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Analyzing the Impact of Vaccination on COVID-19 Spread and Hospitalizations: A Multi-Paradigm Simulation Modeling Approach

Julia Bitencourt[1], Mohsen Nikfar[1], and Konstantinos Mykoniatis[1,*]

[1]Auburn University, Auburn, Alabama, 36849, United States of America

[*]Corresponding author. Email address: kmykoniatis@auburn.edu

Abstract

Multi-paradigm simulation modeling aids the study and analysis of complex systems and their internal interactions. Given the inherent variability that exists in real-world settings, the use of different structures and methods is necessary to accurately represent the system under study. This study integrates Discrete Event Simulation and Agent-Based Modeling, developing a multi-paradigm simulation model to study the emergent COVID-19 crisis. In specific, the goal of this research is to determine how the vaccine distribution affects the spread of COVID-19 as well as hospitalizations for the state of Alabama. The simulation model incorporates three main components, including the supply chain of vaccines, the spread of COVID-19, and hospitalizations. The supply chain of vaccines simulation component studies the availability of trucks for supplying the vaccines and vaccine damage due to inappropriate handling and storage. The spread of the COVID-19 component incorporates the Susceptible Exposed Infected Recovery epidemic model. Lastly, the hospitalizations component considers capacity requirements (in terms of the number of available beds) and treatment times. The multi-paradigm model enables a better understanding of the interactions between variables of interest, helps to evaluate hospital bed requirements, and provides metrics that support the management and control of the epidemic and healthcare system.

Keywords: Discrete Event Simulation, Agent-Based Modeling, SEIR, Vaccines, COVID-19, Modeling and Simulation

1. Introduction

In March 2020, the World Health Organization (WHO) updated the status of the COVID-19 outbreak to a pandemic. One year later, just in the United States, more than 29 million cases were confirmed, and more than 500 thousand lives were lost, corresponding to 20% of the total global deaths related to the spread of SARS-CoV-2, according to the John Hopkins Coronavirus Resource Center (2021a).

Consequently, one of the major concerns raised throughout the pandemic was the costs related to hospitalizations, as well as the burden in the US healthcare system. A simulation study conducted by Bartsch et al (2020) to estimate the potential healthcare cost inflicted by the pandemic concluded that if 20% of the American population get infected by the virus, this would be equivalent to $163.4 billion in direct medical costs, 62.3 million hospital bed days, and 2.7 million Intensive Care Unit (ICU) admissions. In addition to the lives lost and the healthcare system load, the pandemic also had a great impact in different economic sectors, causing the most ruthless economic disruption since World War II (Gössling, 2020). For instance, in the entertainment industry, AMC Theaters reported a net loss of $4.5 billion in 2020, which corresponds to a 3000% increase compared to the same period of 2019 (US Security and Exchange Commission, 2020).

As an attempt to slow down the spread and gradually come back to normality, the scientific community has been working to find solutions to contain the dissemination of COVID-19, especially through the development of an efficient and safe vaccine. In December 2020, The US Food and Drug Administration (FDA) approved an emergency use authorization for COVID-19 vaccines, starting the process of a long-term solution for the coronavirus pandemic (FDA newsletter, 2020).

The initiation of the vaccination program in the US also raised awareness for other issues: how fast vaccines could be broadly available to the public, and how the vaccine distribution would affect the restrain of the virus, and consequently decrease the healthcare system burden. Some work has already been developed to answer these questions. Barnhill (2021) investigated potential problems that might affect the distribution of the COVID-19 vaccine. The latter identified that shortage of resources and capacity for producing, administrating, and distributing the vaccines as the main issues that a government can face while managing such a complex matter.

Although modeling has been widely used to understand the possible consequences of the COVID-19 pandemic in its various aspects, to the best of our knowledge no existing work has been developed connecting the supply chain of vaccines, the spread of COVID-19, and possible impacts in hospitalizations.

