Competition Between MRSA Strains Term Paper

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Contents

1 Introduction

Staph Infections, also known as Staphylococcal infections, are caused by the *Staphylococcus* bacteria. The most common human pathogen in this group of bacteria is *Staphylococcus aureus*, which has over 30 known strains, each affecting the body differently [5]. While most staph infections are mild and treatable with antibiotics, some infections can become severe and lead to life-threatening conditions.

Common symptoms include boils, blisters, and redness on the skin, often around the mouth and nose but can potentially appear anywhere on the body [5]. For breastfeeding mothers, the bacteria can cause mastitis, leading to inflammation and abscesses in the breasts [5]. Certain strains infect the bones, causing osteomyelitis, an inflammatory and painful condition [5]. If the digestive system is infected, symptoms can include food poisoning, vomiting, and diarrhea [5]. When the bacteria enter the lungs, they may lead to pneumonia and breathing difficulties due to abscess formation [5]. In severe cases, *Staphylococcus aureus* can infect the heart and damage the heart valves, leading to heart failure [5]. It can also release toxins into the bloodstream, causing blood poisoning known as septicemia [5].

Certain populations face a higher risk of staph infections. These include individuals who work with children, those who live in crowded conditions, and athletes engaging in high-contact sports [4]. Other high-risk groups include individuals with weakened immune systems either from medications or diseases as well as those frequently in communal environments like dormitories and locker rooms [4]. However, the primary group at an increased risk are patients in hospital settings. The bacteria is extremely dangerous, where in 2017, the U.S. recorded an estimated 119,247 staph infections, leading to 19,832 deaths that year [7]. Despite the MRSA rates declining since 2005, Staph infections continue to pose a substantial challenge in hospital settings [7]. With proper treatment and care, most staph infections heal within one to three weeks, though recovery time varies based on severity [4].

A study in Denmark examined the risks of staph infections across different age groups [2]. Between 2008 and 2015, researchers identified 11,054 cases of Staphylococcus aureus bacteremia (SAB). The median age of infected individuals was 68 years, indicating that older adults are at a higher risk. The highest percentage of cases occurred in individuals aged 60–69 (22.4%) and 70–79 (23.2%). The remaining age distribution was as follows:

- Below age 1: 2.6%
- Ages 01–09: 1.4%
- Ages 10–19: 1.9%
- Ages 20–29: 1.8%
- Ages 30–39: 3.4%

- Ages 40–49: 7.2%
- Ages 50–59: 12.0%
- Ages 80–89: 19.2%
- Age 90 and above: 4.9%

These findings align with other studies, indicating that older populations face the highest risk. However, as discussed earlier, individuals of all ages can contract staph infections, especially those in high-risk environments such as hospitals, sports teams, and healthcare settings.

The most dangerous staph infections are those resistant to antibiotic treatment. The *Methicillin-resistant Staphylococcus aureus* (MRSA) bacteria is a strain that does not respond to Methicillin, a commonly used antibiotic. According to the CDC, 33% of people carry the *S. aureus* bacteria in their noses without symptoms, while 2% of the U.S. population carries MRSA. Although most carriers remain asymptomatic, MRSA is highly contagious and can cause severe infections in vulnerable individuals. MRSA spreads primarily through skin-to-skin contact or nasal colonization, eventually leading to infection. Most cases occur in hospitals and healthcare facilities, such as nursing homes. A CDC study analyzing MRSA cases in various U.S. counties, including San Francisco and Georgia, found that:

- 17.8% of infected patients where in a long-term care facility three days before diagnosis
- 12.8% of infected patients where in an acute-care hospital prior to diagnosis

Some of the data in the study tracked the location of infected patients three days prior to their MRSA diagnosis. Not only are people at risk of contracting MRSA in healthcare facilities, but they are also vulnerable to infection in public settings. Healthcare-Associated MRSA (HA-MRSA) is primarily found in hospitals and nursing homes, where it affects elderly individuals at a higher rate. However, a newer strain, known as Community-Associated MRSA (CA-MRSA), can infect young and healthy individuals, which was a rarity for the traditional MRSA strain. For years, hospitals have been battling the spread of this disease, which accounts for over 100,000 deaths annually. The presence of MRSA in hospitals creates an additional burden for healthcare providers, especially during major public health crises, such as the COVID-19 pandemic.

Instead of focusing solely on treating patients' primary illnesses, hospitals must also worry about controlling MRSA outbreaks, making it more difficult to treat patients. By eliminating the spread of the infection, hospitals can better focus on every patient's needs and illnesses and provide a better opportunity for them to get the help they truly need. Reducing the spread of MRSA would allow hospitals to prioritize patient care, improving treatments.

2 Background

Mathematical modeling has long been used to analyze and predict the spread of diseases, particularly in the field of epidemiology. Epidemiology is the study of epidemics, which are large but short term disease outbreaks. While different diseases behave differently, such as varying transmission patters, there are common factors that influence their spread. treatments, modes of transmission, and disease severity [6]. Additionally, there are population-related factors, such as race, gender, economic status, and geographical factors play a significant role [6]. Mathematical modeling has became an essential tool in epidemiology, allowing researchers to predict how these factors influence disease dynamics. Since the introduction of mathematical modeling in the early 20th century, it has continued to play a big pivotal role in many different diseases, including Staph Infections[6]. Just like the staph infection model, various threshold factors play a crucial role in determining disease dynamics.

These critical values, such as contact number, vector density, and population size, help determine whether the disease will lead to widespread disease, or small outbreak [6]. Similar to our Staph infection model, many epidemiological models categorize the population into three groups: susceptible, infected, and recovered. Focusing on the recovered group, there are different model types to describe it:

- SIS model: In this model, recovered individuals do not develop immunity, meaning they return to the susceptible group after infection. The population cycles between susceptible (S) $\rightarrow$ infected (I) $\rightarrow$ susceptible (S) [6].

- SIR model: Here, recovered individuals gain immunity, preventing them from being reinfected. The population transitions from susceptible (S) $\rightarrow$ infected (I) $\rightarrow$ recovered (R), where recovered individuals do not return to the susceptible group [6].

- SIRS model: In this model, recovered individuals receive temporary immunity. Once immunity wears off, they become susceptible again, transitioning from susceptible (S) $\rightarrow$ infected (I) $\rightarrow$ recovered (R) $\rightarrow$ susceptible (S) [6].

- SI model: This model assumes once an individual becomes infected they remain infected permanently. Following the path of susceptible (S) $\rightarrow$ infected (I) [6].

