(j-1)
         array(i,j,1) = 8;
    else
         array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1) == 2 %patient is in SA
    if r2≥ 0 && r2 < sigma2*probPath(j-1)
        array(i,j,1) = 3;
    else
         array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1) == 3 %patient is in CA
    if r3 ≥0 && r3 < theta1
        array(i,j,1) = 5;
        newInfection(j,1) =  ...
           newInfection(j,1) + 1;
        hospInfection1(j,1) =  ...
           hospInfection1(j,1) + 1;
        %tests(i,j) = 1;
        tests = tests + 1;
    else
         array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1) == 4 %patient is in C
    if r4 ≥ 0 && r4 < theta3
        array(i,j,1) = 5;
        newInfection(j,1) =  ...
           newInfection(j,1) + 1;
        commInfection1(j,1) =  ...
           commInfection1(j,1) + 1;
        tests = tests + 1;
    else
         array(i,j,1) = array(i,j-1,1);
```

```
    end


elseif array(i,j-1,1) == 5 %patient is in IN
    if r5 ≥ 0 && r5 < tau
        array(i,j,1) = 6;
    else
         array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1) == 6 %patient is in IS
    if r6 ≥ 0 && r6 < gamma
        array(i,j,1) = 7;
    else
         array(i,j,1) = array(i,j-1,1);
    end
elseif array(i,j-1,1) == 8 %patient is in CH
    if r8 ≥0 && r8 < theta2
        array(i,j,1) = 5;
        newInfection(j,1) =  ...
           newInfection(j,1) + 1;
        hospInfection1(j,1) =  ...
           hospInfection1(j,1) + 1;
        tests = tests + 1;

    else
        array(i,j,1) = array(i,j-1,1);
    end

else %patient is in R
         array(i,j,1) = array(i,j-1,1);

end



%-------------------------------------------------------------
%           DISCHARGE CALCULATIONS
%-------------------------------------------------------------

disNum = 0.8;
disNum2 = 0.9;

if array(i,j,2) > 42 && (array(i,j,3) > 14  ...
   || array(i,j,3) ==0) %array(i,j-1,3) >  ...
   14       %want to make sure that
    %people haven't gotten sick or recovered
    %reset LOS counter here, reset page 3 here

    if array(i,j,1) == 1 && rand() <  ...
       disNum2 %▵S
```

```
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

        elseif array(i,j,1) == 2 && rand() <  ...
           disNum2 %▵SA
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;


        elseif array(i,j,1) == 3 && rand()<  ...
           disNum %▵CA
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

        elseif array(i,j,1) == 4 && rand()<  ...
           0.99 %▵C
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;


        elseif array(i,j,1) == 7 && rand() <  ...
           disNum %▵R
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

        elseif array(i,j,1) == 8 && rand() <  ...
           disNum2 %▵CH
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

        end
    elseif array(i,j,2) > 56 && array(i,j,1)==7  ...
       %person may have been sick or recovered
        if rand()< disNum2 %▵R + dR
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;
            % disp('sick discharge')
        end
    else


    end

    %-----------------------------------------------------------
```

```
    %           CALCULATING NEW INFECTIONS
    %-------------------------------------------------------------


    if mod(j,30)==0
        monthCount = j/30;
        cumulative30DaySumInfected(w,monthCount)  ...
           = sum(newInfection(j-29:j));

    end

    if mod(j,365) ==0
        m2 = j/365;
        yearlyInfectionCounter(w,m2) =  ...
           sum(newInfection(j-364:j));


    end


    %-------------------------------------------------------------
    %           CALCULATING LENGTH OF  ...
       INFECTIONS PATIENTS
    %-------------------------------------------------------------

    if array(i,j-1,1)==6 || array(i,j-1,1)==5  ...
       %counting sick LOS
        array(i,j,3) = array(i,j-1,3) + 1;
    end

end

    %-------------------------------------------------------------
    %           COUNTING PATIENTS IN EACH CLASS  ...
       ON EACH DAY
    %-------------------------------------------------------------
countDischarge = sum(array(:,:,1)==0,1);
countS = sum(array(:,:,1)==1,1);
countSA = sum(array(:,:,1)==2,1);
countCA = sum(array(:,:,1)==3,1);
countC = sum(array(:,:,1)==4,1);
countIN = sum(array(:,:,1)==5,1);
countIS = sum(array(:,:,1)==6,1);
countR = sum(array(:,:,1)==7,1);
countCH = sum(array(:,:,1)==8,1);

