Methicillin resistant *Staphylococcus aureus* transmission reduction using Agent-Based Modeling and Simulation

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Abstract

Methicillin resistant *Staphylococcus aureus* (MRSA) is a significant ongoing problem in healthcare, most commonly occurring in large, tertiary-care hospitals. Its spread among patients causes many downstream effects, such as longer lengths of stay for patients, higher costs for hospitals and insurance companies, and in a significant number of cases, fatalities. An agent-based simulation model is developed to investigate the dynamics of MRSA transmission in a hospital. The simulation model is used to examine the effectiveness of infection control procedures that could be implemented to reduce or prevent the spread of infection. Specifically, simulation experiments are performed to examine the efficacy of hand hygiene compliance and efficacy, patient screening, decolonization, patient isolation, and healthcare worker-to-patient ratios on the incidence of MRSA transmission and other relevant metrics. The software has produced results comparable to those presented in the literature, by demonstrating varying degrees of improvement within the range of policy initiatives. Outside of extremely high hand hygiene compliance and single HCW-to-patient ratios, patient isolation appears to be the most effective single measure, reducing transmission by the largest amount from a baseline case.

Introduction

In large hospitals, there are many patients and health care workers (HCWs) that come into contact with each other frequently throughout the course of a day. If one of those patients or HCWs becomes colonized with methicillin resistant *Staphylococcus aureus* (MRSA) or another pathogen, the bacteria could spread by way of HCWs to others within the hospital population. As a result, many patients fall victim to hospital-acquired, or nosocomial infection. It is estimated by the Committee to Reduce Infection Deaths (RID) that infections acquired in hospitals lead to over 100,000 deaths per year and an additional $30.5B in hospital costs [1]. More specifically, close to 300,000 (out of 2 million) infection cases involved MRSA, with close to 20,000 of those cases resulting in fatalities.

Many experts agree that hospital-acquired, or nosocomial, infections (HAIs) are almost entirely preventable [2], given a committed and capable healthcare institution. However, studies have shown that such measures have proven difficult to implement and enforce, due to both HCW non-compliance and cost considerations. These infection control policies consist of a number of measures aimed at reducing the incidence of MRSA transmission. Typically, the first measure hospitals take is to create education campaigns aimed at improving hand hygiene compliance of health care workers. The next effort usually involves screening patients for MRSA, at admission and/or with some frequency during their stay. This policy allows for the detection of colonized patients so that further measures can be taken to prevent transmission to other patients in the hospital.

Among these additional measures are patient isolation, decolonization, and reduction of HCW-to-patient ratios. Patient isolation involves moving a detected colonized or infected patient to a single room, so that they are not as likely to colonize other patients. The decolonization process involves a regimen aimed at reducing or removing the presence of bacteria on the skin of patient, which is done typically through the use of antibiotics and alcohol-based bathing. Reducing HCW-to-patient ratios decreases the connectivity of the patient network in the hospital, which decreases the likelihood of transmission from one patient to another.

This research effort seeks to identify the most effective infection control measure or measures that could reduce the incidence of MRSA transmission without becoming cost prohibitive. To accomplish this goal, an agent-based simulation package is designed and developed to model MRSA transmission dynamics and investigate the impact of infection control measures (ICMs) in a hospital.

Methodology

Historically, this problem has been approached using a number of survey and data collection techniques that evaluate a combination of one or more preventive measures [3]. More recently, an expansion in methodology has led to a number of studies using mathematical modeling and simulation [4,5,6,7,8] to investigate the spread of MRSA within hospitals. These computational models allow researchers to evaluate potential solutions in a virtual environment so that hospital administrators can make informed decisions concerning infection control policy. However, mathematical models have limitations as well, as they are driven by derived equations that represent the macroscopic behavior of the system. Even when properly calibrated, these models lack some degree of realism as they fail to depict the low-level interactions that drive the system. These interactions are more naturally represented by agent-based modeling [10], a more recent approach, which is used to develop a software package to further investigate this problem.

Agent-based modeling and simulation (ABMS) is a powerful technique that seeks to generate emergent characteristics from simple, rule-based individual actions. In other words, the goal of ABMS is to determine whether or not macroscopic trends can be generated from microscopic behavior. This technique is used to define agents in a hospital, specifically patients, nurses, physicians, and visitors, that interact with each other throughout the simulation period. The interactions between agents serve as the source of transmission dynamics within the hospital.

Discrete event simulation (DES) is used to propagate the interactions between the agents and serves as an interface to collect data for various configurations of hospital operations, including the implementation of specific ICMs. DES typically offers three design methodologies: time step, event oriented, and process oriented. All methods simulate system dynamics using time-associated events, at which system state variables are updated. Time stepped DES propagates time using a fixed time step until the simulation time of a scheduled event has been reached, at which point the event is processed. A significant disadvantage of time stepped DES is that if the events are distant in time, the simulation could propagate a long time without processing any events, which is an inefficient use of computational resources. Event oriented DES advances time to simulation times at which an event is scheduled to occur. This methodology leads to a serial processing of events, which is straightforward to implement, but cannot be parallelized easily. Process oriented DES operates in a slightly different way, where each simulation component is modeled as a process that executes until the simulation has reached a terminating condition. Process oriented DES also advances to discrete simulation event times, but the execution of the simulation occurs as a series of parallel processes executing through a series of active and inactive states. The process oriented DES methodology is becoming the most prevalent technique because of its correspondence to parallelization, and thus is the method of choice for this software project.

In order to account for the many possible outcomes, the simulation needs to be stochastic, implying that many events must be determined through the use of pseudo-random number generation. The stochastic nature of the simulation requires multiple replications of each scenario to be executed, and thus Monte Carlo methods are also incorporated into the design of the software. Agent-based models are typically computationally expensive, thus running many Monte Carlo replications requires large quantities of processing time. As a result, the software is able to execute serially or in parallel, so that more demanding test cases can be simulated within reasonable amounts of time.

