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The Impact of Vaccines and Behavior on US Cumulative Deaths from COVID-19

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Abstract

We estimate that the combination of changes in behavior to slow the spread of COVID-19 and the delivery of vaccines to a substantial majority of the American population by mid-2021 saved close to 800,000 American lives relative to what would have occurred had vaccines not been developed. We argue that the duration and magnitude of this behavioral response – and thus its overall success in delaying infections – came as a surprise, relative to both our historical experience with pandemic influenza and to model-based projections based on that experience. Thus, we take from our experience with COVID-19 over the past four years the important public health lesson that behavior change can be a powerful force for slowing the spread of a dangerous infectious respiratory disease for a long time. At the same time, these behavioral changes to slow the spread of COVID-19 came at a tremendous economic, social, and human cost. To avoid similar pain from mitigation in the next pandemic, we argue that we need to make investments now not only in vaccine development, but also in data infrastructure so that we can precisely target behavior-oriented mitigation efforts to minimize their economic and social impacts of the next pandemic.

1 Introduction

Starting in March of 2020, the American public undertook massive changes in behavior in response to the threat from COVID-19. These behavioral changes arose partly in response to public mandates and partly as a spontaneous private reaction to this new disease threat. These public and private disease mitigation efforts succeeded in slowing the transmission of SARS-CoV-2 to a remarkable extent through 2020 and well into 2021, by which time effective vaccines had been developed and delivered to much of the American population.

As a result of these mitigation efforts, a large majority of Americans were able to get vaccinated for COVID-19 before experiencing their first infection. We document this using nationwide serology data, which lets us estimate the cumulative number of infections and vaccinations over time (Figure 1). Population-level data on vaccine efficacy indicate that this success in delivering vaccines to many Americans prior to their first SARS-CoV-2 infection substantially reduced the infection fatality rate these Americans suffered when they did contract COVID-19. We document this point using linked vaccine and mortality data in Figure 2.

In this paper, we use these observations, together with a structural epidemiological model, to argue that the combined success in slowing SARS-CoV-2 transmission through behavior change and the widespread delivery of vaccines saved close to 800,000 American lives.

We argue that, relative to historical experience with pandemic influenza and modeling based on this experience, this public health success was a surprise. As of March 2020, it was not at all clear that it would be possible to slow the spread of COVID-19 long enough to develop vaccines and deliver them to the American population in time to save lives. We see this success of behavior-based mitigation with COVID-19 as one of the most important public health lessons of this pandemic — it is, in fact, possible to slow the spread of a dangerous respiratory disease for quite a long time.

But, at the same time, these mitigation efforts came at a tremendous economic, social, and human cost. To avoid similar pain from mitigation in the next pandemic, we argue that we need to make investments now not only in vaccine development, but also in data infrastructure so that we can precisely target mitigation efforts to minimize the economic and social impacts of mitigation with the next pathogen. One might think of these investments in data infrastructure as similar in spirit to the huge investments made in the infrastructure to gather economic data after World War II to better guide economic policy. For population-level infectious disease mitigation policies to be effective at low economic and social cost, they need to be guided by detailed real-time epidemiological data, which is only available in a crisis if one is prepared in advance to gather such data.

1.1 Our Estimate of Lives Saved

We estimate that behavioral mitigation and vaccination together saved close to 800,000 American lives between February 15, 2020, and February 15, 2024. This estimate is based on three data sources: serology data capturing immunity derived from SARS-CoV-2 infection and COVID-19 vaccination in the American population, data on the dynamics of COVID-19-associated deaths, and linked vaccine and COVID-19 mortality data from 30 U.S. States. We describe the construction and interpretation of these data in Section 2.

Our estimate rests on two central premises. First, due to the immune evasion capabilities SARS-CoV-2, the overwhelming majority of Americans would have become infected with SARS-CoV-2 by Feb. 2024 under any realistic vaccination and behavioral mitigation scenario. Second, the health risk of a person's first infection, when unvaccinated, is vastly higher than one's risk after having been vaccinated or previously infected. Thus, the benefit of behavioral mitigation and vaccination came principally from vaccinating individuals before their first SARS-CoV-2 infection. The serology data depicted in Figure 1 indicate that slightly more than two-thirds of the U.S. population were vaccinated prior to their first infection with SARS-CoV-2; it is this group that principally contributes to our estimate of lives saved.

In support of these premises, an estimated 94% of Americans had been infected with SARS-CoV-2 by late 2022, despite the behavioral mitigation and vaccine uptake in the preceding years (Klaassen et al. (2023a)). Population-level data on COVID-19 mortality for those who had been vaccinated versus those who had not been vaccinated gathered from 30 U.S. states with linked mortality and vaccine data and shown in Figure 2 are consistent with the view that COVID-19 was extremely dangerous for those who contracted it for the first time without the protection from vaccines. For those contracting COVID-19 after vaccination or prior infection, the disease is much less dangerous.

Based on these premises, we construct both a back of the envelope calculation of the lives saved by mitigating behavior and vaccines and an estimate from a structural epidemiological model that takes into account behavior, decline in the COVID-19 infection fatality rate over time, and waning immunity against both reinfection and severe disease. The back of the envelope calculation, which conjectures that the 68% of Americans that managed to get vaccinated prior to their first COVID-19 infection would have suffered an infection fatality rate four times higher had they not been vaccinated, leads us to an estimate of 845,000 lives saved.

We develop a full structural model to delve a bit deeper into this calculation and set ourselves up for conducting counterfactual exercises. The model combines a fairly detailed epidemiological description of the various variants of COVID-19

that have appeared over the past four years with a simple model of how mitigating behavior reacts to the rise and fall of daily deaths from the disease as well as parameters governing the administration of vaccines.[1] We argue that this model fits both the dynamics of the data on COVID-19 deaths (see Figure 5) and the dynamics of the serology data on infections and vaccinations (see Figure 6) quite well.

We then simulate the model with vaccines turned off to arrive at a counterfactual prediction for the dynamics of COVID-19 deaths in the absence of vaccines shown in Figure 7, with results for cumulative mortality in our baseline and this counterfactual reported in Table 1. The use of the full structural model with its added detail delivers our preferred estimate of just under 800,000 lives saved.

1.2 Four Lessons

We then draw out four lessons for future pandemics from these data and our counterfactual modeling exercises.

Lesson 1: First, we argue that it was the combination of mitigating behavior and vaccines together that saved lives.

To illustrate this point, we conduct two counterfactual model simulations.

We simulate our model with its baseline specification of mitigating behavior but without vaccines. Without vaccines, behavior alone would have postponed infections, but, in the end, nearly everyone would have been infected and subject to a high infection fatality rate from that first infection. We show the dynamics of COVID-19 deaths in this counterfactual scenario in Figure 7 and the counterfactual scenario for infections in Figure 8.

We find in this scenario with baseline behavior but no vaccines that cumulative mortality from COVID-19 over the past four years would have been 1,975,000 rather than the 1,180,000 in our baseline simulation. It is the difference of 795,000 deaths between these two outcomes that gives us our preferred estimate that vaccines and behavior together saved nearly 800,000 lives.

We then simulate our model with vaccines distributed starting at the end of December 2020, but with no mitigating behavior before that time. In this counterfactual simulation, we see that, without a behavioral response, vaccines would have come too late to save lives. We show the dynamics of COVID-19 deaths in this counterfactual scenario in Figure 9. Our model implies that cumulative COVID-19 deaths would also have been substantially higher in this scenario without mitigation because our serology and deaths data imply that COVID-19 was substantially more dangerous in 2020 than in 2021, and most

[1] We have presented versions of this model in earlier work including Atkeson (2021a), Atkeson (2021b), and Atkeson (2023b).

infections in this scenario would have occurred in 2020.

One might be tempted to use this scenario of an unmitigated epidemic as a benchmark against which to argue that the combination of vaccines and behavior together saved over 2 million lives. We argue that such a comparison would be an overstatement as it seems highly implausible that there would be no private efforts to avoid transmission even in absence of any public mitigation policies. The model simulation of an unmitigated epidemic has the daily death toll peaking at over 60,000 deaths per day. It seems highly likely that people would have reacted on their own to such an outcome even in the absence of any public policies towards the epidemic.

We summarize our model's implications for cumulative mortality from COVID-19 in our baseline model simulation and these two counterfactual simulations in Table 1.

Lesson 2: This success of delaying infections for many months through changes in behavior was a surprise relative to historical experience and modeling of pandemic influenza. We discuss our basis for saying this in Section 4.2. We take, however, as the strongest piece of evidence in favor of this claim the conclusion of Ferguson et al. (2006), a prominent study of mitigation options for a pandemic influenza in the United states, regarding the timing of administration of vaccines that these vaccines would have "almost no effect" if started after 120 days after the first world-wide case because at this time horizon they would be too late to save lives. Clearly, mitigation of COVID-19 bought us many more than 120 days for vaccines to have a significant impact on COVID-19 cumulative mortality.

Lesson 3: To a remarkable extent, this strong behavioral response to COVID-19 through 2020 and 2021 was universal across all 50 states. Certainly there are significant differences in cumulative mortality from COVID-19 across states, but we argue that the outcomes across U.S. states have much more in common than any of them (except New York City) have with the predicted impact of an unmitigated epidemic. We discuss this point in greater detail in Sections 4.3 and 6. We take the data shown in Figure 10 for the dynamics of state-level effective reproduction numbers and that in Figure 11 for serology data on state-level dynamics of infections and vaccinations as the primary pieces of evidence for this conclusion.

We see in these figures that mitigation efforts succeeded in dramatically slowing the growth of the epidemic very rapidly in all 50 states and in slowing the growth of cumulative infections well into 2021 as strong evidence of the importance of an endogenous behavioral reaction to current disease incidence as predicted by many economic models.[2] And, yet, this observation leads us to our fourth lesson.

[2]See, for example Atkeson (2021b), Gans (2022), and Atkeson, Kopecky, and Zha (2023) and the papers cited therein.

Lesson 4: It is unclear what behavioral reaction to expect in response to the next epidemic.