    %-------------------------------------------------------------
    %           YEARLY DISCHARGE COUNT
    %-------------------------------------------------------------

if  mod(j,365) ==0
```

```
            m2 = j/365;
            sumCountDischarge(w,m2) =  ...
               sum(countDischarge(j-364:j));
            testsYearly = [testsYearly; tests];
            tests = 0;
        end


        %-----------------------------------------------------------------
        %           ENVIRONMENT AND PROPORTION OF  ...
           ENVIRONMENT CONTAMINATED
        %           CALCULATIONS
        %-----------------------------------------------------------------

        P(j) = max(0.4*P(j-1) +alphaCH*countCH(j)  ...
           +alphaCA*countCA(j) + alphaC*countC(j) +  ...
           alphaIN*countIN(j) + alphaIS*countIS(j) +  ...
           alphaR*countR(j) - alphaD*countDischarge(j),0);
        probPath(j) = (alpha*enviroBoost*P(j))/(enCo +  ...
           alpha*enviroBoost*P(j));

    end

     %-----------------------------------------------------------------
    %           YEARLY MEANS AND ST DEVS CALCULATIONS
    %-----------------------------------------------------------------


for q=1:length(cumulative30DaySumInfected)
    if mod(q,12)==0
        yearCount = q/12;
        yearlyMean(w,yearCount) =  ...
           mean(cumulative30DaySumInfected(q-11:q));
        yearlyStDev(w,yearCount) =  ...
           std(cumulative30DaySumInfected(q-11:q));
    end

end

for r=1:tt
    if mod(r,365) ==0
        m3 = r/365;
        hospInfYearly(w,m3) = sum(hospInfection1(r-364:r));
        commInfYearly(w,m3) = sum(commInfection1(r-364:r));
        %testsYearly(w,m3) = sum(tests(r-364:r));
    end
end

hospInfSum(w,1) = sum(hospInfYearly(w,:));
commInfSum(w,1) = sum(commInfYearly(w,:));
totalInfSum(w,1) = hospInfSum(w,1) + commInfSum(w,1);
```

```
for v=1:tt
    if mod(v,30)==0
        m4 = v/30;
        hospInfMonthly(w,m4) = sum(hospInfection1(v-29:v));
        commInfMonthly(w,m4) = sum(commInfection1(v-29:v));
        totalInfMonthly(w,m4) = hospInfMonthly(w,m4) +  ...
           commInfMonthly(w,m4);
    end
end

%-------------------------------------------------------------------------
%          COUNTING NUMBER OF TESTS AND ALL INFECTIONS
%-------------------------------------------------------------------------

numberOfTests(w,1) =  ...
   sum(countIN(adjustTime+1 :endTime+adjustTime));
allInfections(w,1) =  ...
   sum(newInfection(adjustTime+1 :endTime+adjustTime));

hospInfection1([1:adjustTime],:) = [];
commInfection1([1:adjustTime],:) = [];

allHospInfPercent(w,1) = sum(hospInfection1) /  ...
   allInfections(w,1);
allCommInfPercent(w,1) = sum(commInfection1) /  ...
   allInfections(w,1);

%testSave = [testSave; tests];
end

%-------------------------------------------------------------------------
%          GETTING RID OF BURN IN YEAR
%-------------------------------------------------------------------------
yearlyInfectionCounter(:,[1:burnInYear]) = [];
yearlyMean(:,[1:burnInYear]) = [];
yearlyStDev(:,[1:burnInYear]) = [];
sumCountDischarge(:,[1:burnInYear]) = [];
hospInfYearly(:,[1:burnInYear]) = [];
commInfYearly(:,[1:burnInYear]) = [];
commInfMonthly(:,[1:12*burnInYear+1]) = [];
cumulative30DaySumInfected(:,[1:12*burnInYear+1]) = [];
hospInfMonthly(:,[1:12*burnInYear+1]) = [];