Implementation

In order to implement the agent-based model, each agent is defined in terms of its characteristics and behavior. This type of modeling is supported best by object-oriented programming (OOP), in which object classes are defined with inherent characteristics and methods. The simulation package is developed in Python, a dynamic object-oriented programming language [11]. In addition to basic Python, the NumPy, SciPy, SimPy, and Parallel Python modules are also useful resources for building the software package. NumPy is a multi-dimensional array-based module that contains a large number of operations for arrays. SciPy is a module used for scientific computation tasks, which provides random number generation functions. SimPy consists of process oriented DES classes and methods which are used to develop the simulation architecture for the software. Parallel Python is used to implement a capability for the software so that Monte Carlo simulation replications can be executed simultaneously on multi-processor machines.

There are two primary object types in SimPy: processes and resources. The interactions between processes and resources are simulated through the use of a scheduler, which advances to discrete points in time to handle specific events. Processes can be used to model many real world objects that are progressing through a system. In SimPy, processes advance through a series of active and passive states defined by their process execution method (PEM) to represent the passing of time. There are a number of ways to start and stop processes during their execution. The first series of methods are yield statements, which cause a process to wait in a passive state until a certain criteria is met, such as a fixed passage of time or until a certain resource has been acquired or released. The second type of process control uses interruptions to awaken a process that is currently waiting. The process that is interrupted can determine the source of the interruption, and is then able to interact with that process in some way. The third method of process control uses event signaling to awaken waiting processes.

The agents in the simulation are all represented as processes, including patients, HCWs, visitors, and even hospitals. The only allowable interactions are between patients and HCWs, and patients and their visitors. Interactions between HCWs are not modeled, because there is not sufficient data to support a significant contribution from such interactions. All agents in the simulation are generated by a source agent, which varies in its operation depending on the type of agent being generated. Patients are generated

continuously so that the hospital remains fully occupied. HCWs are generated at the beginning of the simulation, as specified by parameters. A fixed number of visitors are generated each day, each visiting a single patient in the hospital at random.
There are three classes of resources in SimPy: resources, levels, and stores, two of which are used in the software. Resources can have a finite or infinite capacity and are requested one unit at a time by processes. Hospital beds are modeled as resources that are requested by patients as they enter the hospital. Stores are finite capacity resources that can actually contain processes themselves, which can be requested by other processes in single or multiple quantities. Nurse and physician staffs are modeled as stores, where patients can request either type of HCW for a visit, before returning them so that they become available to other patients.

The transmission of MRSA can occur in one of three ways:

1. A newly admitted patient transmits the bacteria to an HCW,
2. a transiently colonized HCW transmits the bacteria to the patient, or
3. a colonized visitor transmits the bacteria to the patient

The transmission of MRSA between agents is determined stochastically, based on the risk level of the patient and the behavior of the HCWs that visit. Once colonized, a patient remains colonized until the patient either develops an infection or completes a decolonization regimen. The patient can only begin the decolonization or treatment process once the state of the patient has been determined by an HCW. The colonized state of the patient is determined by a screening test whereas the infected state is determined by visual inspection. An HCW can only become colonized through direct contact with a patient. A colonized HCW can become decolonized upon the occurrence of its next hand hygiene activity. The probability of an HCW agent washing its hands is based on its own hand hygiene compliance, factoring in the risk level and isolation status of the patient. Agent interactions and state transitions are summarized in Figure 1.

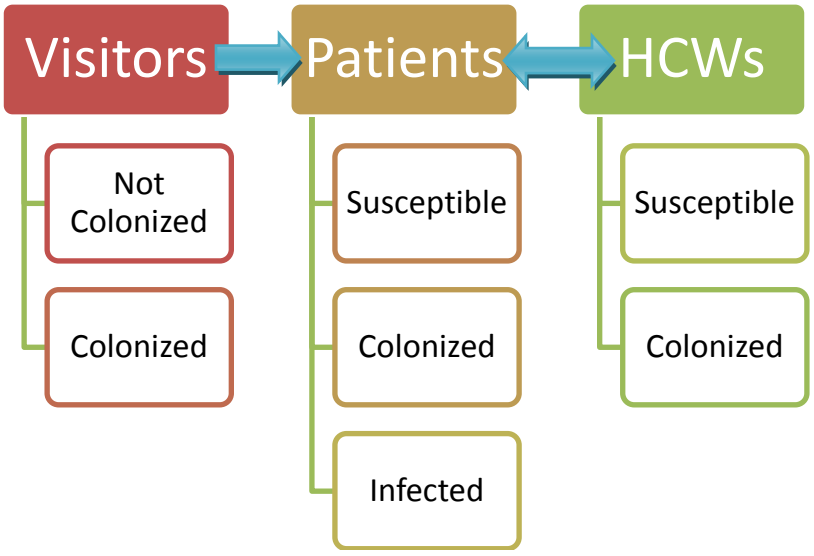

Figure 1: Agent Interactions and State Transitions

The general operation of the software includes three major stages: initialization, simulation, and output of results. During the initialization phase, all of the required modules are loaded into the simulation environment, including the agent class definitions, NumPy, SimPy, SciPy, and Parallel Python modules. In addition, simulation parameters can be input directly into the model or specified by spreadsheet. The primary transmission related parameters are summarized in Table 1. The hospital is also defined in this phase, including the number of single and double rooms, the number of nurses and physicians, and the infection control policy. Additionally, for the parallel case, a job server is defined, to which single replications are submitted.