Epidemiologists have noted the impact of changes in behavior on the dynamics of prior epidemics, particularly in attenuating the initial phase of exponential growth of infections predicted by simple epidemiological models.[3] But figuring out how to predict the quantitative impact of such changes in behavior and how private behavior will respond to public health measures has proved an unsolved challenge.[4]

We see any successful theory of behavior as having to confront a wide range of data across different epidemics. For example, as noted above, the success of public and private changes in behavior in slowing the spread of COVID-19 came as a surprise relative to past experience. And yet, as we see in Figure 13, New York City suffered a terrible first wave of deaths from COVID-19 early on in the pandemic largely due to a delayed reaction to the disease despite clear warnings from the Italian experience a few weeks earlier. Somehow the evidence of COVID in New York City seemed to have a much bigger impact on behavior elsewhere in the U.S. than did the European experience despite objective evidence that air travel links were likely to spread the disease across the globe.

Of particular concern is the question of how our collective experience with COVID-19 over the past four years will influence behavioral responses to the next pandemic for perhaps a generation or more.

And changes in behavior can take many forms. Will these changes be transitory, as appears to have been the case with COVID-19, or longer lasting? As we discuss in Section 4.4, we have seen with the recent Mpox (formerly known as Monkeypox) epidemic that longer lasting behavioral changes appear to have played an important role in driving the effective reproduction number of this disease below one for a sustained period of time, dramatically limiting the impact of this disease and allowing it to be contained with vaccines and traditional public health measures. What accounts for a persistent as opposed to transitory behavioral response? We see these as important questions for future research.

In Section 5, we examine the impact of uncertainty about some key parameters on our estimate of lives saved. We also compare the implications of our model to other estimates of lives saved in the literature.

Following Jia et al. (2023), we examine the impact of increased vaccination coverage on cumulative mortality from COVID-19. The pace of vaccination slowed considerably after the summer of 2021. As a result, many who had neither been vaccinated nor previously infected ended up being infected with the Delta or Omicron variants in the Fall of 2021 and into late February 2022 leading to

[3]See, for example, Chowell et al. (2016) and Eksin, Paarporn, and Weitz (2019).

[4]See, for example, Ferguson (2007) and Funk et al. (2015).

additional deaths that could have been averted with vaccines. We estimate that this failure to expand vaccination coverage in the second half of 2021 cost an additional 273,000 preventable deaths.

We also compare our model's implications to estimates of the impact of vaccines on COVID-19 mortality in Steele et al. (2022) and estimates produced by the Commonwealth Fund using a model described in Moghadas et al. (2021).

In Section 6 we look more closely on the cross-section of outcomes for COVID-19 infections, vaccinations, and deaths across U.S. states. We use our model to argue that the range of outcomes observed are consistent with plausible variation either in the strength of the behavioral reaction or in state-specific structural factors impacting transmission rates. Disentangling the importance of these factors as well as state-level variation in infection fatality rates is something we leave for future research.

In Section 7 we lay out more specifically the types of investments in data infrastructure that we believe would be useful in preparing to do more targeted mitigation in the next pandemic.

Finally, in Section 8, we conclude.

2 Serology and Mortality Data

In this section, we review the serology data and the data on mortality from COVID-19 that we use in choosing parameters for our model and constructing our estimate of the impact of behavior and vaccines on cumulative mortality from COVID-19.

2.1 Serology Data

The serology data we use are drawn from two surveys.

As described in Jones et al. (2021), the CDC measured SARS-CoV-2 seroprevalence (the population-level prevalence of immune markers in the blood) from 2020-2022 by testing for antibodies against two distinct viral antigens in samples from blood donors. One of these antibody types (against type "S" antigen) is generated in response to either a prior infection or vaccination. The other antibody type (against type "N" antigen) is generated only in response to prior infection. Thus, with some caveats,[5] the pair of positive or negative results for each sample allows one to measure whether the individual making the blood donation had been previously infected (with or without vaccination), vaccinated without prior infection,

[5]Such caveats include waning immunity, which can cause a previously infected or vaccinated person to test negative on one or both of the antigen tests, and heterogeneity in the immune response, in which a person can mount an abnormally low immune response to the "N" antigen despite being infected. See also Ong et al. (2021)

or neither vaccinated nor previously infected. We refer to this survey as the Blood Donor Survey.

As described in Bajema et al. (2021), serology data was also collected from samples from commercial blood testing labs. These data measure only whether the person giving the sample had previously been infected. We refer to this as the Commercial Lab Survey.

We note that both of these serology surveys are drawn from different convenience samples — one a sample of blood donors and the other a sample of those having blood drawn as part of their medical checkups or care. We check for consistency of the measure of those infected across these two sources. Unfortunately, no serology data from a sample designed to be representative of the population is available.

In Figure 1, we show the results of the Blood Donor and Commercial Lab serology surveys at the national level for the overall population. The red crosses in each figure show estimates from the Blood Donor survey of the cumulative percentage of the population that had experienced infection by the survey date (showing a response to the "N" antigen). The yellow stars in each figure show estimates from the Commercial Lab survey of the cumulative percentage of the population that had experienced infection by the survey date. We see in these figures that these two separate serology surveys give consistent estimates for the percentage of the population infected at least through the first Omicron wave in early 2022.

The blue circles in each figure show estimates from the Blood Donor survey of combined seroprevalence. That is, it adds to the percentage showing a response of the "N" antigen, the percentage of those showing a response to the "S" antigen but not the "N" antigen. This second group is presumed to be vaccinated but never infected. That is, these blue circles show the sum of those showing antibodies from infection (whether or not they also have been vaccinated) and those showing antibodies from vaccination but not from infection.

Several features of these serology survey data stand out. First, we see that the estimated cumulative percentage of the population infected as of January 2021 was quite low — well below 20% for the overall population. That is, efforts to slow the spread of COVID through 2020 appear to have succeeded in holding cumulative infections to a level that New York City achieved quite quickly at the start of the epidemic and to a much lower level than was attained by the end of 2022.

We see from the gap between the blue circles and the red crosses that the rapid deployment of vaccines succeeded in vaccinating a large portion of the population prior to first infection by the late summer of 2021. Consistent with this rapid deployment of vaccines in the first half of 2021, we see slow growth in the estimate of cumulative infections between January 2021 and July of that year. From the start of 2021 through the summer of that year, the combination of behavior and

vaccinations appeared to be on a path of ending the epidemic.

Unfortunately, due to the combination of new variants (Delta and Omicron) and waning of the immunity provided by vaccines and prior infection, in the fall of 2021, we see infections continue to rise, particularly so in 2022. Given that variants of Omicron have continued to show the ability to infect those who had previously been vaccinated (and reinfect those with prior infections), it is likely that by early 2024, an overwhelming majority of the population has experienced a COVID infection. That is, considerations of herd immunity that were prominently discussed early on in the pandemic have turned out ex-post not to be relevant due to a combination of immune evasion by new variants and waning immunity.

2.2 Mortality Data

We now turn to our data on mortality from COVID-19. We draw these data from the CDC's COVID Data Tracker Website.[6] This data set counts deaths from COVID-19 both the national and state levels, with deaths for New York City broken out separately.

Figure 3 shows weekly COVID deaths for the United States as a whole over the past four years. The number of deaths is shown on the left axis. The weekly death rate per 100K population age-adjusted is shown on the right axis.[7] As shown this figure, the COVID epidemic in the United States has played out in a series of waves, particularly over the first two years of the epidemic. While these waves garnered considerable attention at the time, what we find most striking about this pattern is that, from very early on in the epidemic, cumulative COVID deaths grew roughly linearly, as shown in Figure 4. This linear growth of cumulative deaths is clearly faster in the first two years of the epidemic (from February 2020 through February 2022) than in the second two years of the epidemic.

Why do we find the linear growth of cumulative COVID deaths over the past four years striking? What is missing in Figure 4 is any substantial initial period of exponential growth of cumulative deaths as would be predicted by standard epidemiological models for a novel pathogen. To our minds, this observation of linear growth in cumulative deaths sustained over a four year period is one of the most remarkable features of the COVID epidemic in contrast with historical experience with influenza and the predictions of many epidemiological models. In our model, this outcome is attributed to the strength of the public and private behavioral responses to mitigate transmission of the COVID-19 virus.

[6]The data can be downloaded from `https://data.cdc.gov/NCHS/Provisional-COVID-19-death-counts-rates-and-percen/mpx5-t7tu/about_data`.

[7]The CDC outlines its method for age-adjusting death rates here `https://www.cdc.gov/nchs/hus/sources-definitions/age-adjustment.htm`.

2.3 Implied Infection Fatality Rates

Note that these serology and deaths data together imply that the infection fatality rate for COVID-19 declined over the course of 2020 and 2021 and then again with Omicron. In particular, the Blood Donor and Commercial Lab surveys give identical estimates that 11.5% of the U.S. population had been infected in the December 2020 edition of these surveys. The cumulative COVID death toll by the end of 2020 was close to 390,000. Given a U.S. population of 332 million, this would imply an overall infection fatality rate close to 1%.

Looking at the same numbers prior to the first big Omicron wave, in the November 2021 edition of these surveys, the Blood Donor survey estimated that 27.8% of the population had been infected and the Commercial Lab survey estimated that 31.6% of the population had been infected, while the CDC estimates that just over 800,000 Americans had died of COVID by the end of November 2021, implying that close to 61 million Americans were infected with COVID between January 1 and November of 2021 (if we take 30% infection-induced seroprevalence as our estimate for November 2021). These numbers imply an infection fatality rate closer to 0.66% over the course of 2021 prior to Omicron. The equivalent numbers after the first large Omicron wave show a substantial further decline in the implied infection fatality rate. We use these estimates as a guide for parameterizing the infection fatality rate in our model. We discuss the sensitivity of our results to these assumptions in Section 5.