While other models exist to describe the spread of diseases, these are the primary ones we focused on for our Staph infection model. As mentioned above, each disease has unique factors and modeling associated with it. However, there is significant overlap in the fundamental principles, which allows for similar models to be applied to various diseases.

Mathematical modeling is widely used in studying hospital-acquired infections, known as HAIs. These infections are not present when patients are admitted to hospitals, but are contracted after admission. The infections typically manifest around 48 hours after admission[1]. Individuals at higher risk of acquiring HAIs are those with immunesuppression, older patients, long-term hospital patients, and frequent healthcare facility visitors. Intensive Care Units (ICUs) pose a much higher risk for acquiring HAIs. In fact, a study conducted on 231,459 patients across 947 hospitals found that 19.5% of ICU patients acquired at least one HAI during their stay [1]. Over the years, mathematical modeling has played a crucial role in helping hospitals better analyze and control the spread of these infections. By improving infection prevention strategies, healthcare workers can focus more on caring for the patient's needs without additional worries of managing outbreaks. All strains of MRSA are problematic within hospitals, with studies showing that among pathogens leading to HAIs, *Staphylococcus aureus* accounted for 10.7% of cases, making it the second most common cause after *C. difficile* [1]. With the significant impact of MRSA infections, it was important for us to focus our research on understanding and modeling their spread.

For this paper, we will be focusing on a SIS model, where patients do not develop immunity after recovering from the disease and return to the susceptible patient population. In addition, we will implement the concept of viral interference into our model. Viral infection, also known as superinfection resistance, is the phenomenon where a cell infected by one virus becomes resistant to subsequent infections by other viruses [9]. This interaction can occur within individual cells, hosts, or entire populations [9]. In the context of our model, we apply viral interference to the two strains of MRSA. We assume that individuals can only be infected with one of the two strains, meaning that infection with one strain of MRSA inhibits infection by the other. This approach allows us to focus directly on the dynamics between two competing species, hospital H-MRSA and community C-MRSA. By incorporating viral interference, we can better understand how the presence of one MRSA strand influences the behavior of the other strain.

3 Model

3.1 Previous Models

Our model is based on the standard SIS and SIR models. The typical SIS model is given by the following equation [10]:

1. $\frac{dS}{dt} = -\beta SI + \alpha I$
2. $\frac{dI}{dt} = \beta SI - \alpha I$

The typical SIR model is given by [11]:

1. $\frac{dS}{dt} = -\frac{\beta}{N} SI$
2. $\frac{dI}{dt} = \frac{\beta}{N} SI - \gamma I$
3. $\frac{dR}{dt} = \gamma I$

The SIS model consists of two differential equations, modeling the interaction between the susceptible and infected populations. The key parameters include:

- S: Number of susceptible individuals.
- I: Number of infected individuals.
- β: Infection rate.
- α: Recovery rate

In contrast, the SIR model includes three differential equations, now introducing a recovered population. It shares the same parameters as the SIS model but includes:

- N: Number of individuals in the total poulation.
- γ: Recovery rate (denoted by α in SIS model).

Although our model is based on these previous models, there were still things we wanted to test out. We made modifications to better represent the competition between the two strains of MRSA. Instead of a single infected group, we introduced two distinct infected populations, each corresponding to a different strain of MRSA. Additionally, we assumed that other possible parameters, such as hand hygiene compliance, is already applicable in all hospital settings. Instead, we focused on analyzing the interactions between the two MRSA strains under these controlled conditions.

3.2 Our Model

In our mathematical model the patients in the hospital are divided into three groups: susceptible population S, infected with hospital strain H-MRSA H, and last infected with community strain C-MRSA C. Where N is the total number of patients in the hospital. With initial conditions $S(0) = S_0$, $C(0) = C_0$, and $I(0) = I_0$ specified at time 0. Patients are admitted to the susceptible population at a rate of Λ per day. The fraction of patients with C-MRSA or H-MRSA is denoted as λ_C and λ_H. For simplicity in this model both terms are set equal to zero. β_C and β_H are the infection rates of patients infected C-MRSA and infected H-MRSA patients, respectively. The cure rates of infected CA-MRSA and infected HA-MRSA patients are α_C and α_H, respectively. The death rates of infected CA-MRSA and infected HA-MRSA patients are δ_C and δ_H, respectively. A visualization of the model is shown in Figure 2.

Shown in Figure 1 is a table outlining the meaning and initial value of each parameter. The parameter values used in our model are obtained from the Beth Israel Deaconess Medical Center's computerized database system, which provides patient and infection control data and from the literature [8].

We decided to not distinguish between the colonized and clinically infected with MRSA patients, in large part because being colonized with MRSA puts those at risk of developing infection which will eventually progress to infection. Accordingly the values of the infection rate are a multiplication of the colonized and infection transmission. Each populations of patients S, C, and H are considered to be entirely homogeneous.

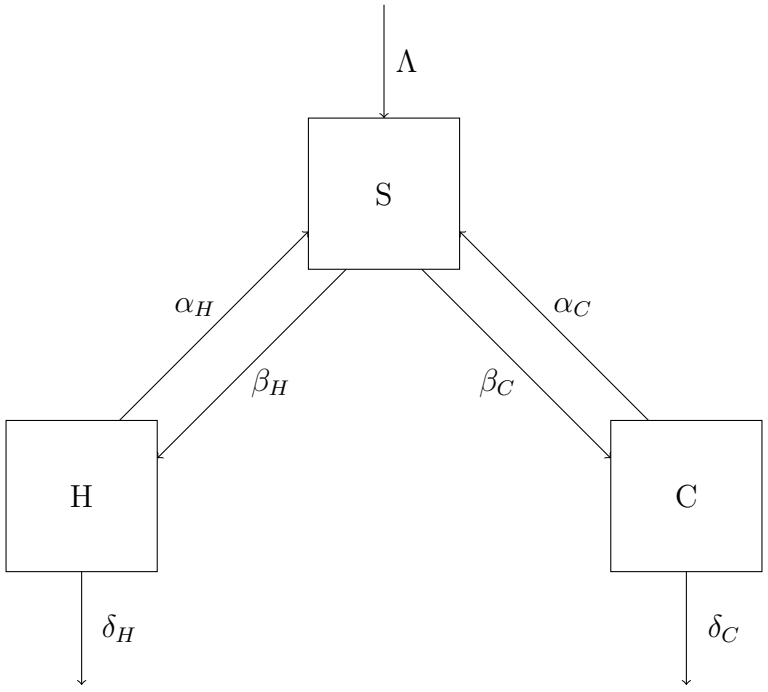
Regarding the death and discharge rates parameter, we decided to make δs strictly the death rate and rather than having a separate discharge rate, we wanted to have all patients return back to the susceptible compartment, because as is somewhat unique to Staph infections, people do not develop immunity after contracting and recovering from the disease. We decided to remove terms from the previous model in [8] that reflected hand hygiene compliance and quarantining of patients, because we decided those extra considerations were not a main concern for our goal.

