# FINAL REPORT

"Optimizing Non-Pharmaceutical and Pharmaceutical Interventions to Mitigate Influenza Pandemic Spread: A Simulation-Based Approach"

By Joel,Wei Sin, Zehao

Simulation Code URL: https://github.com/joel-quek/Georgia-Tech-OMSA/tree/main/ISYE6644%20Simulation/Project

## ABSTRACT

With the most recent flu pandemic of COVID-19 lasting for almost three years starting from 2019, experts believe that it is imperative to investigate and contain the causes of the flu spread. Evidence points to a rapid and systematic response to managing flu spread as the crux for reducing morbidity, mortality, and associated high costs to public communities. Various measures for containing flu spread exist. Non-Pharmaceutical interventions (NPIs) include masks wearing and social distancing, while subsequent Pharmaceutical Interventions (PIs) such as the use of vaccines could be administered to the general population to contain the spread.

In this study, we will develop a simulation model to include the best strategy in the form of an objective function of defined metrics under a set of constraints, and summarize the outcomes of both NPIs and PIs in preventing the spread of a flu pandemic.

## BRIEF APPROACH

In order to comprehensively understand and address the dynamics of influenza pandemic spread, a structured approach is necessary. This entails the construction and analysis of four distinct scenarios.

- Firstly, establishing a baseline scenario devoid of any interventions provides a fundamental understanding of the natural progression of the disease within the population.
- Subsequently, exploring the individual impact of NPIs such as mask-wearing and social distancing enables an assessment of their effectiveness in reducing disease transmission.
- Similarly, investigating the individual impact of PIs like vaccines allows for the evaluation of their efficacy in mitigating the spread of influenza.
- Finally, integrating both NPIs and PIs in combined strategies facilitates an examination of their synergistic effects and overall effectiveness in containing the pandemic.

Through these systematic analyses, insights into the relative contributions of different intervention strategies can be gained, aiding in the development of optimized approaches for pandemic control and management.

# CHAPTER 1: INTRODUCTION

**Context and Background**

Recent pandemics have underscored the critical need for effective pandemic management strategies to minimize health and economic impacts on societies worldwide. The COVID-19 pandemic, in particular, highlighted the importance of rapid and strategic responses to infectious disease outbreaks. During such events, understanding the dynamics of disease spread and the effectiveness of various interventions—both pharmaceutical (PIs) and non-pharmaceutical (NPIs)—is crucial for public health planning and response.

**Problem Statement**

The simulation addresses the problem of how to effectively control and mitigate the spread of an infectious disease within a large population under various intervention strategies. It seeks to explore the implications of different health interventions, such as vaccinations and social distancing measures, on the dynamics of disease spread, economic costs, hospitalization rates, and overall public health outcomes.

**Objectives**

The primary objectives of the simulation study are:

1. To model the spread of an infectious disease within a hypothetical population to understand the baseline dynamics of transmission without interventions.
2. To evaluate the effectiveness of various intervention strategies, including vaccination and hospitalization, in controlling the disease spread.
3. To assess the economic implications of these interventions, focusing on vaccination costs and hospitalization expenses.
4. To provide insights into the optimal mix of interventions that balance health outcomes with economic impacts.

**Scope**

The scope of the study includes:

- Modeling Disease Dynamics: Simulating the natural progression of an infectious disease within a population to establish a baseline scenario.
- Intervention Analysis: Comparing the impact of different interventions, such as vaccination and hospital rates, on the spread of the disease.
- Economic Evaluation: Analyzing the costs associated with each intervention strategy, including direct costs like vaccination and indirect costs stemming from hospitalizations.
- Outcome Optimization: Identifying the most effective strategies that reduce both the health and economic burdens of the pandemic.

**Initial Conditions**
The simulation model starts with a population of 3,000,000 people, initially including 10 infectious individuals and no vaccinated individuals, indicating the beginning of a disease outbreak. The infection probability per contact is set at 0.02, aligning with parameters from previous studies for consistency. The financial parameters include a vaccine cost of $120 per dose and hospitalization costs of $11,275 per patient, with a hospitalization rate of 0.001. This configuration sets the stage to track changes in the numbers of susceptible, infectious, vaccinated, recovered, and deceased individuals throughout the simulation, facilitating an analysis of various public health interventions' impacts on disease spread and economic costs.