Therefore, this paper aims to describe how vaccine distribution can affect the spread of COVID-19 as well as hospitalizations for the state of Alabama using a multi-method modeling approach. Compliance with mitigation strategies was also explored in the model using different contact rate scenarios. We chose the state of Alabama, mainly for geographical proximity reasons. Furthermore, the state of Alabama also presented one of the highest Intensive Care Units (ICU) occupation rates in the US in January 2021, reaching 96% occupation (John Hopkins Coronavirus Resource Center, 2021b).

To model the vaccine distribution, this study will consider the following factors: supply of vaccines, and vaccine damage due to inappropriate handling and storage. To model the spread of COVID-19, we used Agent-Based Modeling (ABM). Every individual in the population can be categorized into one of the four main states: Susceptible-Exposed-Infected-Recovered (SEIR). Finally, the number of hospitalizations is also incorporated in the model as a Discrete Event Simulation (DES), allowing the investigation of interactions between the different variables, and helping to assess capacity requirements through the utilization of hospital beds.

The remainder of the paper is organized as follows: Section 2 provides a brief literature review of the current work developed, Section 3 describes the research methodology and data collection process, Section 4 details the experimentation and results, and in Section 5 we discuss conclusions, limitations and future work.

2. Literature Overview

Several studies using different modeling methods have already been conducted to understand the dynamics of transmission and patterns behind many infective diseases. For instance, De Paz and Flores (2014) compared the performance of two propagation models (ABM and SIR) to examine the spread of H1N1 flu under different epidemiological scenarios.

For the COVID-19 pandemic, although the mathematical representation of compartmental models (e.g. SEIR) and statistical growth models are the most commonly used approaches in the literature (Gnanvi, Salako, Kotanmi & Kakaï, 2021), modeling and simulation (M&S) techniques such as ABM, DES, and, to a lesser extent, System Dynamics (SD) have also been adopted. Cuevas (2020) used ABM to simulate the transmission process and risks inside a facility considering spatial aspects, social characteristics, and health conditions. Silva et al (2020) proposed a model that combines SEIR and ABM to simulate the pandemic dynamics according to seven different scenarios and provide input to policymakers concerning the adoption of mitigation strategies. Similarly, Sy et al (2020) developed a model to support policy development through a SD approach, which captures the relationships, feedbacks, and delays inherent to the diseases.

One of the main consequences of the rapid spread of COVID-19 is the burden on the healthcare system. M&S, especially DES, has been extensively used to model the hospital environment and its key indicators, such as ICU occupation and bed requirements. In this context, Wood, McWilliams, Thomas, Bourdeaux, and Vasilakis (2020) developed a stochastic DES model to evaluate the dynamics of ICU admissions. The latter suggests that capacity-dependent deaths can be reduced by 75% when the number of hospital beds is increased, which consequently reduces the length of stay and peak of demand. More recently, Melman, Parlikad, and Cameron (2021) also took advantage of DES to propose a decision support model for resource allocation considering both COVID-19 and non-COVID-19 care. Finally, Das (2020) used a DES model to analyze the impact of COVID-19 on the workflow and performance indicators of ambulatory endoscopy centers. In addition to DES representations, other M&S methods are also mentioned in the literature to simulate a hospital setting. For instance, Weissman et al (2020) utilized a Monte Carlo simulation to study hospital capacity (beds and ventilator machines) and to estimate peaks in demands under the COVID-19 impact. Using the Susceptible-Infectious-Recovered (SIR) model, the authors estimated the time until capacity would be exceeded.

As vaccines become available, and with them the hope for returning to normalcy, M&S becomes an essential tool for assessing the different scenarios that the supply chain (SC) system is going to face to make doses accessible to the maximum range of people during vaccination campaigns. Golan, Trump, Cegan, and Linkov (2020) pointed out the importance of a resilient vaccine SC for fulfilling vaccination plans. They emphasized that a quantitative criterion and a comprehensive approach towards SC resilience are crucial to fight back the pandemic. Moreover, Li and Giabbanelli (2021) developed an agent-based simulation model to investigate how effective a national vaccine campaign could be when using vaccines with different efficacies. The authors also considered the effect of people's willingness to receive the vaccine, as well as different daily vaccination capacities according to two distinct federal plans. Furthermore, exploring vaccination alternatives, Asgary, Najafabadi, Karsseboom, and Wu (2020) developed a multi-paradigm simulation model combining ABM and DES to simulate a mass vaccination drive-through facility, providing insight about processing and waiting times, as well as maximum throughput.