From these parameters we created a double SIS model shown in Figure 3. The goal of our model and this project, is to find the stable fixed points for certain parameters that reflects the real world behavior of *Staphylococcus aureus* infections. For our numerical analysis, we utilized data from a previous model [3].

Figure 1: Table of parameters

Symbol	Interpretation	Value
N	Total Number of patients in the hospital	$N_0 = 410$
S(t)	Number of susceptible patients	$S_0 = 400$
C(t)	Number of patients infected with community strain	$C_0 = 5$
H(t)	Number of patients infected with hospital strain	$H_0 = 5$
Λ	Growth rate of the susceptible population (admission rate - discharge rate)	70
δ_C	Rate at which patients exit the community strain compartment due to death	0.0033
δ_H	Rate at which patients exit the hospital strain compartment due to death	0.0111
α_C	Decolonization rate from community strain compartment	0.6
α_H	Decolonization rate from hospital strains compartment	0.6
β_C	Rate of infection (transmission rate) of the community strain	0.36×0.09
β_H	Rate of infection (transmission rate) of the hospital strain	0.27×0.07

Figure 2: Diagram of Subgroups in the Hospital Setting



The equations of our model is as follows:

Figure 3: Mathematical Model

- $\frac{dS}{dt} = \underbrace{\Lambda}_{\text{admissions}} + \underbrace{\alpha_H H + \alpha_C C}_{\text{recovery}} - \underbrace{(\beta_H H + \beta_C C)S}_{\text{infection}}$
- $\frac{dC}{dt} = \underbrace{\beta_C SC}_{\text{infected}} - \underbrace{(\alpha_C + \delta_C)C}_{\text{recovered or died}}$
- $\frac{dH}{dt} = \underbrace{\beta_H SH}_{\text{infected}} - \underbrace{(\alpha_H + \delta_H)H}_{\text{recovered or died}}$
- N = S + C + H

4 Stability Analysis

4.1 Finding fixed points

Let's find the sets of fixed points (S^*, C^*, H^*) where $\frac{dS}{dt} = \frac{dC}{dt} = \frac{dH}{dt} = 0$.

4.1.1 Finding (S_1^*, C_1^*, H_1^*)

$\frac{dC}{dt} = 0 = \beta_c S^* C^* - (\alpha_C + \delta_C)C^*$
$\beta_C S^* C^* = (\alpha_C + \delta_C)C^*$
$S^* = \frac{(\alpha_C + \delta_C)\cancel{C^*}}{\beta_C \cancel{C^*}}$
$S^* = \frac{\alpha_C + \delta_C}{\beta_C}$, when $C^* \neq 0$

$\frac{dH}{dt} = 0 = \beta_H S^* H^* - (\alpha_H + \delta_H)H^*$
If $S^* = \frac{\alpha_C + \delta_C}{\beta_C} \neq \frac{(\alpha_H + \delta_H)}{\beta_H}$, then $\frac{dH}{dt} = 0$ requires that $H^* = 0$.

$\frac{dS}{dt} = 0 = \Lambda + \alpha_H H^* + \alpha_C C^* - (\beta_H H^* + \beta_C C^*)S$
If $H^* = 0$, then $0 = \Lambda + \alpha_C C^* - \beta_C C^* S^*$
If $S^* = \frac{\alpha_C + \delta_C}{\beta_C}$, then $0 = \Lambda + \alpha_C C^* - \beta_C C^* \frac{\alpha_C + \delta_C}{\beta_C}$
$\cancel{\beta_C} C^* (\frac{\alpha_C + \delta_C}{\cancel{\beta_C}}) = \alpha_C C^* + \Lambda$
$\cancel{\alpha_C C^*} + \delta_C C^* = \cancel{\alpha_C C^*} + \Lambda$
$\delta_C C^* = \Lambda$
$C^* = \frac{\Lambda}{\delta_C}$

Thus, one of our sets of fixed points is $\boxed{(S_1^*, C_1^*, H_1^*) = (\frac{\alpha_C + \delta_C}{\beta_C}, \frac{\Lambda}{\delta_C}, 0)}$

(S_1^*, C_1^*, H_1^*) represents the situation where disease H is eradicated, C is endemic, and the total population is steady. The proportion of total population afflicted with C at any moment under this equilibrium condition is inversely related to the death rate of C (δ_C), which is people leaving the Susceptible & Infected (S+I) population pools. It's also directly related to the admission rate (Λ), which is people entering the S+I population pools. So the proportion of sick people is a measure of the "immigration"/"emigration" rate of the total S+I pools.

There's one more interesting idea suggested by the (S_1^*, C_1^*, H_1^*) result. It says that a more deadly C results in a lower proportion of people infected with C at equilibrium. However, there's no direct dependence between the amount of C at equilibrium and the transmission parameter α_C. Intuitively, you might expect that a higher transmission rate α_C would shift the S-C equilibrium towards C, but this does not seem to be the case. In fact, a higher α_C would cause more S to exist at equilibrium, which is the opposite of expectation. It's possible that a high transmission α_C may have a direct relationship with the value of C or the speed at which C increases or decreases, at nonequilibrium conditions.

4.1.2 Finding (S_2^*, C_2^*, H_2^*)

If you perform the same mathematical procedure as above except starting by setting $\frac{dH}{dt} = 0$, then you get a complementary fixed point that arises when $S^* = \frac{\alpha_H + \delta_H}{\beta_H} \neq \frac{\alpha_C + \delta_C}{\beta_C}$, forcing $C^* = 0$.

Thus, another set of fixed points is $\boxed{(S_2^*, C_2^*, H_2^*) = (\frac{\alpha_H + \delta_H}{\beta_H}, 0, \frac{\Lambda}{\delta_H})}$

This result (S_2^*, C_2^*, H_2^*) is complementary to (S_1^*, C_1^*, H_1^*). Therefore, any analysis of this result would be a repetition of what was discussed for (S_1^*, C_1^*, H_1^*), except C is the one being eradicated instead of H.

