The Potential Impact of Pharmaceutical and Non-Pharmaceutical Interventions to Mitigate the COVID-19 Crisis in the United States: A Model-Based Analysis

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April 21, 2020

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Introduction

The COVID-19 pandemic originated in Wuhan, China in December 2019 and quickly spread across the globe. On March 11, 2020 the World Health Organization (WHO) officially declared COVID-19 a pandemic and by April 21, 2020, there were more than 2.5 million confirmed cases and over 175,000 deaths globally.

In the United States (US), the situation evolved swiftly after the first case was confirmed on January 19, 2020. Limited testing posed disease surveillance challenges, and the spread of the disease gave rise to exponential growth in the number of cases, followed shortly thereafter by a rise in deaths. A major outbreak in the New York metropolitan area soon led to the US becoming the worldwide epicenter of the pandemic. As the strategy shifted from containment to mitigation, social distancing policies were adopted and the majority of US states issued stay-at-home orders. Fearing significant hospital stress and overload in areas with surging cases, efforts were made to increase healthcare system capacity to manage the crisis. As of April 21, 2020, over 820,000 confirmed cases and over 44,000 deaths have been reported in the US.

As state and federal policymakers monitor, prepare for, and respond to the COVID-19 pandemic, they have relied on statistical models to help predict the pandemic's course and to understand how various strategies and interventions may affect health outcomes. To aid these efforts, we developed an infectious disease model and conducted a series of scenario analyses. The model is intended to help inform and educate policymakers—and the wider public—about the broad potential outcomes of mitigation strategies and future interventions. It is not intended to be predictive, as the actual outcomes of the pandemic will depend on the specific actions undertaken. Specific objectives include estimating the potential impact of the level of disease transmission, increasing health system capacity, timing of social distancing, level of social distancing, easing of social distancing, and a hypothetical drug intervention.

Methods

We developed a COVID-19 susceptible-exposed-infected-recovered (SEIR) model, with additional compartments for treatment and death, from a US perspective. In the model, people transition between the compartments over time as the disease spreads through the population. Disease transmission is represented in the model by the basic reproduction number (R_0). R_0 is influenced by characteristics of the virus and human behavior. An R_0 value of less than 1 leads to the disease eventually extinguishing, while a value greater than 1 has the potential to spread exponentially and generate an epidemic or pandemic.

The model estimates the number of people in each compartment (susceptible, exposed, infected, treated, recovered, and dead) daily over a 1-year period (January 1, 2020–December 31, 2020). The total number of emergency department (ED), hospital, and intensive care unit (ICU) visits and their associated costs were also calculated. Model inputs were obtained through a literature review of recent published studies and other publicly available sources. Values for the contact and infection rates were estimated by calibrating the model to observed US death rates up to April 14, 2020. The model was used to conduct various scenario analyses, including reducing contacts to assess the effect of social distancing, increasing healthcare capacity, and reducing hospital length of stay (LOS) and mortality to assess the effect of potential pharmaceutical interventions.

Model Scenarios and Findings

Impact of level of disease transmission: Analyses were conducted to examine the potential impact of the level of disease transmission by varying R_0, while assuming that social distancing reduces contact by 75% through the remainder of the year. Under these circumstances, we estimate the peak health system capacity will not be exceeded. The estimated number of total infections ranged from 14.1 million (R_0 = 2.2) to 57.4 million (R_0 = 4.2), while the number of deaths ranged from 93,000 (R_0 = 2.2) to 376,000 (R_0 = 4.2). Total healthcare costs ranged from $13 billion ($R_0$ = 2.2) to $53 billion ($R_0$ = 4.2). The base-case estimate (R_0 = 3.2) results in 21.4 million infections, 141,000 deaths, and nearly $20 billion in total costs.

Impact of health system capacity change: To examine the potential impact of changes in health system capacity, we devised 2 scenarios, where health system capacity is exceeded due to lower compliance with social distancing policies, and evaluated the impact of a small increase (+25%) and a large increase (+50%) in healthcare system capacity. In the tested scenarios, increasing healthcare system capacity reduced deaths by 5% to 16%. Increasing healthcare system capacity was sufficient to manage the scenario with minimal overcapacity (when increased by 50%) but was not sufficient to manage a scenario with substantial overcapacity. Avoidance of substantial healthcare system overcapacity through effective use of social distancing would be advisable.

Impact of timing of social distancing: We examined the potential impact of implementing social distancing 1 week earlier and 2 weeks earlier, assuming R_0 = 3.2 and a 75% reduction in contact due to social distancing. Initiating social distancing 1 week earlier led to a 68% decrease in infections and deaths compared to the base case, with an estimated 6.9 million infections and 45,000 deaths. If social distancing was started 2 weeks earlier, a 90% decrease in infections and deaths would be achieved, with 2.1 million infections and 14,000 deaths.

Impact of level of social distancing: We looked at the potential impact of the level or degree of social distancing from April 15, 2020 onward. This encompasses such factors as the types of public policies in place and the level of compliance by the public. The scenarios include low, moderate, and high levels of social distancing (60%, 75%, and 90% reduction in contact, respectively) and assume that the level of social distancing is maintained through the end of 2020. In the low scenario, the healthcare system capacity is exceeded in terms of hospital beds, ICU beds, and ventilators, while capacity is not exceeded in the other scenarios. The number of deaths varied substantially, with 1.05 million deaths for the low social distancing scenario, 141,000 deaths for the moderate scenario, and 77,000 deaths for the high scenario. Estimated healthcare costs varied significantly as well.

Impact of easing social distancing: We examined scenarios to ease social distancing policies in order to “reopen” the US economy. In all scenarios, we assumed that easing of social distancing resulted in a change from a 75% reduction in contact to a 50% reduction in contact. First, we considered uniform easing of social distancing beginning on June 1 with R_0 = 3.2 (base case) and R_0 = 2.2. When R_0 = 3.2, a resurgence of cases could occur in the early fall, resulting in a total of 203.6 million infections and 1.7 million deaths. On the other hand, if R_0 = 2.2, uniform easing of social distancing would result in a slow but steady increase in infections, without a significant resurgence, resulting in a total of 24.6 million infections and 153,000 deaths. Second, we considered intermittent easing of social distancing, alternating between 2 months of easing (beginning on June 1) followed by 1 month of reimplementation of social distancing and alternating thereafter. In contrast to uniform easing, intermittent easing when R_0 = 3.2 would significantly reduce the extent of resurgence, resulting in 127.8 million infections and 938,000 deaths. And, when R_0 = 2.2, intermittent easing would result in a step-down and virtual elimination of cases over the course of the year, resulting in 17.3 million infections and 113,000 deaths.

Impact of a hypothetical drug intervention: A final set of scenarios were created to assess the potential impact of a hypothetical drug treatment. These scenarios use base-case assumptions (R_0 = 3.2 and 75% social distancing) in which the health system is not at overcapacity. These scenarios assume the new treatment becomes available on July 1, 2020 and that it reduces hospital LOS and mortality to varying degrees. Using these assumptions, the model estimated the hypothetical treatment would potentially save 5,000 to 15,000 lives over the remainder of the year. An effective drug intervention with a substantial reduction in mortality has the potential to change the risk/benefit calculus and may aid efforts to ease social distancing.

Limitations

These analyses are not intended as predictions but as examples of what could happen over the course of the pandemic based on potential state and federal policies adopted and actions taken. The analysis utilizes a basic SEIR model to deterministically model disease transmission at a US population level and is based on limited available data for some key model parameters (eg, R_0, infection fatality rate, extent of social distancing).

Conclusion

This analysis was intended to inform policymakers on the potential impact of various pharmaceutical and non-pharmaceutical interventions to mitigate the COVID-19 crisis in the US. Social distancing is the primary intervention available to mitigate the pandemic, and outcomes are significantly affected by both its timing and extent. In areas where social distancing efforts fail, planning and preparations to increase health system capacity will save lives but may not be sufficient to manage surge conditions. Careful consideration should be given to when and how to ease social distancing given the potential exponential growth of COVID-19. Large-scale testing and disease surveillance to monitor conditions will be essential to successful easing of social distancing and to determine when strengthening social distancing policies may prove necessary. Effective utilization of these policy tools, and others, will help policymakers to navigate the pandemic and help to minimize the adverse health impacts and economic burden until more effective treatments, and ultimately a vaccine, become available.

KEY LEARNINGS FOR POLICYMAKERS

- The impact of an unmitigated COVID-19 pandemic would be dire, with a substantial number of deaths and a vastly overwhelmed healthcare system.
- Social distancing is the single most effective intervention we currently have to mitigate the COVID-19 pandemic (until the availability of a highly efficacious treatment or vaccine).
    - The timing of social distancing is critical: Due to the potential of COVID-19 cases to grow exponentially, early intervention makes a substantial difference in the number of infections and lives lost.
    - The level of social distancing is critical: Maintaining an effective R of <1 is the dividing line between avoiding and incurring a pandemic.
- Increasing health system capacity to manage surge conditions is an effective life-saving intervention.
    - Anticipating and predicting the timing and extent of a surge (eg, via testing and modeling) are critical to effective mobilization of resources.
    - However, no amount of capacity increase will be sufficient to handle a large surge; therefore, the preferred strategy is to utilize social distancing to avoid a surge.
- Easing of social distancing involves a tactically and strategically complex cost-benefit balancing act.
    - Testing and surveillance will be crucial to monitor the effectiveness of social distancing policies and whether easing is warranted based on risks and benefits.
    - Large-scale testing followed by contact tracing and isolation may allow for easing of broader and blunter social distancing policies.
    - Public education is needed to avoid the “pandemic response paradox,” where policies leading to effective mitigation result in the call for removal of those policies as “not necessary.”
- Pharmaceutical interventions currently under investigation may eventually reduce health system burden and patient mortality.
    - Significant reductions in mortality would have the potential to change the cost-benefit landscape.
    - Development of an effective vaccine would essentially eliminate the need for social distancing and help to end the pandemic.

INTRODUCTION

Background

Overview of COVID-19

COVID-19 is a disease caused by the novel SARS-CoV-2 coronavirus, a family of viruses that include forms of the common cold and more severe respiratory conditions such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). While most COVID-19 cases are mild and may even present as asymptomatic, a minority of patients, predominantly the elderly and immunocompromised, experience serious respiratory symptoms and require hospitalization. In more severe cases, patients develop acute respiratory distress syndrome (ARDS) and require intensive care unit (ICU) support and mechanical ventilation.[1]

The SARS-CoV-2 virus was first identified following an outbreak of pneumonia cases of unknown origin that occurred in Wuhan, Hubei, China in December 2019.[2] Since then, the disease has rapidly spread across the globe to over 200 countries.[3] The World Health Organization (WHO) officially declared COVID-19 a pandemic on March 11, 2020.[4] As of April 21, 2020, there were over 2.5 million confirmed cases of COVID-19 and over 175,000 associated deaths globally.

COVID-19 in the United States (US)

The first confirmed US case was on January 19, 2020 in Washington state a few days after an infected individual returned from travel to Wuhan, China.[5] Shortly thereafter, the White House issued a travel suspension on foreign nationals from China that took effect on February 2.[6] The first community-acquired case occurred on February 28 in California, followed by the first US death in Washington state on February 29. It soon became evident that efforts to contain the disease were failing, and the US declared a national emergency on March 13.[7] Inadequate access to diagnostic testing and asymptomatic transmission challenged early disease surveillance efforts, limited opportunities for contact tracing and case isolation, and ultimately led to further spread of COVID-19 in the US.

On March 16, the White House issued social distancing guidelines, and several states quickly followed with stay-at-home orders to limit the spread of COVID-19.[8] By April 7, a total of 42 states plus the District of Columbia had enacted stay-at-home orders.[9] These strategies were intended to "flatten the curve" (ie, reduce the size of the peak in COVID-19 cases) by minimizing contacts and transmission of the disease to reduce health system burden. Despite these efforts, the US became the worldwide epicenter of the pandemic, with over 820,000 confirmed cases and over 44,000 deaths as of April 21, 2020. The New York metro area and others with surge conditions faced shortages of hospital beds, ICU beds, ventilators, medical staff, and personal protective equipment (PPE).

Forecasting the Pandemic

As healthcare resources became scarcer, and cases and deaths per day increased exponentially, efforts to model the potential impact of the pandemic grew. Epidemiological models can help inform policymakers of potential outcomes of diseases to better plan mitigation strategies and manage resources. Projections from an infectious disease model developed by the Imperial College London were released on March 16, 2020 and were effective in encouraging broader implementation of social distancing across the globe.[10] Another infectious disease model developed by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington has been widely utilized by US state and federal officials to inform policymaking related to resource allocation and implementation of social distancing measures during the pandemic.[11] As the pandemic progresses, it is imperative to continue to refine current COVID-19 models and develop new ones to ensure the US response to the crisis is in alignment with the best available projections.

Objective

To examine the potential impact of various public health policy options and mitigation strategies on the COVID-19 pandemic in the US, we developed an infectious disease model and conducted a series of scenario analyses. The model is intended to help inform and educate the public and policymakers about the potential outcomes of mitigation strategies and future interventions. It is not intended to be predictive, as the actual outcomes of the pandemic will depend to a large extent upon the specific actions taken.