As pointed out in the latter example, multi-paradigm simulation models have also been employed in the context analyzed by this paper. Multi-paradigm simulation models are characterized by a combination of two or more modeling and simulation approaches (DES, SD, or/and ABM) to describe a complex system (Mykoniatis & Angelopoulou, 2020). One of the advantages of using multi-paradigm simulation models instead of single modeling approaches is that the latter can face various challenges to represent the complexity of real systems, resulting in an oversimplified model that excludes critical components (Mykoniatis, 2015). Borschev (2013) describes the process of combining DES and ABM for supply chain and health care systems. He provides a process for integrating DES inside agents that represent supply chain elements. He also shows how to model agents who are temporally transformed to entities for requesting treatment from a health care center, which is captured by a DES paradigm. Djanatliev and German (2013, December) applied the three M&S paradigms (DES, ABM, and SD) to assess health care technology. They applied SD for the macroscopic level of abstraction to capture population and disease dynamics and combined ABM with DES to model the hospital environment. DES deployed for the meso levels of abstraction, to capture workflow aspects, and ABM was used for micro levels of abstraction to capture details of heterogeneous interactions on the individual level. Other examples of multi-paradigm models can be observed in Chahal, Eldabi, and Young (2013); Viana, Brailsford, Harindra, and Harper (2014); and more recently, in Jalayer, Orsenigo, and Vercellis (2020).

This paper describes the implementation and evaluation of a multi-paradigm simulation model which combines aspects of ABM and DES to investigate how vaccine distribution can affect the dynamics of the spread of COVID-19, as well as hospitalizations. Compliance with mitigation strategies during the vaccination campaign was also investigated by the model.

3. Modeling the Impact of Vaccines on the COVID-19 Spread and Hospitalizations

This section describes the methodology that we followed for the development of a multi-paradigm DES and ABM simulation model. Modeling an ordered sequence of well-defined events is one of the unique features of DES, whereas capturing the heterogeneity of agents across a population is one of the differentiating aspects of ABM compared to DES and SD (Mykoniatis, 2015; Angelopoulou and Mykoniatis, 2018). Deploying DES and ABM simulation into the development of this vaccine distribution model using a geographic information system (GIS) becomes essential to capture both the spatial and temporal characteristics of the COVID-19 Spread and hospitalizations.

For the development of the hybrid DES and ABM model we considered the following assumptions:

- The demand for vaccines remains constant over time.
- Only two-doses COVID-19 vaccines are considered.
- Fully vaccinated individuals cannot infect other agents in the transmission model.
- The death rate is equal to the birth rate. Therefore, we do not eliminate agents from the population.
- Storage limitations and requirements are not assessed by the model.
- Hospital bed availability has a limited and fixed capacity.

Furthermore, for modeling the supply of vaccines, we considered distribution centers with the same initial number of trucks for delivering doses. However, the model’s interface allows the user to adjust the total number of trucks, the contact rate of the virus transmission, and the spoilage rate to allow for testing different scenarios. Figure 1 depicts the user interface.

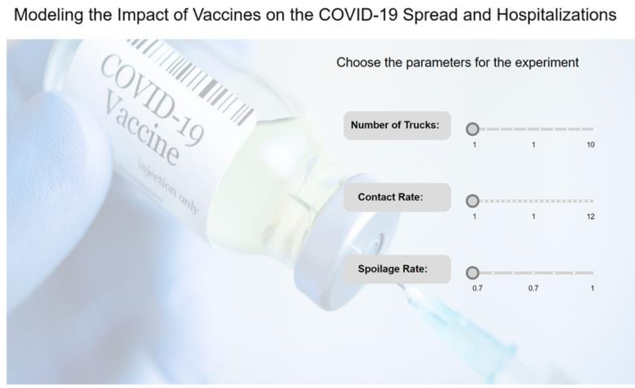

Figure 1. Model Interface.

For the development of the model, we used AnyLogic PLE version 8.7.4, which allows the user to combine different modeling and simulation approaches, as well as capture distinct abstraction levels of the system under analysis.