2.4 Mortality by Vaccine Status

There are many clinical studies of the effectiveness of vaccines in protecting against severe disease and death. We do not review that evidence here. Instead, we make use of population level data on the realized COVID mortality rates of the vaccinated and unvaccinated. As discussed in Jia et al. (2023), 30 states of the United States integrated their vaccine databases with their reporting of mortality data. Thus, for these states, on a weekly basis, one can measure the number of COVID related deaths among those who had received the two doses of the primary series of vaccines at least 14 days before death and COVID deaths among those who had not received these primary vaccines. The CDC also estimates the number of people in these states in these two groups, and thus one can construct a weekly COVID mortality rate for the vaccinated and unvaccinated populations.

In the left panel of Figure 2, we show data on the weekly age-adjusted COVID mortality rates for those with two doses of a primary vaccine (from the first half of 2021) at least 14 days prior to death (in blue) and those without this protection from vaccines (in orange).[8] The dates given on the x-axis are the year and week

[8]We use the data available here `https://data.cdc.gov/Public-Health-Surveillance/`

number used in the CDC's Mortality and Morbidity Weekly Review (MMWR). We see in this figure that the weekly mortality rate for the unvaccinated was much higher than for the vaccinated in 2021. After the first big Omicron wave, the weekly COVID mortality rate for the unvaccinated falls to meet the low mortality rate for the vaccinated.

In the right panel of Figure 2, we show the ratio of these two mortality rates. We see in the panels of this figure that vaccination reduced the COVID mortality rate on the order of 85% until the first Omicron wave. After that first Omicron wave, we see that the difference in mortality rates by vaccination status was much smaller. We conjecture, based on the serology data, that this outcome arose as the majority of the unvaccinated had come to have the protection of a prior COVID infection. Thus, the mortality rates for the unvaccinated fell to a level much closer to that for the vaccinated as both groups were largely protected after this first Omicron wave.

Figure 15 shows data on deaths by vaccine status from the same data source broken down by age. This figure is from Jia et al. (2023). We can see that vaccines played a particularly important role in protecting the elderly.

In our model, we match the observation that some of those who were vaccinated died from COVID-19 with the assumption that for some fraction of the vaccinated population (75%), protection against severe disease was complete, while for the remainder of the vaccinated population (25%), vaccination failed to provide any protection against severe disease. We take this as a simplified method for capturing partial vaccine effectiveness.

2.5 Waning Immunity and the Long Tail of COVID Deaths

With the emergence of Omicron variants we have seen that both vaccines and prior infection provide only temporary protection against new infections. As a result, the prevalence of COVID infections has remained high over the past two years despite the fact that by the end of the first quarter of 2022 the overwhelming majority of the U.S. population had already been vaccinated or experienced a prior COVID infection or both.

This outcome is a result of two factors. One is that the protection offered by vaccines and prior infection against re-infection wanes over time. The other is that the continual evolution of the virus allows new versions of it to evade immune defenses. After two years of Omicron and three years of experience with mRNA vaccines, it is clear that both processes are at work with COVID. Both

Rates-of-COVID-19-Cases-or-Deaths-by-Age-Group-and/d6p8-wqjm/about_data.

processes also play an important role in seasonal influenza. It is unclear the relative importance of these two forces for COVID. See, for example, Jung et al. (2023).

In our model we capture these two processes of waning immunity (or immune evasion) against infection and waning immunity against severe disease separately. To capture the relatively rapid risk of re-infection with Omicron, we model breakthrough infections that have a low infection fatality rate. To capture the slower process of waning immunity against severe disease, we model agents as losing their immunity and facing the same risks as a person who has never been exposed to COVID at a slow rate. It is this second process that largely accounts in the model for the long tail of COVID deaths that we see over the past two years.

We now turn to a description of our model.

3 Summary Description of The Model

We now present our structural model of the impact of behavior and vaccines on cumulative mortality from COVID in the United States over the period February 15, 2020 to February 15, 2024. This model extends that in Atkeson (2023b). A full description of this model is given in Appendix A.

3.1 Purpose and Fit of the Model

Recall that our estimate of the impact of behavior and vaccines on cumulative COVID mortality is based primarily on an accounting of the number of Americans who were able to get vaccinated prior to their first COVID infection, and to a lesser degree on an estimate of the benefits of delaying infections due to a decline over time in the infection fatality rate of COVID-19. We see this model as a formal accounting device to take into account the dynamics of the COVID infection fatality ratio implied by the serology data and the transition of the epidemic towards an endemic steady-state.

Thus, while we do not formally estimate the parameters of this model, we do evaluate it as an accounting device on the basis of its fit to the dynamics of COVID-19 infections and vaccinations at the national level as measured by the serology data in Figure 1 as well as the dynamics of deaths from COVID-19 at the national level as shown in Figures 3 and 4.

To that end, we show the fit of our model to the dynamics of COVID-19 deaths in Figure 5, with the model fit to cumulative COVID-19 deaths shown in the left panel and the fit to weekly COVID-19 deaths in the right panel.

We show the model fit to the serology data in Figure 6. The left panel of Figure 6 compares the model estimate of the fraction of the population with protection from severe disease due to prior infection taking into account waning immunity

as described below (this fraction can be either vaccinated or not) to the serology data on the fraction of the population showing antibodies from prior infection.

The right panel of Figure 6 compares the model estimate of the fraction of the population showing antibodies from vaccination but not prior infection, again taking into account waning immunity as described below, to the serology data on the fraction of the population showing antibodies from vaccination but not prior infection.

In these three figures, we see that the fit of the model with its baseline parameters to the dynamics of infections, vaccinations, and deaths is quite good.

We then use this model to conduct several counterfactuals to estimate the impact of behavior and vaccines on cumulative mortality from COVID-19 in the United States over the past four years. It is here that the structure of the model is harder to assess as we do not observe these counterfactual outcomes in the data. As we describe the model, we aim to describe what features of the data that we do observe allow us to "identify" the key parameters driving our model's implications for these counterfactuals. In particular, we focus on describing why we have some confidence in our choices for the parameters governing the nature and strength of the behavioral response in the model.

3.2 Model Structure

The model is an SEIHRS model with waning immunity and introduction of the Alpha, Delta, and Omicron variants as the epidemic progresses. This model extends the workhorse SIR epidemiological model in several dimensions. We explain the reasons for these extensions after reviewing some basic epidemiological concepts.

To begin, a standard SIR model of an epidemic views the population at any point in time as being divided into three categories: susceptible to infection $S(t)$, currently infected and capable of spreading the disease $I(t)$, and resistant to the disease $R(t)$ either from natural immunity (including that induced by prior infection) or from vaccination.

This distribution of characteristics across the population is assumed to evolve over time as follows. Those that are currently infectious ($I(t)$) are assumed to stop being infectious at rate γ per unit time. A fraction η of those who stop being infectious do so because they die. We thus refer to η as the *infection fatality rate*.

Those currently infectious encounter other agents in the population at random and transmit their disease to those agents met at a rate $\beta(t)$ per unit time. We refer to $\beta(t)$ as the *transmission rate*. We allow the transmission rate to depend on factors inherent to the pathogen and the environmental location as indicated by a parameter $\bar{\beta}$ as well as time dependent factors such as seasonality and behavioral responses.

Since the expected length of time that an infectious agent is expected to be in this state is $1/\gamma$, the average number of agents that an infectious person will transmit their disease to is given by $\beta(t)/\gamma$. Since only fraction $S(t)$ of those agents are actually susceptible to the disease, the expected number of new infections caused by a single infectious agent is given by what is called the *effective reproduction number*

$$\mathcal{R}_{eff}(t) = \frac{\beta(t)}{\gamma} S(t)$$

Note that the average length of time that an infectious agent remains infectious (here $1/\gamma$) in this model also corresponds to the average length of time between one individual becoming infectious and subsequent infections caused by that individual. This length of time is referred to as the *generation interval*.

The effective reproduction number is related to the SIR model implied growth rate of the fraction of the population that is infectious by

$$\frac{\dot{I}(t)}{I(t)} = \left(\mathcal{R}_{eff}(t) - 1\right) \gamma$$

where $\dot{I}(t)$ denotes the derivative of infections with respect to time.

We note two points from this formula. First, we see that the question of whether epidemic (in terms of $I(t)$) is growing or shrinking over time is determined by whether the effective reproduction number is above or below one.

Second, the speed of growth of infections per unit time is determined both by the effective reproduction number and the generation interval. Thus, to match data on the growth rate of infections (or deaths) per unit time, one must take a stand on these two parameters. In our model, we hold the generation interval fixed across variants and aim to match the dynamics of weekly deaths in the data with differences in inherent transmissibility of different variants, a seasonal influence on transmissibility, and a behavioral response to the current level of deaths.

We now explain the dimensions in which we extend this simple model and why we do so. We then review our choices for parameter values, with a focus on the generation interval, infection fatality rates, transmission rates, and the impact of behavior on these transmission rates.

We add compartments to the simple SIR model as follows. We add both an exposed state E and the hospitalized state H. Agents in the exposed state have contracted the disease but are not yet infectious. This is a common modification of the SIR framework. Inclusion of this state enriches the dynamics of initial growth of the epidemic. We describe below the purpose of the hospitalized state H. We also add a vaccinated state V to count those who have been vaccinated prior to their first COVID infection. In terms of protection against infection and severe

disease, this state is equivalent to the R state counting those with immunity from prior infection.

To allow for different COVID variants to have different transmission rates and different infection fatality rates, the compartments E and I are further broken down by variant i, where i indexes the original variant, and the Alpha, Delta, and Omicron variants.

The rate at which agents leave the E_i compartment for both the normal and more transmissible variants is σ and the rate at which agents leave the I_i compartments for all variants is γ. We also include compartments E_i and I_i corresponding to those experiencing breakthrough Omicron infections. These individuals are modeled as having immunity to previous variants but not to Omicron. The purpose of these additional states is to allow the infection fatality rate for breakthrough infections to differ from that of other infections.

With these assumptions, the mean generation time for the model is then $1/\sigma + 1/\gamma$. We set this generation time in line with estimates from the CDC.[9] As mentioned above, this generation time sets the time-scale of the epidemic implied by the model.