The model examines the potential impact of both non-pharmaceutical and pharmaceutical interventions. Specific objectives include estimating the outcomes for the following scenarios:

- Unmitigated pandemic (for comparison)
- Impact of R_0 (level of disease transmission)
- Impact of increasing health system capacity
- Impact of timing of social distancing
- Impact of level of social distancing
- Impact of easing social distancing
- Impact of a hypothetical drug intervention

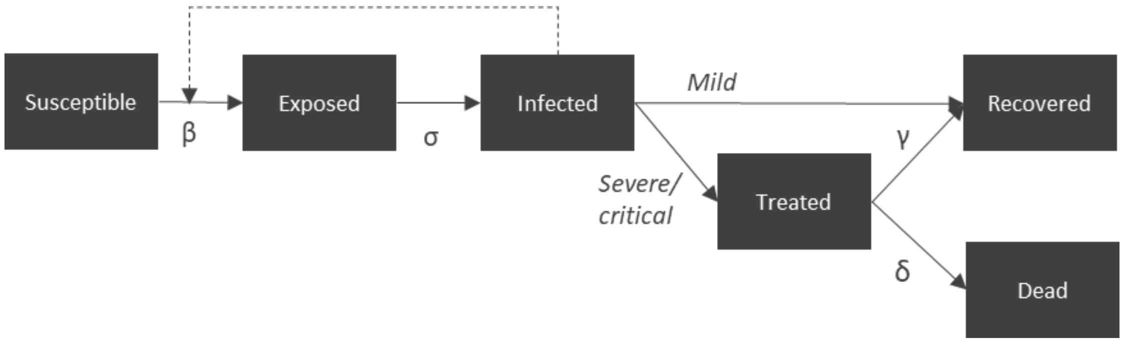
METHODS

Model Design

We modeled the COVID-19 pandemic in the US using a susceptible-exposed-infected-recovered (SEIR) model.[12] SEIR models utilize compartments that people transition between over time to model the transmission of a disease through a population (eg, people start in the susceptible compartment, may move to the exposed compartment, then to the infected compartment, and finally to the recovered compartment). The exposed compartment represents the latent period from when the disease has been transmitted to the time that a person becomes infectious. SEIR models are operationalized through a series of differential equations governed by a set of parameters to reflect the dynamics of disease transmission and recovery.

There are variations on the SEIR model, and for the purposes of this analysis, we supplemented a basic SEIR model with additional compartments for treated and dead to better model the treatment and recovery process for the novel coronavirus. The treated group was divided into two separate compartments for hospitalization and ICU. In the model, infected patients with mild disease were assumed to recover, while patients with severe disease are treated in the hospital, and critical patients are treated in the ICU. Hospitalized patients either recover or die. Our model, therefore, represents a susceptible-exposed-infected-treated-recovered-dead (SEITRD) model as shown in Figure 1. The model equations are shown in Appendix B (Figure B1).

Figure 1. Model Structure



Beta (β) represents the infection parameter, which is characterized by the infection rate per infected person per day. Sigma (σ) represents the latency parameter, the rate per day at which exposed people become infectious. Gamma (γ) represents the recovery parameter, the rate per day at which the infected recover. Finally, delta (δ) represents the mortality parameter, the proportion of those infected who die. The dotted line signifies that the infected transmit the disease to the susceptible. The interaction between the susceptible and infected population makes disease transmission models highly dynamic and very sensitive to changes in certain parameters such as the contact rates. The model was designed to incorporate the potential effect of health system overcapacity on mortality. When the number of patients requiring a resource (ie, hospital bed, ICU bed, ventilator) exceeds the capacity of the healthcare system, an additional relative risk is applied to the mortality rate for hospitalized patients and is scaled to the extent of overcapacity, resulting in an increase in the effective infection fatality rate (IFR).

The model was constructed to allow assessment of the potential impact of various interventions on the course of the pandemic and outcomes. Interventions include both non-pharmaceutical interventions to mitigate the spread and pharmaceutical interventions (drugs to treat the disease). We considered 2 non-pharmaceutical interventions: (1) reducing contacts (ie, social distancing) to reduce the effective R and (2) increasing health system capacity (number of hospital beds, number of ICU beds, and number of ventilators) to reduce the impact of health system overcapacity on mortality. We also assessed the potential impact of a hypothetical pharmaceutical intervention that would improve the recovery rate among hospitalized patients and thereby reduce hospital length of stay (LOS) and mortality. Appendix B (Figure B2) outlines how these interventions act on the model structure.

Model Inputs

Model inputs were obtained through a literature review to identify plausible values based on the data available at the time of the analysis. Population parameters were based on the US Census, and the model was seeded with an assumed single US case on January 1, 2020, two weeks prior to the first known case on January 15. Parameters for disease infection dynamics were based on values for the latent and infectious period from the literature. Values for the contact and infection rates were estimated by calibrating the model to observed US death rates (see "Model Calibration" for additional information). The distribution of infected patients by disease severity was estimated based on observed data and recent published studies. Values for baseline mortality parameters were obtained from published studies and calibrated to yield an overall IFR consistent with values from the literature. The impact of mortality due to health system overcapacity was estimated based on data from a published literature review and on observed data for New York (overcapacity) compared to other regions in the US (not overcapacity). Healthcare system capacity was based on estimates from publicly available sources. Healthcare utilization parameters (eg, occupancy, ventilator utilization, and length of stay) were obtained from published studies and publicly available sources. Finally, cost estimates were obtained from publicly available sources.

Appendix A (Table A1) provides a full list of the model parameters, values, sources, and other relevant information.

Basic Reproduction Number: R_0

The basic reproduction number (R_0) is a measure of the dynamics of disease transmission. The R_0 represents the number of people that each infected person will, on average, infect. The R_0 determines whether an epidemic will occur within a population. If the R_0 is <1, the disease will extinguish, while if it is >1, it has the potential to spread exponentially and generate an epidemic. The R_0 is a function of the infection rate multiplied by the contact rate multiplied by the duration of infectiousness.[13] The R_0 is influenced by characteristics of the virus and human behavior.[14]

Reducing contacts through "social distancing" provides a means to avoid or mitigate an epidemic. Reducing contacts changes the basic reproduction number to an effective reproduction number (R). To avoid an epidemic, R must be reduced below 1, which means that the percentage reduction in contacts required is $1 - 1/R_0$. Note that this also represents the proportion of the population that must be vaccinated (or recovered) to achieve herd immunity.

Model Outputs

The model estimates the number of people in each compartment (susceptible, exposed, infected, hospital, ICU, recovered, and dead) daily over a 1-year (365-day) period from January 1, 2020 to December 31, 2020. From these data, we obtain the estimated peak day for infections and hospitalizations. The maximum utilization of healthcare resources (ie, hospitals beds, ICU beds, and ventilators) is calculated as the number needed divided by the capacity and expressed as a percentage. The cumulative number and percentage of susceptible, infected, recovered, and dead were estimated at the end of the year, with the number recovered and dead expressed as a percentage of those infected.[a] Finally, the model calculates the number of emergency department (ED), hospital, and ICU visits as well as ED, hospital, ICU, and total costs.

[a] Note that to attempt to better reflect the number of actual cases (including asymptomatic and undiagnosed cases), we are utilizing an infection fatality rate rather than a case fatality rate, the difference being that the former is the fatality rate among all infected persons, whereas the latter is the fatality rate among confirmed cases.

Model Calibration

Given the availability of data regarding the course of the pandemic to date, we calibrated the model to the time series data for COVID-19 deaths in the US from the Johns Hopkins University Coronavirus Resource Center.[15] The baseline input for the contact rate (which influences the R_0) was calibrated to yield modeled deaths approximating the observed deaths through April 14, 2020. The observed deaths provide the most reliable metric for purposes of model calibration, as the deaths due to COVID-19 better represent the true number of fatalities than the confirmed cases represent the true number infected. While both are likely an undercount, as even some COVID-19-related deaths may not be properly counted (eg, due to a failure to test, false negative test, or classification of a COVID-19 death due to other cause), the number of confirmed cases is a greater undercount of the infected population due to limited testing and the presence of a significant number of mild and asymptomatic cases that go undetected.[16] This approach is similar to that utilized by IHME in the development of their COVID-19 analysis.[11] Appendix B (Figure B4 and Figure B5) shows the modeled and observed deaths and cases, respectively, through April 14, 2020. The model estimates that approximately 1 out of 15 infected patients has been diagnosed, which is consistent with the high 20% test positivity rate in the US that is indicative of a substantial undiagnosed population.[17]

MODEL SCENARIOS AND FINDINGS

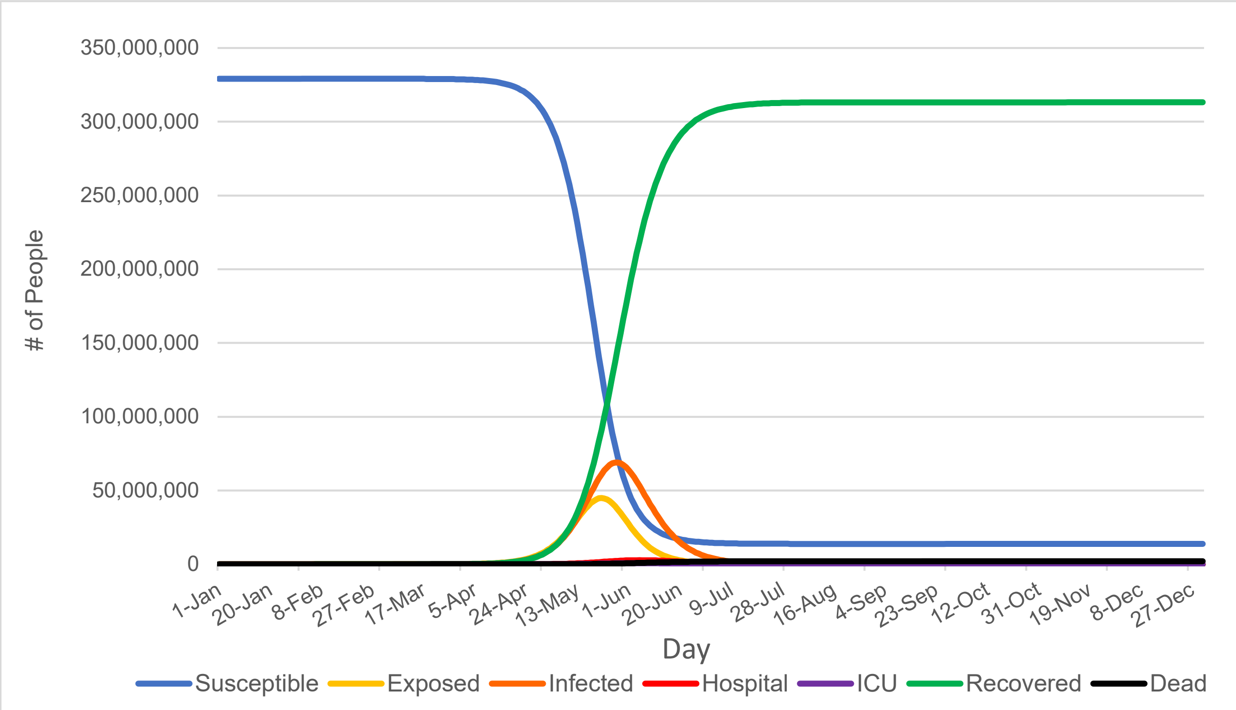
Unmitigated Scenarios

Analyses were conducted to estimate the potential impact of an unmitigated pandemic with scenarios for low R_0, moderate R_0, and high R_0, along with a scenario for a moderate R_0 with inclusion of the impact of increased mortality due to health system overcapacity (Appendix A, Table A2). Note that these analyses are not calibrated to the actual data to date and represent a theoretical maximum impact of the pandemic, as they all assume that no actions are undertaken to mitigate or reduce the spread of disease. Accordingly, these results should not be interpreted as predictions of the COVID-19 pandemic but are provided instead to understand the potential dynamics of the pandemic for purposes of comparison.

Lower R_0 results in a later peak, lower peak utilization, fewer infections and deaths, and lower costs, while higher R_0 results in earlier peak, higher peak utilization, more infections and deaths, and higher costs. In an unmitigated pandemic, the model estimates 1.83 million deaths when $R_0 = 2.2$ (Appendix B, Figure B5), 2.07 million deaths when $R_0 = 3.2$ (Figure 2), and 2.13 million deaths when $R_0 = 4.2$ (Appendix B, Figure B6). None of these estimates includes the potential impact of health system overcapacity. When we add in the effect of health system overcapacity, with an $R_0 = 3.2$, mortality increases to an estimated 2.89 million deaths, representing a 40% increase in mortality, demonstrating the potentially significant impact of health system overcapacity on mortality.

These scenarios represent a theoretical “worst case” scenario such that if the virus were allowed to spread unchecked and no one changed their behavior at all, the consequences would be very severe. Most of the population would be infected, and the healthcare system would be overloaded at levels ranging from 600% to 2,700%. Healthcare costs would be substantial, ranging from $250 to $300 billion.

Figure 2. Unmitigated Pandemic (R_0 = 3.2)



Impact of R0 (Level of Disease Transmission)

Analyses were conducted to examine the potential impact of varying R_0 from April 15 onward using the model calibrated to US deaths through April 14. These scenarios also include the impact of social distancing measures adopted in mid-March through early April. The extent of social distancing (Appendix B, Figure B7) was estimated based on the timing of state stay-at-home orders and the proportion of the US population represented by those states, assuming that states with stay-at-home orders reduced contact by 75% while states without stay-at-home orders only reduced contact by 25%. It was also assumed that prior to the introduction of stay-at-home orders issued by states that social distancing began to take effect on March 16, when social distancing guidelines were issued by the federal government. Finally, these scenarios all assume that social distancing remains in effect at a 75% reduction in contact through the remainder of the calendar year.