## CHAPTER 2: LITERATURE REVIEW

Our flu spread simulation model incorporates methodologies from several pivotal studies. We utilize the FluTE model's detailed stochastic approach for modeling influenza transmission across large populations. Insights from "Strategies for Mitigating an Influenza Pandemic" guide our inclusion of various intervention strategies. The SEIR multiplex network model's focus on social interactions informs our approach to modeling interaction dynamics. Additionally, integrating food distribution logistics from the Georgia study highlights the socio-economic impacts of pandemics. These referenced studies collectively inspire our simulation, ensuring a comprehensive and effective modeling of flu spread scenarios.

**1. Strategies for Mitigating an Influenza Pandemic**
This paper uses simulation models to explore various strategies for mitigating influenza pandemics, focusing on Great Britain and the United States. It examines interventions like school closures, antiviral treatments, and travel restrictions, using a large-scale epidemic simulation model. The findings suggest that internal travel restrictions and border controls are largely ineffective unless extremely stringent. The most effective strategies include school closure combined with antiviral prophylaxis, which can significantly reduce peak attack rates. Additionally, household-based interventions, such as quarantine and prophylaxis, could effectively reduce transmission if highly compliant.

**2. Modeling Singapore COVID-19 Pandemic with a SEIR Multiplex Network Model**
This paper presents an agent-based SEIR model that utilizes a multiplex network to account for various types of social interactions (household, workplace, and public gatherings) during the COVID-19 pandemic in Singapore. The model is designed to assess the effectiveness of interventions like social distancing, work from home policies, and lockdowns. It concludes that without effective measures, such as the "Circuit Breaker" lockdown, the spread within densely populated areas could lead to uncontrolled outbreaks. The model also highlights the role of asymptomatic carriers and the importance of rapid testing to mitigate the spread.

**3. FluTE Model**
FluTE is an individual-based simulation model of influenza that uses stochastic modeling to simulate the spread of influenza across large populations like metropolitan areas or the entire United States. It incorporates complex natural history, intervention strategies, and realistic social contact networks. The model allows for various intervention strategies to be tested, such as vaccination and social distancing, and runs on personal computers. FluTE is particularly notable for its detailed representation of each

individual within the simulation, which can help public health officials plan and respond to influenza outbreaks effectively.

**4. Modeling Influenza Pandemic, Intervention Strategies, and Food Distribution**

This paper focuses on the logistics of food distribution during an influenza pandemic, integrating a disease spread model with a facility location and resource allocation network model. It explores the impact of intervention strategies like school closures and voluntary quarantine on the spread of disease and food distribution needs. The model was applied to the state of Georgia, providing insights into the number of meals needed and the design of the supply chain network. It finds that voluntary quarantine might be more effective and less disruptive than school closures.

These summaries helped provide foundational knowledge for creating a simulation model in Python for pandemic flu spread simulations.

## CHAPTER 3: METHODOLOGY

**Model Description**

The simulation model evaluates the spread and control of an infectious disease within a population, focusing on three key processes:

| **Code Section** | **Description** |
|---|---|
| Part A: Calculating New Infections | Calculating New Infections - Simulates daily interactions between infectious and susceptible individuals, calculating new infections based on a set transmission probability of 0.02. |
| Part B: Updating Status | Uses a stochastic approach to determine daily recoveries and deaths within the infectious population, with predefined recovery and death rates. |
| Part C: Applying Vaccination | Implements daily vaccinations based on a variable rate, adjusting the susceptible and vaccinated populations accordingly and tracking associated costs. |

This model provides a dynamic framework to assess the effectiveness of health interventions and their impact on disease spread and population health. Each part of the model will be elaborated below.