3.3 The Model of Behavior and Disease Transmission

We use an ad-hoc model of the impact of behavior on transmission rates. Specifically, the reduced-form for the behavioral response of the transmission rate to the level of daily deaths is given by

$$\beta_i(t) = \bar{\beta}_i \exp(-\kappa(t)\frac{dD(t)}{dt} + \psi(t))$$

where the parameters $\bar{\beta}_i$ control the inherent transmissibility of the original and subsequent variants of COVID, the parameter $\psi(t)$ is used to introduce seasonality in transmission, and $\kappa(t)$ is the semi-elasticity of transmission with respect to the level of daily deaths. Thus, public and private behavior impacting transmission is assumed to respond only to the current level of daily deaths.

Five comments regarding this model of behavior are in order.

1. First, we have assumed that behavior reacts to the current level of daily deaths. As described in Atkeson (2021b), this form of behavior serves to regulate the effective reproduction number and drive it down to one in the initial phase of the epidemic and then keep it close to one for the remaining

[9] See `https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html`. On that webpage, the CDC notes a mean time of approximately six days between symptom onset in one person to symptom onset in another person infected by that individual.

course of the epidemic. More specifically, such behavior regulates the model-implied growth rate of cumulative deaths to remain roughly constant over time. We argue throughout this paper that this outcome of roughly linear growth of cumulative COVID deaths is one of the most striking features on the data on COVID deaths, not only in the United States, but around much of the world. While this outcome might be predicted by economic theory, it is not universally observed across epidemics. For example, as we disucss elsewhere, mitigating behavior seems to have taken a different, and more persistent form, in the recent Mpox epidemic. Thus, it is not clear that behavior will take the same form in the next epidemic.

2. Our second comment concerns the role of the dual assumptions that behavior responds to the daily death rate and not the level of infections and that, due to the presence of the H compartment, daily deaths are essentially a distributed lag of past levels of $I(t)$. As discussed in the appendix of Atkeson (2021b), these assumptions appear to be remarkably successful in allowing the model to match the size of the waves of COVID deaths with each new variant over the past four years. Models in which behavior reacts to the level of infections directly or that do not include this lag have difficulties in matching the size of these waves as, in these cases, behavior is too successful at keeping the effective reproduction number close to one. That is, mitigating behavior reacts so quickly to changes in the level of infections that waves are cut off. On this point see Droste and Stock (2021) and Atkeson, Kopecky, and Zha (2021).

3. Third, we see the introduction of new variants as exogenous shocks to transmission rates that allow us to identify the strength and timing of the behavioral response of the model. We thus take the observation that the model can match the size and shape of the waves of deaths associated with the introduction of the Alpha, Delta, and Omicron variants as validation of the parameter choices governing the behavioral response in the model, including the delay induced by the H compartment. Moreover, we take from the Omicron wave in which new infections spiked much higher than in previous waves and much higher than deaths did as validation of the assumption that behavior responds to deaths and not infections

4. Fourth, the waves of COVID-19 deaths shown in Figure 3 appear to have a seasonal pattern, with summertime lows, that we match with our seasonal factor $\psi(t)$ chosen to follow a sine wave, and

5. Fifth, ideally, one would want to build a model in which agents are fully rational and make decisions about their mitigation behavior, particularly for

understanding behavioral responses in the counterfactuals that we consider. To build such a model, however, one must take a stand on what agents believe about the risks that they face from the disease, and this can be hard to do in real time. Moreover, it might also be difficult to incorporate the delayed responses of behavior that appear to be critical in reproducing the dynamics of the epidemic that we have observed. We leave these challenges to future research.

Fitting this model to the data has been an ongoing project starting with a first version in Atkeson (2021a). The goal has been to explore whether one could account for the dynamics of the COVID-19 epidemic with a simple model with a stable formulation of behavior.

In previous work and in this model, we find that the strength of the response of public and private behavior impacting transmission to the level of daily deaths as indexed by $\kappa(t)$ appears to have relaxed in the late fall of 2020 and then remained consistent since then. Specifically, we choose an initially high value of $\kappa(t)$ for the period February 15, 2020 until November 2020, and then $\kappa(t)$ declines to a new level equal to 35% of its intial value. We refer to this apparent relaxation of behavior in the face of the level of daily COVID deaths as "fatigue". We find that this one-time change in behavior in our model is required for the model to match the height of the waves of COVID in late 2020 and beyond.[10] This formulation of behavior was chosen early on in this modeling process starting with the first version of this model in February of 2021 and has been kept constant since that time.

3.4 Key Parameters

We set the infection fatality rates for the COVID variants prior to Omicron to be a declining function of time. As discussed above, the serology data estimates for the percentage of the population infected as of the end of 2020 and the data on cumulative deaths at that time imply an infection fatality rate of 1% for 2020. We use that value for this time period. The corresponding infection fatality rate implied by the serology and deaths data for 2021 period to prior Omicron is 0.5%.

To match the big jump in infections with the first Omicron wave with an increase in deaths that is modest in comparison to what would have happened if Omicron was as deadly as prior variants, we use a lower infection fatality rate of 0.15% for those infected out of the S compartment. We also allow Omicron to infect those in the R compartment (those with protection from prior infection or

[10] Andersson et al. (2021) and Gaetano et al. (2023) argue that the impending arrival of effective vaccines may have caused such a relaxation of behavior.

vaccination) with a very low infection fatality rate. We refer to such infections as *breakthrough infections*.

Having chosen these parameters, we choose the parameters for inherent transmissibility $\bar{\beta}_i$ to match the dynamics of the waves of deaths associated with each of them. As described in the Appendix, these parameters imply a relative transmissibility across variants indexed by the ratio of these parameters that is in line with established estimates.

In modeling the transmissibility of Omicron, one must set two parameters — the constant $\bar{\beta}_i$ reflecting its inherent transmissibility and a parameter governing the probability that a vaccinated or recovered individual suffers a breakthrough infection. These two parameter combine to give Omicron a growth advantage over Delta. There is considerable uncertainty regarding the relative importance of these two parameters. We choose them to match data from South Africa that Omicron had a growth advantage of a factor of three relative to Delta in a population with 85% protected by prior immunity as well as our serology and deaths data in that first Omicron wave. We find that our model's implications for the first wave of Omicron deaths are largely invariant to the particular choice of $\bar{\beta}_i$ for Omicron. What does vary as this parameter is varied (and the probability of a breakthrough infection modified to keep the growth advantage of Omicron over Delta at 3 times) is the size of the wave of initial Omicron infections. We have chosen a pair of parameters to match this growth advantage for Omicron and this wave of infections as indicated in the serology data.

To model the impact of vaccines, we set the rate at which susceptible agents are moved from the S compartment directly to the V compartment equal to $\lambda(t) = 0.0065$ starting on January 1, 2021 and zero before that date. Vaccines are administered at this rate for the first 185 days of 2021. The rate of vaccination then drops to $\lambda(t) = 0.0065/5$ until the end of 2022 and then $\lambda(t)$ is set to zero after that. In the model, the V compartment is equivalent to the R compartment and is simply used to count vaccinations prior to infection.

In our model, agents in compartment $V(t)$ enjoy full protection from infection by the Alpha and Delta variants and substantial protection against death from Omicron in the same way as agents with prior infection (in the R compartment). Thus, we regard the number of agents in this compartment as representing the population that is both vaccinated prior to a first COVID infection and that gained protection from that vaccination. To model that vaccines are not 100% effective, we assume that the portion of those who actually arrive in the V compartment is 75% of the total vaccinated. Thus, when we compare the model implications for $V(t)$ to the measures from the serology data on those vaccinated but not infected in Figure 6, we plot $V(t)/0.75$ as a measure of the total population vaccinated.

We assume that agents flow out of the V and R compartments back to the

S compartment thus and become susceptible again to severe disease at a rate corresponding to expected duration of protection against severe disease of 3 years. Because Omicron can also infect those in the R and V compartments with breakthrough infections (but with a much lower infection fatality rate), our model allows protection against reinfection to wane much faster than protection against severe disease. It is this second process that largely accounts in the model for the long tail of COVID deaths that we see over the past two years. Both estimates for the speed of waning are subject to considerable uncertainty.

4 Main Model Results: Four Lessons

We now use the model to conduct counterfactual experiments to explore the impact of behavior and vaccines on cumulative mortality from COVID-19 in the United States over the past four years. We focus on drawing four lessons from them model.

The first of these lessons is that behavior and vaccines together saved close to 800,000 lives. Without vaccines, behavior would have had a much smaller impact on cumulative mortality. Without behavior, vaccines would have come too late to save lives.

The second lesson is that the effectiveness of behavior in slowing transmission in 2020 and 2021 was a surprise relative to historical experience with pandemic influenzas and model implied scenarios for the impact of mitigation on transmission of such a pandemic influenza.

The third lesson is that the strong behavioral response mitigating transmission was common to all fifty states. That is, in terms of their responses to COVID-19, the states have more in common with each other than they do with historical experience or pre-COVID model-implied outcomes with pandemic influenza.

The fourth lesson is that while this strong behavioral response to COVID did buy considerable time to develop and distribute effective vaccines, it is unclear whether the response will be the same in the next pandemic.

We now flesh out each of these lessons in turn.

4.1 Lesson 1: Behavior and Vaccines Together

As discussed above, we show our model's baseline implications for the dynamics of COVID-19 deaths, infections, and vaccinations in Figures 5 and 6. We show the model's implications for cumulative COVID-19 mortality over the four year period from February 15, 2020 to February 15, 2024 in the first row of Table 1.

We show the model implications for COVID deaths with the baseline parameters governing behavior but with no vaccines in Figure 7 and in the second row of Table 1. As indicated in the second row of Table 1, the model implies that

absent vaccines, the cumulative death toll over the past four years would have been 1,975,000. That is, our model implies that, given baseline behavior, vaccines saved 795,000 lives. We take this as the headline result of this paper.