4.1.3 Finding (S_3^*, C_3^*, H_3^*)

It's possible to have a case where $S^* = \frac{\alpha_H + \delta_H}{\beta_H} = \frac{\alpha_C + \delta_C}{\beta_C}$. On its own, it allows $\frac{dH}{dt} = \frac{dS}{dt} = 0$. However, we still need to find the H^* and S^* that permits $\frac{dS}{dt} = 0$.
$\frac{dS}{dt} = 0 = \Lambda + \alpha_H H^* + \alpha_C C^* - (\beta_H H^* + \beta_C C^*) S^*$
$\Lambda + \alpha_H H^* + \alpha_C C^* = (\beta_H H^* + \beta_C C^*) S^*$

$\Lambda + \alpha_H H^* + \alpha_C C^* = \frac{\cancel{\beta_H} H^*(\alpha_H + \delta_H)}{\cancel{\beta_H}} + \frac{\cancel{\beta_C} C^*(\alpha_C + \delta_C)}{\cancel{\beta_C}}$
$\Lambda + \cancel{\alpha_H H^*} + \cancel{\alpha_C C^*} = \cancel{\alpha_H H^*} + \delta_H H^* + \cancel{\alpha_C C^*} + \delta_C C^*$
$\Lambda = \delta_H H^* \delta_C C^*$
$H^* = \frac{\Lambda}{\delta_H} - \frac{\delta_C}{\delta_H} C^*$
This implies a linear relationship between H^* and C^* when $\frac{\alpha_H + \delta_H}{\beta_H} = \frac{\alpha_C + \delta_C}{\beta_C}$.

Final set of fixed points is $\boxed{(S_3^* = \frac{\alpha_H + \delta_H}{\beta_H} = \frac{\alpha_C + \delta_C}{\beta_C}, H_3^* = \frac{\Lambda}{\delta_H} - \frac{\delta_C}{\delta_H} C_3^*)}$

(S_3^*, C_3^*, H_3^*) intuitively represents the situation where both H and C have the same (emigration from infected)/(immigration to infected) rate. For the sake of this discussion, if you can consider the strength of a virus to be how long they keep a person infected, then these two diseases would be equally strong.

In this situation, it seems that H and C can coexist in the long-term. It would be interesting to evaluate whether this is a stable condition where H and C are equally "strong", whether one disease will still dominate the other depending on initial conditions, or if there's any center behavior around the fixed point.

4.2 Determining stability

We first compute the Jacobian of the system, where
$f_1 = \frac{dS}{dt} = \Lambda + \alpha_H H + \alpha_C C - (\beta_H H^* + \beta_C C)S$
$f_2 = \frac{dC}{dt} = \beta_c SC - (\alpha_C + \delta_C)C$
$f_3 = \frac{dH}{dt} = \beta_H SH - (\alpha_H + \delta_H)H$

So $J = \begin{pmatrix} \frac{\partial f_1}{\partial S} & \frac{\partial f_1}{\partial C} & \frac{\partial f_1}{\partial H} \\ \frac{\partial f_2}{\partial S} & \frac{\partial f_2}{\partial C} & \frac{\partial f_2}{\partial H} \\ \frac{\partial f_3}{\partial S} & \frac{\partial f_3}{\partial C} & \frac{\partial f_3}{\partial H} \end{pmatrix} = \begin{pmatrix} -(\beta_H H + \beta_C C) & \alpha_C - \beta_C S & \alpha_H - \beta_H S \\ \beta_C C & \beta_C S - (\alpha_C + \delta_C) & 0 \\ \beta_H H & 0 & \beta_H S - (\alpha_H + \delta_H) \end{pmatrix}$

4.2.1 Stability of (S_1^*, C_1^*, H_1^*) fixed point

To determine the stability of the (S_1^*, C_1^*, H_1^*) fixed point, we need to plug in S^*, C^*, H^* into the Jacobian and solve for $det(J_1 - \lambda I) = 0$

$$0 = |J_1 - \lambda I| = \begin{vmatrix} \frac{-\beta_C \Lambda}{\delta_C} - \lambda & -\delta_C & \alpha_H - \beta_H \frac{\alpha_C + \delta_C}{\beta_C} \\ \frac{\beta_C \Lambda}{\delta_C} & -\lambda & 0 \\ 0 & 0 & \beta_H \frac{(\alpha_C + \delta_C)}{\beta_C} - (\alpha_H + \delta_H) - \lambda \end{vmatrix}$$

$$0 = (\beta_H \frac{(\alpha_C + \delta_C)}{\beta_C} - (\alpha_H + \delta_H) - \lambda) \begin{vmatrix} \frac{-\beta_C \Lambda}{\delta_C} - \lambda & -\delta_C \\ \frac{\beta_C \Lambda}{\delta_C} & -\lambda \end{vmatrix}$$

So $\lambda_{11} = \beta_H \frac{(\alpha_C + \delta_C)}{\beta_C} - (\alpha_H + \delta_H)$

If $\beta_H(\alpha_C + \delta_C) > \beta_C(\alpha_H + \delta_H)$, then $\lambda_{11} > 0$, so the system would be unstable with respect to the H-axis (since this eigenvalue originated from the third column of the Jacobian). Any initial condition that starts on the H axis with $H \neq 0$ would move away from $H = 0$.

Following that, if $\beta_H(\alpha_C + \delta_C) < \beta_C(\alpha_H + \delta_H)$, then $\lambda_{11} < 0$ indicating that the system is stable with respect to the H-axis, so any initial condition that starts on the H axis with $H \neq 0$ would converge towards $H^* = 0$.

$$0 = \begin{vmatrix} \frac{-\beta_C \Lambda}{\delta_C} - \lambda_{12} & -\delta_C \\ \frac{\beta_C \Lambda}{\delta_C} & -\lambda_{13} \end{vmatrix}$$

$$M \equiv \begin{vmatrix} \frac{-\beta_C \Lambda}{\delta_C} & -\delta_C \\ \frac{\beta_C \Lambda}{\delta_C} & 0 \end{vmatrix}$$

$tr(M) = \frac{-\beta_C \Lambda}{\delta_C} + 0 < 0.$

$det(M) = 0 + \beta_C \Lambda > 0.$

Since all constants are non-negative, the trace is negative and determinant is positive, so $\lambda_{12,13}$ should both have a negative real part, indicating some kind of stability (either stable node or stable spiral). If $\mathrm{tr}(M)^2 - 4\det(M) > 0$, AKA $\frac{\beta_c \Lambda}{\delta_C^2} > 4$, then it means $\lambda_{12,13}$ has no imaginary part, indicating a stable node with respect to S and C, at (S_2^*, C_2^*). Conversely, if $\mathrm{tr}(M)^2 - 4\det(M) < 0$, AKA $\frac{\beta_c \Lambda}{\delta_C^2} < 4$, then it means $\lambda_{12,13}$ has an imaginary part, indicating a stable spiral with respect to S and C, towards the (S_2^*, C_2^*) coordinate.