3.1. Discrete Event Simulation Module

Discrete-event simulation (DES) has primarily been used as a decision support tool to analyze and assess complex system concepts, layout, and control logic. DES approach has also been deployed in daily operational processes and planning of healthcare facilities. In this study, we used DES to model the hospitalization process. Specifically, we applied DES to capture the entities/agents that request treatment and their statistics considering both the availability of inpatient hospital beds in the state of Alabama reported by the John Hopkins Coronavirus Resource Center (2021c), as well as the average days COVID-19 patients spend in the hospital. The average length of stay was estimated according to a study conducted by Richardson et al (2020) with 5,700 patients hospitalized in the NYC area. The study found an overall length of stay of 4.1 days (IQR, 2.3-6.8), which is represented in our model as a triangular distribution with a mode of 4.1 days, a maximum of 6.8 days, and a minimum of 2.3 days. The model also accounts for the deaths that might occur during the treatment, estimated as 2% of the total of people treated. Figure 2 illustrates the process flow of the individuals who request treatment in a clinic.

Figure 2. DES Model for Hospitalizations.

3.2. Agent Based Modeling Module

The agent-based module is composed of self-adaptive agents that represent the population of the state of Alabama. The reason for modeling the population as heterogeneous agents with unique attributes is that we can accurately capture the transmission of the disease through the individual agents' interactions among each other and within their environment (GIS network).

A modified Susceptible, Exposed, Infected, Recovered (SEIR) model was created to capture each agent's behavior of COVID-19 transmission. Each individual's behavior in the transmission model is modeled by a state chart with five states, as shown in Figure 3. The states are defined as follows:

- Susceptible: individuals in this state can contract the virus.
- Exposed: individuals in this state were exposed to the virus. In the model, the transition from Susceptible to Exposed is defined as a message sent from infective agents that interact with susceptible individuals at a certain contact rate.
- Infected: individuals in this state are infected and can transmit the virus to other individuals in the population. The transition from Exposed to Infected is defined by a rate representing the mean latency duration of the virus.
- Recovered: individuals in this state are recovered and immune to COVID-19 for a certain period of time. The transition from Infected to Exposed is defined by a rate representing the mean infection duration. Furthermore, we considered the period of waning immunity varying according to a uniform distribution from 90 to 180 days.
- Hospitalized: individuals in this state requested treatment in a hospital facility. The hospitalized state is triggered by a condition that checks the age attributed to the agent. If the age attributed to the agent is greater than 65 years old, the probability of hospitalization assigned is 0.55. Otherwise, the probability assigned is 0.13. The predicted probabilities were estimated using data extracted from Dashti, Roche, Bates, Mora, and Demler (2021) in a study conducted with 12,347 patients in the US.

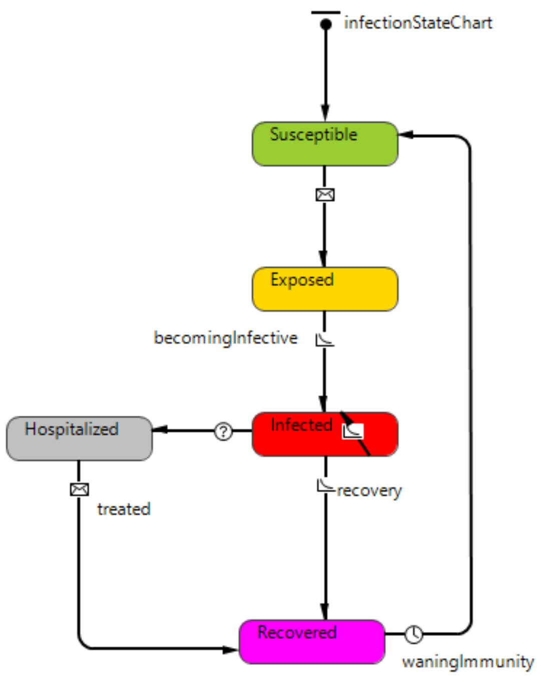

Figure 3. SEIR-infection-hospitalization State Chart.