We see in Figure 7 that most of these additional deaths would have occurred in 2021. That is, after the first big Omicron wave in early 2022, the model implications for COVID deaths with and without vaccines are nearly the same. This is because, in the absence of vaccines, the model implies that close to 95% of the population would have experienced their first COVID infection by the end of that first Omicron wave and thus the level of population protection against severe disease after that point would have been similar with or without vaccines. This prediction of our model for the dynamics of infections in the absence of vaccines is shown in Figure 8.

In our model, we assume that vaccination reduced the infection fatality rate from first infection with COVID in 2021 from 0.005 to 0.0013 (or 25% of the IFR for the naive unvaccinated).[11] Thus, to understand our counterfactual estimate of the COVID death toll in the absence of vaccines, imagine that this 68% of the population had instead been infected without the protection of vaccines and had, as a result, suffered the full infection fatality rate of 0.005 rather than 0.0013. Had this occurred, the counterfactual death toll from COVID in the absence of vaccines would have been 847,000 higher than the baseline with vaccines. [12] Our full model delivers a slightly lower estimate of lives saved due to the arrival of Omicron in late 2021, which had a lower infection fatality rate than prior variants, and the assumption that the protection against severe disease offered by vaccines (and prior infection) wanes over time. But one can clearly see from this calculation the simple logic underlying our estimate of the impact of behavior and vaccines on cumulative mortality from COVID-19 in the U.S.

These blood serology data highlight how important the interaction of behavior change and vaccine development and deployment were in saving lives. Had SARS-CoV-2 swept through the U.S. population in an unmitigated epidemic, it is likely that the overwhelming majority of the U.S. population would have been infected by early fall of 2020, leaving much less room for people to benefit from being vaccinated prior to their first infection.

We illustrate this point in Figure 9 in which we simulate the model with the behavioral parameter $\kappa(t) = 0$. In this simulation, the vast majority of the U.S. population gets infected by the late summer of 2020.[13] We report the implied

[11] Recall that we assume that 25% of those who receive a vaccine do not end up with protection, while the other 75% gain complete protection until either their immunity wanes or they suffer a breakthrough infection with Omicron.

[12] The calculation is 0.68*0.75*0.005*332000000 where the last term is the U.S. population.

[13] Our results for the cumulative mortality of an unmitigated epidemic during 2020 are worse than those in Ferguson et al. (2020) in part because our estimate of the basic reproduction

cumulative death toll in the third row of Table 1. Here we see an extraordinary model-implied death toll, consistent with an infection fatality rate of 1% applied to nearly the entire U.S. population in 2020 together with subsequent deaths in later years due to waning immunity.

Clearly, any estimate of lives saved depends on the assumed counterfactual. How should this impact our thinking about the next pandemic? From an ex-ante perspective as of March of 2020, the other premises on which our ex-post estimation is based would have been hard to predict. Was it going to be possible to delay transmission for the time required to develop and deliver effective vaccines? If vaccines had taken much longer to arrive or had offered less protection against severe disease, would the whole exercise of slowing transmission have been a wasted effort?

Based on these simulations comparing the death toll with baseline behavior and no vaccines to that with no mitigating behavior, we argue, in short, no – as such mitigation efforts would have still helped to reduce strain on a severely overburdened healthcare system and bought critical time to learn how to better care for patients with severe disease even in the absence of vaccines. Such considerations are important to bear in mind when considering which behavioral interventions should be adopted. Without behavioral responses to the epidemic an unmitgated epidemic would have been much more severe than even our counterfactual with behavior but without vaccines.

One might be tempted to use this scenario of an unmitigated epidemic as a benchmark against which to argue that the combination of vaccines and behavior together saved over 2 million lives. We argue that such a comparison would be an overstatement as it seems highly implausible that there would be no private efforts to avoid transmission even in absence of any public mitigation policies. The model simulation of an unmitigated epidemic has the daily death toll peaking at over 60,000 deaths per day. It seems highly likely that people would have reacted on their own to such an outcome even in the absence of any public policies towards the epidemic.

4.2 Lesson 2: Strength and Duration of the Behavioral Response was a Surprise

We argue now that the success in slowing the spread of COVID-19 during 2020 and 2021 evident in the serology data came as a surprise relative to both historical experience with pandemic influenza and model-based estimates of the impact of

number of the original variant is higher (we assume 3 while they assumed 2.5) and thus an unmitigated epidemic infects more of the population and in part because our estimated IFR at the start of the epidemic is slightly higher (1% vs. 0.9%).

mitigation measures on transmission based on that historical evidence.

In many ways, pandemic influenza was the closest historical and epidemiological parallel to the COVID-19 epidemic. Both diseases are fast-moving respiratory diseases with potentially high infection fatality rates. The case of the 1918-1919 "Spanish Flu" epidemic was viewed as particularly relevant, but the epidemics of 1957, 1968, and 2009 also served as examples.

The risk of a new pandemic influenza has been viewed as a substantial threat for a long time. See, for example, the disease and economic scenarios laid out by the President's Council of Economic Advisors in September of 2019 in CEA (2019) which foresaw the potential for hundreds of thousand of deaths and trillions of dollars of economic disruption from a pandemic influenza.

In response to this threat from pandemic influenza, epidemiologists have invested considerable effort into studying historical experiences with pandemic influenza and modeling the impact of various mitigation options on influenza transmission.[14].

Of particular interest in this regard is Figure 1 in Hollingsworth et al. (2011) which shows the duration (in weeks) and effectiveness (in terms of percentage reduction in transmission rates) of historical interventions to slow the spread of the 1918-19 influenza and SARS-CoV-1. That figure estimates that interventions in the 1918-19 influenza epidemic reduced transmission rates by less than 50% in all cases and much less than that amount in many cases. Moreover, these interventions were sustained for less than 15 weeks. As shown in this figure, mitigation efforts for SARS-CoV-1 were estimated to be much more effective, but these were also sustained for less than 15 weeks. In comparison, with regard to COVID-19, we see from the serology data that efforts to slow disease spread substantially had an impact for many months through late 2021.

Prominent studies of the possibilities for using public health interventions to contain an new influenza strain at its source include Longini et al. (2005) and Ferguson et al. (2005). Prominent modeling studies of the use of broader public health measures including school closures and social distancing to slow the spread of a pandemic influenza that broke through efforts to contain it at the source include Ferguson et al. (2006) and Germann et al. (2006). Universally, these studies predict short periods of very rapid spread of disease even in the modeled presence of intense public health efforts to slow disease spread so that available flu vaccines can be administered.

Particularly telling in this regard is the caption of Figure 4 in Ferguson et al. (2006) that notes regarding the timing of administration of vaccines that these

[14]For examples of studies of transmission during the 1918-19 influenza pandemic see Mills, Robins, and Lipsitch (2004), Fraser et al. (2011), and Eggo, Cauchemez, and Ferguson (2011). For studies of the impact of mitigation on transmission during the 1918-19 influenza pandemic see, for example, Bootsma and Ferguson (2007), Hatchett, Mecher, and Lipsitch (2007), Correia, Luck, and Verner (2022), and Velde (2022)

vaccines would have "almost no effect" if started after 120 days after the first world-wide case.[15] This conclusion is clearly too pessimistic about the possibility of controlling the spread of a respiratory pathogen through behavioral mitigation, as COVID-19 vaccines still had a major benefit despite arriving more than a year after the first world-wide case. The COVID-19 pandemic fundamentally changed our conception of what is possible with respect to behavioral mitigation.

This contrast between the anticipated and observed impact of behavioral change on slowing the transmission of COVID-19 is even more remarkable given that the original strain of SARS-CoV-2 was more contagious than a pandemic influenza strain was expected to be, had the ability to spread prior to the onset (or in the absence) of symptoms, and ultimately generated new variants with substantially increased transmissibility. The cards were stacked against us, even relative to the modeled scenarios for pandemic influenza that served as our basis for our earliest understanding of SARS-CoV-2.

To see this point, consider the scenarios for pandemic influenza expected by modelers as laid out in Meltzer et al. (2015). Table 1 of that paper lays out the range of scenarios for transmissibility and clinical severity of potential new pandemic influenzas typically considered and Figure 1 of that paper places historical pandemics in this space of transmissibility and clinical severity. The original strain of COVID-19 had higher transmissibility than the worst-case scenario and was near to the worst-case scenario in terms of its clinical severity.

The fact that COVID-19 could be transmitted prior to showing symptoms made epidemiologists (including ourselves) pessimistic that its spread could be effectively controlled. As described in Fraser et al. (2004), "the success of ... control measures is determined as much by the proportion of transmission occurring prior to the onset of overt clinical symptoms (or via asymptomatic infection) as the inherent transmissibility of the etiological agent (measured by the reproductive number $\mathcal{R}(0)$)". Likewise, early in the COVID-19 epidemic Hellewell et al. (2020) pointed to the pre- and a-symptomatic transmission of COVID-19 as a reason to be pessimistic about our ability to contain its spread.

These features of COVID-19, together with the hazy prospects as of March 2020 for developing an effective vaccine in time to be useful, meant that, despite all the planning for a pandemic influenza, the set of actionable targeted mitigation policies available to slow the spread of COVID-19 in a cost-effective manner was very small as of March of 2020. In fact, in an early and highly cited article from March 9, 2020 giving broad outlines of options for mitigating the coming pandemic, Anderson et al. (2020) remarked that "it is easy to suggest a 60% reduction in transmission will do it or quarantining within 1 day from symptom onset will control transmission, *but it it is unclear what communication strategies or social*

[15] See also Figure 2 in Germann et al. (2006).

distancing actions individuals and governments must put in place to achieve these desired outcomes" (emphasis added).

We argue that one of the main lessons of our experience with COVID-19 is that there are far greater possibilities for slowing transmission of a deadly respiratory virus than previously thought. Given that new knowledge, we should work urgently to determine how to achieve similar behavioral mitigation in the next pandemic but at far lower cost.

4.3 Lesson 3: Behavior and State level outcomes

There has been great interest in comparing the impact of COVID-19 across states of the U.S. in the press and in some academic work.[16] Certainly the outcomes for cumulative mortality for COVID vary widely across the states of the U.S. What accounts for these differences? We address this question in greater detail in section 6.