In the context of the whole system, it means that as long as $\frac{\beta_H(\alpha_C + \delta_C)}{\beta_C} < \alpha_H + \delta_H$ and S is close to S_1^*, then H will be eradicated, and S and C will move towards a stable nonzero equilibrium. There is a critical point of $\frac{\beta_C \Lambda}{\delta_C^2} = 4$ where the behavior of the $S - C$ plane around this fixed point shifts from being a stable spiral to being a regular fixed node.

4.2.2 Stability of (S_2^*, C_2^*, H_2^*) fixed point

The calculations to find this stability point are pretty similar to the one for (S_1^*, C_1^*, H_1^*). You would find that stability along the C-axis varies depending on whether $\beta_C(\alpha_H + \delta_H) > \beta_H(\alpha_C + \delta_C)$ which suggests instability along the C-axis, or $\beta_C(\alpha_H + \delta_H) < \beta_H(\alpha_C + \delta_C)$ which suggests stability along the C-axis.

By analyzing the 2x2 M matrix corresponding to this fixed point, you would again find that $\text{tr}(M) < 0$ and $\det(M) > 0$, suggesting a stable spiral along the S and H axes, towards the (S_2^*, H_2^*) coordinate.

In the context of the whole system, it means that as long as $\beta_C(\alpha_H + \delta_H) < \beta_H(\alpha_C + \delta_C)$ and S is close to S_2^*, then C will be eradicated, and S and H will move towards a stable nonzero equilibrium. There is a critical point of $\frac{\beta_H \Lambda}{\delta_H^2} = 4$ where the behavior of the S-H plane around this fixed point shifts from being a stable spiral to being a regular fixed node.

4.2.3 Stability of (S_3^*, C_3^*, H_3^*) fixed point

Keep in mind that for a three-variable system, stability can be evaluated between three planes: S-H, H-C, and C-S. The stability along the S-C plane was most evaluated in the (S_1^*, C_1^*, H_1^*) analysis, and stability along the S-H plane was evaluated in the (S_2^*, C_2^*, H_2^*) analysis because they are interesting. However, this doesn't give a full picture of the stability along other planes (S-C & C-H for (S_1^*, C_1^*, H_1^*), and S-H & C-H for (S_2^*, C_2^*, H_2^*).

Thus, even though we got some "stable" results for the other two fixed points, that doesn't preclude us from also getting "stable" results for this fixed point, depending on along which plane the stability lies.

We start by plugging in $S^* = \frac{\alpha_H + \delta_H}{\beta_H} = \frac{\alpha_C + \delta_C}{\beta_C}$ into the Jacobian, and get the resulting matrix:

$$J_3 = \begin{pmatrix} -(\beta_H H_3^* + \beta_C C_3^*) & -\delta_C & -\delta_H \\ \beta_C C_3^* & 0 & 0 \\ \beta_H H_3^* & 0 & 0 \end{pmatrix}$$

$$|J_3 - \lambda I| = \begin{pmatrix} -(\beta_H H_3^* + \beta_C C_3^*) - \lambda & -\delta_C & -\delta_H \\ \beta_C C_3^* & -\lambda & 0 \\ \beta_H H_3^* & 0 & -\lambda \end{pmatrix}$$

After some solving, we find that the characteristic equation has a factor of λ at the front,

meaning that one of our eigenvalues $\lambda_{31} = 0$. This may reflect lack of movement along the line $H_3^* = \frac{\Lambda}{\delta_H} - \frac{\delta_C}{\delta_H} C_3^*$. Since all the points along this have neutral stability relative to each other. It doesn't fall under the dichotomy of stable vs unstable where values converge or diverge from a specific point. Thus, $\lambda_{31} = 0$, indicating neutral stability.

Since the fixed point (S_1^*, C_1^*, H_1^*) is stable along the S-C plane, then it means the adjacent fixed point (S_3^*, C_3^*, H_3^*) must be unstable along the S-C plane. And since (S_2^*, C_2^*, H_2^*) is stable along the S-H plane, then it means (S_3^*, C_3^*, H_3^*) must be unstable along the S-C plane. Thus, the behavior around this fixed point is unstable with respect to both S-H and S-C.

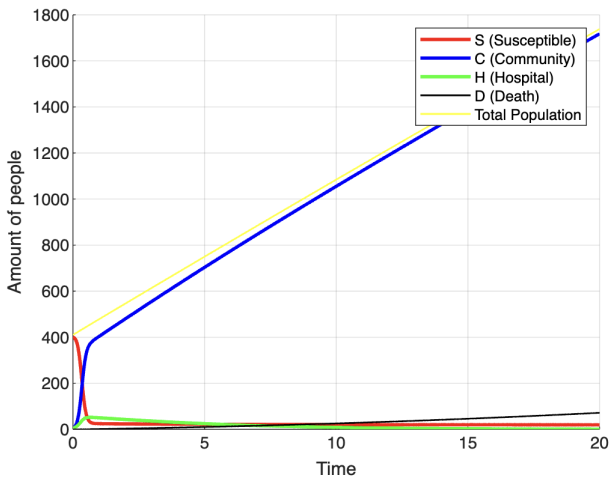
The overall interpretation of this result is that unless the system starts out at (S_3^*, C_3^*, H_3^*), then one disease should dominate over the other, depending on initial conditions. This is true even when both diseases are equally "strong" in the sense that $\frac{\alpha_H + \delta_H}{\beta_H} = \frac{\alpha_C + \delta_C}{\beta_C}$. Although this model doesn't include a direct parameter of competition between these two diseases, this could be considered a case of the competitive exclusion principle applied to an SIR model.