In addition to the SEIR state chart, a model simulating a vaccination campaign was incorporated inside the agent representing the population. The vaccination campaign model consists of four states. Primarily, agents go through a checkpoint that guarantees that individuals just get vaccinated if doses are available (CheckAvailability1). Then, if vaccines are available, agents get the first dose (GetDose1). After 28 days, the agents go again for a checkpoint (CheckAvailability2), and if doses are available, they get the second shot (GetDose2). Agents are considered fully vaccinated just after the second dose.

For the vaccination state chart, there is also a period of waning immunity following the same distribution of the transmission model. When immunity is lost, agents will return to the first state and restart the vaccination cycle. Figure 4 illustrates the vaccination state chart.

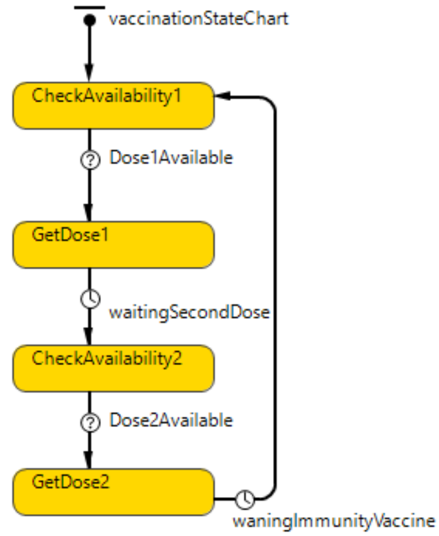

Figure 4. Vaccination State Chart.

Finally, to incorporate the distribution of vaccines into the model, we used agents representing (i) distribution centers/hubs where the vaccines arrive from the manufacturers, (ii) clinics where the vaccine is administered, and (iii) trucks that deliver the doses from the distribution centers to the vaccination clinics.

The model also considers the spoilage of vaccines during the transportation of doses due to mishandling. The spoilage happens at a certain rate on every trip and can be defined by the user.

The clinics' weekly demand was estimated according to the average number of administered doses reported by the Alabama Department of Public Health (2021) from 03/03/2021 to 04/13/2021. The demand was proportionally distributed over 67 of Alabama's counties according to the population size.

As it is illustrated in Figure 5, trucks leave the distribution center (atDistributionCenter) to fulfill the orders created by the nearest clinic (toClinic). In the clinic, if the truck receives a message from another clinic, it will check the number of orders with the remained doses of vaccines available in the truck. If the truck has enough vaccines for the next clinic, it will depart the current clinic towards the next one (fromClinicToClinic). The trucks return to distribution centers according to a condition (goingBackToDistributor) whenever the truck is empty or it does not receive any orders from other clinics.

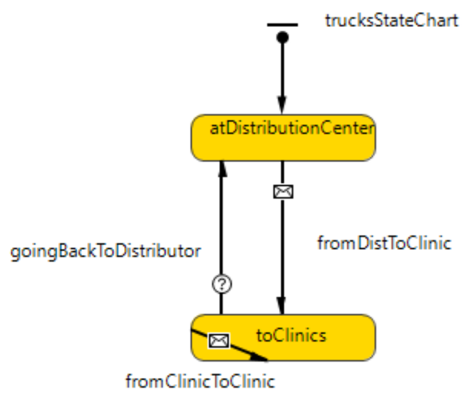

Figure 5. Trucks State Chart.

3.3. GIS Network Module

In this model, we used the AnyLogic GIS Network for the distribution of vaccines. The GIS space allowed us to place the clinic and distributor agent types into a geospatial environment defined with a GIS map. For the distribution of vaccines, we considered four distribution centers which are located in four of the most populated cities of Alabama (Birmingham, Huntsville, Mobile, and Montgomery). The distribution centers supply the clinics with vaccines by using truck agents, as described in Section 3.2.

The GIS space supports the functionality to set and retrieve the current truck location, to move the trucks that distribute vaccines using an average specified speed from distributor locations to clinic locations, to execute actions upon arrival, to animate the (static or moving) trucks at its location, as well as to establish connections based on agent's layout. On the GIS map, we have placed 67 clinics, one for each county of Alabama state.