Here we make the argument that, relative to the historical and modeling benchmarks for pandemic influenza discussed above, residents of all 50 states made surprisingly strong and lasting efforts to slow the spread of COVID-19 so that vaccines came in time to save a considerable number of lives.

To illustrate this point, we show Figure 10, taken from Chitwood et al. (2022), which depicts the dynamics of the effective reproduction number for COVID-19 for each of the 50 states of the United States. In this figure, we observe that behavior in all 50 states changed rapidly and dramatically so as to drive the effective reproduction number of COVID-19 in the state down to one very early on in the epidemic. Moreover, this behavior was sustained so as to keep this effective reproduction number close to one throughout 2020. Atkeson, Kopecky, and Zha (2023) find similar results for both U.S. States and many countries.

As we have discussed above, if the effective reproduction number of a disease remains close to one, then the growth rate of current infections is close to zero. Equivalently, the growth rate of cumulative infections and deaths is then roughly constant. This is precisely the dynamics we observe in cumulative COVID-19 mortality at the state level.

To illustrate this point, in Figure 12, we show the dynamics of cumulative COVID-19 deaths as an age-adjusted death rate per 100K of the population for selected states. In the left panel of this figure, we show the dynamics of cumulative COVID-19 deaths for California, Florida, New York (excluding New York City), and Texas. We see that New York had a very rapid growth of cumulative deaths in the initial phase of the epidemic, and then settled in to a lower growth rate.

[16] See, for example, Barro (2022), Bollyky et al. (2023), and Kerpen, Moore, and Mulligan (2023).

Texas had a high growth rate of cumulative deaths throughout the first two years of the epidemic. Given the rhetoric surrounding this topic, we find it striking how similar the age-adjusted outcomes for COVID-19 deaths have been for California and Florida over the past four years.

In the right panel of Figure 12, we show the dynamics of cumulative COVID-19 deaths as an age-adjusted death rate per 100K of the population for New York City and seven other states representing extreme high and low mortality outcomes across states. With the exception of New York City, we see largely linear growth in cumulative deaths over the first two years of the COVID-19 epidemic for all of these locations. As evident in the figure, New York City suffered exceptionally rapid initial growth of cumulative COVID-19 deaths in the first wave of the epidemic, likely due to the surprise introduction of a large number of hidden cases from Europe in early 2020.

For futher evidence of this commonality of responses across U.S. states, in Figure 11, we show estimates from the Commercial Lab and Blood Donor serology surveys of cumulative infections (in red) and combined seroprevalence (in black) for the 50 states of the United States. While these surveys show considerable variation in the estimated percent infected across states, we see in this figure that all of the states followed similar dynamics of slow growth in infections in the first two years of the epidemic and rapid deployment of vaccines in the first half of 2021.[17] We discuss these state-level serology data in greater detail in Section 6.

Based on this evidence, we argue that the most important feature of the outcomes across U.S. states (and even countries around the world) is how much they have in common relative to outcomes that were expected given prior epidemiological modeling of and past experiences with pandemic influenza. To a large extent, residents of every state in the United States outside of New York City reacted very strongly to COVID-19 very early on and took significant actions to slow its spread all through 2020 and 2021. We regard the observation that this could be done, and done nearly universally across different states of the U.S., as a great surprise.

To expand further on this point, observe that the model-based forecast in Ferguson et al. (2020) for peak deaths with unmitigated spread of COVID-19 was over 16 deaths per day per 100K population (implying over 50,000 deaths per day in the U.S. as a whole) with 75% of the population being infected by late summer of 2020. This forecast was not out of line with what was experienced in locations that did little to mitigate the spread of SARS-CoV-2. For example, we note that seroprevalence studies in Manaus, Brazil indicated an attack rate of 75% in their

[17] Chitwood et al. (2022) argues that the serology data underestimates the true portion of the population ever infected for a variety of reasons. This paper presents alternative estimates of the state-level portion of the population infected through 2020 in its Figure 7.

first wave of the pandemic.[18] We see nothing like this rapid spread of COVID-19 in the serology data across U.S. states.

In March and April of 2020, New York City experienced the worst wave of COVID-19 infections and mortality of anywhere in the U.S. over the past four years. Its peak weekly mortality rate was 60 per 100K population (less than 10 per 100K per day) — in the range of one half that predicted in Ferguson et al. (2020) for peak deaths with unmitigated spread. Seroprevalence estimates for New York City indicate up 20% of that population of 8 million people was infected in the first wave in Spring of 2020.[19]

We illustrate the extent to which the first wave of COVID-19 deaths in New York City was an outlier in Figure 13. In that figure, we show the dynamics of weekly COVID-19 deaths for the 50 states at an age-adjusted rate per 100K of population in gray. We show these dynamics for New York City in red and for the United States overall in blue. As is clear from the figure, the first wave of COVID-19 deaths in New York City was much larger than any other wave experienced in any state in the United States. That is, as shown in Figure 10 and here in Figure 13, the response to flatten the curve and dramatically slow the transmission of COVID-19 was universal across the 50 states of the United States.

We now turn to our fourth lesson regarding the prospects for a similar behavioral response next time.

4.4 Lesson 4: Unclear if behavior will be the same next time

From our perspective, the success of this sustained and fairly uniform behavioral response to slow transmission for this length of time to allow for the deployment of vaccines and improved medical care is perhaps the biggest surprise of the COVID-19 pandemic. Clearly, a strategy of slowing transmission for 8-15 months as needed to develop and deliver an effective vaccine is based on the premise that people can be persuaded to go along with that plan. To an extent that seems well outside historical experience with pandemic influenza and predictions based on that historical experience, Americans did go along with that plan, with or without mandates from state governments.

Many economists, one of us included, have argued ex-post that this pattern of adjusting behavior to keep the growth rate of new infections and deaths relatively close to zero observed nearly universally in the U.S. and across many countries is precisely the response that economic theory would predict.[20]

[18] See Buss et al. (2021).

[19] See Stadlbauer et al. (2021).

[20] See Atkeson (2021b), Atkeson (2023a), and Atkeson, Kopecky, and Zha (2023). See Gans (2022) for a broader survey of the economics papers on this topic.

But this argument then raises the puzzle of why did we not see a quantitatively similar response to pandemic influenzas, in particular the 1918 Spanish Flu? And comparison of these different outcomes for pandemic influenza and COVID-19 raises the question of which behavioral response should we expect to see in the next pandemic? Will it be a short sharp wave as for COVID-19 in New York City in March and April of 2020 and in most cities for which we have data in 1918? Or will it be a long drawn out affair as for COVID-19 in the rest of the United States? The answer to this question will have a big impact on the range of mitigation strategies available in the fact of the next pandemic and is a great challenge in epidemiological modeling.[21]

The world has already experienced an outbreak of another emerging pathogen. Starting in May of 2022, Mpox, formerly known as monkeypox, began to spread rapidly primarily through sexual contact between men, with this spread being particularly alarming since it showed up in a large number of countries in a short period of time. Mpox is an example of a known pathogen endemic to a relatively small area (in West Africa) suddenly spreading rapidly well outside that region.

Simple examination of the exponential growth of cases in the United States between May and August of 2022 shown in Figure 22 indicated that this disease had the potential to spread quite broadly, at least within a subset of the U.S. population. Instead, as shown in Figure 22, the number of cases began to die out rapidly in late August and new cases in the United States have been held at a low level throughout 2023. What explains this path of this epidemic?

What we find interesting about this Mpox epidemic is that it appears that through a combination of a sustained change in private sexual behavior and the targeted application of vaccines, it was possible to dramatically reduce the cumulative number of cumulative cases relative to what would be predicted for an unmitigated epidemic. In other words, the behavioral response to Mpox appears to be a remarkable success.

Zhang et al. (2023) quantifies the impact of behavior and vaccines on the spread of Mpox with an epidemiological model using data on the Mpox outbreak in the United Kingdom, which exhibited an epidemic curve similar to that in Figure 22. These authors argue that changes in behavior and vaccination together played an important role in shaping this epidemic.

We find it interesting to note, however, that their accounting of the impact of behavior and vaccines on the trajectory of this epidemic is quite different from our accounting of the impact of these factors on the trajectory of the COVID epidemic. In particular, they find that the response of behavior (in terms of men reducing the numbers of their sexual partners) was strong and persistent enough to drive the effective reproduction number of Mpox below one on a sufficiently sustained

[21] See Funk et al. (2015).

basis to drive the number of new cases to a very low level. This never happened with COVID-19. They then estimate that the use of pre-exposure vaccines for susceptible men limited the threat of resurgence.

The estimated combined impact of these interventions was then very substantial in limiting the size of the outbreak: the U.K. had 3250 observed cases over the study period relative to an estimated final size of an uncontrolled epidemic of 169,400. We see these estimates, together with the discussion in Daskalakis, Romanik, and Jha (2024), as driving home the message that targeted interventions in combination with vaccination can have a powerful impact on outcomes of an epidemic.

Another factor to consider going forward is the extent to which our experience with COVID-19 will shape reactions to new epidemics going forward for decades to come. Will the public be more skeptical of public health warnings about new pathogens? Or will our collective experience with significant mortality from an infectious disease outbreak lead us to take future threats more seriously? Addressing such questions seems of first-order importance for research going forward.

5 Comparison to Other Estimates in the Literature

We have taken an approach of estimating the impact of behavior and vaccinations on cumulative COVID mortality based on an estimate of the fraction of the U.S. population that were vaccinated before they were first infected with COVID derived from serology data, an estimate of the fraction of those individuals who would have been infected with COVID absent vaccines based on an estimate of the final size of the COVID epidemic, and an estimate of the difference between the infection fatality rate for those first infected by COVID before being vaccinated and those first infected by COVID after being vaccinated.

5.1 Key Sources of Uncertainty Regarding our Estimate of Lives Saved

Our estimate of lives saved is subject to uncertainty due to uncertainty in each of the numbers entering this calculation.