The R_0 in the US was estimated in the calibrated model based on observed data from January 1, 2020 through April 14, 2020 to be approximately 4.2. Note that this value is higher than other estimated R_0 values for the coronavirus. However, this is because the US pandemic to date is largely composed of data from New York, the largest and fastest growing outbreak in the world. New York is a likely outlier, due to its high population density and levels of local and international travel; therefore, we assumed from April 15 onward as the pandemic spreads through the rest of the US a lower R_0 of 3.2 for our base-case analysis, along with a variety of scenarios for alternative lower and higher values (Appendix A, Table A3). The R_0 may also change due to seasonal effects on virus transmission.[18]

In all tested scenarios, so long as social distancing with a 75% contact reduction is maintained throughout the remainder of the year, we estimate the peak health system capacity will not be exceeded. The peak number of infections and hospitalizations will occur in April, except for a high R_0 of 4.2, in which case they peak in May. The estimated number of deaths ranges from a low of 93,000 (R_0 = 2.2) to a high of 376,000 (R_0 = 4.2). The number of infections ranges from 14.1

million (R_0 = 2.2) to 57.4 million (R_0 = 4.2). Finally, total healthcare costs range from $13 billion ($R_0$ = 2.2) to $53 billion ($R_0$ = 4.2). The base-case estimate (R_0 = 3.2) results in 21.4 million infections and 141,000 deaths. Figure 3 shows the forecast outcomes for the base-case scenario (R_0 = 3.2) with social distancing of 75% maintained through the rest of the year. Figure 4 shows the outcomes for the base-case scenario with the susceptible and recovered groups removed for clarity.

Figure 3. Base-Case Scenario (All Outcomes)

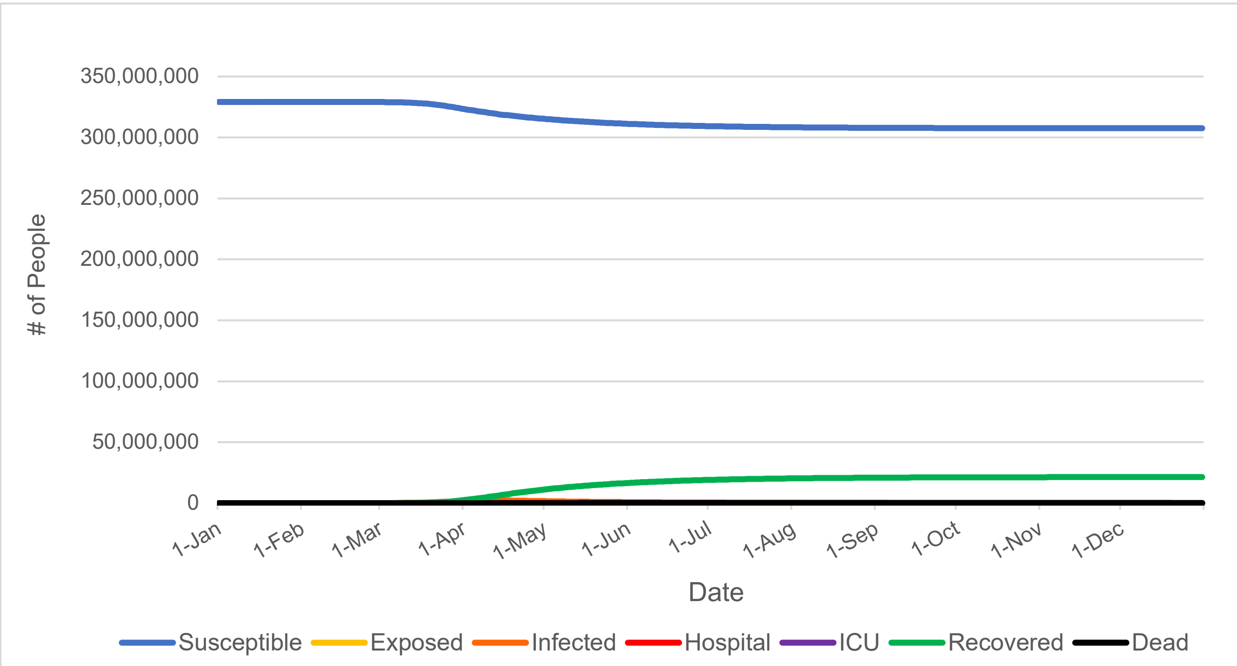
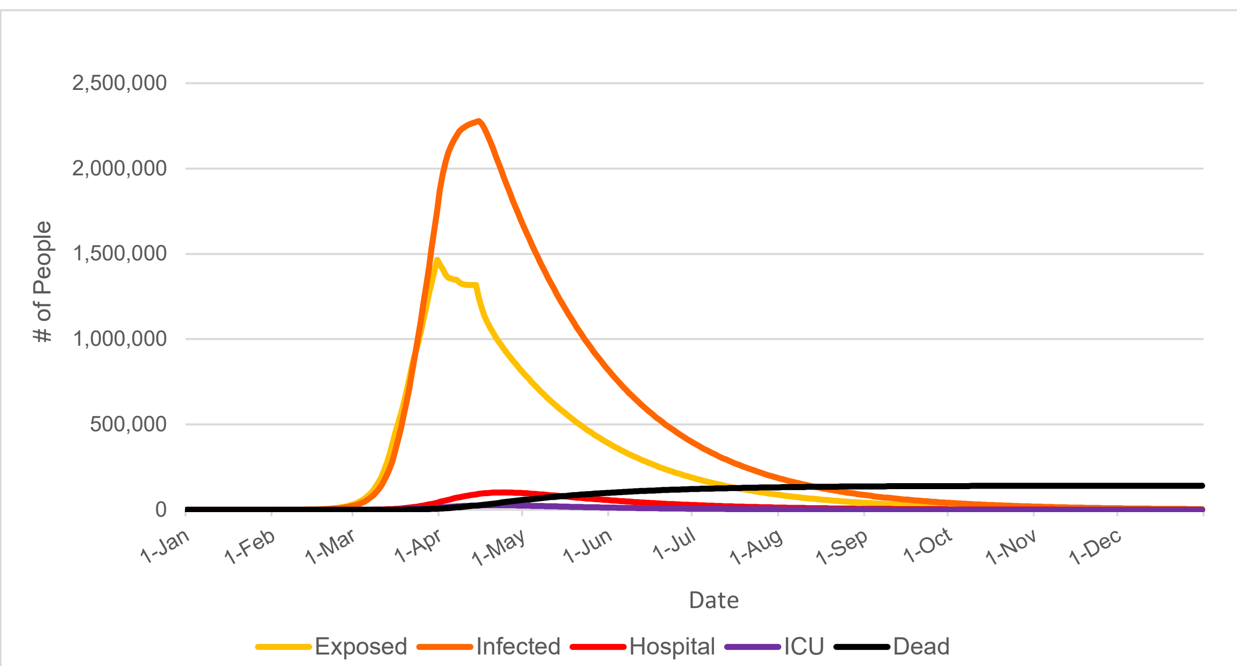


Figure 4. Base-Case Scenario (Susceptible and Recovered Groups Removed)



Impact of Health System Capacity Change

To examine the potential impact of changes in health system capacity, we devised 2 scenarios where health system capacity is exceeded, because if social distancing is maintained at a 75% reduction (base case) or greater, the healthcare system is not expected to be at overcapacity. The first scenario involves very low compliance of social distancing with a 50% contact reduction. The second scenario is low compliance of social distancing with 60% contact reduction. In each of these scenarios, we evaluated the impact of changes in healthcare system capacity by assessing the effect of a small increase in capacity (+25%) and a larger increase in capacity (+50%) (Appendix A, Table A5).

Figure 5 and Figure 6 show the potential impact of increasing health system capacity. In each scenario for the base case (+0% increase), the healthcare system is substantially overcapacity. In the base case, ICU beds and ventilator capacity are more overutilized than hospital beds. Increasing overall health system capacity by 25% or 50% is not enough to accommodate all patient needs in the 50% social distancing scenario. In the 60% social distancing scenario, increasing capacity by 50% is sufficient to meet patient treatment needs. This demonstrates that increasing capacity can potentially help to ameliorate moderate levels of overcapacity but likely not high levels of overcapacity. The model incorporates the potential impact of health system overcapacity on mortality, and in these scenarios, by increasing health system capacity, the potential reduction in deaths is estimated to be 5% to 16%.

Figure 5. Impact of Increasing Health System Capacity (With 50% Social Distancing)

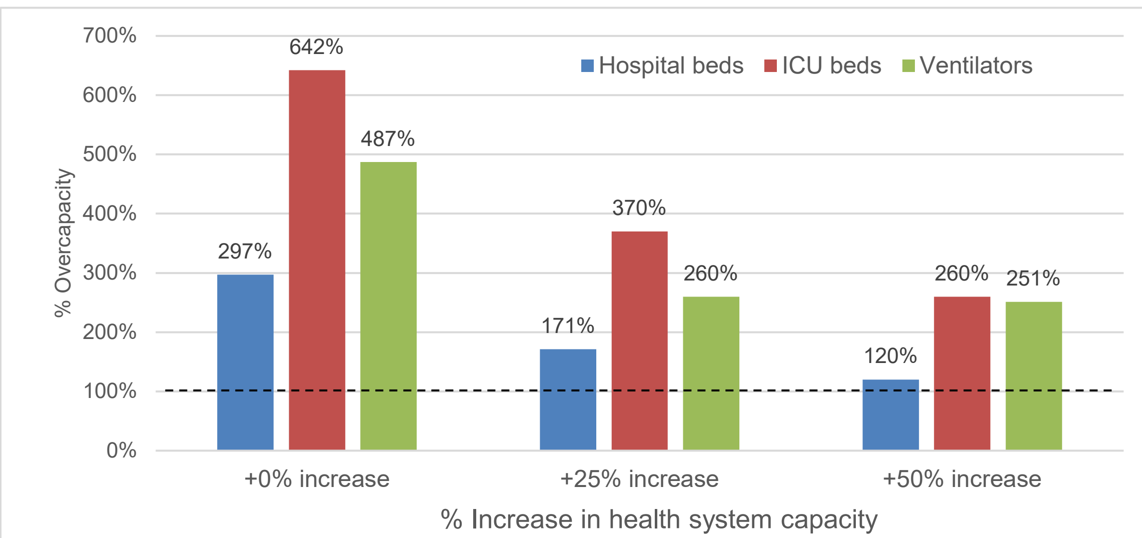
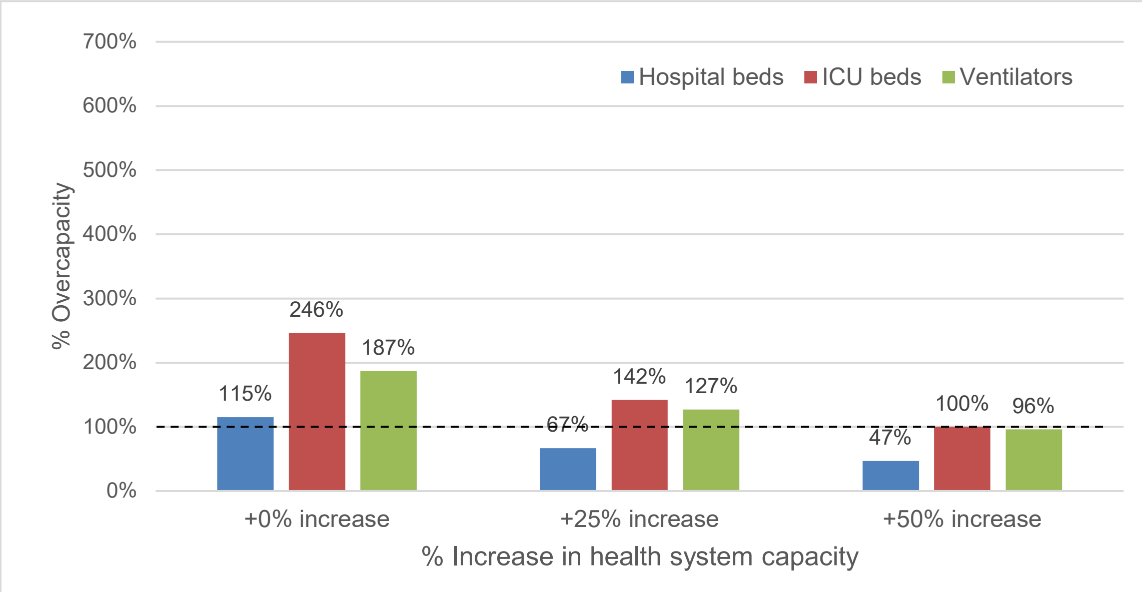


Figure 6. Impact of Increasing Health System Capacity (With 60% Social Distancing)

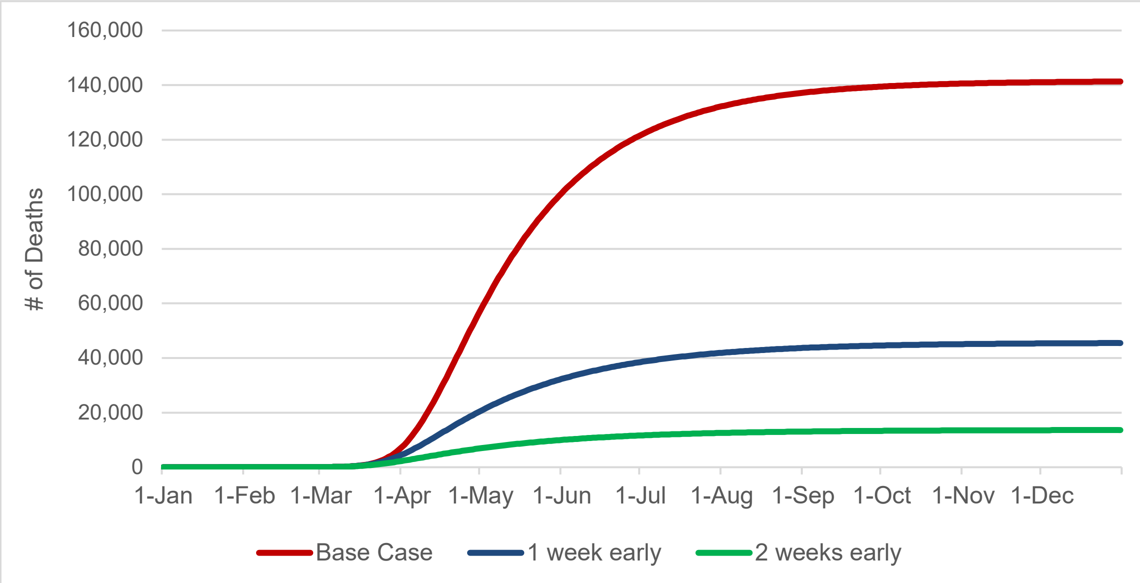


Impact of Timing of Social Distancing

We also conducted analyses to examine the potential impact of earlier implementation of social distancing (Appendix A, Table A5). The scenarios include implementing social distancing policies 1 week earlier (beginning on March 9) or 2 weeks earlier (beginning on March 2). Note that all scenarios assume an R_0 of 3.2 and the same 75% reduction in contact that persists through the remainder of the year.