allYearsInfectionsMeans =   ...
   mean(yearlyInfectionCounter,'all');
allYearsInfectionsStDev =  ...
   std(yearlyInfectionCounter,0,'all');

allMonthsInfectionsMeans =  ...
```

```
   mean(cumulative30DaySumInfected,'all');
allMonthsInfectionsStDev =  ...
   std(cumulative30DaySumInfected,0,'all');

allYearsHospInfMeanPercent = mean(allHospInfPercent, 'all');
allYearsHospInfCountMean = mean(hospInfYearly, 'all');
allYearsCommInfMeanPercent = mean(allCommInfPercent, 'all');
allYearsCommCountMean = mean(commInfYearly, 'all');

%testsYearly(:,[1:burnInYear]) = [];
%testYearlySum = sum(testsYearly');
%allYearlyMeanTests = mean(testsYearly,'all');

for b=1:length(testsYearly)
    if mod(b,11) == 1
        testsYearly(b) = nan;
    end
end

allYearsAvTests = nanmean(testsYearly);

aa = [allYearsCommInfMeanPercent;  ...
   allYearsHospInfMeanPercent; allYearsCommCountMean;  ...
   allYearsHospInfCountMean; allMonthsInfectionsMeans;  ...
   allMonthsInfectionsStDev; allYearsInfectionsMeans;  ...
   allYearsInfectionsStDev; allYearsAvTests];
aa = aa';


countHospCol = countCH + countCA;


x = [1:1:366];

% figure
% plot(x,P)
% legend('Amount of Pathogen')
%
% figure
% plot(x,probPath,'r')
% legend('proportion of pathogen in environment')
%



figure
plot(x,countHospCol(:,[365:730],1), 'r', x,  ...
   countC(:,[365:730],1), 'm',  ...
   x,countIN(:,[365:730],1), 'b', x,  ...
   countIS(:,[365:730],1), 'c')
legend('Hospital-onset, Colonized',  ...
```

```
    'Community-acquried, Colonized', 'Infected, not  ...
    tested', 'Infected, positive test')
xlabel('Time (days)');
ylabel('Number of patients');
```

Appendix F

MATLAB CODE – ADI- MODEL

```
clear

%-------------------------------------------------------------------------
%           PARAMETERS
%-------------------------------------------------------------------------
endSim = 1;
yearlyInfectionCounter(1) = 0;
testsYearly = [];
double = 2;
half = 0.5;


for w=1 :endSim
    endTime = 6*365;
    burnInYear = 1;
    adjustTime = 365; %run program for this long before  ...
       making calculations
    tt = endTime + adjustTime;
    newInfection = zeros(tt,1);
    hospInfection1 = zeros(tt,1);
    commInfection1 = zeros(tt,1);
    tests = 0;
    cleanRoom = 0;


    %CANNOT ADJUST - LIT VALUES
    gamma = 1/10; %recovery from C.diff,
    tau = 1; %testing accuracy
    lambda = 1/6;
    theta1 = 1/10;
    b = 0.8; % proportion of patients coming in susceptible

    %CAN ADJUST
    sigma1 = 0.01;  %becoming colonized from susceptible
    sigma2 = 0.05;  %becoming colonized from  ...
       susceptible on antibiotics
    theta2 = 1/60; % moving from colonized in hospital  ...
       to infectious
```

```
theta4 = 1/60;
alphaCA = 1;%1.06;
alphaCS = 1;%;1.06;
alphaCH = 1;%1.06;
alphaIN = 2;
alphaIS = 1;%;1.03;
alphaR = 1;%1.015;
alphaD = 1;%1.1;
alpha = 1;
enCo = 1000;
enviroBoost = 6;

%-------------------------------------------------------------------
%           INITIALIZING PATIENT STATES & ENVIRONMENT
%-------------------------------------------------------------------