**Part A: Calculating New Infections**
This section of the model simulates the daily interactions of infectious individuals with others in the population and calculates the number of new infections. Each infectious individual can have between 0 and 15 interactions per day. The probability of transmission per interaction is set to match the infection probability defined in your initial conditions (0.02). If an interaction results in transmission (which statistically happens 20% of the time given the 0.02 probability), the number of susceptible individuals decreases, and the number of new infections increases.

**Part B: Updating Status**
This part updates the status of the infectious population by calculating the number of recoveries and deaths each day using stochastic methods (specifically, the binomial distribution). The model assumes recovery and death rates (10% and 1%, respectively). The calculated changes (recoveries and deaths) are then adjusted to ensure they don't exceed the number of currently infectious individuals. This section provides dynamic updates on the health status of the population, impacting the counts of infectious, recovered, and deceased individuals.

**Part C: Applying Vaccination**
The vaccination part of the model applies daily vaccinations to the susceptible population. The vaccination rate is dynamically calculated with a base rate of 1% and an added daily variation of up to 0.5%. The actual number of vaccinations administered is calculated based on this rate and adjusted so it does not exceed the number of susceptible individuals. The costs associated with vaccinations are also tracked, providing a financial aspect to the impact assessment of the vaccination strategy.

**Population Setup**
Population Size: 3,000,000 individuals.
Initial Conditions:
- Infected: 10 initially infected individuals, starting the spread of the disease.
- Vaccinated: 0 initially, reflecting the scenario before vaccination begins.
- Susceptible: Calculated as the total population minus the initially infected and vaccinated individuals.

**Transmission Dynamics**
- Interaction Rules: Each infectious individual can have between 5 and 15 interactions per day, randomly determined.
- Infection Probabilities: Set at 0.02, implying a 2% chance of disease transmission per interaction, reflecting typical contagion probabilities for respiratory illnesses.

**Recovery and Mortality Rates**
- Recovery Rate: 10% chance of recovery per day, indicating that each infectious individual has a probability of recovering daily.
- Death Rate: 1% chance of death per day, representing the fatality rate among the infectious individuals.
- Calculation: Both rates are applied stochastically using a binomial distribution to determine the actual number of recoveries and deaths each day.

**Vaccination Strategy**

- Base Vaccination Rate: 1% of the susceptible population per day, adjustable to reflect daily variations.
- Daily Variation: Up to 0.5% variation in the daily vaccination rate to simulate real-world inconsistencies in vaccine distribution.
- Mechanism: The number of vaccinations administered daily is calculated based on the current susceptible population and the adjusted daily rate. The process continues until 70% of the total population is vaccinated.

**Parameters**

- Population Size: Chosen to simulate a large community or city.
- Initial Infectious and Vaccinated Counts: Reflects the early stage of an outbreak.
- Infection Probability, Recovery, and Death Rates: Based on epidemiological data typical of respiratory infections.
- Vaccination Rate and Variation: Mimics real-world vaccination efforts where daily rates can fluctuate due to supply and logistical issues.

**Simulation Process**

1. Initialization:
   - Set initial counts for infected, vaccinated, and susceptible populations.
   - Define and initialize all rates and probabilities.
2. Daily Loop Execution:
   - Day Start: Increment the day counter.
   - New Infections Calculation: For each infectious individual, randomize the number of interactions and apply the infection probability to potentially increase the number of infections.
   - Status Update: Calculate recoveries and deaths using the recovery and death rates, adjust the infectious count, and update the recovered and deceased totals.
   - Vaccination Administration: Randomize the daily vaccination rate within the specified range, calculate the number of vaccinations, and update the susceptible and vaccinated counts.
   - Cost Calculation: Compute daily and total vaccination costs.
   - Threshold Check: End the simulation if 70% vaccination coverage is reached or the simulation reaches its day limit.
3. Output Results:
   - Display final statistics on vaccination, recovery, death, and infection rates, along with total costs associated with vaccination.