Our base-case scenario, which includes social distancing beginning to increase on March 16, results in 21.5 million infections and 141,000 deaths. By starting social distancing 1 week earlier on March 9, the model estimates that there would be 6.9 million infections and 45,000 deaths, a 68% decrease in infections and deaths. If social distancing were started 2 weeks earlier (on March 2), the model estimates that there would be 2.1 million infections and 14,000 deaths, a 90% decrease in infections and deaths. Figure 7 shows the estimated deaths over time by timing of social distancing. Estimated healthcare costs are also reduced substantially, from $20 billion in the base case to $6 billion if initiated 1 week earlier to $2 billion if initiated 2 weeks earlier.

Figure 7. Estimated Deaths Over Time by Timing of Social Distancing

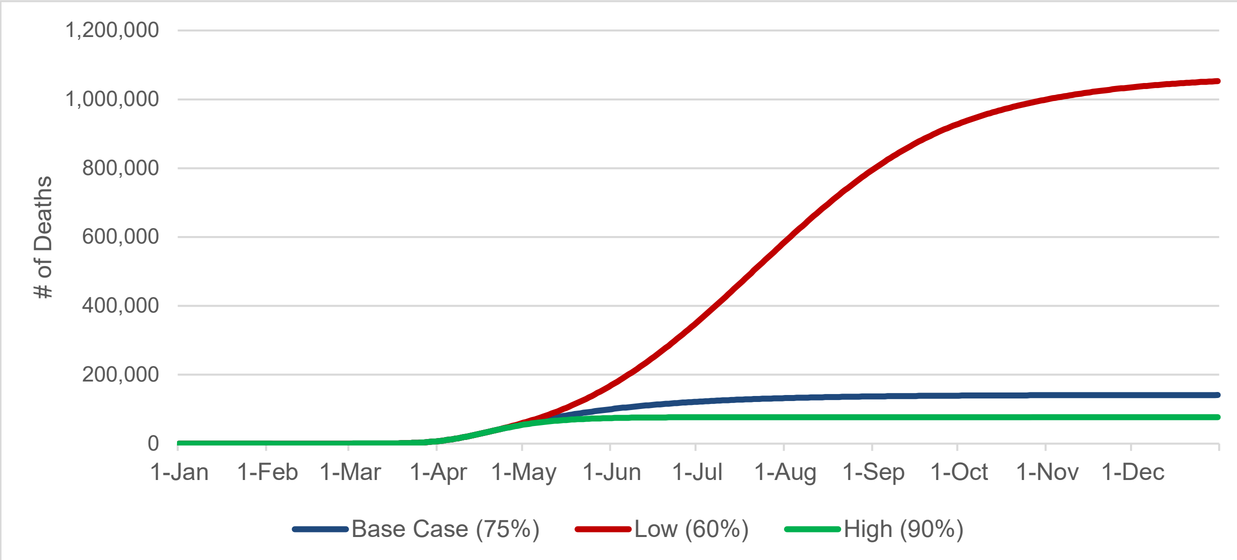


Impact of Degree of Social Distancing

Additional analyses examined the potential impact of the degree or extent of social distancing (Appendix A, Table A6) from April 15 onward. The extent of social distancing can vary due to the types of policies put into place and the level of compliance by members of the public. The scenarios include a low level of social distancing (60% reduction in contact), moderate social distancing (75% reduction in contact), and high social distancing (90% reduction in contact). These reductions are consistent with the amount of reduction in visits to places outside the home from a recent study in New York City.[19] All scenarios assume that the level of social distancing is maintained through the end of the year.

In the scenarios with moderate and high levels of social distancing, the pandemic peaks in April and healthcare system capacity is not exceeded. However, in the low social distancing scenario, the pandemic does not peak until July and the healthcare system capacity is exceeded in terms of the number of needed hospital beds, ICU beds, and ventilators. The numbers of infections and deaths vary substantially across these 3 scenarios: low social distancing led to 136.4 million infections and 1.05 million deaths; moderate social distancing led to 21.5 million infections and 141,000 deaths; high social distancing led to 11.7 million infections and 77,000 deaths. Figure 8 shows the impact of degree of social distancing on the estimated number of deaths. Estimated healthcare costs vary significantly based on the degree of social distancing: $125 billion (low social distancing), $20 billion (moderate social distancing), and $11 billion (high social distancing).

Figure 8. Estimated Deaths Over Time by Degree of Social Distancing



Impact of Easing Social Distancing

We looked at a variety of potential scenarios involving easing of social distancing policies to allow for increased economic activity (Appendix A, Table A7). First, we considered uniform easing of social distancing on June 1 under our base-case scenario with an R_0 of 3.2 and under a scenario with an R_0 of 2.2. For each of these scenarios, we assumed that easing of social distancing resulted in change from a 75% reduction in contact to a 50% reduction in contact. While it is difficult to say exactly what policies might result in this level of change, it could be a combination of factors such as removing stay-at-home orders; opening schools and workplaces; allowing non-essential travel; loosening policies on group gatherings; reopening restaurants, theaters, bars, and other communal spaces; adjusting guidelines on proximity, mask use, etc; and changing the degree to which testing, contact tracing, and isolation are implemented. We also considered intermittent easing of social distancing (involving 2 months of easing beginning on June 1 followed by 1 month of reimplementation of social distancing and alternating thereafter) under our base-case scenario with an R_0 of 3.2 and with a lower R_0 of 2.2.

The potential impact of uniform easing of social distancing without adequate testing, contact tracing, and isolation could be significant. Figure 9 shows that if early easing of social distancing were to occur on June 1, assuming an R_0 of 3.2, without adequate surveillance to adopt potential corrective measures, a resurgence of cases could occur in the early fall period, resulting in a total of 203.6 million infections, 1.7 million deaths, and $187 billion total costs. On the other hand, as Figure 10 shows, with an R_0 of 2.2, uniform easing of social distancing would result in a slow steady increase in cases, without a significant resurgence, resulting in a total of 24.6 million infections, 153,000 deaths, and $22 billion total costs. Alternatively, as Figure 11 shows, intermittent easing (alternating 2 months off and 1 month on) with an R_0 of 3.2 would significantly reduce the extent of resurgence compared to uniform easing, resulting in 127.8 million infections, 938,000 deaths, and $116 billion total costs. Finally, as Figure 12 shows, with an R_0 of 2.2, intermittent easing would result in a step-down and virtual elimination of cases over the course of the year, resulting in 17.3 million cases, 113,000 deaths, and $16 billion total costs.

Figure 9. Impact of Uniform Easing of Social Distancing (R_0 = 3.2)

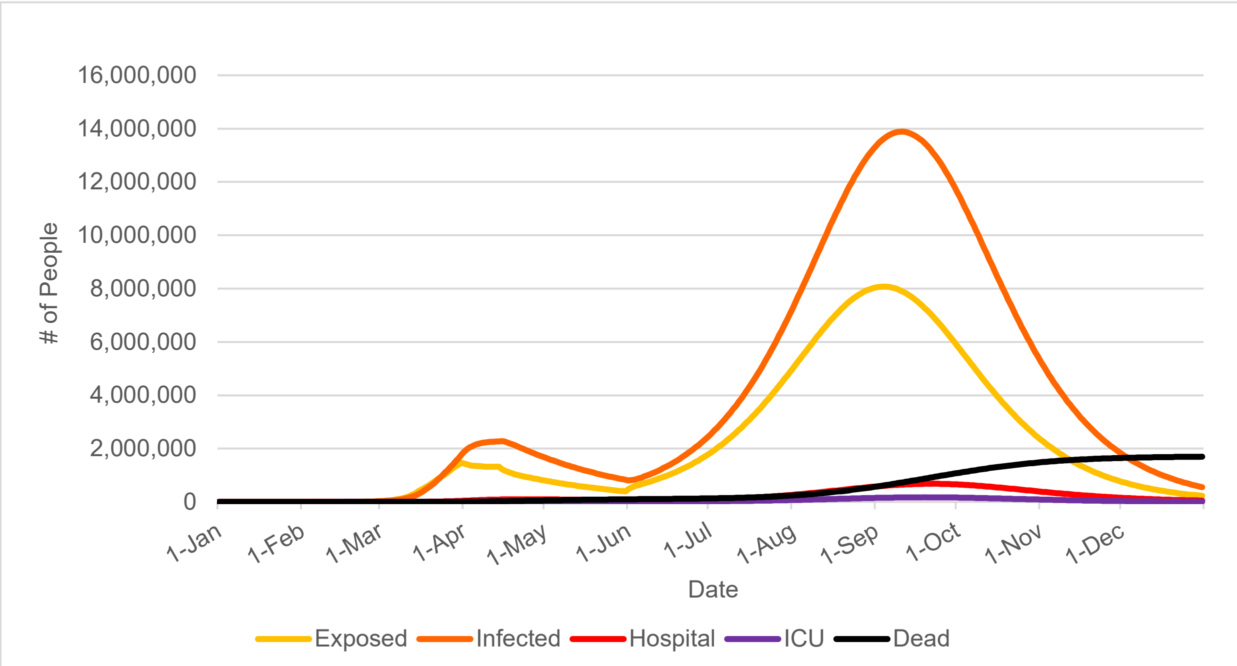


Figure 10. Impact of Uniform Easing of Social Distancing (R_0 = 2.2)

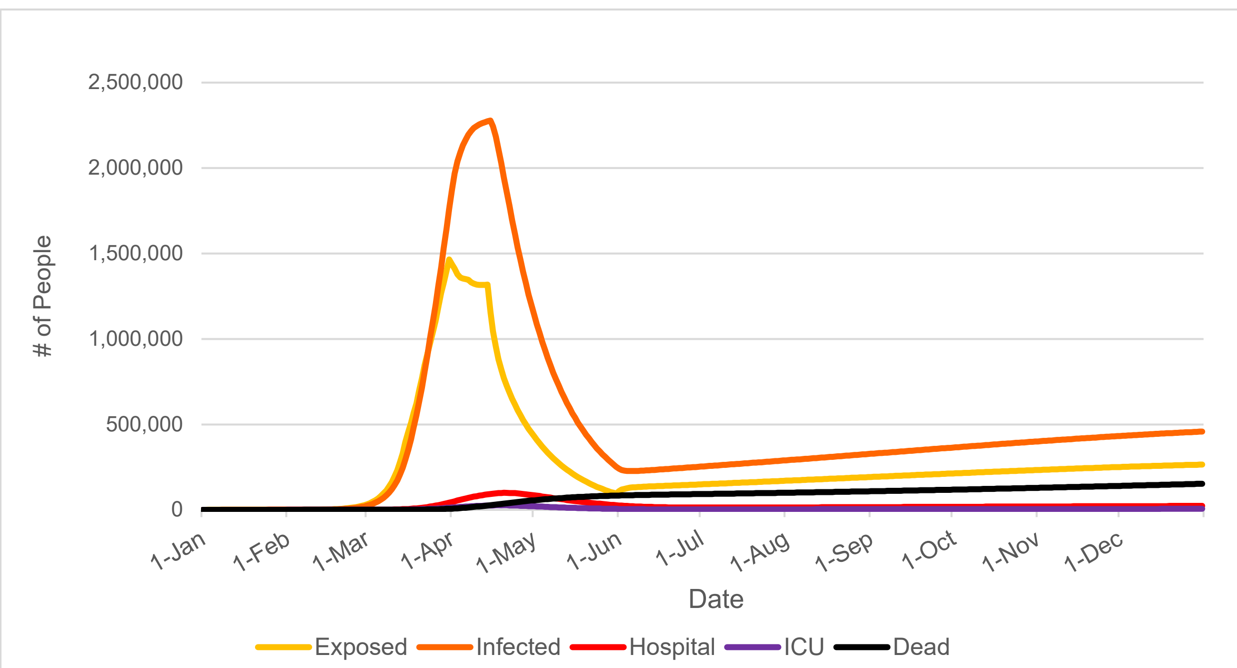


Figure 11. Impact of Intermittent Easing of Social Distancing (R_0 = 3.2)