Parameter Name	
• **Hand hygiene compliance** • **Hand hygiene efficacy** • **HCW to patient ratios**	Performance Related
• **Transmissibility** - **Patient to HCW** - **HCW to Patient** - **Visitor to Patient** • **Length of stay** • **Number of daily contacts** • **Number of colonized patients admitted**	External Factors

Table 1: Transmission Factors

During the simulation phase, all of the processes are activated and progress through their process execution methods. Patient agents enter the hospital and request a bed. When a bed becomes available, the patient is admitted and possibly screened if specified by the hospital infection control policy. If a bed is not yet available, the patient occupies a space in the hospital waiting room. Patient lengths of stay and the required number of visits are specified by the user and are defined once the patient is admitted. Patients are visited each day by nurse and physician agents, and sometimes visitor agents, if they are fortunate enough to have friends and family. If active surveillance is enforced, the patient may be screened periodically for colonization. Once the screening test results have returned, the patient may receive treatment based on the results. If the patient tests positive for colonization or shows signs of an infection, the patient may undergo decolonization or be moved to isolation. During each visit, MRSA can be transmitted to or from the patient. Once the visit is complete, the nurse or physician has the opportunity to wash their hands, which may or may not be successful depending on the efficacy of the hand washing agent. If a patient develops an infection, their stay is extended for treatment; otherwise, that patient is released at the end of their stay and another patient is allowed to enter the hospital.

At the end of each replication, statistics are accumulated before moving on to the next replication. Once all of the replications have been simulated, auxiliary functions can be called to print, store, and plot the results of the simulation. The output displays three categories of information, including the basic simulation parameters, infection control policy, and the simulation results averaged over the number of replications. The first set of statistics summarize the population statistics within the hospital, such as the total number of patients, the number of patients discharged, and the average length of stay. The next set of statistics display information related to the implemented ICMs, such as the number of screening tests or the number of patients that completed the decolonization process. The last series of statistics relate to the infection metrics, which summarize the spread of infection within the hospital. The parallel execution also produces some statistics on the execution times of the job server.

Computing

Agent-based models can require large amounts of processing because of their explicit representation of interactions. Consequently, executing many Monte Carlo replications can become computationally prohibitive, when done so in a serial manner. However, each replication is independent of the others, so it is advantageous to run as many simulations as possible in parallel. In order to assess the effectiveness of parallel computing, two scenarios were tested: a small case with many replications and a large case with a small number of replications. These two scenarios were run on the Genome cluster at the University of Maryland. The machine used contained 32 processors and 128 GB RAM. The results of the comparison are shown in Tables 2 and 3.

Small Case
▪ 100 days, 250 replications
▪ 10 single/10 double rooms
▪ 10 nurses/5 physicians
▪ 10 day length of stay
▪ 5 daily contacts
▪ No infection control measures

Table 2: Parameters and results of running a small case on Genome cluster

N	Job Time Sum (s)	Run Times (s)	Speedup
1	747	747	-
2	752	377	1.98
4	746	188	3.97
8	752	96	7.78
16	761	50	14.94
32	941	33	22.64

As shown from the data, multiple processors improve the speedup dramatically, by a factor almost equal to the number of processors for smaller numbers of processors. As the number of processors increases, there is some degradation in speedup due to the extraction of results from a larger number of processors, ass indicated by the total job time sum. However, even with this degradation, the run times are still lower with more processors, so there is still something to be gained from a larger number of processors.

Large Case
▪ 500 days, 25 replications
▪ 50 single/150 double rooms
▪ 50 nurses/20 physicians
▪ 10 day length of stay
▪ 5 daily contacts
▪ All infection control measures

Table 3: Parameters and results of running a large case on the Genome cluster

N	Job Time Sum (m)	Run Times (m)	Speedup
1	136.9	136.9	-
2	138.4	71.84	1.91
4	136.1	37.91	3.61
8	133.7	21.10	6.49
16	141.3	11.88	11.52
32	182.3	8.96	15.28

For larger cases, it is clear that simulations are more difficult to run quickly, as single replications are still computationally intensive. The degradation in speedup is even more apparent, as each processor loses efficiency by running less replications. However, the benefit of parallelization is even greater in this case, as the feasibility of running larger numbers of replications in serial comes into question.

Overall, parallelization in the execution of agent-based modeling and simulation is a valuable capability, allowing for a faster execution in every case. Even with the degradation in speedup as the number of processors increases, the run times continue to decrease. In addition, there is no penalty for doing so, as the replications are independent and therefore no accuracy is lost.

Verification, Validation, and Testing

There are a number of standard metrics from the literature that are used to evaluate the prevalence of MRSA and the potential for its spread within a hospital ward. These metrics can be used to determine the effectiveness of various infection control procedures. The first of these is the *successful introduction rate*, which is the number of secondary MRSA cases arising from transmission within the hospital. This metric gives a clear depiction of the susceptibility of the hospital to outbreaks. Another important metric is *mean ward prevalence*, which is the percentage of hospital days on which at least one colonized patient was present. This metric describes the degree to which MRSA is present within the hospital, which correlates with the ability to eliminate the bacteria completely. The percentage of *colonized patient days* represents the proportion of days spent as a colonized or infected patient in the hospital. This metric is a good representation of quality, as low proportions indicate not only a low incidence of cross-transmission, but a quick response to those patients who have become colonized or infected. The *attack rate* is calculated as the ratio of MRSA transmissions to uncolonized patient days. The inverse of metric is also useful, representing the number of average number of uncolonized patient days between secondary cases of MRSA. Finally, the *basic reproduction number*, R_0, is a key indicator of whether an outbreak will occur. R_0

is the mean number of secondary cases that results from a single index patient. Typically, if $R_0 > 1$, then an outbreak is likely to occur within the hospital, as the average colonized patient will transmit MRSA through an HCW to at least one other patient.

Verification

The verification process involved ensuring that the implementation correctly represents the agent definitions and interactions specified by the conceptual model. Most importantly, verification tests are performed to check that the software receives the correct parameter values and executes each process properly during the simulation. In order to facilitate this process, an event logging system was implemented to monitor the critical events in the simulation, such as patient admissions and discharges, HCW visits to patients, transmissions between agents in the hospital, and execution of various infection control procedures.