5 Numerical Simulation

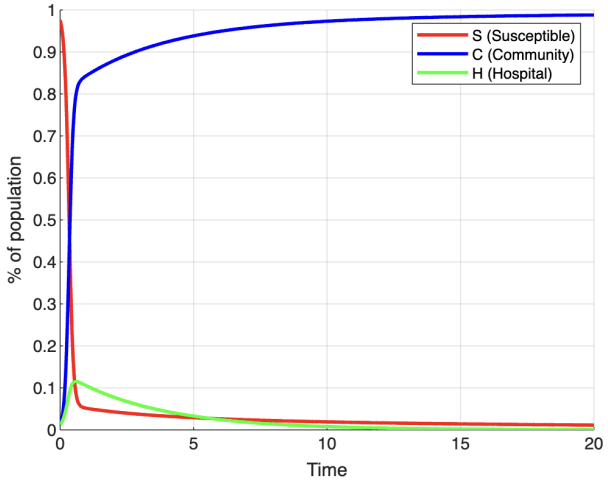
For this numerical simulation, we will analyze the interaction between the two MRSA strains under different initial conditions:

- An equal number of individuals initially infected with H-MRSA and C-MRSA.
- A greater number of individuals initially infected with H-MRSA than C-MRSA.
- A greater number of individuals initially infected with C-MRSA than H-MRSA.

We began with a set of parameter estimates derived from model established in [8]. The parameters were obtained from the Beth Israel Deaconess Medical Center's computerized database system, which provides patient and infection control data and from the literature. Running the simulation with the parameter values from Figure 1 yielded the following graph:



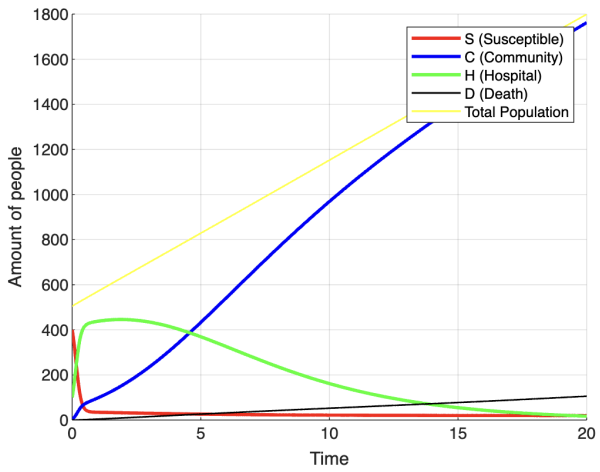
(a) Amount of people simulation.



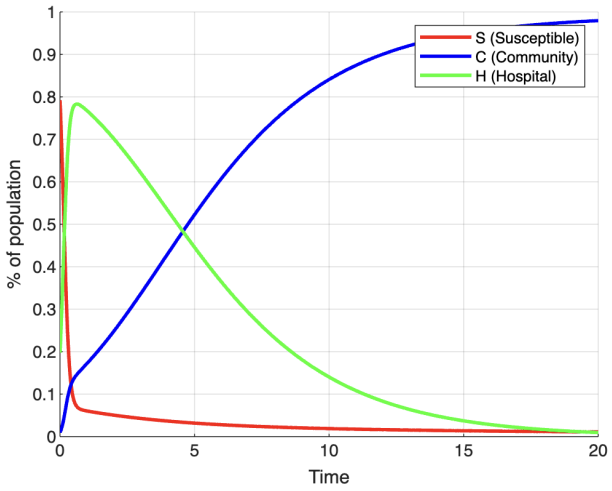
(b) Percentage of population simulation.

As shown in these graphs, the Community MRSA strain dominates. In graph (a), the majority of the total population becomes infected with C-MRSA, while the number of individuals infected with H-MRSA, the number of deaths, and the number of susceptible individuals stabilize near zero. In graph (b), the percentage of susceptible individuals and those infected with H-MRSA remains near zero, while nearly the entire population becomes infected with the Community strain (reaches nearly 1). This behavior is driven by the higher infection rate and lower death rate of the Community strain compared to the Hospital strain.

Given these results, we sought to observe a different outcome, one where the Hospital MRSA strain becomes more dominant. To test this, we increased the initial value of $H(t)$ from 5 to 100, meaning the population initially had twenty times as many individuals infected with H-MRSA as with C-MRSA. Running the numerical simulation with these new conditions produced the following results:



(a) Amount of people simulation $H(t) = 100$.



(b) Percentage of pop. simulation $H(t) = 100$.

The behavior observed in these two graphs is consistent with our previous findings. Regardless of how many individuals are initially infected with H-MRSA, the C-MRSA eventually dominates the population over time.

Increasing the initial number of individuals infected with the Hospital strain results in a higher and longer peak of H-MRSA infections. However, the number and percentage of individuals infected with H-MRSA eventually stabilizes at zero. Given these results, we modified the differential equations slightly by introducing a new parameter to better represent competition between the two strains.

In the updated numerical simulation model, a term representing viral interference was introduced. The parameter σ represents the strength of interference, where $\sigma = 0$ indicates no interference (strains do not affect each other), and $\sigma = 1$ represents perfect interference (one strain completely prevents infection by the other).In the $\frac{dC}{dt}$ equation, the term $(1-\sigma H)$ is included, while in the $\frac{dH}{dt}$ equation, the term $(1-\sigma C)$ is used. These terms imply that an individual infected with one strain has a reduced likelihood of acquiring the other strain. In other words, as the number of individuals infected with H-MRSA increases, the multiplying factor in the $\frac{dC}{dt}$ equation decreases, and vice versa. This modification better reflects the idea that prior infection with one strain decreases susceptibility to the other. The inclusion of this interference term resulted in the following equations:

- $\frac{dS}{dt} = \underbrace{\Lambda}_{\text{admissions}} + \underbrace{\alpha_H H + \alpha_C C}_{\text{recovery}} - \underbrace{(\beta_H H + \beta_C C)S}_{\text{infection}}$
- $\frac{dC}{dt} = \underbrace{\beta_C SC}_{\text{infected}} \cdot \underbrace{(1-\sigma H)}_{\text{competition}} - \underbrace{(\alpha_C + \delta_C)C}_{\text{recovered or died}}$