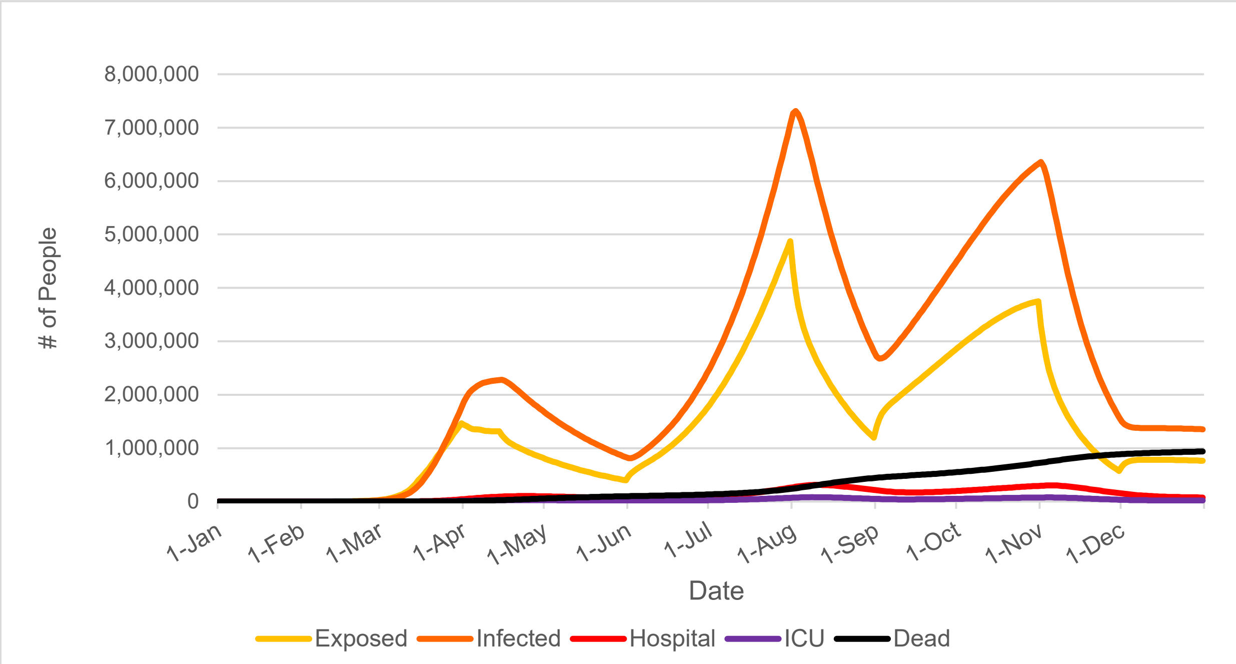
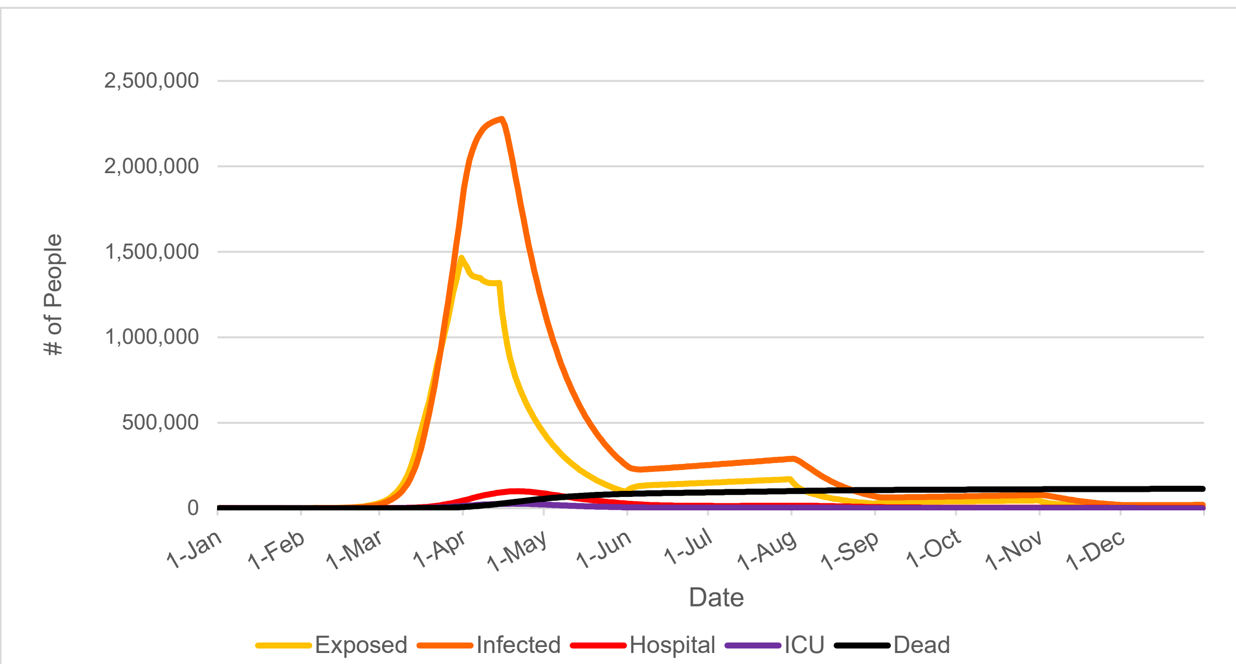


Figure 12. Impact of Intermittent Easing of Social Distancing (R_0 = 2.2)

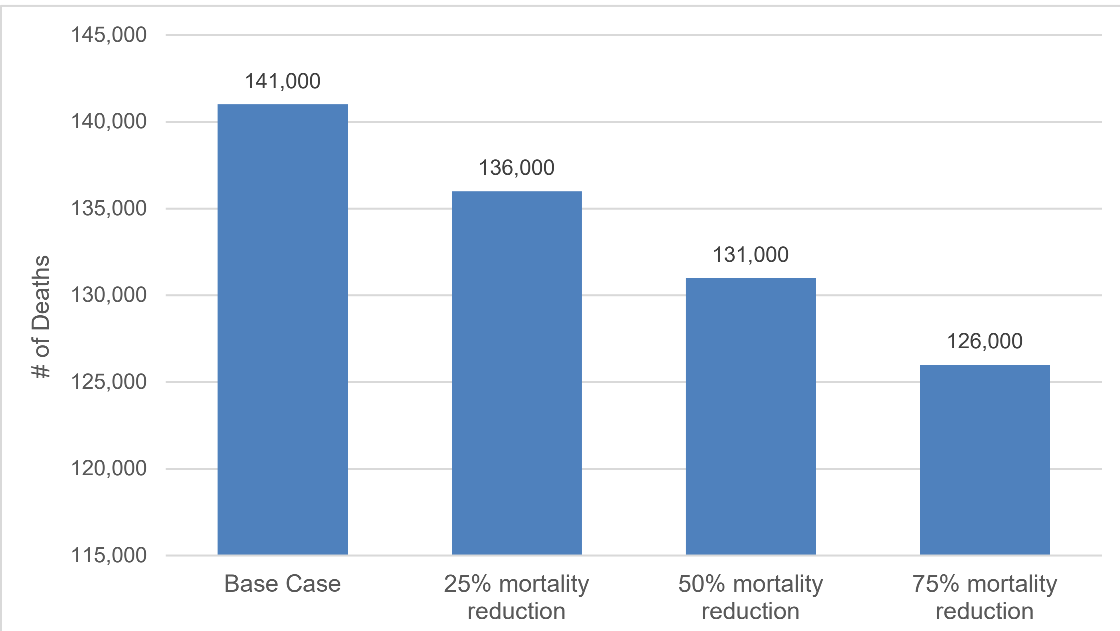


Impact of Hypothetical Drug Interventions

Pharmaceutical interventions offer another tool to mitigate the pandemic. Drugs that effectively treat the disease can help to reduce hospital LOS and mortality, particularly for patients with severe symptoms. Reducing LOS also has the additional benefit of reducing the demand on the healthcare system. Note that these scenarios (Appendix A, Table A8) compare to the base-case scenario ($R_0 = 3.2$ and 75% social distancing) in which the health system is not at overcapacity. These scenarios assume a hypothetical new treatment becomes available on July 1 that reduces LOS and mortality as follows: (1) reduce LOS by 15% and mortality by 25%; (2) reduce LOS by 25% and mortality by 50%; and (3) reduce LOS by 50% and mortality by 75%.

Figure 13 shows that a drug intervention introduced on July 1 could potentially save 5,000 to 15,000 lives over the remainder of this year under the base-case scenario. The potential effect is somewhat attenuated since most deaths would have already occurred by July 1 under a scenario where social distancing is maintained at 75% through the rest of the year. If, however, social distancing is eased and cases increase, the potential benefit of a drug intervention would increase significantly.

Figure 13. Impact of a Drug Intervention on Deaths



DISCUSSION

This model-based analysis examined the potential impact of pharmaceutical and non-pharmaceutical interventions to mitigate the COVID-19 crisis in the US. We developed a SEITRD model and parameterized the model using available data to assess various scenarios and interventions. Non-pharmaceutical interventions are already being employed by policymakers to mitigate the pandemic. Pharmaceutical interventions may soon become available as various existing and investigational drugs are being studied in human clinical trials for COVID-19. It is our intention that these analyses may provide some insights and assist policymakers with implementing strategies to better navigate the pandemic.

Our unmitigated analysis ($R_0 = 3.2$), representing a theoretical "worst case" scenario, estimated 2.07 million deaths and is in line with estimates from other analyses. The Imperial College London model estimated 2.2 million deaths in the US over the course of an unmitigated pandemic.[10] Worst case projections from a Centers for Disease Control and Prevention (CDC) model estimated a potential 1.7 million deaths,[20] while a separate analysis led by a former CDC director estimated up to 1.6 million deaths in the US.[21] Notably, these analyses do not include the potential impact of health system overcapacity on mortality. Our analysis attempts to account for this by adding the additional risk of mortality during conditions of overcapacity. When this is added to the unmitigated analysis, the model estimates 2.89 million deaths, a substantial increase.

Our base-case analysis utilizes an R_0 value of 3.2 and estimates 141,000 deaths. This R_0 is higher than preliminary estimates for SARS-CoV-2, which range from 2.2 to 2.7,[22] and higher than the 2.4 value used in the Imperial College London model.[10] However, the author of that study is reported to have since adopted a revised R_0 estimate of over 3.[23] A recent study estimated an R_0 value as high as 5.7 after reassessment of the data from China.[22] When we calibrated our model to real-world data for US deaths, we obtained an estimated R_0 of 4.2. However, for the base case, we utilized a value of 3.2 given that the calibrated value was largely based on the impact of the exponential growth observed in the New York metropolitan area, which we believe is likely to be an outlier for the rest of the country.

Since the R_0 value may have a significant impact on the model outcomes, we conducted a series of analyses to explore the potential outcomes of the calibrated model with different R_0 values under the assumption that the current levels of social distancing remain in place for the remainder of 2020. We estimate 14.1 million (R_0 = 2.2) to 58.3 million (R_0 = 4.2) infections and 93,000 (R_0 = 2.2) to 376,000 (R_0 = 4.2) deaths in the US over the course of 2020. These estimates are roughly in line with other available estimates. The White House provided initial estimates of 100,000 to 240,000 deaths in 2020.[24] Analyses from IHME initially estimated 81,114 cumulative deaths (95% confidence interval [CI]: 38,242–162,106) from COVID-19 through July 2020 and, as of April 19, these have been revised down to 60,308 deaths (95% CI: 34,063–140,381) on their website.[11] Note that the IHME projections for April 18 were 34,897 deaths, while actual deaths according to Johns Hopkins were higher at 38,664. At the end of July, our base-case model (R_0 = 3.2) estimates a total of 132,000 cumulative deaths, while our scenario analysis with an R_0 of 2.2 estimates a cumulative 92,000 deaths, figures that are higher than the IHME model, but both lie within their CIs. Additional models have provided various estimates which are available on a CDC website.[25]

Many states and communities have been preparing for a surge in hospital demand by COVID-19 patients. These efforts include canceling elective surgeries, adding beds, expanding staff, obtaining additional medical equipment, setting up field hospitals, and transferring patients to alternative sites of care. Our analysis shows that modest levels of health system overcapacity can potentially be managed by increasing capacity. However, if the pandemic is not well controlled and there is a large surge in cases, these efforts may not be enough, as healthcare demand could still potentially exceed capacity by 10- to 12-fold. For instance, hospitals in the New York metropolitan area were overwhelmed despite the state's extensive efforts to expand capacity. On the other hand, in some less dense and rural areas that have implemented effective social distancing policies, hospitals have been well undercapacity with concern about having to lay off under-utilized staff. Navigating a course through the pandemic to avoid unmanageable surges while maintaining hospital financial stability will require careful policy and resource coordination between local, state, and federal policymakers.

The timing of social distancing makes a dramatic impact on both the number of infections and deaths and on costs. Starting social distancing 1 week earlier would have reduced the number of infections and deaths by 68% (saving an estimated 96,000 lives). Initiating social distancing 2 weeks earlier would have reduced infections and deaths by 90% (saving an estimated 127,000 lives). These estimates are very similar to estimates from other researchers showing a 60% reduction in estimated deaths (23,000 vs 60,000) if social distancing were implemented 1 week earlier and a 90% reduction (6,000 vs 60,000) if implemented 2 weeks earlier.[26] Policymakers should be keenly aware of the potential impact of conditions of exponential growth and the importance of acting expeditiously based on timely surveillance and sufficient testing.

Our analysis also demonstrates the potentially dramatic impact of the degree of social distancing on outcomes. For social distancing to effectively mitigate disease transmission, the effective R must be reduced to near or preferably below 1, and near this value there are significant non-linearities (ie, small changes in social distancing can result in large impacts). In the base-case analysis, an R_0 of 3.2 and a 75% reduction in contact results in an effective R of 0.8 and the pandemic is controlled. However, when social distancing is weakened to 60% (R = 1.28), deaths increase by over a factor of 7. When it is strengthened to 90% (R = 0.32), deaths are nearly cut in half compared to the base case. These scenarios reflect the importance of maintaining effective levels of social distancing. Indeed, real-world evidence to date, in the US and around the world, has demonstrated that social distancing is the single best intervention we currently have to mitigate and suppress the spread of COVID-19. However, some geographic areas have experienced weaker implementation and maintenance of social distancing policies, with poor compliance and backlash by a portion of the public and some questioning the need for social distancing once levels of infection have been reduced.[27] Some Asian countries that initially responded with the most strict and effective policies to control the virus have recently begun to experience a resurgence in cases as social distancing policies were eased.[28] Research on the effectiveness of social distancing policies would better inform policymakers and help them to adopt high-value policies that minimize the spread of disease with minimal impacts on people, communities, and businesses.