In addition to programmatic testing, simple test cases were performed to ensure that the software was producing reasonable output. There are two types of techniques that were used in this phase: corner case testing and relative value testing. Corner case testing involves setting parameters to their extreme values where their outputs are known. For example, setting the proportion of colonized admitted patients to zero should not produce any transmission within the hospital, as there are no colonized patients to transfer MRSA to HCWs. Relative value testing involves changing parameters to see if they affect the output in the right direction. For example, decreasing hand hygiene compliance to zero results in a massive outbreak whereas increasing it to one nearly prevents transmission completely. Corner case and relative value testing were performed on each of the relevant input parameters.

Validation

The validation process for ABMS at this stage of its use is not consistently agreed upon. However, Axtell et al. describe a useful convention for three varying degrees of validation for agent-based models [12]. The authors speak of a *replication standard*, used for re-creating agent-based models described in the literature. It is also a useful standard for validating agent-based models with other types of models, such as mathematical or conventional simulation models. The three level of validation, in order of decreasing precision, are numerical identity, distributional equivalence, and relational alignment. Numerical identity implies that the results from two models are exactly the same, which provides a high degree of confidence for both models. Distributional equivalence typically comes into play when comparing models where at least one model contains stochastic elements. In these cases, it is very unlikely that validation tests will produce numerical identity; therefore the goal is typically to demonstrate that each model produces a similar distribution of numerical results. Finally, relational alignment provides at least some degree of confidence, implying that the two models produce the same trends as a result of varying input parameters. This type of standard can be the best case scenario, especially when comparing models that use different input parameters to

model the same system. Models that fail to display any degree of relational alignment may need to undergo additional conceptualizing and/or verification.

The ABMS validation process involved performing simulation experiments from the literature and comparing the results. The first comparison was performed with the standard SIR model from epidemiology [3]. This model consists of nonlinear differential equations that represent the transition from **S**usceptible to **I**nfected to **R**ecovered states. These equations are shown in Table 4 and operate under the assumption that the population is homogenous, closed (i.e. no migration), and well-mixed.

State	Model Equation
Susceptibles	$\frac{dS}{dt} = -\beta SI$
Infecteds	$\frac{dI}{dt} = \beta SI - \gamma I$
Recovered	$\frac{dR}{dt} = \gamma I$

Table 4: SIR Model Equations

Agent-based modeling can reproduce similar transmission dynamics, even though the conceptual models differ considerably. This comparison was performed for a hospital population of 100 patients, only considering the susceptible and colonized (infected) states, as there is no recovered state for MRSA patients since they are always susceptible to colonization. A comparison of the two models is shown in Figures 2 and 3.

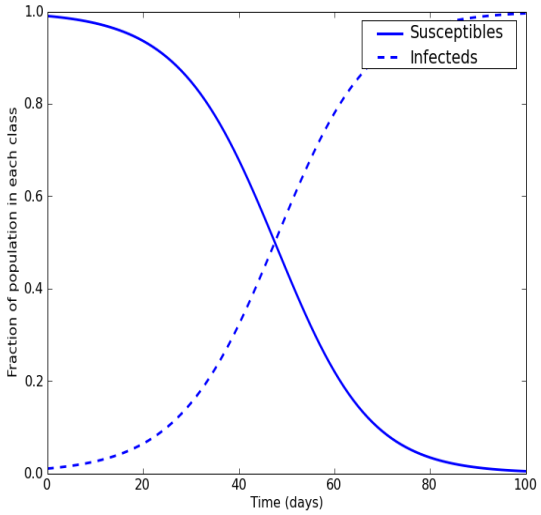

Figure 2: SIR Model

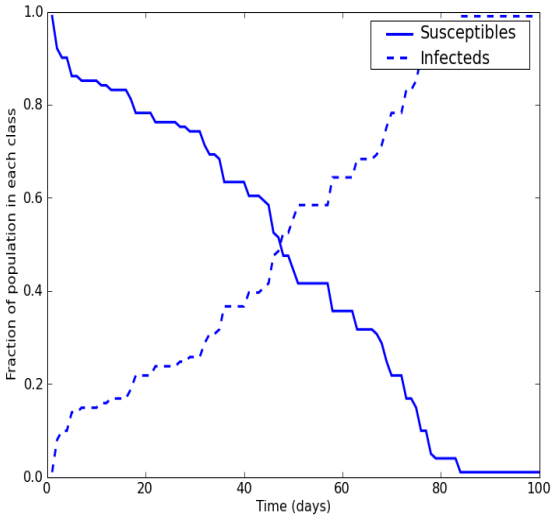

Figure 3: ABMS

In addition to comparing ABMS to mathematical epidemiology models, it is also necessary to look at more recent computational models. Beggs, Shepherd, and Kerr [9] developed a deterministic model to explore the effects of hand hygiene compliance in depth. The primary model equations allow for an analytical expression to compute R0,

which is shown in Table 5 with a related and necessary expression involving hand hygiene compliance. Three coupled simulation experiments were performed, which examined the effect of hand hygiene compliance and efficacy, transmissibility, and daily contacts on R_0. A comparison of the results is shown in Figures 4, 5, and 6.

$$R_0 = \frac{(n-1)\beta\beta'}{(\mu+\gamma)n'\mu'\lambda'} \quad (1) \qquad \mu' = \frac{cnf_h}{n'(1-f_h)} \quad (2)$$

Parameter	*Meaning*	*Default Value*
n	Number of patients	20
n'	Number of HCWs	3
μ	Patient removal rate	0.10 per day
μ'	Hand washing rate	14.0 per day
λ'	Average efficacy of each hand washing event	0.5
γ	Detection rate of colonized patients	0.10 per day
c	Patient-HCW contact rate	5 per patient per day
p,p'	Transmissibility	0.1
β,β'	Transmission rate (cp, cp')	0.5