% S = 1, SA = 2, CA = 3, CH = 4, IN = 5, CS = 6, IS  ...
   = 7, R = 8

p1 = 1;
p2 = 1;
p3 = 1;
p4 = 1;
p5 = 1;
p6 = 1;
p7 = 1;
p8 = 1;
p9 = 1;
p10 = 1;
p11 = 1;
p12 = 1;
p13 = 1;
p14 = 1;
p15 = 1;
p16 = 2;
p17 = 2;
p18 = 2;
p19 = 2;
p20 = 2;
p21 = 3;


vector = [p1; p2; p3; p4; p5; p6; p7; p8; p9; p10;  ...
   p11; p12; p13; p14; p15; p16; p17; p18; p19;  ...
   p20; p21];
vectorNames = {'p1'; 'p2'; 'p3'; 'p4'; 'p5'; 'p6';  ...
   'p7'; 'p8'; 'p9'; 'p10'; 'p11'; 'p12'; 'p13';  ...
   'p14'; 'p15'; 'p16'; 'p17'; 'p18'; 'p19'; 'p20';  ...
   'p21'};
P(1) = 0;
```

```
probPath(1) = 0;

array = zeros(length(vector) , endTime, 4);
array(:,1,1) = vector;
numPatients = size(vector);

initialLOS = [randi([0,42],1);randi([0,42],1);  ...
   randi([0,42],1);  ...
   randi([0,42],1);randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1);  ...
   randi([0,42],1); randi([0,42],1)];
array(:,1,2) = initialLOS;


%-------------------------------------------------------------------
%           BIG LOOP ITERATING THROUGH PATIENTS ON  ...
   INSIDE (i)
%           AND DAY SIMULATION ON THE OUTSIDE (j)
%-------------------------------------------------------------------


for j=2:(tt)

    for i=1:numPatients %want to iterate this over  ...
       entire vector except for environment
        r0 = rand();
        r1 = rand();
        r2 = rand();
        r3 = rand();
        r4 = rand();
        r5 = rand();
        r6 = rand();
        r7 = rand();

        %-------------------------------------------------------------
        %           ADDING TO THE LOS
        %-------------------------------------------------------------

        array(i,j,2) = array(i,j-1,2) + 1;

        %-------------------------------------------------------------
        %           PATIENT TRANSITION STATEMENTS
        %-------------------------------------------------------------

        if array(i,j-1,1) == 0
```

```
    if r0 ≥ 0.2
        array(i,j,1) = 1;
        tests = tests + 1;
    else
        array(i,j,1) = 6;
        tests = tests + 1;
    end
elseif array(i,j-1,1) == 1 %if patient is  ...
   in S
    if r1 ≥0 && r1 < sigma1*probPath(j-1)  ...
       %go to 3 via sigma with environment  ...
       weight factored in
        array(i,j,1) = 4;
    elseif r1 ≥ sigma1*probPath(j-1) && r1  ...
       < sigma1*probPath(j-1) + lambda %go  ...
       to 2 via lambda
        array(i,j,1) = 2;
    else
        array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1) == 2 %if patient is  ...
   in SA

    if r2 ≥ 0 && r2 < sigma2*probPath(j-1)
        array(i,j,1) = 3; %go to 4 via beta  ...
           with environment weight factored in
    else
        array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1) == 3 %if patient is  ...
   in CA
    if r3 ≥ 0 && r3 < theta1
        array(i,j,1) = 5;
        newInfection(j,1) =  ...
           newInfection(j,1) + 1;
        hospInfection1(j,1) =  ...
           hospInfection1(j,1) + 1;
        tests = tests + 1;
    else
        array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1) == 4 %if patient is  ...
   in CH
    if r4 ≥ 0 && r4 <  theta2
        array(i,j,1) = 5;
        newInfection(j,1) =  ...
           newInfection(j,1) + 1;
        hospInfection1(j,1) =  ...
```

```
            hospInfection1(j,1) + 1;
        tests = tests + 1;
    else
        array(i,j,1) = array(i,j-1,1);
    end
elseif array(i,j-1,1) == 5 %if patient is  ...
   in IN
     if r5 ≥ 0 && r5 < tau
        array(i,j,1) = 7;
         %newInfection(j,1) =  ...
            newInfection(j,1) + 1;
     else
        array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1)==6 % patient is in CS
    if r6 ≥ 0 && r6 < theta4
        array(i,j,1) = 7;
        newInfection(j,1) =  ...
           newInfection(j,1) + 1;
        commInfection1(j,1) =  ...
           commInfection1(j,1) + 1;
        tests = tests + 1;
    else
        array(i,j,1) = array(i,j-1,1);
    end