Figure 6 illustrates the trucks delivering vaccines from distribution centers to clinics using the AnyLogic GIS network in Alabama state.

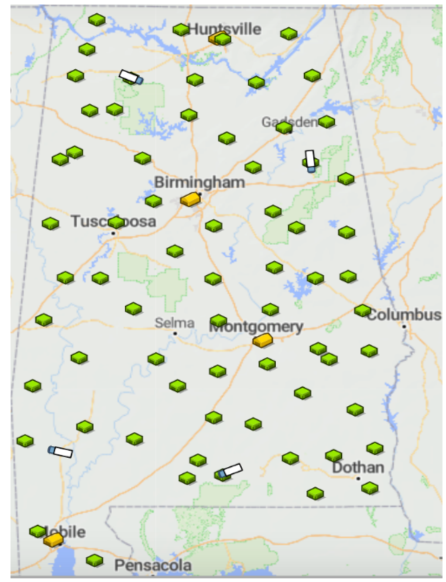

Figure 6. GIS Map.

4. Results and Discussion

This section provides information about the experimental design and results. Before conducting the experiments, we successfully tested and verified the correction of the DES logical flow, agents' state transitions, and the dynamics of the disease by observing the animation of the simulation output and the state diagrams.

4.1. Analyzing the Impact on Hospitalizations

For investigating the effects of vaccine distribution in hospitalization, we analyzed the impact of the number of available trucks for delivering the doses (1, 3, and 10 trucks) and spoilage rate (10%, 20%, and 30%) on hospital bed utilization. For each scenario, we conducted 10 runs and 10 replication per iteration, resulting in a 95% confidence interval (CI). Tables 1 and 2 show the results for the assessed scenarios.

Table 1. Hospital bed utilization for different number of trucks.

Number of Trucks	Average Bed Utilization	Bed Utilization (95% CI)
1	0.856	[0.82, 0.892]
3	0.821	[0.771, 0.871]
10	0.784	[0.726, 0.842]

Table 2. Hospital bed utilization for different spoilage rates.

Spoilage Rates	Average Bed Utilization	Bed Utilization (95% CI)
0.1	0.795	[0.739, 0.851]
0.2	0.807	[0.756, 0.858]
0.3	0.831	[0.785, 0.877]

The effect of different contact rates (1, 4, and 12) was also explored in the model. Lower contact rates represent the population complying with mitigation strategies during the vaccination campaign. Table 3 presents the results obtained for the distinct contact rates.

Table 3. Hospital bed utilization for different contact rates.

Contact Rates	Average Bed Utilization	Bed Utilization (95% CI)
1	0.562	[0.495, 0.629]
4	0.796	[0.743, 0.849]
12	0.885	[0.848, 0.922]

To compare the scenarios, we used the following rule of thumb: if there is an overlap between CI, the difference between groups is not statistically significant. Otherwise, the difference will be statistically significant.

As Table 1 demonstrates, the average bed utilization decreases when we increase the number of trucks (0.856, 0.821, and 0.784 for 1, 3, and 10 trucks, respectively). However, all the confidence intervals overlap. Therefore, the difference between their means is not statistically significant.

For different spoilage rates, the average hospital bed utilization obtained was 0.795, 0.807, and 0.831 for 0.1, 0.2, and 0.3 spoilage rates, respectively. Using the same rule of thumb, we concluded that the differences between the means are not significant.

On the other hand, contact rate has a substantial impact. The average bed utilizations for contact rates 12 and 4 are statistically different from the average for contact rate 1, reinforcing the importance of complying with mitigation strategies to slow down the spread of COVID-19 and, consequently, decrease the pressure on the healthcare system, especially when considering the waning immunity effect.

4.2. Analyzing the Impact in the Spread of COVID-19

Using the same parameter variations, we also analyzed the effects of vaccine distribution and different contact rates on the spread of COVID-19 observing the SEIR graph output.

Figures 7, 8, and 9 show the effect of the number of trucks on the spread of COVID-19 disease.