Much of the US has yet to reach the peak of the COVID-19 epidemic, and there has already been considerable attention focused on easing social distancing and “reopening” the economy. The economic pressures are profound, with the economic fallout from the pandemic expected to exceed the Great Recession of 2008 and perhaps even rivaling the impact of the Great Depression. As of April 16, 2020, the US Bureau of Labor Statistics reports that 22 million jobs have been lost.[29] A variety of plans for reopening the economy have recently been released.[30] The White House has also issued a set of guidelines to state and local officials regarding reopening of their economies.[31] However, projections from the Department of Health and Human Services forecast that cases and deaths may rise, potentially substantially, when social distancing is eased.[32] And a new analysis by Harvard researchers showed that the transmissibility of the SARS-CoV-2 virus may require intermittent social distancing until 2022 to adequately mitigate the pandemic until herd immunity is acquired or a vaccine becomes available.[18] Planning and implementing an effective reopening strategy that balances health and economic outcomes is arguably the greatest challenge faced by countries right now. Substantial testing will be necessary to both monitor disease transmission to prevent outbreaks and to reduce transmission of active cases, particularly asymptomatic patients, as social distancing policies are eased.

To understand the potential impact of easing social distancing, we conducted a set of 4 scenario analyses: (1) uniform easing of social distancing (R_0 = 3.2); (2) uniform easing of social distancing (R_0 = 2.2); (3) intermittent easing of social distancing (R_0 = 3.2); (4) and intermittent easing of social distancing (R_0 = 2.2). In scenario 1, after social distancing successfully drives down COVID-19 cases, we encounter an even larger resurgence in the fall of 2020, which would likely require an extended shutdown period, potentially worsening economic outcomes and resulting in substantially more deaths. In scenario 2, after successful social distancing, we may find that easing social distancing results in a slow and steady increase in cases, which may be manageable, particularly if an effective treatment for COVID-19 becomes available. In scenario 3, intermittent social distancing helps to provide significantly better control of COVID-19 than uniform easing but at an additional economic cost and burden that must be weighed by the public and policymakers. Finally, scenario 4 is the most favorable, where intermittent social distancing could potentially quell the threat posed by COVID-19 until a vaccine becomes available while limiting the economic impact.

Finally, in addition to social distancing, drugs can be impactful with the potential to reduce LOS and mortality in patients with COVID-19 with severe or critical disease. Reductions in LOS would help to address issues of health system overcapacity by allowing earlier discharge of patients. Reductions in mortality, if substantial enough, would potentially help shift the cost-benefit calculus on easing some of the more restrictive social distancing policies. For instance, if our baseline assumption of an IFR of 0.66% is approximately correct, then a drug that can reduce mortality by around 80% would reduce the IFR to 0.13%. This IFR would be more in the range of the fatality associated with the seasonal flu and could provide policymakers and the public with the reassurance they need to ease social distancing for the benefits of a more open economy. Currently, clinical trials are underway for remdesivir, hydroxychloroquine, ritonavir/lopinavir, and ritonavir/lopinavir with interferon-beta.[33] New data suggest hydroxychloroquine may not be effective and may cause potentially fatal heart rhythm disorders.[34] Preliminary evidence indicates that remdesivir, originally developed as a treatment for Ebola, may improve patient outcomes, including both reducing LOS and improving survival.[35] In the meantime, while the world awaits the availability of safe and effective treatments, non-pharmaceutical interventions remain our primary policy tool.

Limitations

There are a few important limitations to this analysis. First and foremost, the modeling scenarios provided herein are intended as hypothetical analyses of the following form: if these conditions are met, then these outcomes would be anticipated. It should be stressed that the scenarios and outcomes are not intended as predictions of what *will* happen. The primary reason for this, as should be evident from the analyses, is that what *will* happen is largely a matter of what policies are enacted, when they are enacted, and the extent to which they are followed. A pandemic is not a deterministic phenomenon, and human behavior from now and over the remainder of the pandemic will largely determine what happens.

Second, the SIR compartment model approach used in this analysis is a relatively simple form of epidemiologic modeling that assumes random and uniform mixing in a closed population and may potentially overestimate the extent of disease transmission. We modeled the disease and outcomes for the US population as a whole; however, the US is geographically heterogeneous and composed of communities with very different characteristics (eg, extent and timing of initial infections, density, size of households, degree of contact within and outside of the community, and extent to which social distancing policies are adopted and when). These characteristics could result in very different disease transmission dynamics within and across communities, as could seasonal effects in transmissibility.[18] Our model does not incorporate the impact of age, which appears to have a significant effect on disease transmission and mortality. Other models have conducted analyses at the state or even county level,[11] while some have conducted microsimulations to model potential interactions between individuals in households, schools, and workplaces.[10] While these more sophisticated methods may offer some advantages, the results of this analysis are generally consistent with these analyses, and we believe a simpler analysis may be more accessible and instructive for policymakers to help understand the broad effects of different types of available interventions.

Third, despite the growing amount of COVID-19 research, there are still limited available data regarding some key parameters to inform models.[36] For instance, data on the IFR are limited due to a lack of information regarding the true number of infected people, since the confirmed case counts represent a significant underestimate. Eventually serologic studies will allow for more precise estimates. In the meantime, a relatively small change in the IFR can result in a significantly different number of estimated deaths in the analysis. While the number of deaths is less likely to represent an undercount, some patients without a confirmed diagnosis (eg, due to lack of testing) may have their death attributed to other causes. Furthermore, the real impact of the COVID-19 crisis extends even beyond patients with the disease, as many patients with other conditions may suffer morbidity or mortality from lack of access to medical care and medicines.[37] The true reproduction number (R_0) and the extent of social distancing in the community (eg, most current measures such as miles traveled are proxies) are notably difficult to estimate. Costs are also extremely difficult to estimate under current circumstances. We utilized publicly available cost estimates that may not generalize to a pandemic setting, where hospitals must acquire additional and costly durable medical equipment, incur additional staffing costs, acquire scarce medications and supplies at inflated costs, and even set up field hospitals. The true costs of the COVID-19 pandemic will not be known for some time. Accordingly, the model results should be interpreted with appropriate caution given these uncertainties.

Finally, modeling in general involves a considerable simplification of complex systems. The COVID-19 pandemic involves biological systems (the virus and human anatomy), systems of human behavior, healthcare systems and medical technology, and the economy. At this point in time, we simply do not know what future awaits us: implementation of large-scale testing and contact tracing could substantially curtail disease transmission; the transmissibility of the virus may be altered seasonally[18]; mutations may render the virus more or less infectious or lethal; prior infection may not impart immunity; a highly effective treatment or vaccine may be discovered; people may behave in unpredictable ways; and substantial economic pressures may alter the decision landscape. As the well-known aphorism has it, “all models are wrong, but some are useful,” and when it comes to policy models, even a rough approximation to the truth may be enough to render them useful, particularly in times of great urgency.

CONCLUSIONS

This model-based analysis is intended to inform policymakers on the potential impact of various pharmaceutical and non-pharmaceutical interventions to mitigate the COVID-19 crisis in the US. Social distancing is currently the primary intervention available to mitigate the pandemic; therefore, it is essential that policymakers effectively utilize it and engage public support. Meanwhile, policymakers should be prepared with plans to mobilize resources and increase health system capacity should social distancing fail to control infections and a surge begins to occur within their local community or state. Careful consideration should be given to when and how to ease social distancing, as the timing and the degree of social distancing are critical when dealing with the potential exponential growth of COVID-19. Adequate testing and disease surveillance will be essential to successfully implement easing of social distancing and to monitor for when reimplementation of social distancing policies may be necessary. Effectively utilizing these techniques will help to minimize the adverse health effects of the pandemic and the economic burden on society until more effective treatments, and ultimately a vaccine, become available to change the risk-benefit calculus or bring about herd immunity. Successfully navigating the COVID-19 pandemic will require that policymakers coordinate across local, state, and federal government; that evidence-based research inform policymaker perspectives; that developed plans are flexible and responsive to changing conditions; that critical resources (such as testing and an expanded public health workforce) are fully mobilized; and that innovative and available technologies are effectively employed.

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APPENDIX A: TABLES

Table A1. Model Parameters

Population

Parameter	Value	Source	Comment
US population	329,135,084	US Census 2020[38]	Estimated US population as of January 1, 2020
Initial immunity	0%	Assumption	Based on SARS-CoV-2 being a novel virus
Initial infected	1	Holshue 2020[39]	Based on the first US documented case on January 15, 2020 (note that we assumed the first case in the US occurred a few weeks earlier on January 1)

Infection Dynamics

Parameter	Value	Source	Comment
Contacts/day	6.0	Assumption	Estimated by calibrating the model to the US mortality data through April 15, 2020 (beyond that date, this parameter was varied to reflect alternative R_0 scenarios and changes in social distancing)
Infections/contact	10%	Assumption	This parameter works in conjunction with contacts/day to yield β, which along with the infectious period, determines the R_0
Latent period	4 days	Sanche 2020[22]	Estimated based on a reported incubation period of 5 days (note that the latent period is slightly shorter than the incubation period if asymptomatic transmission is possible)
Infectious period	7 days	Sanche 2020[22]	Estimated based on a latent period of 4 days and a serial interval of 7–8 days (note that the serial interval = the latent period plus half of the infectious period; therefore, with a latent period of 4 days and infectious period of 7 days the model assumes a serial interval of 7.5 days, which is in line with estimates of 7–8 days for the serial interval)

Disease Severity

Parameter	Value	Source	Comment
Mild	96%	Worldometer 2020[3]	Based on 4% of active cases worldwide being serious or critical and 96% being mild (as of 4/14/20)
Severe	3%	Wu 2020[40]	Estimated based on approximately three-quarters (14% out of 19%) of those hospitalized being severe
Critical	1%	Wu 2020[40]	Estimated based on one-quarter (5% out of 19%) of those hospitalized being critical

Mortality (Baseline)

Parameter	Value	Source	Comment
Hospital	5.2%	Rajgor 2020,[41] Verity 2020[42]	Calibrated to yield a baseline infection fatality rate of 0.66%
ICU	50.0%	Bhatraju 2020[43]	Study reported that 50% of critically ill patients died

Mortality (Overcapacity)

Parameter	Value	Source	Comment
Hospital bed	1.2 RR	Eriksson 2016[44]	Based on a review that found that hospital inpatient overcapacity increased mortality by 0%–30%, we assumed a 20% increase in risk of mortality

ICU bed	1.2 RR	Eriksson 2016[44]	Based on a review that found that hospital inpatient overcapacity increased mortality by 0%–30%, we assumed a 20% increase in risk of mortality
Ventilator	1.6 RR	Assumption, CNN[45]	Assumed 60% increase in risk of mortality, which results in an 80% chance of mortality (note that together, these parameters generate an overall 40% increase in IFR from 0.66%–0.9%, which is consistent with data showing a case fatality rate 40% higher for New York City [4.7%] than the rest of the country [3.4%] as reported by CNN)

Healthcare Capacity

Parameter	Value	Source	Comment
Hospital beds	826,331	AHA 2020[46]	Number of non-ICU beds
ICU beds	97,776	AHA 2020[46]	Number of ICU beds
Ventilators	62,000	Johns Hopkins 2020[47]	Based on 62,000 full-feature mechanical ventilators (note that we did not include the 98,000 additional non-full-featured ventilators)

Utilization

Parameter	Value	Source	Comment
Hospital bed occupancy	66%	NCHS 2018[48]	Occupancy rate for all hospitals in 2015 (Table 89)
ICU bed occupancy	66%	NCHS 2018[48]	Occupancy rate for all hospitals in 2015 (Table 89)
Ventilators already in use	47%	Wunsch 2013[49]	Estimated based on approximately 30% of ICU patients being on mechanical ventilation
ED visit (% among infected)	10%	CDC 2020[50]	Estimated based on the number of ED visits for COVID-like illness as of the 14th week of 2020 divided by the number of estimated infections in the model
Hospital LOS	12	Bhatraju 2020[43]	Median LOS among all patients (patients who survive and die)
ICU LOS	9	Bhatraju 2020[43]	Median LOS among all patients (patients who survive and die)
Ventilator required for critical COVID-19 patient	75%	Bhatraju 2020[43]	Study reported that 75% of critically ill COVID-19 patients required mechanical ventilation

Costs

Parameter	Value	Source	Comment
ED visit	$934	Muhuri 2019,[51] BLS 2020[52]	$934, based on mean ED cost of $840 for influenza patients inflated from 2016 (CPI 463.675) to 2020 (CPI 515.605) using the medical care component of the BLS CPI
Hospitalization	$17,875	AHRQ 2020,[53] BLS CPI[52]	$17,875, based on HCUP cost of $16,075 (ICD-10 J12.89, viral pneumonia) inflated from 2016 (CPI 463.675) to 2020 (CPI 515.605) using the medical care component of the BLS CPI
Critical care	$29,002	AHRQ, 2020,[53] BLS 2020[52]	$29,002, based on HCUP cost of $26,081 (ICD-10 J80, acute respiratory distress syndrome) inflated from 2016 (CPI 463.675) to 2020 (CPI 515.605) using the medical care component of the BLS CPI

Table A2. Results: Unmitigated Scenarios (No Calibration)

Scenario	Low R_0 = 2.2	Moderate R_0 = 3.2	High R_0 = 4.2	Moderate R_0 = 3.2 (With Mortality Due to Overcapacity)
Peak (day)				
Infections	August 16	May 28	April 25	May 28
Hospital	August 26	June 5	May 3	June 5
Peak utilization (%)				
Hospital bed	638%	995%	1,190%	995%
ICU bed	1,414%	2,270%	2,763%	2,270%
Ventilator	1,073%	1,722%	2,097%	1,722%
Outcomes (#, %)				
Susceptible	49.6M (15.1%)	13.8M (4.2%)	4.1M (1.2%)	13.8M (4.2%)
Infected	279.5M (84.9%)	315.3M (95.8%)	325.1M (98.8%)	315.3M (95.8%)
Recovered[a]	277.7M (99.3%)	313.2M (99.3%)	322.9M (99.3%)	312.4M (99.1%)
Dead[a]	1.83M (0.66%)	2.07M (0.66%)	2.13M (0.66%)	2.89M (0.92%)
Visits (#)				
ED	28.0M	31.5M	32.5M	31.5M
Hospital	8.4M	9.5M	9.8M	9.5M
ICU	2.8M	3.2M	3.3M	3.2M
Costs ($)				
ED	$26,109M	$29,448M	$30,361M	$29,448M
Hospital	$149,904M	$169,074M	$174,318M	$169,074M
ICU	$81,072M	$91,440M	$94,276M	$91,440M
Total[b]	$257,085M	$289,962M	$298,956M	$289,962M

[a] For recovered and dead, percentage is percentage of those infected (not of entire population).