elseif array(i,j-1,1)==7 %patient is in IS
    if r7 ≥ 0 && r7 < gamma
        array(i,j,1) = 8;
    else
        array(i,j,1) = array(i,j-1,1);
    end
else %if patient is in R
    array(i,j,1) = array(i,j-1,1);

end

%-------------------------------------------------------------
%           DISCHARGE CALCULATIONS
%-------------------------------------------------------------

disNum = 0.8;
disNum2 = 0.9;

if array(i,j,2) > 42 && (array(i,j,3) > 14  ...
   || array(i,j,3) ==0) %array(i,j-1,3) >  ...
   14       %want to make sure that
    %people haven't gotten sick or recovered
    %reset LOS counter here, reset page 3 here
```

```
        if array(i,j,1) == 1 && rand() < disNum  ...
           %▵S + dS
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

            %disp('discharge from 1')
        elseif array(i,j,1) == 2 && rand() <  ...
           disNum %▵SA + dSA
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

            %disp('discharge from 2')
        elseif array(i,j,1) == 3 && rand()<  ...
           disNum %▵C + dC
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

            %disp('discharge from 3')

        elseif array(i,j,1) == 4 && rand()< disNum
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

        elseif array(i,j,1) == 6 && rand()< disNum
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;
            if j > 365
            cleanRoom = cleanRoom + 1;
            end

        elseif array(i,j,1) == 8 && rand() < disNum
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;

            %disp('discharge from 6')
        end
    elseif array(i,j,2) > 56 && array(i,j,1)==8  ...
       %person may have been sick or recovered
        if rand()< disNum2 %▵R + dR
            array(i,j,1) = 0;
            array(i,j,2) = 0;
            array(i,j,3) = 0;
            %disp('sick discharge')
        end
    else
```

```
        %disp(array(i,j-1,2))
        %disp(array(i,j-1,1))

    end

    %-------------------------------------------------------------
    %           CALCULATING NEW INFECTIONS
    %-------------------------------------------------------------

    if mod(j,30)==0
        monthCount = j/30;
        cumulative30DaySumInfected(w,monthCount)  ...
           = sum(newInfection(j-29:j));
    end

    if mod(j,365) ==0
        m2 = j/365;
        yearlyInfectionCounter(w,m2) =  ...
           sum(newInfection(j-364:j));

    end



    %-------------------------------------------------------------
    %           CALCULATING LENGTH OF  ...
       INFECTIONS PATIENTS
    %-------------------------------------------------------------

    if array(i,j-1,1)==5 || array(i,j-1,1)==7  ...
       %counting sick LOS
        array(i,j,3) = array(i,j-1,3) + 1;
    end

end

%-------------------------------------------------------------
%           COUNTING PATIENTS IN EACH CLASS ON  ...
   EACH DAY
%-------------------------------------------------------------
countDischarge = sum(array(:,:,1)==0,1);
countS = sum(array(:,:,1)==1,1);
countSA = sum(array(:,:,1)==2,1);
countCA = sum(array(:,:,1)==3,1);
countCH = sum(array(:,:,1)==4,1);
countIN = sum(array(:,:,1)==5,1);
countCS = sum(array(:,:,1) ==6,1);
countIS = sum(array(:,:,1)==7,1);
countR = sum(array(:,:,1)==8,1);

%-------------------------------------------------------------
```

```
        %           YEARLY DISCHARGE COUNT
        %-------------------------------------------------------------

        if  mod(j,365) ==0
            m2 = j/365;
            sumCountDischarge(w,m2) =  ...
               sum(countDischarge(j-364:j));
            testsYearly = [testsYearly; tests];
            tests = 0;
        end

        %-------------------------------------------------------------
        %           ENVIRONMENT AND PROPORTION OF  ...
           ENVIRONMENT CONTAMINATED
        %           CALCULATIONS
        %-------------------------------------------------------------