Table 5: Beggs, Shepherd, and Kerr model equations and parameter definitions and values

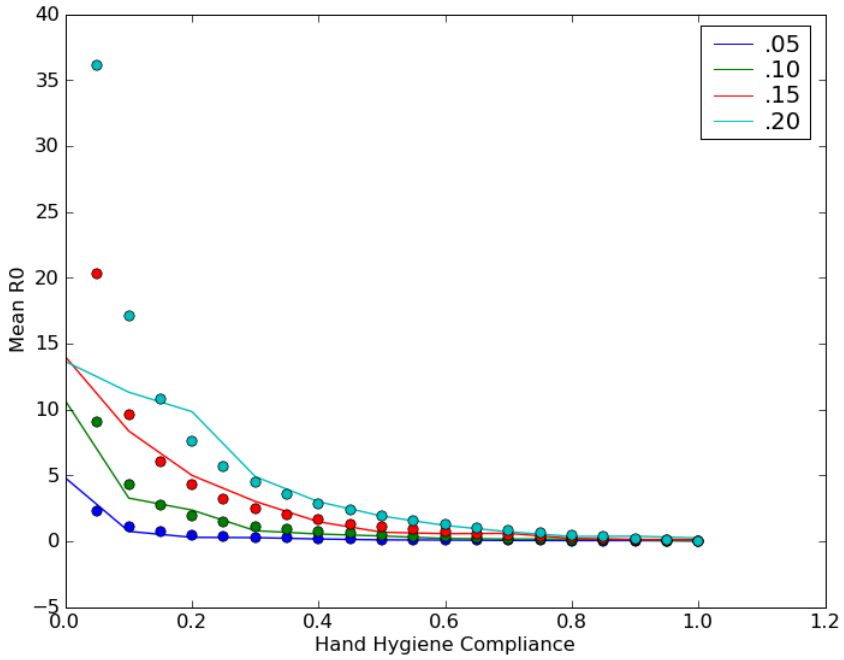

Figure 4: Comparison of ABMS with Beggs, Shepherd, and Kerr hand hygiene compliance and transmissibility experiment

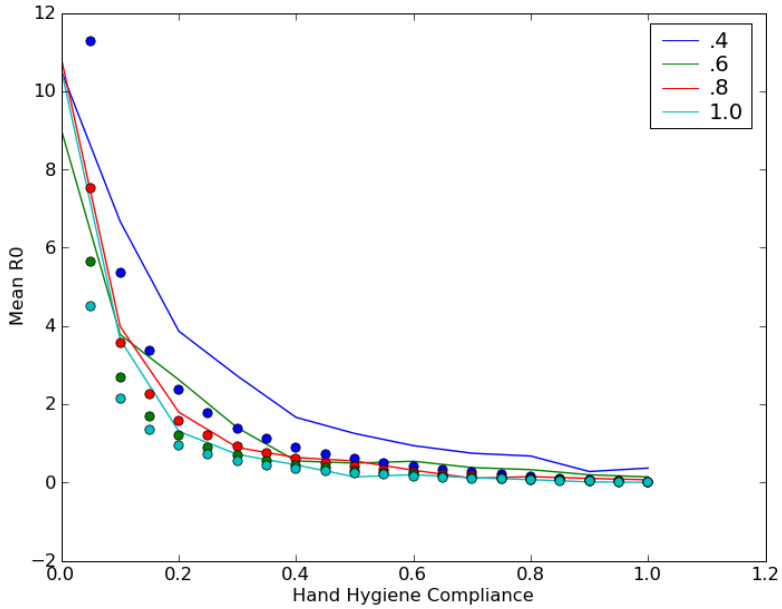

Figure 5: Comparison of ABMS with Beggs, Shepherd, and Kerr hand hygiene compliance and efficacy experiment

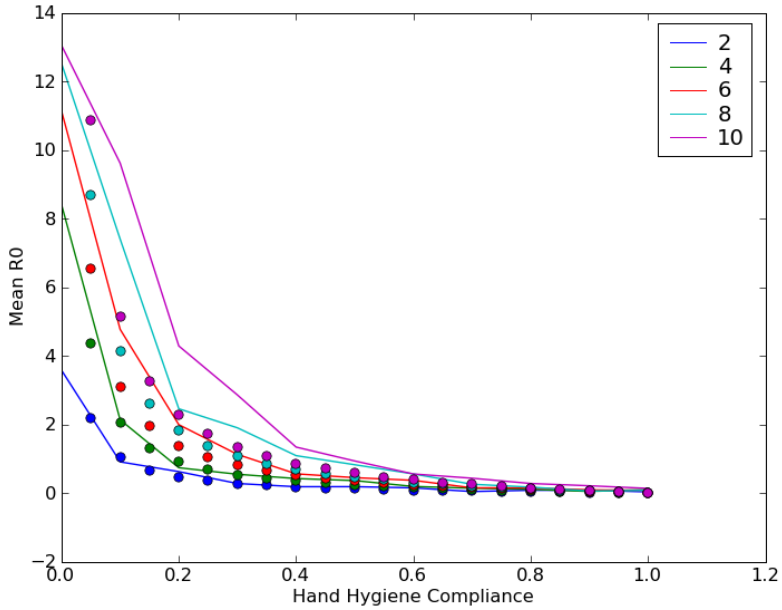

Figure 6: Comparison of ABMS with Beggs, Shepherd, and Kerr hand hygiene compliance and daily contacts experiment

As shown by the figures above, hand hygiene compliance displays a couple of key behaviors. The first of these behaviors is similar to the law of diminishing returns. An increase in compliance from 0 to 40% results in a significant improvement in transmission from a massive outbreak to containment. On the other hand, an incremental increase in compliance above 40% results in very little improvement, requiring a significant increase to reduce R_0 by any significant amount. This behavior clearly indicates that additional control measures are needed to further reduce transmission, as extremely high compliance rates are typically not feasible.