[b] Values may not sum due to rounding.

Table A3. Results: Impact of Basic Reproduction Number (R_0)

Scenario	Low R_0 = 2.2	Low/Moderate R_0 = 2.7	Moderate R_0 = 3.2 (Base Case)	Moderate/High R_0 = 3.7	High R_0 = 4.2
Peak (day)					
Infections	April 15	April 15	April 15	April 15	May 4
Hospital	April 21	April 22	April 24	April 28	May 22
Peak utilization (%)					
Hospital bed	35%	36%	36%	38%	42%
ICU bed	80%	80%	81%	82%	89%
Ventilator	61%	61%	61%	63%	68%
Outcomes (#, %)					
Susceptible	315.0M (95.7%)	312.4M (94.9%)	307.6M (93.5%)	296.6M (90.1%)	270.8M (82.3%)
Infected	14.1M (4.3%)	16.7M (5.1%)	21.6M (6.5%)	32.5M (9.9%)	58.3M (17.7%)
Recovered[a]	14.1M (99.3%)	16.6M (99.3%)	21.4M (99.3%)	32.2M (99.3%)	57.4M (99.3%)
Dead[a]	93,000 (0.66%)	110,000 (0.66%)	141,000 (0.66%)	212,000 (0.65%)	376,000 (0.65%)
Visits (#)					
ED	1.4M	1.7M	2.2M	3.2M	5.8M
Hospital	424,000	501,000	646,000	974,000	1.7M
ICU	141,000	167,000	215,000	325,000	578,000
Costs ($)					
ED	$1,321M	$1,560M	$2,013M	$3,037M	$5,429M
Hospital	$7,587M	$8,956M	$11,555M	$17,409M	$31,003M
ICU	$4,103M	$4,844M	$6,249M	$9,415M	$16,767M
Total[b]	$13,012M	$15,359M	$19,818M	$29,862M	$53,199M

[a] For recovered and dead, percentage is percentage of those infected (not of entire population).

[b] Values may not sum due to rounding.

Table A4. Results: Impact of Healthcare System Capacity

Scenario	+25% Capacity (50% SD)	+25% Capacity (60% SD)	+50% Capacity (50% SD)	+50% Capacity (60% SD)
Peak (day)				
Infections	June 26	July 12	June 26	July 12
Hospital	July 7	July 23	July 7	July 23
Peak utilization (%)				
Hospital bed	171%	67%	120%	47%
ICU bed	370%	142%	260%	100%
Ventilator	331%	127%	251%	96%
Outcomes (#, %)				
Susceptible	116.9M (35.5%)	192.8M (58.6%)	116.9M (25.5%)	192.8M (58.6%)
Infected	212.3M (64.5%)	136.4M (41.4%)	212.3M (64.5%)	136.4M (41.4%)
Recovered[a]	210.5M (99.2%)	134.9M (99.3%)	210.6M (99.3%)	135.0M (99.3%)
Dead[a]	1.76M (0.83%)	945,000 (0.70%)	1.68M (0.79%)	887,000 (0.65%)
Visits (#)				
ED	21.2M	13.6M	21.2M	13.6M
Hospital	6.4M	4.1M	6.4M	4.1M
ICU	2.1M	1.4M	2.1M	1.4M
Costs ($)				
ED	$19,825M	$12,721M	$19,825M	$12,721M
Hospital	$113,817M	$72,861M	$113,817M	$72,861M
ICU	$61,556M	$39,406M	$61,556M	$39,406M
Total[b]	$195,198M	$124,988M	$195,198M	$124,988M

SD – social distancing.

[a] For recovered and dead, percentage is percentage of those infected (not of entire population).

[b] Values may not sum due to rounding.

Table A5. Results: Impact of Timing of Social Distancing

Scenario	March 16 (Base Case)	March 9	March 2
Peak (day)			
Infections	April 15	April 8	April 1
Hospital	April 24	April 17	April 11
Peak utilization (%)			
Hospital bed	36%	11%	3%
ICU bed	81%	24%	7%
Ventilator	61%	18%	5%
Outcomes (#, %)			
Susceptible	307.6M (93.5%)	322.2M (97.9%)	327.1M (99.4%)
Infected	21.6M (6.5%)	6.9M (2.1%)	2.1M (0.6%)
Recovered[a]	21.4M (99.3%)	6.9M (99.3%)	2.1M (99.3%)
Dead[a]	141,000 (0.66%)	45,000 (0.66%)	14,000 (0.66%)
Visits (#)			
ED	2.2M	694,000	208,000
Hospital	646,000	208,000	62,000
ICU	215,000	69,000	21,000
Costs ($)			
ED	$2,013M	$648M	$194M
Hospital	$11,555M	$3,721M	$1,114M
ICU	$6,249M	$2,013M	$602M
Total[b]	$19,818M	$6,382M	$1,910M

[a] For recovered and dead, percentage is percentage of those infected (not of entire population).

[b] Values may not sum due to rounding.

Table A6. Results: Impact of Level of Social Distancing

Scenario	Low = 60%	Moderate = 75% (Base Case)	High = 90%
Peak (day)			
Infections	July 12	April 15	April 15
Hospital	July 23	April 24	April 19
Peak utilization (%)			
Hospital bed	115%	36%	35%
ICU bed	246%	81%	79%
Ventilator	187%	61%	60%
Outcomes (#, %)			
Susceptible	192.8M (58.6%)	307.6M (93.5%)	317.4M (96.4%)
Infected	136.4M (41.4%)	21.6M (6.5%)	11.7M (3.6%)
Recovered[a]	134.8M (99.2%)	21.4M (99.3%)	11.6M (99.3%)
Dead[a]	1.05M (0.78%)	141,000 (0.66%)	77,000 (0.66%)
Visits (#)			
ED	13.6M	2.2M	1.2M
Hospital	4.1M	646,000	351,000
ICU	1.4M	215,000	117,000
Costs ($)			
ED	$12,721M	$2,013M	$1,094M
Hospital	$72,861M	$11,555M	$6,280M
ICU	$39,406M	$6,249M	$3,396M
Total[b]	$124,988M	$19,818M	$10,770M

[a] For recovered and dead, percentage is percentage of those infected (not of entire population).

[b] Values may not sum due to rounding.

Table A7. Results: Easing of Social Distancing

Scenario	Uniform Easing (R_0 = 3.2)	Uniform Easing (R_0 = 2.2)	Intermittent Easing (R_0 = 3.2)	Intermittent Easing (R_0 = 2.2)
Peak (day)				
Infections	September 10	April 15	August 2	April 15
Hospital	September 21	April 21	August 10	April 21
Peak utilization (%)				
Hospital bed	243%	35%	111%	35%
ICU bed	523%	80%	247%	80%
Ventilator	397%	61%	188%	61%
Outcomes (#, %)				
Susceptible	125.6M (38.1%)	304.5M (92.5%)	201.4M (76.7%)	311.8M (94.7%)
Infected	203.6M (61.9%)	24.6M (7.5%)	127.8M (23.3%)	17.3M (5.3%)
Recovered[a]	201.0M (99.2%)	23.7M (99.4%)	124.6M (99.4%)	17.2m (99.3%)
Dead[a]	1.70M (0.84%)	153,000 (0.64%)	938,000 (0.75%)	113,000 (0.66%)
Visits (#)				
ED	20.3M	2.4M	12.7M	1.7M
Hospital	6.1M	717,000	3.8M	518,000
ICU	2.0M	239,000	1.3M	173,000
Costs ($)				
ED	$18,993M	$2,275M	$11,861M	$1,615M
Hospital	$108,749M	$12,818M	$67,373M	$9,262M
ICU	$58,815M	$6,932M	$36,437M	$5,009M
Total[b]	$186,558M	$22,025M	$115,671M	$15,885M

[a] For recovered and dead, percentage is percentage of those infected (not of entire population).

[b] Values may not sum due to rounding.

Table A8. Results: Impact of Pharmaceutical Interventions

Scenario	Base Case (R_0 = 3.2, SD = 75%)	Reduce LOS 15%, Mortality 25%	Reduce LOS 25%, Mortality 50%	Reduce LOS 50%, Mortality 75%
Peak (day)				
Infections	April 15	April 15	April 15	April 15
Hospital	April 24	April 24	April 24	April 24
Peak utilization (%)[a]				
Hospital bed	36%	36%	36%	36%
ICU bed	81%	81%	81%	81%
Ventilator	61%	61%	61%	61%
Outcomes (#, %)				
Susceptible	307.6M (93.5%)	307.6M (93.5%)	307.6M (93.5%)	307.6M (93.5%)
Infected	21.5M (6.5%)	21.5M (6.5%)	21.5M (6.5%)	21.5M (6.5%)
Recovered[b]	21.4M (99.3%)	21.4M (99.4%)	21.4M (99.4%)	21.4M (99.4%)
Dead[b]	141,000 (0.66%)	136,000 (0.63%)	131,000 (0.61%)	126,000 (0.59%)
Visits (#)				
ED	2.2M	2.2M	2.2M	2.2M
Hospital	646,000	646,000	646,000	646,000
ICU	215,000	215,000	215,000	215,000
Costs ($)				
ED	$2,013M	$2,013M	$2,013M	$2,013M
Hospital	$11,555M	$11,555M	$11,555M	$11,555M
ICU	$6,249M	$6,249M	$6,249M	$6,249M
Total[c]	$19,818M	$19,818M	$19,818M	$19,818M

SD – social distancing.

[a] Note that peak utilization values do not change despite impact on LOS since peak utilization occurs before the introduction of the pharmaceutical intervention on July 1.

[b] For recovered and dead, percentage is percentage of those infected (not of entire population).

[c] Values may not sum due to rounding.

APPENDIX B: FIGURES

Figure B1. Model Equations

$$\frac{dS}{dt} = -\beta\frac{SI}{N}$$

$$\frac{dE}{dt} = \beta\frac{SI}{N} - \sigma E$$

$$\frac{dI}{dt} = \sigma E - \gamma I$$

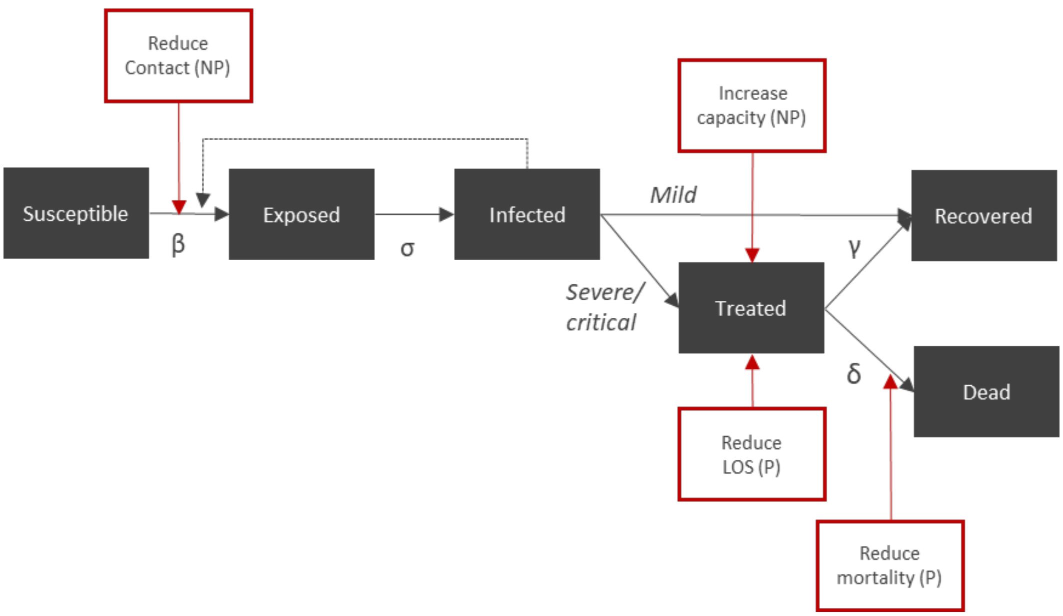
$$\frac{dT}{dt} = \gamma I_{Severe} - \gamma T$$

$$\frac{dR}{dt} = \gamma I_{Mild} + \gamma T \times (1 - \delta T)$$

$$\frac{dD}{dt} = \gamma T \times \delta T$$

Where β = infection parameter; σ = latency parameter; γ = recovery parameter (separate values were used for mild and severe patients); δ = mortality parameter.