        P(j) = max(0.4*P(j-1) + alphaCA*countCA(j)  ...
           +alphaCH*countCH(j) + alphaCS*countCS(j) +  ...
           alphaIN*countIN(j) + alphaIS*countIS(j) +  ...
           alphaR*countR(j) - alphaD*countDischarge(j),0);
        probPath(j) = (alpha*P(j))/(enCo + alpha*P(j));


    end

    %-------------------------------------------------------------
    %           YEARLY MEANS AND ST DEVS CALCULATIONS
    %-------------------------------------------------------------

    for k=1:length(cumulative30DaySumInfected)
        if mod(k,12)==0
            yearCount = k/12;
            yearlyMean(w,yearCount) =  ...
               mean(cumulative30DaySumInfected(k-11:k));
            yearlyStDev(w,yearCount) =  ...
               std(cumulative30DaySumInfected(k-11:k));
        end

    end
    for r=1:tt
        if mod(r,365) ==0
            m3 = r/365;
            hospInfYearly(w,m3) =  ...
               sum(hospInfection1(r-364:r));
            commInfYearly(w,m3) =  ...
               sum(commInfection1(r-364:r));
           % testsYearly(w,m3) = sum(tests(r-364:r));
        end
    end
hospInfSum(w,1) = sum(hospInfYearly(w,:));
```

```
commInfSum(w,1) = sum(commInfYearly(w,:));
totalInfSum(w,1) = hospInfSum(w,1) + commInfSum(w,1);


    for v=1:tt
        if mod(v,30)==0
            m4 = v/30;
            hospInfMonthly(w,m4) =  ...
               sum(hospInfection1(v-29:v));
            commInfMonthly(w,m4) =  ...
               sum(commInfection1(v-29:v));
            totalInfMonthly(w,m4) =  ...
               hospInfMonthly(w,m4) + commInfMonthly(w,m4);
        end
    end
    %-----------------------------------------------------------------
%          COUNTING NUMBER OF TESTS AND ALL INFECTIONS
%-----------------------------------------------------------------

allInfections(w,1) = sum(newInfection(adjustTime+1:tt));

hospInfection1([1:adjustTime],:) = [];
commInfection1([1:adjustTime],:) = [];

allHospInfPercent(w,1) = sum(hospInfection1) /  ...
   allInfections(w,1);
allCommInfPercent(w,1) = sum(commInfection1) /  ...
   allInfections(w,1);


end



%-----------------------------------------------------------------
%          GETTING RID OF BURN IN YEAR
%-----------------------------------------------------------------
yearlyInfectionCounter(:,[1:burnInYear]) = [];
yearlyMean(:,[1:burnInYear]) = [];
yearlyStDev(:,[1:burnInYear]) = [];
sumCountDischarge(:,[1:burnInYear]) = [];
hospInfYearly(:,[1:burnInYear]) = [];
commInfYearly(:,[1:burnInYear]) = [];
commInfMonthly(:,[1:12*burnInYear+1]) = [];
cumulative30DaySumInfected(:,[1:12*burnInYear+1]) = [];
hospInfMonthly(:,[1:12*burnInYear+1]) = [];


allYearsInfectionsMeans =   ...
   mean(yearlyInfectionCounter,'all');
allYearsInfectionsStDev =  ...
```

```
   std(yearlyInfectionCounter,0,'all');

allMonthsInfectionsMeans =  ...
   mean(cumulative30DaySumInfected,'all');
allMonthsInfectionsStDev =  ...
   std(cumulative30DaySumInfected,0,'all');

allYearsHospInfMeanPercent = mean(allHospInfPercent, 'all');
allYearsHospInfCountMean = mean(hospInfYearly, 'all');
allYearsCommInfMeanPercent = mean(allCommInfPercent, 'all');
allYearsCommCountMean = mean(commInfYearly, 'all');

for b=1:length(testsYearly)
    if mod(b,11) == 1
        testsYearly(b) = nan;
    end
end

allYearsAvTests = nanmean(testsYearly);

aa = [allYearsCommInfMeanPercent;  ...
   allYearsHospInfMeanPercent; allYearsCommCountMean;  ...
   allYearsHospInfCountMean; allMonthsInfectionsMeans;  ...
   allMonthsInfectionsStDev; allYearsInfectionsMeans;  ...
   allYearsInfectionsStDev; allYearsAvTests];
aa = aa';

countHospCol = countCH + countCA;