In order to validate the additional control measures, a baseline case was defined, as specified in Table 6. From the baseline case, infection control measures were implemented to assess their effectiveness.

Baseline Case
▪ **100 days, 250 replications**
▪ **30 patients, 5 HCWs**
▪ **10 single, 10 double rooms**
▪ **5% of patients admitted are colonized with MRSA**
▪ **5 daily contacts per patient, U(0,10) day LOS**
▪ **50% hand hygiene compliance, 80% efficacy**
▪ **No interventions**

Table 6: Baseline case parameters

The first set of experiments involved coupling patient screening on admission with patient isolation and decolonization, as these measures require the detection of colonized patients to take effect. For both patient isolation and decolonization, a pair of figures shows the effects of the proportion of patients screened on the number of isolations and decolonizations as well as the system effect on transmission, in terms of mean R_0. It is clear that as the proportion of patients screened on admission increases, the number of isolations and decolonizations both increase linearly, indicating that screening more patients continues to produce improvement. It is also clear from the figures that with more isolations and decolonizations, which result from more patient screenings, the mean R_0 value decreases linearly as well. It is also quite clear that patient isolation is a better control measure than decolonization, although the difference in mean R_0 values only becomes significant at higher screening probabilities.

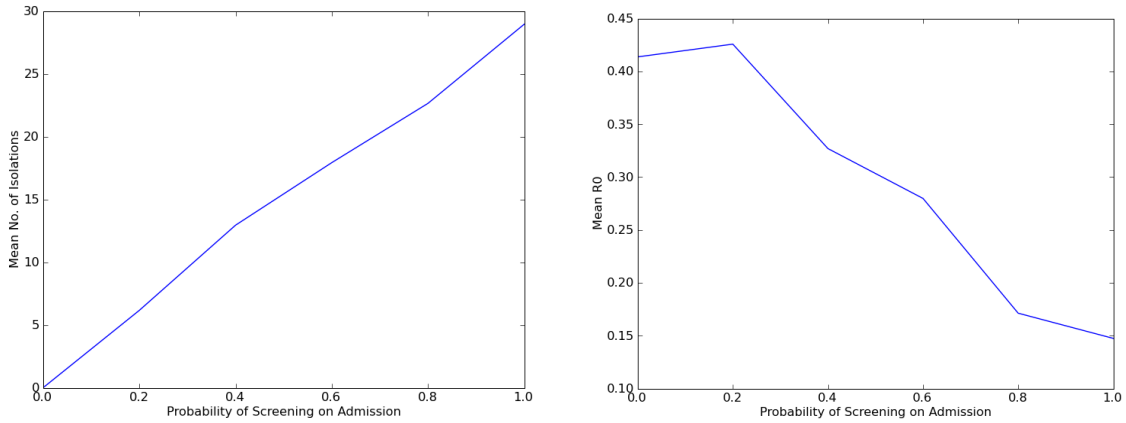

Figure 7: Mean number of isolations and mean R_0 plots as a function of patient screening probability

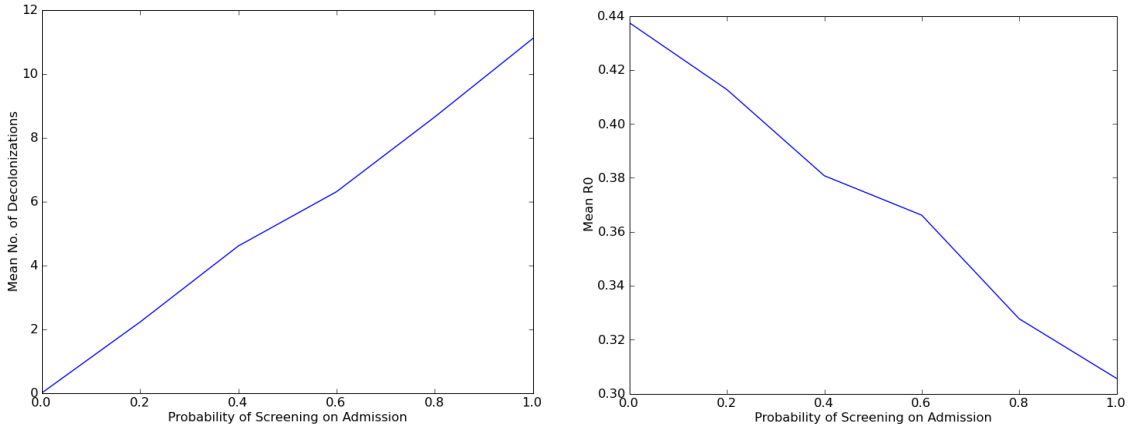

Figure 8: Mean number of decolonizations and mean R_0 plots as a function of patient screening probability

The last measure to consider is HCW-to-patient ratios. The effect on mean R_0 is shown in Figure 9. As expected, a HCW-to-patient ratio of unity nearly eliminates transmission, as colonized patients that are admitted are unable to transmit to other patients. However, it is interesting to see that extremely low ratios are required to have a significant effect on R_0. It appears that ratios higher than 3 do not have much benefit at all.