**Part D: Daily Simulation Loop**

Part D extends the simulation model over a set period, repeating the infection, recovery, and vaccination processes daily to assess long-term trends and outcomes. Here's a brief description of this component:

Daily Simulation Loop: The model runs for up to 300 days or until 70% of the population is vaccinated. Each day consists of:

- Calculating New Infections: Infectious individuals interact with others, leading to new infections based on the infection probability.
- Updating Status: Daily recoveries and deaths are calculated stochastically, updating the counts for infectious, recovered, and deceased individuals.
- Applying Vaccination: Vaccinations are administered based on a variable daily rate, adjusting for the percentage of the susceptible population that gets vaccinated each day.
- Cost Calculation: The cost of vaccinations administered each day is calculated, along with a cumulative total.

The loop tracks the progress of the disease and the impact of interventions over time, providing a comprehensive view of the pandemic's dynamics and the effectiveness of the vaccination strategy. The simulation ends when the vaccination threshold is met or the designated number of days is reached, summarizing key metrics such as percentages of vaccinated, recovered, deceased, and total contracted cases, along with total vaccination costs.

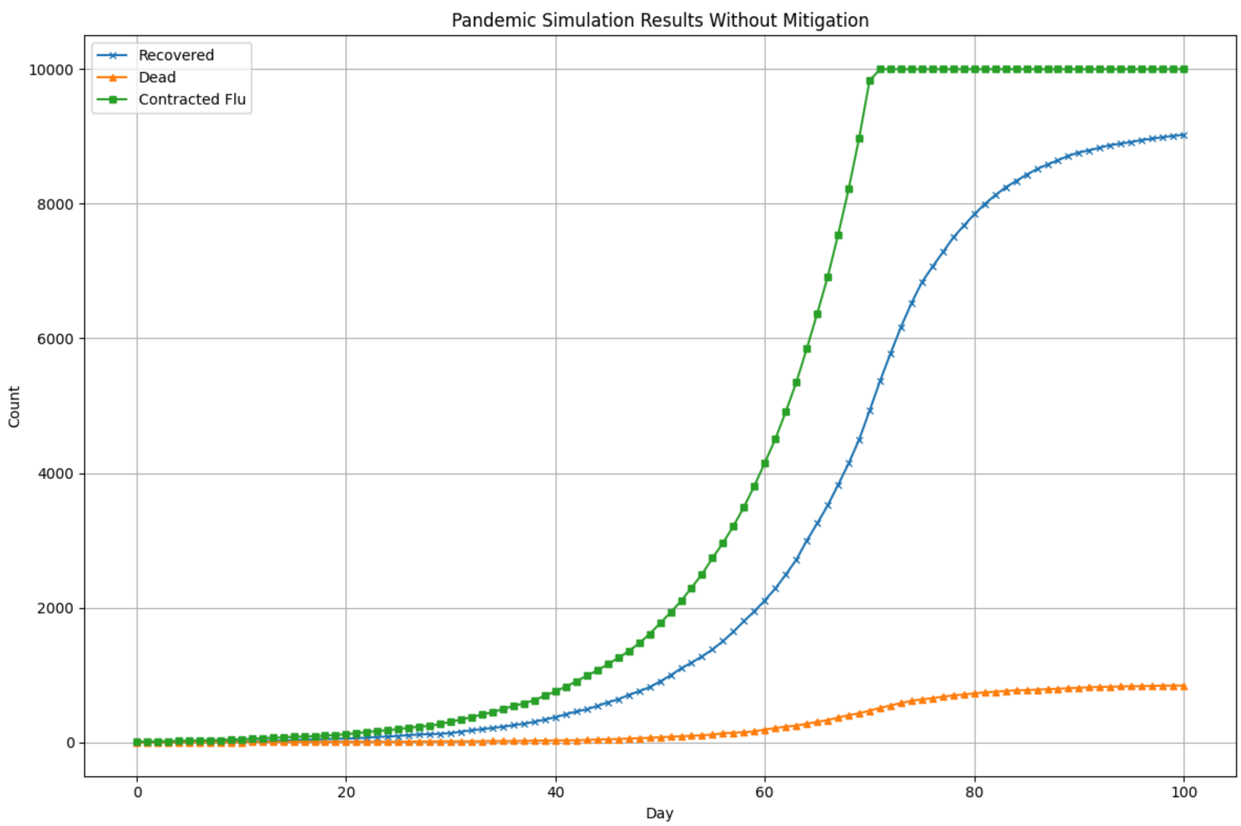
## CHAPTER 4: RESULTS

### Simulation without Mitigation

This baseline simulation explores the progression of an infectious disease over 100 days without any interventions. Starting with an initial count of 10 infectious individuals within a population of 10,000, the model tracks daily infections, recoveries, and deaths, assuming interaction ranges and probabilities of infection, recovery, and mortality.

**Key Elements:**

- Infectious interactions range from 5 to 15 per day.
- Fixed infection, recovery, and death probabilities are used to calculate daily changes.
- Results are plotted to show the progression of recovered, deceased, and total contracted cases over the simulation period.



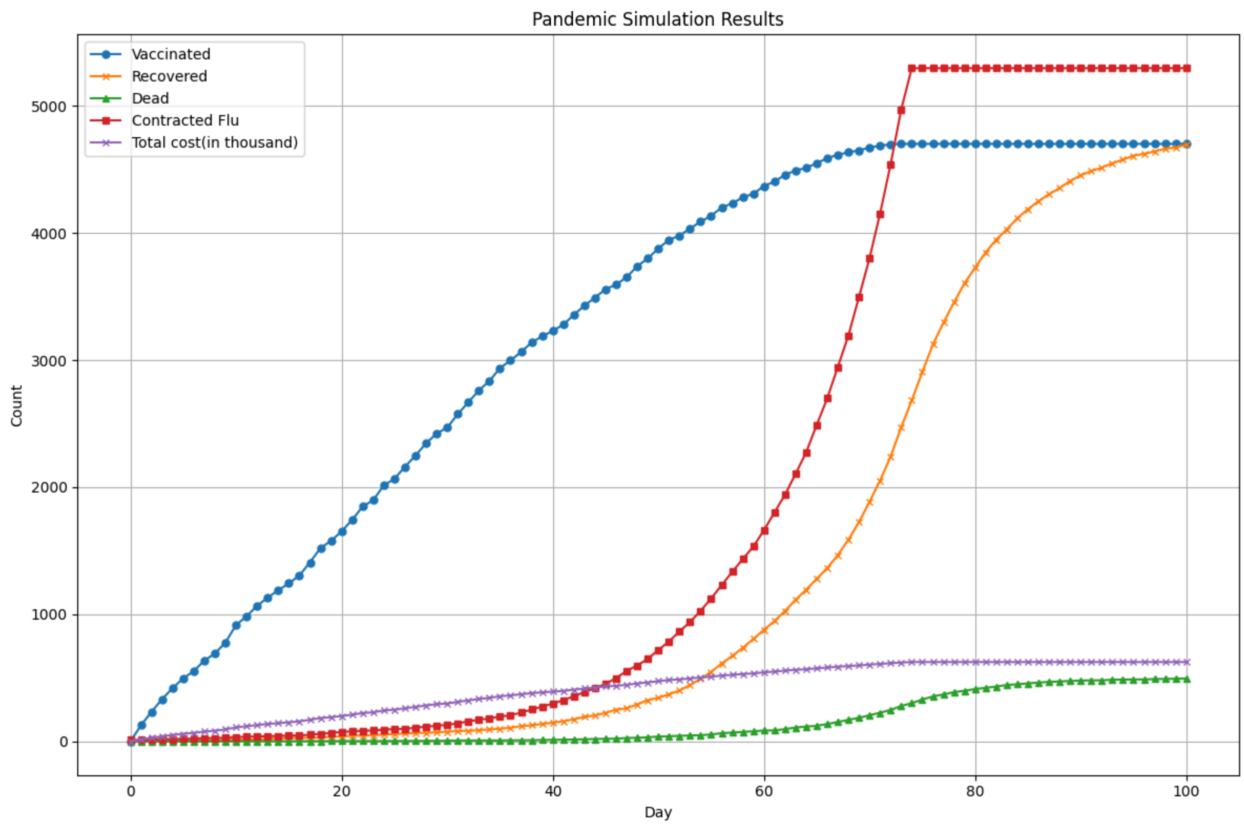

Simulation ended on day 100.
Percentage recovered: 90.24%
Percentage dead: 8.43%
Percentage contracted the flu: 100.00%