%x = [1:1:j-364];
x = [1:1:366];

%
% figure
% plot(x,P)
% legend('Amount of Pathogen')
%
% figure
% plot(x,probPath,'r')
% legend('proportion of pathogen in environment')
%
% figure
% plot(x,countS(:,:,1), x,countSA(:,:,1),  ...
   x,countCA(:,:,1), x,countCN(:,:,1), x,  ...
   countCS(:,:,1), x,countIN(:,:,1), x, countIS(:,:,1),  ...
   x, countR(:,:,1))
% legend('Susceptible','Susceptible on Antibiotics',  ...
   'Colonized on antibiotics', 'Colonized, not  ...
   screened', 'Colonized, screened','Infected, not  ...
   screened','Infected, screened','Recovered')
```

```
% xlabel('Time (days)');
% ylabel('Number of patients');

figure
plot(x,countHospCol(:,[365:730],1), 'r', x,  ...
   countCS(:,[365:730],1), 'm',  ...
   x,countIN(:,[365:730],1), 'b', x,  ...
   countIS(:,[365:730],1), 'c')
legend('Hospital-onset, Colonized',  ...
   'Community-acquried, Colonized', 'Infected, not  ...
   tested', 'Infected, positive test')
xlabel('Time (days)');
ylabel('Number of patients');
```

Appendix G

MATLAB CODE – T-TEST FOR ABM

```
% MUST RUN non-ADI model or ADI-model first

filename = '/Users/kellyreagan/Documents/Research/Cases  ...
   in BMT unit.xlsx';
T = readtable(filename);
data = T([1:77],2);
A = table2array(data);
% figure
% qqplot(A)
%
% figure
% histogram(A)

meanData = mean(A);
stdData = std(A);
varData = var(A);

simData = cumulative30DaySumInfected;
simData = simData';
simData = simData(:)';
simSample=datasample(simData,77);
simSample = simSample';
meanSim = mean(simSample);
stdSim = std(simSample);
varSim = var(simSample);

%figure
%histogram(simSample)

% testing to see if variances are equal -- F-test
% null hypothesis is that the variances are the same
% alter hypothesis is that the variances are not
% h =1 means reject the null hypothesis at the default  ...
   1% significance
% level
% ci contains the lower and upper boundaries of the 99%  ...
   confidence interval
% for the true variance ratio
%
```

```
[h,p,ci,stats]=vartest2(A,simSample, 'Alpha', 0.01)

%cannot reject the null hypothesis that the variances  ...
   are the same
%Now I can run a two sample t-test
[h2,p2,ci2,stats2]=ttest(A,simSample,'Alpha',0.01)

%returned value of h=0 indicates that I cannot reject  ...
   the null hypothesis
```

VITA

Kelly Anne Reagan grew up in Midlothian, VA where she accelerated her early love for mathematics by attending the Mathematics and Science High School at Clover Hill High School in Midlothian, VA. Starting in August 2013, she attended Elon University in Elon, NC as a Presidential Scholar and Elon College Fellow. Her Elon College Fellows research focused on mathematically modeling the spread of dengue fever incorporating human mobility. She also participated in the 2016 Summer Research Experience at the National Institute for Mathematical and Biological Synthesis in Knoxville, TN where she worked on mathematically modeling human emotions. She graduated cum laude from Elon University in May 2017 with a Bachelor of Science in Applied Mathematics with minors in Computer Science and Public Health Studies. While at Elon, she was President of Kappa Delta Sorority- Eta Chi Chapter, co-captain of the women's club lacrosse team and she published her Elon College Fellows research. After graduating from Elon, she moved back to Richmond, VA to be close to her family and to pursue a Ph.D. in Systems Modeling and Analysis at Virginia Commonwealth University. During her five years in the program, she focused her studies on mathematical biology. Since starting research at Elon, she has published four papers as first author. After graduating, Kelly and her senior rescue dog will move to Atlanta, GA where she has accepted an offer to be a mathematical modeler for the Centers for Disease Control and Prevention Steven M. Teutsch Prevention Effectiveness Fellowship. During the two-year postdoctoral fellowship, she will use her quantitative skills to complete research with the Division of Cancer Prevention and Control.