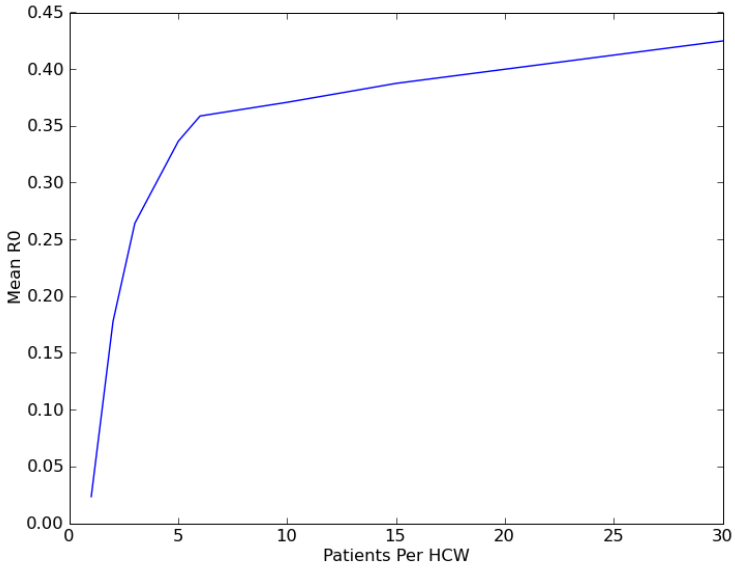

Figure 9: Mean R_0 plot as a function of healthcare worker to patient ratios

The best case results for each infection control measure are summarized in Table 7. It is clear that 1:1 HCW-to-patient ratios result in the best performance, but such ratios are typically infeasible, especially outside of intensive care units. The next best control measure is clearly patient isolation, which outperforms even the 2:1 HCW-to-patient ratio with respect to the attack rate and R_0 measures, which provide the best assessment of transmission in the hospital. Decolonization appears to be the least effective measure,

although it is slightly more effective at reducing ward prevalence, essentially because it is the only method for eliminating colonization.

Mean Statistic	Baseline	Isolation	Decolonization	Cohorting	
				1:1	*2:1*
Patients Colonized	51.46	39.56	45.42	**34.79**	40.65
Colonized Patients Admitted	36.50	34.48	34.76	**33.85**	33.89
No. of Secondary Cases	14.97	5.08	10.66	**0.94**	6.75
Ward Prevalence	82.51%	81.44%	**78.82%**	78.99%	80.57%
Colonized Patient Days	6.49%	5.66%	5.72%	**5.14%**	5.64%
Attack Rate	0.004989	0.001693	0.003553	**0.000313**	0.002251
R_0	0.4098	0.1474	0.3056	**0.0272**	0.1991

Table 7: Summary of infection control measure performance

Additional Testing

Now that ABMS has demonstrated results consistent with the literature, simulation experiments can be performed to provide insight to questions relevant to hospitals. One such question relates to determining which type of HCW, namely nurses or physicians, is responsible for the majority of transmission. Another relevant question is concerned with determining the circumstances under which a high-performance hospital could become susceptible to an outbreak. These questions are now considered in turn.

The question of who colonizes more, nurses or physicians, is important for hospitals who do not know who to target primarily with education programs. Both populations have different cultures and varying degrees of interaction with patients, and therefore would require a different approach to reduce transmission. Nurses typically see patients much more often, but they wash their hands more often. Physicians typically see many more patients, but less frequently. These contrasting service patterns make it difficult to predict the primary source of transmission.

Two experiments were conducted in a 50 patient hospital with 10 nurses. Both experiments varied the proportion of patient visits from nurses and measured the proportion of patients colonized by nurses. In the first experiment, the number of physicians was varied from 1 to 5, with equal hand hygiene compliance, to determine the effects of nurse-to-physician ratios on transmissions. The second experiments examined the effects of physician hand hygiene compliance, which was at best equal to that of nurses. The results of these experiments are summarized in Figure 10.

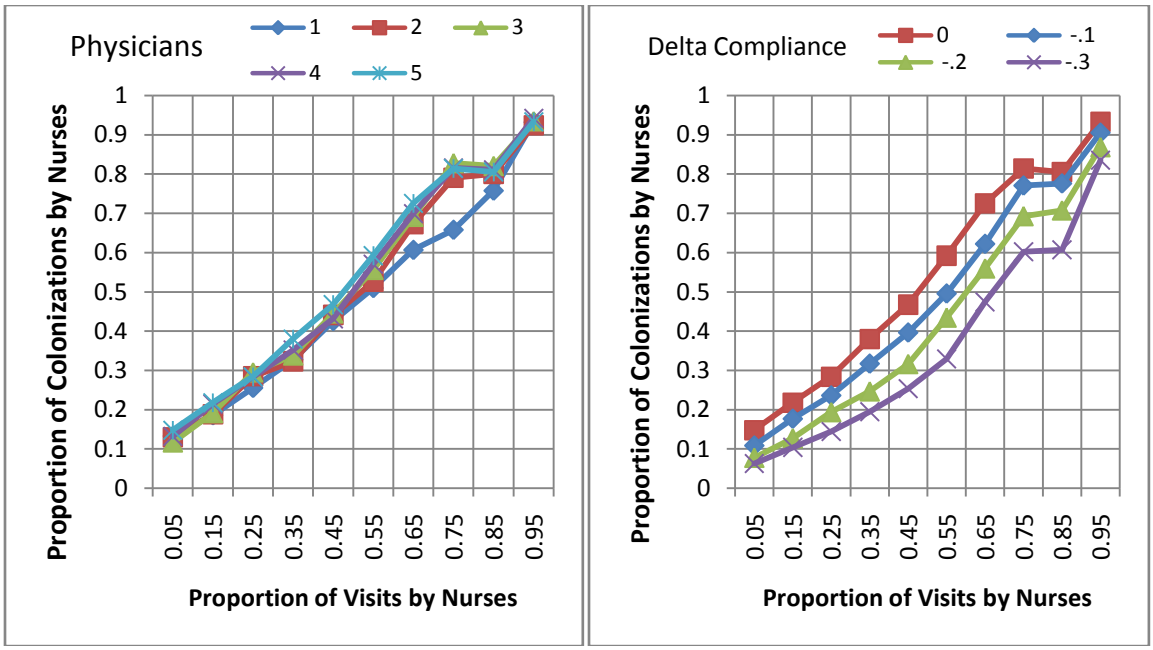

Figure 10: Proportion of colonization plots, varying the number of physicians and difference in physician hand hygiene compliance

In the first experiment, it is clear that the nurse-to-physician ratio does not have a significant impact on the transition point where nurses colonize more patients than physicians. For this scenario, it is clear that whoever receives the majority of patient visits is likely to be the more significant source of transmission. In the second experiment, the difference in hand hygiene compliance significantly impacts the transition point, shifting it further to the right as the difference grows. For the case where physicians are 30% less likely to wash their hands, nurses must visit patients approximately two-thirds of the time to colonize more patients. In practice, however, nurses typically visit patients 80-90% of the time, clearly indicating from these results that nurses account for the significant majority of colonizations.