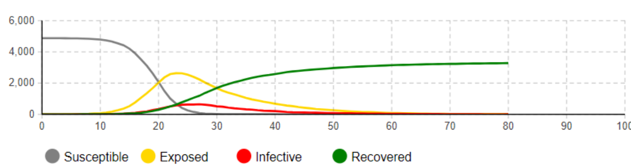

Figure 7. SEIR model graph using 1 truck.

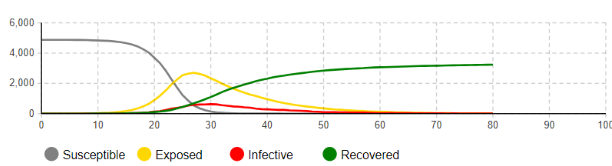

Figure 8. SEIR model graph using 3 trucks.

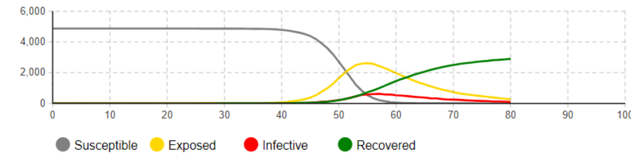

Figure 9. SEIR model graph using 10 trucks.

Figures 10, 11, and 12 demonstrate the effect of vaccine spoilage rates on the spread of COVID-19 disease.

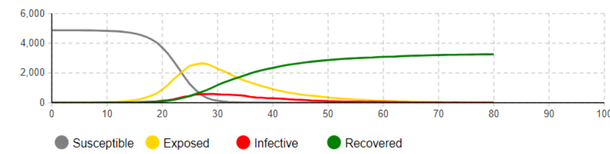

Figure 10. SEIR model graph using 0.1 spoilage rate.

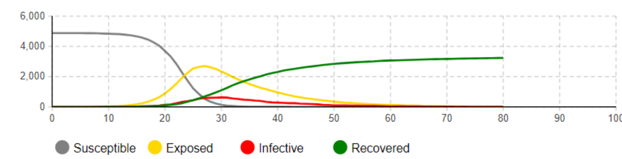

Figure 11. SEIR model graph using 0.2 spoilage rate.

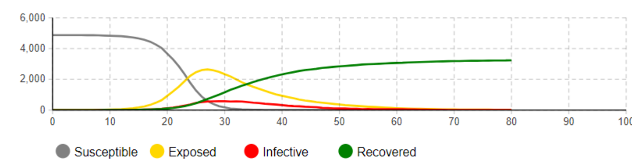

Figure 12. SEIR model graph using 0.3 spoilage rate.

Finally, Figures 13, 14, and 15 display the effect of contact rate on the spread of COVID-19 disease.

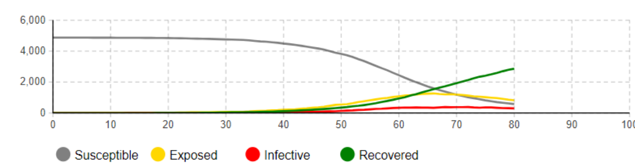

Figure 13. SEIR model graph using 1 for contact rate.

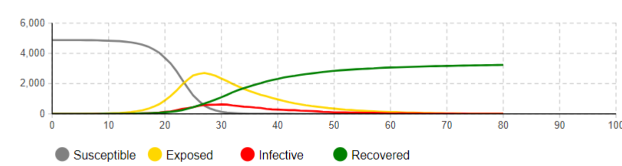

Figure 14. SEIR model graph using 4 for contact rate.

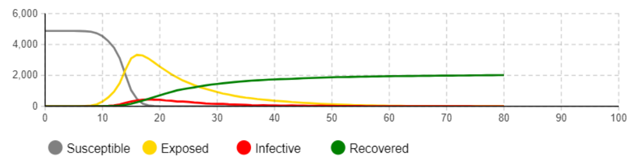

Figure 15. SEIR model graph using 12 for contact rate.

For the number of trucks, the SEIR graphs indicate a very similar behavior when using 1 or 3 trucks to deliver the vaccines. On the other hand, when using 10 trucks, the peak for Exposed and Infective is delayed. Despite a delay being observed, indicating that the population is more resistant to the infection, the height of the peak is very similar to the other scenarios assessed. One of the reasons for this fact is that, although there is a greater number of people fully vaccinated, the proportion of immune individuals is not enough for containing the spread.