Our model may lead to an overestimate of lives saved because blood serology data may undercount infections prior to vaccination or overstate the protection offered by vaccination either because it is not representative of the entire population or because of waning antibodies or both. See, for example, Chitwood et al. (2022). We do not consider this concern as having a significant impact on our estimate of lives saved by vaccines. In particular, Atkeson (2023b) conducts a similar exercise estimating the impact of vaccines on lives saved using an estimate of cumulative

infections over the course of 2020 closer to that in Chitwood et al. (2022) and arrives at an estimate of lives saved close to 750,000, not far from the updated estimate in this paper.

Our model may lead to an underestimate of lives saved because old people got vaccinated early and did more to avoid getting infected early. In Figure 14 we show serology data from the Blood Donor and Commercial Lab surveys for the population 65 years old and older at the national level. By comparing this figure to Figure 1, we see that infections spread more slowly through this older population in 2020 and 2021 and that vaccinations were deployed more rapidly in this population in early 2021 than was the case for the general population as shown in Figure 1.

Absent vaccines, this elderly population would have likely become infected, and once infected they would have died at a rate higher than our assumed infection fatality rate. To illustrate this point, we see in the serology data shown in Figure 14 and in Figure 21 at the state level, that for those over 65 years of age, 80% had been vaccinated before they were infected as of July 2021. Clearly, given the high infection fatality rate of COVID-19 for the elderly, the counterfactual of a much higher infection rate among this age group would imply a very high death toll and thus a much larger estimate of lives saved.

We note that some argued for an approach to COVID mitigation based on focused protection of the elderly. See "The Great Barrington Declaration" at `https://gbdeclaration.org/`. The serology data both at the national level shown in Figure 1 and at the state level discussed below are consistent with the view that those over 65 did manage to get infected at a substantially slower rate than the general population. Would this greater mitigation by the elderly have made a difference for overall mortality absent vaccines? Given the arrival of the Delta and Omicron variants, we think not. It is unclear whether this success in avoiding infection by the elderly would have been more than temporary absent the development of vaccines. Of course, our statement here is based on the benefit of our ex-post knowledge of the emergence of these highly transmissible variants. Perhaps focused protection might have greater effect in the context of a different disease. Importantly, focused protection is most effective when overall infection rates are kept low, as targeted protection of just a single group – like the elderly in the context of COVID-19 – would likely fail in the absence of substantial mitigation efforts in the rest of the population as well.

5.2 Alternative Estimation Approaches

There are a number of alternative approaches to estimating the impact of vaccination on COVID mortality available in the literature that we review here.

Jia et al. (2023) apply an interesting methodology to construct an estimate of a different measure of the impact of vaccines on COVID mortality. They aim to measure the marginal impact on mortality if vaccination (here corresponding to the first two shots in the primary series) had happened faster or had been pushed further than it actually was. They focus on the time period from the end of May 2021 (when vaccination was well underway) and the beginning of September of 2022.

Their estimate of this marginal impact is based on the use of two data inputs. The first data input is a count of weekly COVID deaths by vaccination status over the study time period. That is, it consists of a weekly count of the number of COVID deaths among those who had not received their primary series of vaccinations 14 days prior to death and those that had received those vaccinations. These counts of COVID deaths by vaccination status are stratified by age and are available for 30 U.S. states that integrated their state-level vaccine records with their reporting of vital records statistics reported to the CDC. The second data input is a measure of the size of the vaccinated and unvaccinated populations in these 30 states derived from their state-level vaccine records.

These counts of COVID deaths by vaccination status can be combined with measures of the size of the vaccinated and unvaccinated populations to estimate the weekly COVID population mortality rate by age and vaccination status. We reproduce the results from this calculation by Jia et al. (2023) reported in their figure S3 here in Figure 15. The associated weekly measures of the population by vaccination status in these age groups used to derive the COVID mortality rates shown in Figure 15 are reported by Jia et al. (2023) in their figure S2 reproduced here in Figure 16

Jia et al. (2023) construct an estimate of additional lives saved had vaccination been extended to the entire population by constructing a counterfactual estimate of the number of COVID deaths that would have occurred had everyone been vaccinated by the end of May 2021. To construct this counterfactual COVID death toll, they apply the weekly COVID mortality rate for the vaccinated population shown in Figure 15 to the unvaccinated population shown in Figure 16. The difference between the observed death toll in the unvaccinated population and this counterfactual death toll is their estimate of additional lives saved. Using this methodology, they find that, had the entire population received the primary round of two shots by the end of May 2021, an additional 232,000 lives could have been saved.[22]

[22]Zhong et al. (2023) conduct a related analysis of the mortality impact of marginal increases in the rate of vaccination on COVID mortality over the period January 2021 through April 2022. They report that increasing vaccination coverage to 85% of the adult population over this time period would have saved an additional 178,000 lives and increasing it to 100% of the adult population would have saved 319,000 lives. Again these estimates are of the benefit of increasing

We note several striking features of these data shown in Figures 15 and 16.

First, in Figure 16 we see that the administration of vaccines in 2021 covered a large portion of the population by the late summer of 2021, with this level of coverage being particularly high for the elderly population. Thus, these administrative data on vaccination are consistent with the serology data we discussed above. These observations of high levels of vaccine coverage by late summer of 2021 are also consistent with the hypothesis that the marginal impact on COVID mortality of raising vaccination coverage from observed levels to 100% of the population is significantly smaller than the impact on COVID mortality of raising vaccine coverage from 0% to observed levels that we aim to estimate.

Second, in Figure 15, we see that the weekly COVID mortality rate for the unvaccinated was much higher than that for the vaccinated in the Delta and first Omicron waves in the fall of 2021 and early 2022. We see this evidence as consistent with the hypotheses that a first infection with COVID Delta or Omicron was quite dangerous for the unvaccinated and that vaccines provided considerable protection against severe disease during those episodes.

We note in Figure 15, the COVID mortality rate for the unvaccinated falls markedly even for the elderly after late March or early April of 2022. We see this decline in the mortality rate for the unvaccinated as consistent with the hypothesis that, after the first Omicron wave, the large majority of the unvaccinated population had likely already been exposed to COVID and hence had some protection from severe disease due to that prior infection. Note that this hypothesis is also consistent with the finding in Barro (2022) from cross-state regressions that the impact of vaccination rates on subsequent COVID mortality appears to decline substantially after the first COVID wave.

In our model, and in the data, the pace of vaccinations slows considerably in the second half of 2021. One might ask, as do Jia et al. (2023), how many lives might have been saved if the initially rapid pace of administering vaccines had been continued through the second half of 2021 and continued through into 2024.

We show our model results for this scenario in the first row of Table 2. Here we find that with continued rapid vaccination, the cumulative death toll would have been 907,000 over the four year duration of the epidemic. In comparison with our baseline death toll of 1,180,000, this counterfactual simulation suggests that more rapid vaccination continuing through the fall of 2021 would have saved an additional 273,000 lives.

As shown in Figure 23, nearly all of this benefit is realized from the model's implication that more rapid vaccination would have very much reduced the wave of deaths associated with the Delta variant in the fall of 2021 and would have

vaccination rates above those actually achieved. We focus on estimating the impact of achieved vaccination rates.

substantially mitigated the initial waves of deaths associated with the Omicron variant in early 2022. Continued rapid vaccination after early 2022 would have had a much smaller marginal impact on the model implied COVID death toll. We see these findings as in line with the results of Jia et al. (2023).

Steele et al. (2022) develop an estimate of the impact of vaccines on COVID mortality over the time period December 2020 to September 2021 based on an alternative approach to calculating this impact. Their approach is based on an estimate of flows of new potential infections over the study time period. That is, they develop a structural model of the epidemic similar to an SIR model and attempt to estimate the rate per unit time at which infected individuals would have transmitted their infection to vaccinated individuals had those individuals not been vaccinated together with the associated COVID deaths that would have followed those counterfactual infections.[23] They arrive at an estimate of 235,000 lives saved from December 2020 to September 2021.

This estimate is substantially lower than our estimate primarily because the estimation methodology is different. In particular, if we apply an incremental IFR of 0.05% to their estimate of 235,000 lives saved, we see that this corresponds to an estimate of 47 million additional infections in their counterfactual without vaccines over the period from December 2020 to September 2021, equal to 14% of the U.S. population. What their estimate leaves out relative to ours is an estimate of the additional infections and deaths that would have occurred as the COVID epidemic continued after September 2021 in the counterfactual without vaccines. It is these additional infections and deaths that we aim to count by incorporating an estimate of the final size of the epidemic in our estimation procedure.

To draw a comparison between our model results and those in Steele et al. (2022), we simulate our model with baseline behavior with and without vaccines through September 15, 2021. We report these results in the third and fourth rows of Table 2. In this table, we see that we obtain an estimate that vaccines saved 448,000 lives through that date. Note, in our counterfactual, vaccines averted substantially more infections during this time period than estimated in Steele et al. (2022).

The Commonwealth Fund has produced a series of estimates of lives saved by vaccines.[24] The authors of these estimates use an agent-based model based on the

[23]The model is based on one used to estimate the impact of vaccines on seasonal influenza here Tokars et al. (2018). See also Jones, Khader, and Branch-Elliman (2022) for an editorial commentary on this article.

[24]See, for example, `https://www.commonwealthfund.org/blog/2022/impact-us-covid-19-vaccination-efforts-march-update`. This estimate is an update of a previous estimate from December of 2021at `https://www.commonwealthfund.org/publications/issue-briefs/2021/dec/us-covid-19-vaccination-program-one-year-how-many-deaths-and`. That estimate

model in their earlier paper Moghadas et al. (2021).

They report an estimate that, through March 2022, "Without vaccinations, there would have been an estimated 66 million additional COVID infections". That corresponds to an estimate that an additional 20% of the U.S. population would have been infected absent vaccines. This is an underestimate of counterfactual infections relative to our calculation of averted infections prior to Omicron based on a simple count of those vaccinated before infected as implied by the serology data together with our estimate of the final size of the COVID epidemic.