**Simulation with Vaccination but without Mask Wearing**

This scenario introduces vaccination without other mitigation measures like mask-wearing. It simulates the same population and disease dynamics but incorporates a vaccination strategy targeting 70% population coverage.

**Key Elements:**

- Daily vaccination rates are adjusted stochastically around a base rate.
- Vaccination impacts the number of susceptible individuals directly, reducing potential new infections.
- Economic factors include vaccination costs and hospitalization fees, with total costs calculated and plotted.



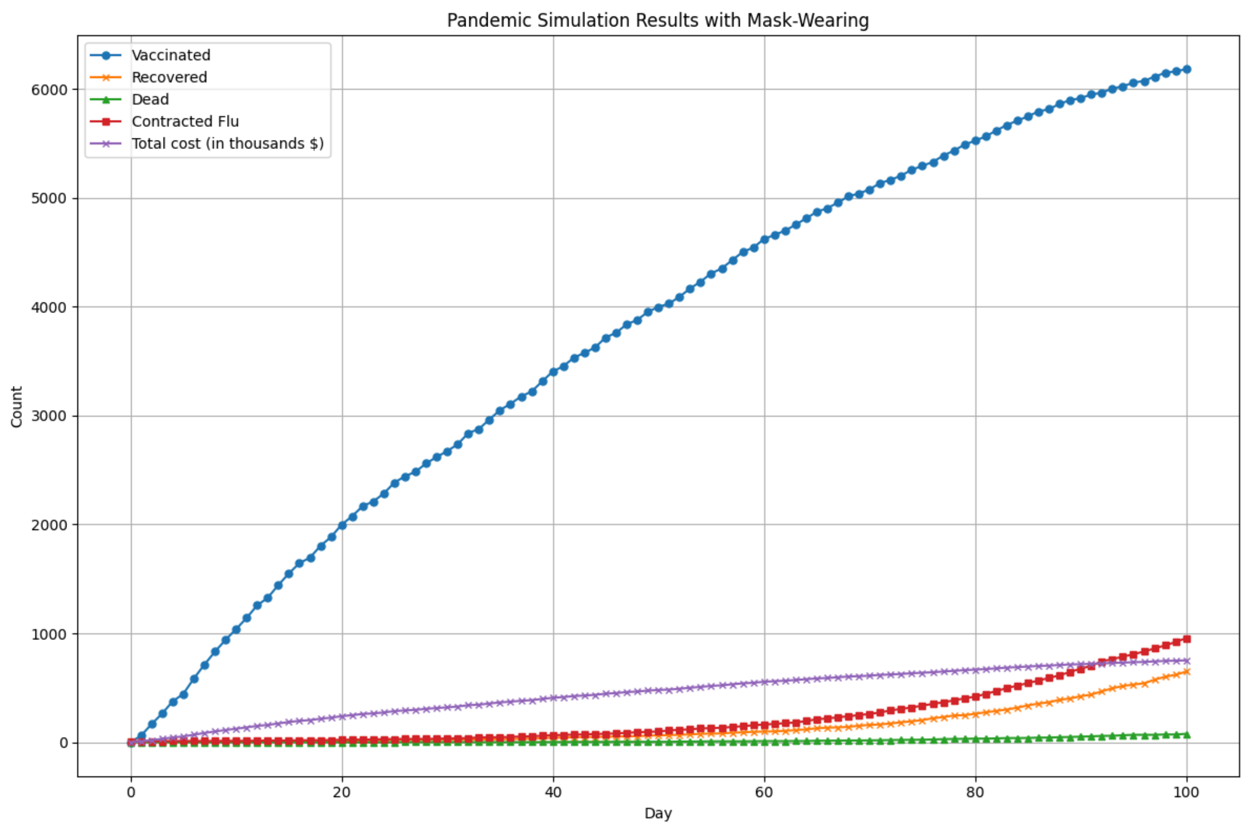

Simulation ended on day 100.
Percentage vaccinated: 47.02%
Percentage recovered: 46.96%
Percentage dead: 4.94%
Percentage contracted the flu: 52.98%
Total cost: 564240
Total cost: 59622.200000000004