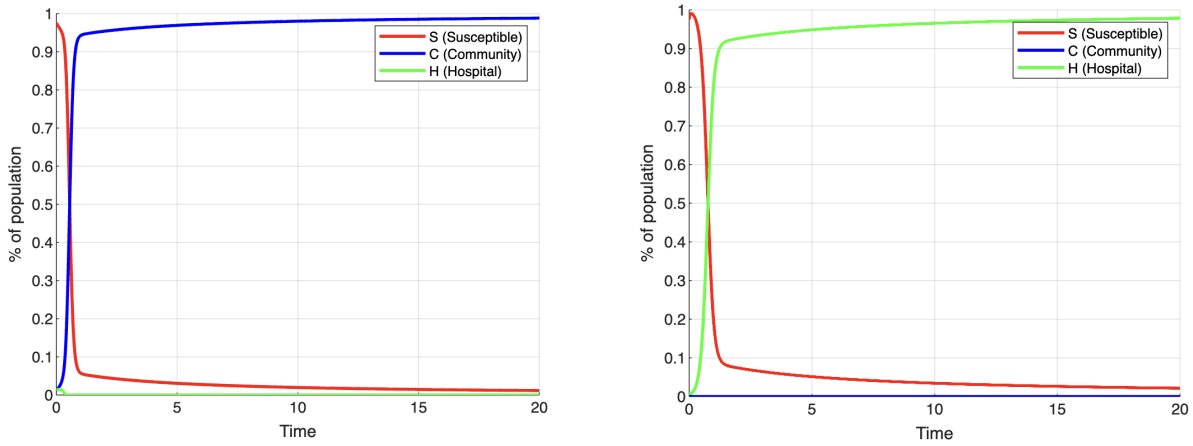
- $\frac{dH}{dt} = \underbrace{\beta_H SH}_{\text{infected}} \cdot \underbrace{(1-\sigma C)}_{\text{competition}} - \underbrace{(\alpha_H + \delta_H)H}_{\text{recovered or died}}$

- N = S + C + H

Using these updated equations, we re-examined the three scenarios: an equal number of individuals initially infected with H-MRSA and C-MRSA, a higher number of individuals infected with H-MRSA than C-MRSA, and a higher number of individuals infected with C-MRSA than H-MRSA.When one strain had more initial infections, we increased the infected count by one, setting the comparison to six individuals infected with one strain and five with the other. The goal of this simulation was to determine the critical value of σ at which the dominance shifts from one strain to the other.

5.1 Simulation 1: Equal Initial Infections of H-MRSA and C-MRSA

For this simulation, we maintained the same initial values used in previous tests. We first examined values of σ at opposite ends of the spectrum, setting $\sigma = 0.1$ and $\sigma = 0.9$. These values produced the following graphs:



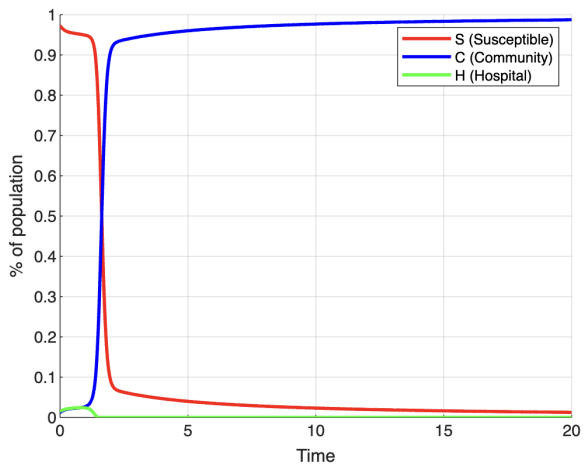
(a) Percentage of population simulation $\sigma = 0.1$. (b) Percentage of population simulation $\sigma = 0.9$.

As shown in graph (a), the Community MRSA strain initially experiences an outbreak, representing an epidemic phase of the infection. Over time, the infection stabilizes near 100%, meaning it is becoming an endemic in the long run. Similarly, graph (b) illustrates the same scenario, but with the Hospital MRSA strain undergoing an initial epidemic phase before stabilizing at nearly 100% to become endemic. To determine the critical viral interference value at which dominance shifts between the two strains, we adjusted the value of σ until

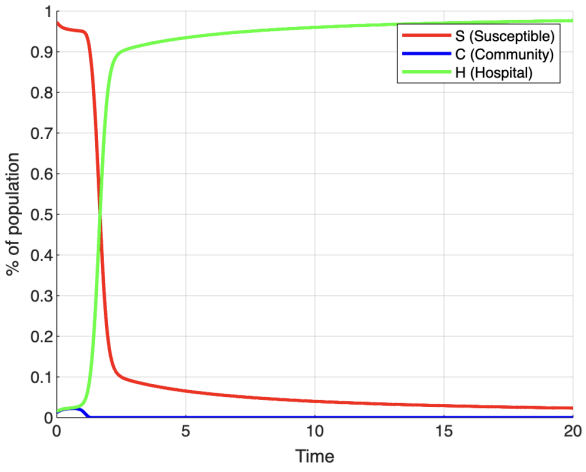
we identified the critical point where one strain overtakes the other. After testing multiple values, we found that the critical value of σ lies between 0.2134 and 0.2135, the point at which dominance transitions between H-MRSA and C-MRSA. This result suggests that when one strain makes up between 21.34% and 21.35% of infections, it becomes strong enough to suppress the other strain and eventually drive it to extinction. Below 21.34%, C-MRSA dominates, while above 21.35%, H-MRSA takes over.

5.2 Simulation 2: More Individuals Initially Infected with H-MRSA than C-MRSA

For this simulation, we set $H(0) = 6$ and $C(0) = 5$, giving the Hospital MRSA strain a slight initial advantage over the Community MRSA strain. Through this analysis, we identified the critical value of σ to be between 0.1066 and 0.1067, marking the interval where the dominance shifts between the two strains. This result suggests that when one strain has between 10.66% and 10.67% of infections, it becomes strong enough to suppress the other strain and eventually drive it to extinction. When σ is below this critical value, the Hospital MRSA strain undergoes an epidemic phase with a steep initial increase, eventually stabilizing at nearly 100% to become endemic. When σ exceeds this threshold, the same pattern occurs, but with the Community MRSA strain instead. Below are the graphs illustrating the behavior at the lower and upper bounds of the identified critical value:



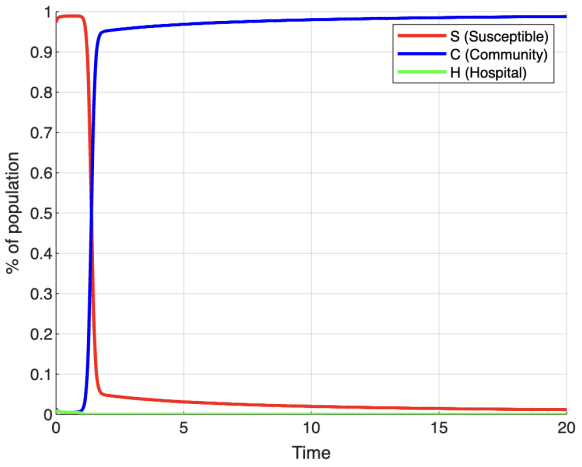
(a) Percentage of population simulation with $\sigma = 0.1066$.