Figure B2. Model Structure With Interventions



NP – non-pharmaceutical; P – pharmaceutical

Note: The intervention to reduce contacts (social distancing) is parameterized with 2 values: a percentage reduction and a start date (although scenarios with various degrees of social distancing over time and those involving multiple dates such as relaxing/removing social distancing were also implemented). The intervention to increase healthcare system capacity was parameterized by the percentage increase in the available resource for the 3 separate resources (hospital beds, ICU beds, and ventilators). No start date was applied as it was assumed that these increases in resources would occur early (ie, before the epidemic peak when they would be required). The interventions to reduce LOS and mortality are parameterized with 2 values, the percentage reduction in LOS/mortality and a start day.

Figure B3. Calibration of Observed Deaths vs Modeled Deaths

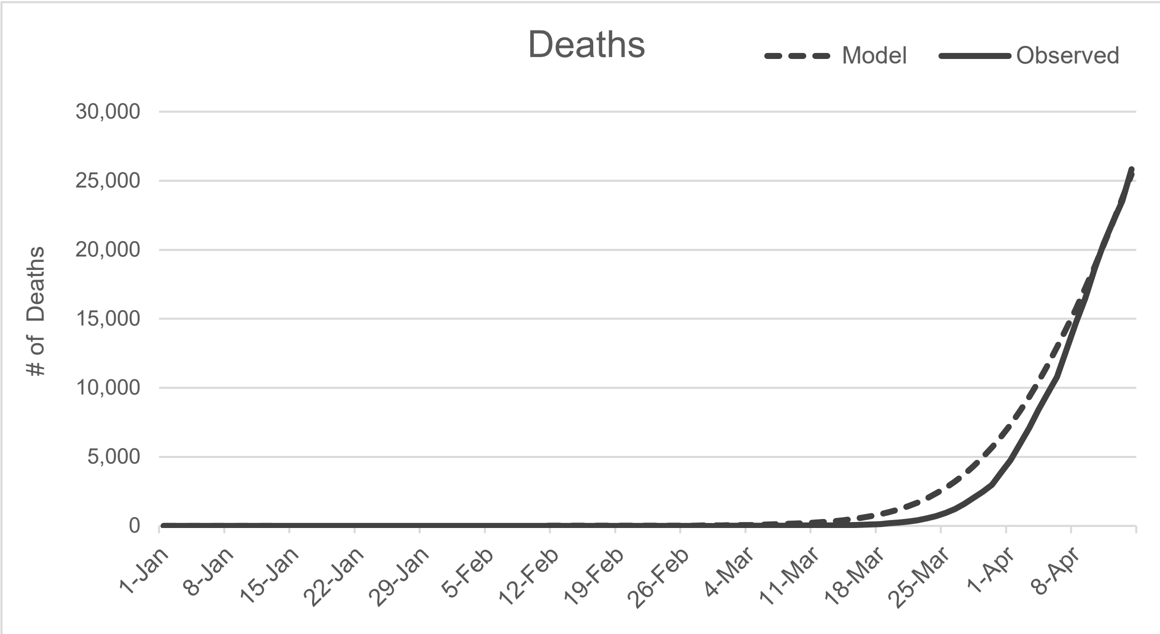
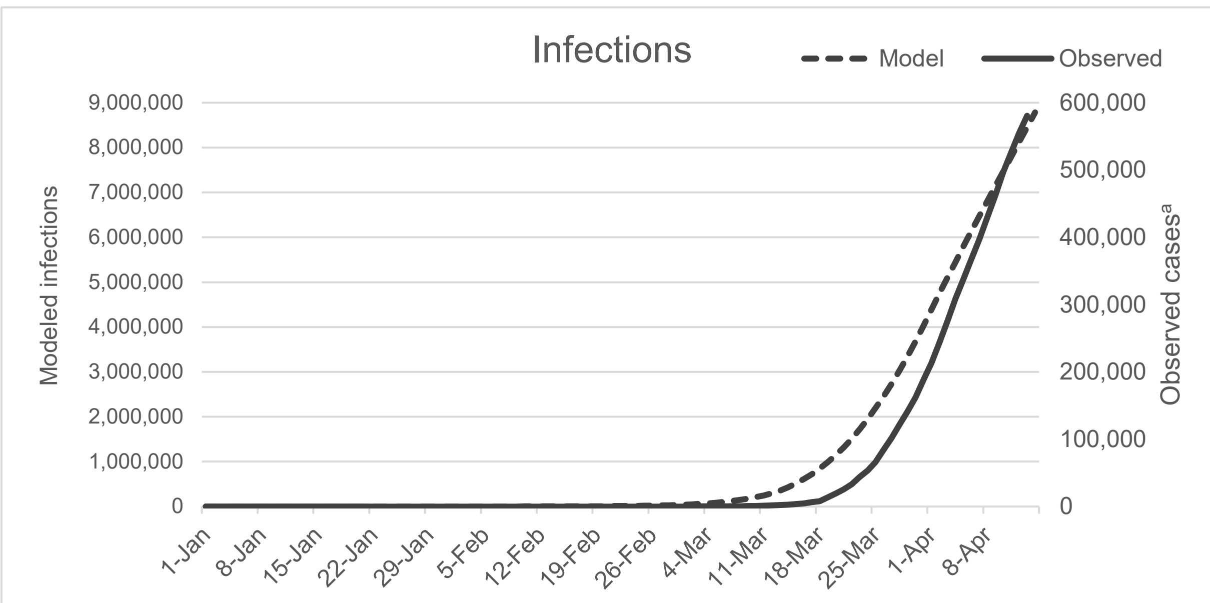


Figure B4. Calibration of Observed Cases vs Modeled Infections



[a] Observed cases are those confirmed through diagnostic testing and represent a fraction of all infected.

Figure B5. Unmitigated Pandemic (R_0 = 2.2)

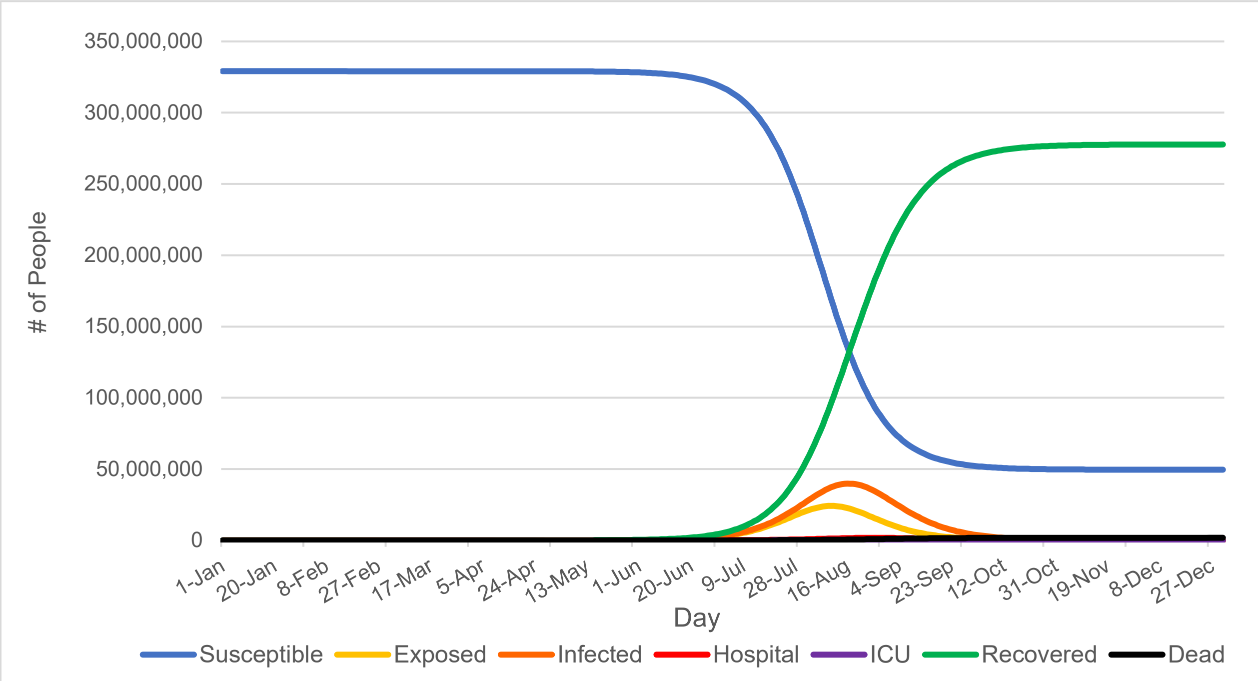


Figure B6. Unmitigated Pandemic (R_0 = 4.2)

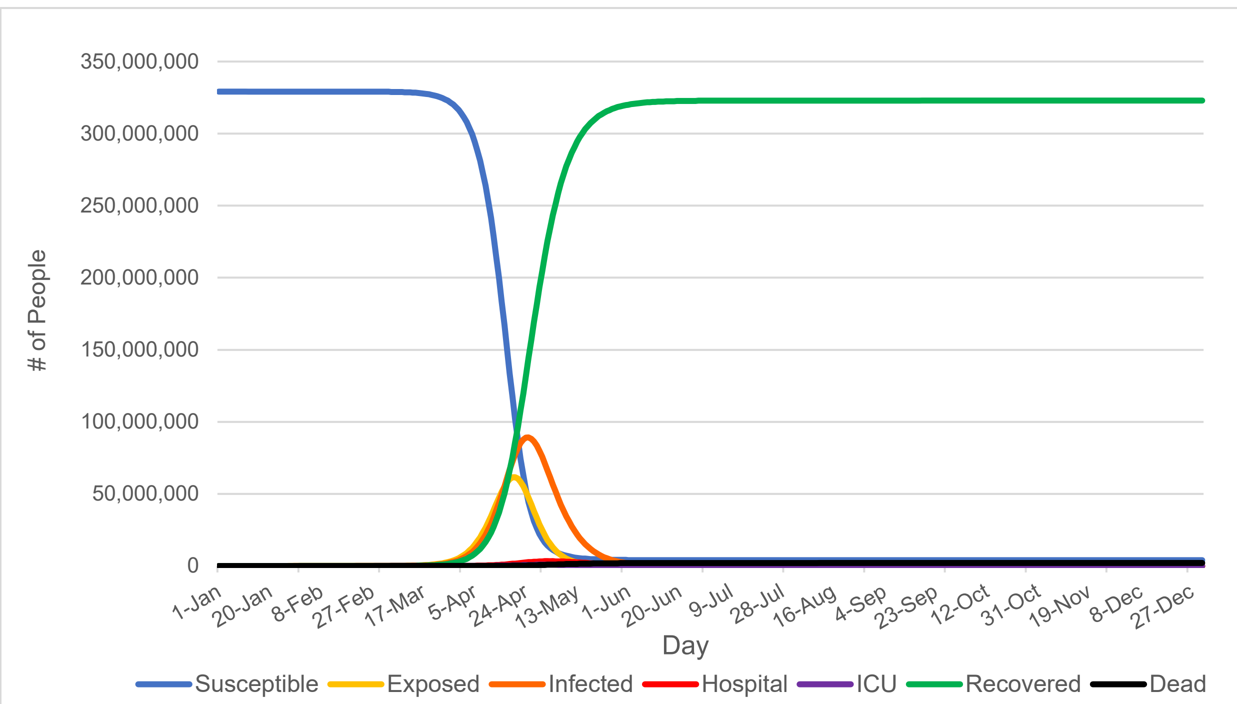
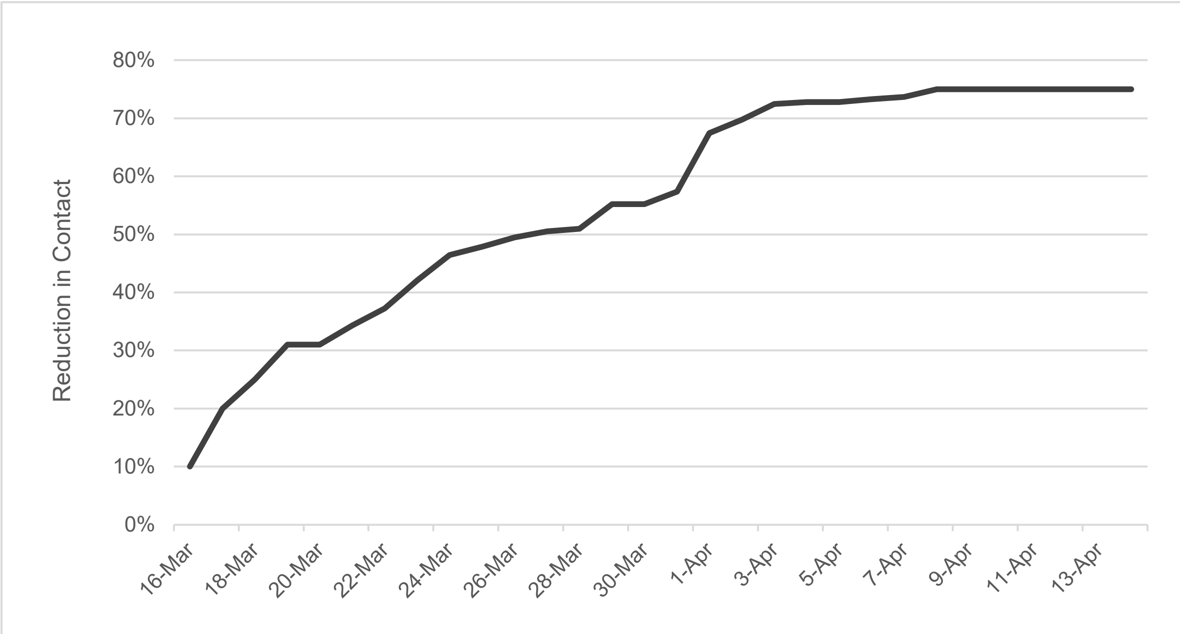


Figure B7. Estimated Reduction in Contact Due to Social Distancing



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