**Simulation with both Vaccination and Mask Wearing**

The third scenario adds mask-wearing to the vaccination strategy. Mask efficacy and adoption rates are factored into the infection probability, reducing the chance of transmission per interaction when masks are worn.

**Key Elements:**

- Mask adoption and efficacy reduce the effective infection probability for interactions involving masked individuals.
- The combined effects of vaccination and mask-wearing are modeled to evaluate their synergistic impact on disease control.
- Economic calculations consider both vaccination and hospitalization costs, providing a comprehensive view of financial implications.




Simulation ended on day 100.
Percentage vaccinated: 61.80%
Percentage recovered: 6.49%
Percentage dead: 0.78%
Percentage contracted the flu: 9.57%
Total cost of vaccination: $741,600.00
Total cost of hospitalization: $10,677.43

## CHAPTER 5: INTERPRETATION OF RESULTS

<table>
<tr><th></th><th>Simulation without Mitigation</th><th>Simulation with Vaccination but without Mask Wearing</th><th>Simulation with Vaccination and Mask Wearing</th></tr>
<tr><td>Percentage Vaccinated</td><td>Not applicable (no vaccination strategy)</td><td>47.02%</td><td>61.80%</td></tr>
<tr><td>Percentage Recovered</td><td>90.24%</td><td>46.96%</td><td>6.49%</td></tr>
<tr><td>Percentage Dead</td><td>8.43%</td><td>4.94%</td><td>0.78%</td></tr>
<tr><td>Percentage Contracted the Flu</td><td>100.00%</td><td>52.98%</td><td>9.57%</td></tr>
<tr><td>Total Cost of Vaccination</td><td rowspan="2">Not applicable (no vaccination or other intervention costs)</td><td>$564,240</td><td>$741,600.00</td></tr>
<tr><td>Total Cost of Hospitalization</td><td>$59,622.20</td><td>$10,677.43</td></tr>
</table>

**Analysis:**

- Vaccination Impact: The simulations with vaccination (with and without mask-wearing) achieved significantly lower percentages of individuals contracting the flu compared to the simulation without mitigation. This demonstrates the effectiveness of vaccination in reducing disease transmission.
- Mask-Wearing Impact: Introducing mask-wearing in addition to vaccination further reduced the percentage of individuals contracting the flu, as well as the associated costs of hospitalization and vaccination.
- Economic Considerations: The total costs associated with vaccination and hospitalization were substantially higher in the simulation without mask-wearing compared to the simulation with both vaccination and mask-wearing. This highlights the potential cost-saving benefits of implementing multiple intervention strategies.

Overall, these comparisons emphasize the importance of multi-faceted approaches, including vaccination and non-pharmaceutical interventions like mask-wearing, in mitigating the spread of infectious diseases and minimizing associated costs.

.

## CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

### Summary of Findings

- The simulations presented in this study demonstrate the effectiveness of various pandemic response strategies in mitigating the spread of infectious diseases and reducing associated morbidity, mortality, and economic costs. Key findings include:
- Vaccination, when implemented alone, significantly reduces the percentage of individuals contracting the flu and leads to a substantial decrease in mortality rates compared to scenarios without vaccination.
- The combination of vaccination and non-pharmaceutical interventions such as mask-wearing further enhances the effectiveness of pandemic response efforts, resulting in even lower rates of disease transmission and mortality.
- Economic considerations play a crucial role in pandemic response planning, with the simulations highlighting the potential cost-saving benefits of implementing comprehensive intervention strategies.