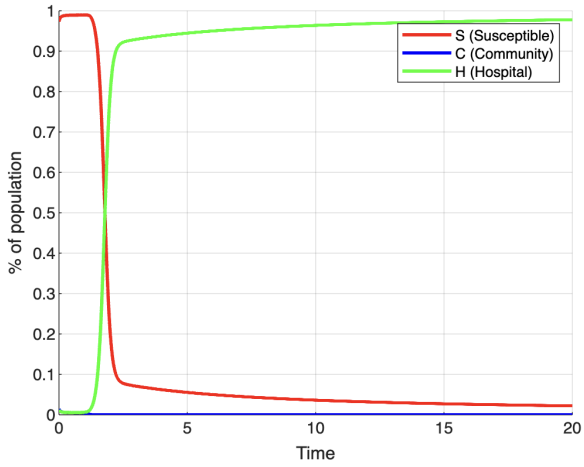
(b) Percentage of population simulation with $\sigma = 0.1067$.

5.3 Simulation 3: More Individuals Initially Infected with C-MRSA than H-MRSA

For this simulation, we set $C(0) = 6$ and $H(0) = 5$, giving the Community MRSA strain a slight initial advantage over the Hospital MRSA strain. Using the same approach as in the previous simulations, we identified the critical value of σ to be between 0.4187 and 0.4188. This indicates that when one strain accounts for between 41.87% and 41.88% of infections, it becomes strong enough to drive the other strain to extinction. As shown in the following graphs, below the critical viral interference value, C-MRSA dominates over time. Above the critical value, H-MRSA takes over and becomes the dominant strain:



(a) Percentage of population simulation with $\sigma = 0.4187$.



(b) Percentage of population simulation with $\sigma = 0.4188$.

5.4 Classification of Critical σ Value

The results from the numerical simulation suggest that when more individuals are initially infected with C-MRSA than H-MRSA, the critical σ value is the highest among the three scenarios. This indicates that a stronger viral interference effect is required to shift dominance between the two strains. The second highest critical σ value occurred when the initial number of infections with both strains was equal. On the other hand, when more individuals were initially infected with H-MRSA than C-MRSA, the critical viral interference value was the lowest, meaning that C-MRSA required less interference to eventually dominate. This suggests that the Community strain is inherently more competitive in this model, requiring only a small level of interference to dominant the Hospital strain over time.

These critical σ values represent a threshold where the system's long-term behavior shifts. Below the critical value, C-MRSA dominates while H-MRSA dies out. Above the critical

value, H-MRSA dominates, leading to the extinction of C-MRSA. At these critical σ values, the system undergoes a bifurcation, meaning that a small change in σ results in a shift where one strain becomes dominant instead of the other. This bifurcation is likely a transcritical bifurcation for the following reasons:

- Two equilibrium states exchange stability at the critical viral interference value.
- Before the bifurcation, one strain dominates while the other goes extinct.
- After the bifurcation, the other strain dominates.
- There is no coexistence, just a switch in which strain survives and dominates.

This demonstrates how a small change in the viral interference parameter σ can completely determine which MRSA strain becomes endemic. Identifying the bifurcation point helps predict the conditions where one strain will dominate the other. The system's sensitivity to σ shows the importance of viral interference in shaping MRSA dynamics, which could help inform healthcare strategies for controlling the spread of these infections.

6 Conclusion

In this paper we analyzed MRSA strain competition through stability analysis and numerical simulations. The analysis provides us with the insight into the long-term dynamics of hospital-associated (H-MRSA) and community-associated (C-MRSA) infections. The theoretical stability analysis revealed that the dominance of one strain depends on key parameter relationships, particularly the infection and recovery rates. Numerical simulations supported this finding, demonstrating that C-MRSA consistently out competes the H-MRSA due to its higher transmission rate β and lower mortality rate δ, even when initial conditions favor H-MRSA.

To better capture real-world dynamics, we introduced a viral interference parameter σ, allowing us to model direct competition between strains. Future work could explore additional factors such as antibiotic resistances, hand washing by patients, quarantining of patients, and including spread of disease by health care workers. By refining our model and incorporating empirical data, we can improve predictions of MRSA prevalence and inform public health strategies for infection control.

The model we describe in this paper has some salient limitations. Most notably the equations are completely continuous by representing patient populations in non-integer values, while in real life only an integer amount of patients can be counted, there are no fractions

of patients in hospitals. In addition to this, the differential equations we describe are a simplification removing actions a hospital administration could do take to reduce transmission including hand washing, quarantining, and patient education. In our model we also omit a discharge rate proportional to the amount of susceptible population in the hospital, this term would be $-\gamma_S \times S(t)$ with $\gamma_S = 0.2$. By excluding this term we assume that the discharge rate is a flat amount and this allows the population in the hospital to balloon up to thousands of patients. While in reality a hospital may not be able to support so many patients, due to limited resources including bed space, staff, and supplies. We also assume a lack of randomness in transmission by using fixed parameter values. On top of that our model is inherently deterministic and not stochastic, while in actuality transmission of Staph infections has an inherently random component due to factors that influence spread of disease. One last consideration that could be limiting the direct application of our analysis to real life is including other strains of . By only including two the hospital and community strains we are inherently not representing the entire dynamic bacteria ecosystem.

The model used in our analysis simulated a hospital environment with patients admitted and discharged at a fixed rate. We believe a reasonable extension of this work would be to conduct similar modeling of Staph infections in nursing homes. Nursing homes represent a large population of vulnerable seniors with similar risks of developing Staph infections. However, the epidemiology in nursing homes is different to hospitals in many ways. Nursing homes hava smaller influx and efflux of residents compared with hospitals, residents of nursing homes tend to stay in the facilities longer, and nursing homes are more community-like in that residents may share a room and involve in social activities [3]. Looking into nursing homes would require more look into finding representative parameters. Yet we believe it is worthwhile to help look into a disease affecting our most vulnerable populations.

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