For the different spoilage rates tested, the peaks of Exposed and Infective occurred almost at the same time and magnitude. Therefore, no perceived effect was observed on the spread.

Once again, contact rates demonstrated the most impactful outcome. Examining the Exposed and Infective curves, for lower contact rates, a flatter peak can be perceived, while for higher contact rates, the peak happens faster and more abruptly, emphasizing the importance of mitigation strategies.

4.3. Analyzing the Impact of a Second Outbreak

In addition, we ran a simulation experiment and tested the effect of a second outbreak when a portion of the population is already vaccinated. Figure 16 illustrates the SEIR disease dynamics for the first outbreak where just a few doses were administered to the population. Figure 17 illustrates the scenario where approximately 50% of the population is already vaccinated.

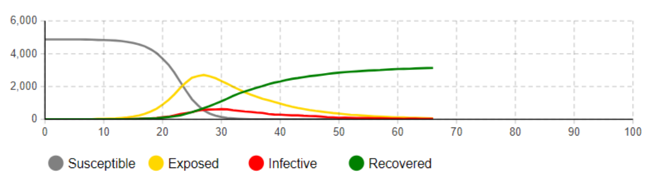

Figure 16. SEIR model graph for the first outbreak.

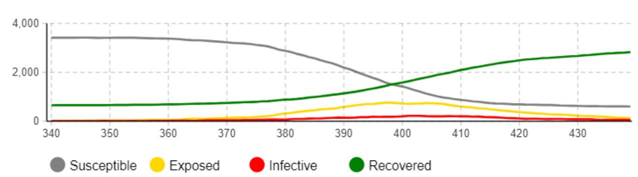

Figure 17. SEIR model graph for the second outbreak.

As one can observe, Figure 17 presents a flattened curve of the number of infected and exposed people as expected. The results reinforce the importance of a strong vaccination campaign to minimize the effects of COVID-19 spread.

5. Conclusions

In this work, we tested the effect of the vaccine distribution as well as different contact rates on the spread of COVID-19 and hospitalizations in the state of Alabama. We created our model based on the real data provided by governmental resources and academia. After verification and validation of our model, we implemented different scenarios to investigate the effect of the different number of trucks for delivering vaccines, vaccine spoilage rate, and contact rate on hospitalization and spread of the disease.

The results show when we consider a waning effect for vaccines, the importance of following mitigation strategies like social distancing and quarantine is still significant. Increasing the number of available trucks and reducing vaccine spoilage rates can reduce the average hospital bed utilization. Nevertheless, we observed the differences between means are not statistically significant. The spoilage rate did not display any significant effect on the spread of the disease. An increasing number of trucks caused a delay in a peak in the number of exposed and infected people, demonstrating that having just a small proportion of the population fully vaccinated is not enough to contain an outbreak. The most promising results came from decreasing contact rate, which can be achieved by complying with mitigation strategies. Reducing the contact rate from 12 to 1 can significantly reduce hospital bed utilization from 0.885 to 0.562. It also can flatten the curve for the number of infected people and cause a delay in the time that the peak happens. Considering our findings, we conclude that if we consider the waning immunity effect for vaccines, mitigation strategies can still be critical for reducing the burden on hospitals and their personnel. The discussed interventions were shown to be efficacious on a small scale (for Alabama State) and or under controlled conditions. However, we anticipate that these initiatives can be effectively scaled up and be expanded under real-world conditions to reach a greater proportion of the eligible population and consider other territorial contexts while retaining effectiveness.

Some of the limitations faced by this study are related to the aforementioned assumptions. Assessing additional storage constraints and requirements could provide a more realistic model of how vaccine distribution affects the pandemic scenario.

In the future, we plan to enhance the simulation model by exploring how the number of available resources, such as nurses and professionals able to administer vaccines, can affect the model. Furthermore, storage limitations in both clinics and distribution centers can be implemented. Finally, another direction for future work will be to consider the process of hospitalization and vaccination in each county aiming to provide more specific actions to the individual needs of each region.

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