### Limitations

Despite the insights provided by the simulations, several limitations should be acknowledged:

- The model simplifies complex real-world dynamics and may not fully capture all factors influencing disease transmission and intervention effectiveness.
- Assumptions regarding parameters such as infection probabilities, recovery rates, and intervention efficacy may not accurately reflect real-world conditions and could impact the validity of the results.
- The simulations do not account for variations in population demographics, healthcare infrastructure, or behavioral factors that could affect the outcomes of pandemic response strategies.

### Future Research

- Areas for further research and improvement in the model include:
- Incorporating more nuanced representations of population dynamics, including age-specific susceptibility and transmission rates, to better capture the heterogeneous nature of disease spread.
- Enhancing the model's ability to account for dynamic changes in intervention effectiveness over time and in response to evolving epidemiological trends.
- Conducting sensitivity analyses to assess the robustness of the model outputs to variations in key parameters and assumptions.
- Validating the model against real-world data from past pandemics or controlled experimental settings to assess its predictive accuracy and reliability.

### Implications for Policy and Practice

- Vaccination Prioritization: The simulations highlight the importance of prioritizing vaccination efforts to reduce the spread of infectious diseases. Policymakers should focus on achieving high vaccination coverage rates to effectively mitigate disease transmission within the population.
- Combining Interventions: Implementing multiple intervention strategies, such as vaccination and non-pharmaceutical interventions like mask-wearing, can lead to more effective control of

pandemics. Policymakers should consider integrating these interventions into comprehensive pandemic response plans to maximize their impact.

**Cost-Benefit Analysis**: The simulations underscore the economic implications of different pandemic response strategies. Policymakers should conduct thorough cost-benefit analyses to evaluate the financial implications of implementing various interventions and prioritize interventions that offer the greatest public health benefits while minimizing costs.

**Public Health Messaging**: Effective communication and public health messaging are crucial for promoting compliance with intervention strategies such as vaccination and mask-wearing. Policymakers should invest in clear, evidence-based communication strategies to inform the public about the importance of these interventions and address any concerns or misconceptions.

**Health Equity Considerations**: Policymakers should prioritize equitable access to vaccination and other interventions to ensure that vulnerable populations, including those with limited access to healthcare or higher risk of exposure, are adequately protected. Efforts should be made to address disparities in vaccine distribution and access to healthcare resources to promote health equity during pandemics.

Overall, the results of the simulations underscore the importance of comprehensive, evidence-based pandemic response strategies that prioritize vaccination, integrate multiple intervention approaches, consider economic implications, and address health equity considerations. Policymakers should use these insights to inform the development and implementation of effective pandemic response plans at local, national, and global levels.

**REFERENCES**

1. Chao, D. L., Halloran, M. E., Obenchain, V., & Longini, I. M. (2010). FLUTE, a publicly available stochastic influenza epidemic simulation model. *PLOS Computational Biology*, *6*(1), e1000656. https://doi.org/10.1371/journal.pcbi.1000656

2. Ekici, A., Keskinocak, P., & Swann, J. (2014). Modeling influenza pandemic and planning food distribution. *Manufacturing & Service Operations Management*, *16*(1), 11–27. https://doi.org/10.1287/msom.2013.0460

3. Cooper, I., Mondal, A., & Antonopoulos, C. G. (2020). A SIR model assumption for the spread of COVID-19 in different communities. *Chaos, Solitons & Fractals*, *139*, 110057. https://doi.org/10.1016/j.chaos.2020.110057

4. A mathematical model of COVID-19 transmission
Jayatilaka et al.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8642156/

5. Ferguson, N. M., Cummings, D. A. T., Fraser, C., Cajka, J. C., Cooley, P. C., & Burke, D. S. (2006). Strategies for mitigating an influenza pandemic. Nature, 442(7101), 448-452.
https://doi.org/10.1038/nature04795

6. Chung, N. N., & Chew, L. Y. (2021). Modelling Singapore COVID-19 pandemic with a SEIR multiplex network model. Scientific Reports, 11, 10122.
https://doi.org/10.1038/s41598-021-89515-7