With the respect to the question of the susceptibility of high performance hospitals to MRSA outbreaks, we consider a 100 patient hospital with 20 nurses and 10 physicians. The HCWs comply with hand washing 70% of the time, and the hospital employs patient screening on admission with one-day test result return times, patient isolation, and decolonization. On first look, this hospital would seem impermeable to MRSA outbreaks due to the significant effort to prevent and control infection. For the most part, this assessment is true, as moderate changes in a number of transmission factors, such as hand hygiene efficacy, daily contacts, proportion of colonized admitted patients, screening test return times, and patient lengths of stay, do not have a significant impact on transmission with such a high hand hygiene compliance rate. Only two cases appear to lead the system to an outbreak, a highly transmissible pathogen (greater than 0.28 for this case) and a high visitor rate (greater than 200 per day at 2% transmission rate). To the first case, a highly transmissible pathogen transfers between patients and HCWs much more frequently, spreading more frequently throughout the hospital. The second case can lead

to an outbreak due to the ‘small-world effect’, as visitor introductions create new pockets of colonization, allowing for transmission to occur along different vectors in the hospital.

Conclusions

Agent-based modeling and simulation provides a powerful capability to analyze complex systems. When applied to epidemiological problems, it is straightforward to represent individuals and the interactions between them to model both the transmission dynamics of some disease and the effectiveness of various infection control measures. Parallel processing is also an extremely valuable capability, as agent-based models are typically computationally intensive, requiring a large number of computer cycles to simulate. Being able to execute Monte Carlo simulations in parallel allows for results to come faster and more reliably, as more replications can be simulated in reasonable amounts of time.

As to the specific problem of reducing MRSA transmission in hospitals, the best defense involves two main approaches: decrease the connectivity of the patient network and decrease the likelihood of transmission between patients and HCWs. High incidences of transmission occur when the patient population is well-mixed, meaning that many patients share the same HCWs, allowing for transmission to occur easily. Isolating patients and maintaining low HCW-to-patient ratios can serve to segment the patient population, so that colonized patients are less likely to transfer the bacteria to others. HCWs can reduce the probability of transmission by practicing proper hand hygiene and hospitals can do so by minimizing patient lengths of stay and the number of daily contacts.

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Appendix A: Project Schedule

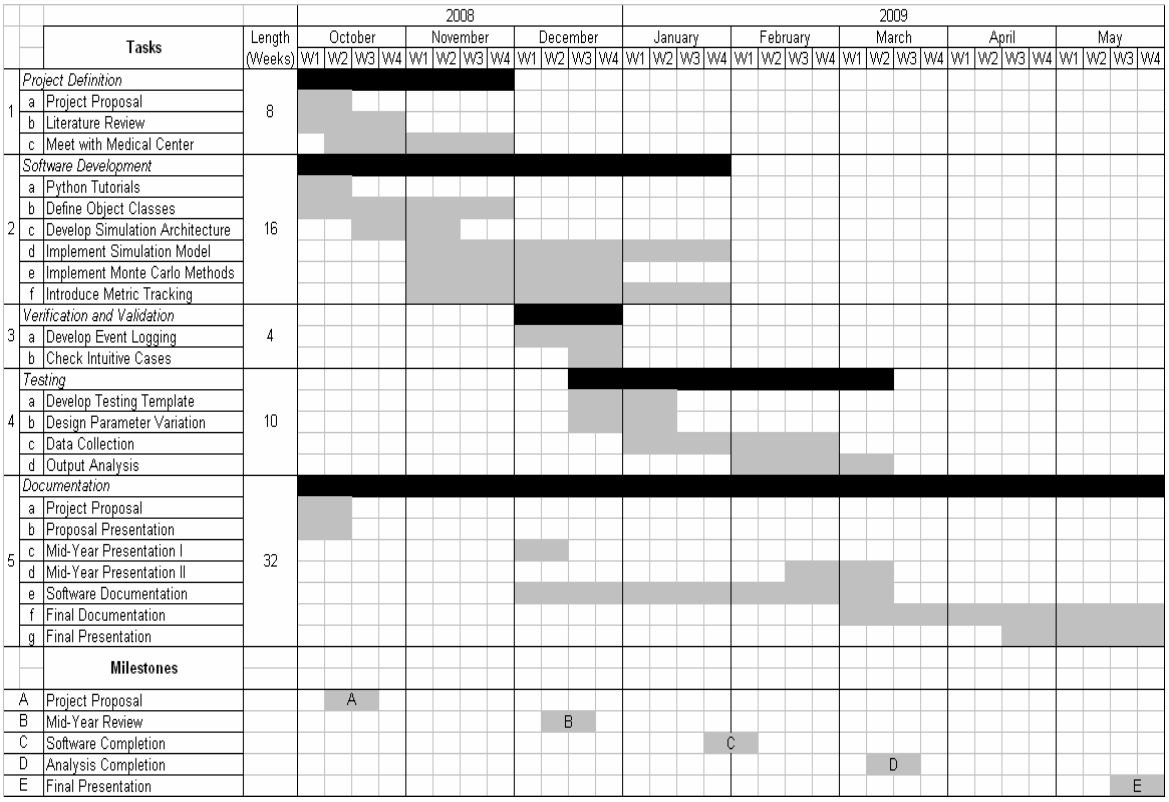

Figure 11: Project Schedule