They then report an estimate of 2,265,222 deaths averted. This estimate of deaths averted seems very high in light of their estimate of infections averted. Using their estimate of infections averted, this estimate of deaths averted implies that those 66 million additional infections would have had an infection fatality rate of 3.4%. It is unclear what evidence this estimate of the incremental infection fatality rate is based on.

6 What Drove Differences in State Level Outcomes?

As we have discussed above, there has been great interest in comparing the impact of COVID-19 across states of the U.S. in the press and in some academic work. We have argued that, in terms of broad strokes, the dynamics of the COVID-19 epidemic have more in common across states than would be expected from historical experience or projections from pandemic influenza models. We now examine the cross-section outcomes across states and argue that these outcomes are consistent with reasonable variation in either structural factors impacting virus transmissibility that might vary across states (such as weather, density, etc.) and/or reasonable variation in the strength of the behavioral response across states.

6.1 Cross-State Cumulative COVID Mortality and Infections

We start with a review of cross-state outcomes for cumulative deaths shown in Figure 17. The different linear growth rates of cumulative COVID deaths across states of the United States, sustained over time, led to significant differences in cumulative outcomes through the first two years of the epidemic.

In the left panel of Figure 17, we show cumulative deaths by state from the beginning of the epidemic through April 4, 2022 as an age-adjusted rate per 100K of population. This dispersion in cumulative COVID death rates is quite wide. In the right panel of Figure 17, we show the cumulative deaths by state for the period April 4, 2022 through December 30, 2023 on the same scale. Here we see that the

was for 36 million infections averted and 1.1 million lives saved, again implying an incremental IFR over 3%.

growth in cumulative deaths over the past two years has been much slower and more uniform across states than during the first two years.

In Figure 18 we show results for seroprevalence measured in the Blood Donor Survey from the first quarter of 2022 (at the end of the first big Omicron wave) broken down at the state level. In the left panel of this figure, we see that there is considerable dispersion in the measure of the cumulative percentage of the population infected across states by the end of the first big Omicron wave, with some locations showing only 25-30% of the population infected and others showing roughly 70% of the population infected. In the right panel of this figure, we see, in contrast, that the population in nearly all states had achieved a high level of combined protection from either prior infection or vaccines by the end of the first Omicron wave.[25]

At a mechanical level, the different outcomes for cumulative deaths across states through the first quarter of 2022 shown in the left panel of Figure 17 are largely accounted for by differences in cumulative infections in the serology data with moderate variation in the implied infection fatality rates across states. Thus, it appears that the serology data are giving a meaningful measure of cumulative infections.

We illustrate this point in Figure 19. The left panel of that figure shows a scatter plot of the state-level measure of the cumulative percent of the population infected from the Blood Donor Survey in the first quarter of 2022 on the x-axis and state-level cumulative COVID mortality at an age-adjusted rate per 100K population as of April 4, 2022 on the y-axis. The red line in that figure is a regression line with the intercept set to zero. The slope of that line is consistent with an estimated cumulative infection fatality rate very close to 0.5% based on the cross-state variation in measured infections and deaths by the end of the first quarter of 2022.

The right panel of that figure shows the implied cumulative infection fatality rate at the state level obtained by taking the ratio of the state-level cumulative COVID age-adjusted mortality rate as a percentage of the population and the state-level measure of the cumulative percentage of the population infected as of the 2022 Q1 Blood Donor Survey. (Note that this variation in state-level infection fatality rates can be both real and due to errors in measurement.) From these figures, we argue that the serology data provide a meaningful measure of the progress of the COVID epidemic at the state level.

We note that, relative to the overall population in each state, the elderly

[25]Klaassen et al. (2023b) Figures 1, 2 and 3 present alternative estimates of the portion of the population at the state level with effective protection from severe disease from either prior infection or vaccination over the course of 2021. These estimates are also consistent with the view that the population across U.S. states had attained high levels of protection from severe disease by the end of 2021.

managed to avoid infection through the first quarter of 2022 at a fairly uniform rate. In Figure 21 we show a scatter plot of measures of the cumulative percentage of the overall population infected from the Blood Donor Survey from the first quarter of 2022 on the x-axis and the cumulative percent of the population 65 and over infected from the same survey. We see that the scale of y-axis lies well below that on the x-axis.

After the first large Omicron wave in early 2022, the impact of further increases in measures of infections from serology data on further COVID deaths gets much weaker, consistent with the view that vaccination prior to a first infection with COVID protected substantially against COVID mortality from Omicron. In fact, after the first quarter of 2022, the differences in infection rates across states fell dramatically as Omicron managed to infect the vaccinated at a high rate.

In Figure 20, we show a scatter plot of the state-level measures of the portion of the population previously infected from the 2022 Q1 Blood Donor Survey and the same measure at the state-level from the 2022 Q4 Blood Donor Survey. In that figure, we see that the percentage of the population infected at the state level in the first quarter of 2022 ranged from a low of roughly 25% to a high of roughly 70%. By the end of 2022, this dispersion in the percentage of the population infected shrank considerably, with the low end in particular now over 60%.

We thus conclude that this relationship between cumulative infections and deaths breaks down after the first big Omicron wave. Over the past two years, the incremental growth of cumulative deaths has been uniformly much smaller across U.S. states despite huge and differential growth in infections measured in the serology data over the course of the remainder of 2022. We argue that these observations of relatively uniform outcomes over the past two years are best accounted for by the observation that by the end of the first quarter of 2022, nearly everyone had been vaccinated or infected or both so that the mortality impact of further infections has been much reduced and now depends largely on the biologically determined speed with which the protection against severe disease offered by vaccination or prior infection wanes or fails due to immune evasion by new variants.

6.2 Moderate Differences in Behavior and Transmissibility Can Account for These Cross-State Outcomes

We now use our model to consider the range of variation in the strength of behavior and of structural factors impacting transmission required to account for this dispersion in outcomes for COVID-19 mortality across states.

We first simulate our model with all baseline parameters except that we consider the strength of behavior as indexed by $\kappa(t)$ to be either twice its baseline value

(strong behavior) or half its baseline value (weak behavior). Results are reported in the first two rows of Table 3, with the predicted dynamics of COVID deaths shown in Figure 24. We see in this figure that in both cases, the model produces the linear growth of cumulative deaths seen in the state level data, just with different slopes. This variation in behavior also produces a wide range of mortality outcomes when cumulated over time.

We then simulate our model with all baseline parameters except that we consider the transmission constants $\bar{\beta}_i$ to be either 1.5 times or 0.66 times their baseline values, corresponding to faster or slower transmission.[26] Results are reported in the first two rows of Table 3, with the predicted dynamics of COVID deaths shown in Figure 25.

What is to be learned from this dispersion in infection and mortality outcomes across U.S. states? To what extent did specific actions or policies or patterns of private behavior account for these different outcomes across states? Or inherent differences in infection fatality rates? These questions are hard to answer given all of the confounding factors that also influenced infection and mortality outcomes across states. In particular, it is difficult to assess to what extent it was ex-ante differences in structural factors such as density or weather across states states that might have led to faster or slower transmission or differences in public and private behavior that caused the different growth rates of infections and deaths observed across states.

We do not attempt such an analysis in this paper. Moreover, we argue that the universally strong behavioral response in all 50 states is the most striking feature of the state level data.

7 What is needed to make mitigation less painful next time?

The behavioral mitigation measures undertaken during the COVID-19 pandemic helped to save many thousands of lives, but they came at a high social and economic cost. Uncertainty about key features of COVID-19 and about the human behaviors that impact its spread forced us to take stronger, more widespread, and longer-lasting behavioral mitigation measures that might have been necessary in a more information-rich setting. Likewise, individuals largely lacked the tools they needed to make informed assessments about their risk of becoming infected or transmitting disease. For example, widespread and cheaply available diagnostic tests - along with clear guidance on how to report and interpret them - could have

[26] See Ives and Bozzuto (2021) and Sy, White, and Nichols (2021) for estimates of the range of variation in COVID transmission rates across regions of the U.S.

helped alleviate the need for general physical distancing measures like school and workplace closures that lasted for many months into the pandemic.[27]

The next pandemic may look very different than COVID-19, but it will nevertheless be critical to find ways to rapidly reduce our uncertainty about the pathogen's characteristics and the human behaviors that underlie its spread, and likewise to rapidly develop and deploy the tools that will empower individuals to make informed behavioral choices. This will require developing off-the-shelf research protocols for learning about transmission routes, the natural history of infection, and the dynamics of immunity for an emerging pathogen soon after it is first detected. In the meantime, we must also invest in ongoing data collection efforts to provide baseline measurements against which data on an emerging infectious disease can be meaningfully compared. A detailed discussion of the steps needed to effectively prepare for the next pandemic is provided by Lipsitch et al. (2023). Here, we outline a few key considerations.

7.1 Assessing transmission routes

When an emerging outbreak is detected, a critical first task is to determine the pathogen's routes of transmission. Beyond the most basic information on transmission route (e.g., sexual vs. vector-borne vs. respiratory, and (if respiratory) droplet vs. aerosol vs. fomite), it is also important to identify the venues and behaviors that are most conducive to spread. For example, it became evident early in the COVID-19 pandemic that outdoor transmission was far less common than indoor transmission,[28] and that singing was a particularly high-risk activity.[29] Pre-approved study designs, backed with funding for rapid deployment, would help to more rapidly clarify how and where the bulk of transmission occurs in the event of an emerging outbreak.

To place these studies in the proper context, we also require detailed studies on interpersonal contact patterns, both at baseline and as they evolve over the course of an outbreak, much like the CoMix study[30] did in the context of COVID-19. Such studies recruit representative cohorts and ask questions about their behaviors (e.g., conversational or sexual contacts) that may be relevant to the spread of disease. Mobility data, gathered for example using mobile phones, can also be useful,[31] though such data must be interpreted with care since the owners of mobile devices or the users of a given app may not be representative of the broader population.[32]

[27] See, for example, the discussion in Atkeson et al. (2020).
[28] Bulfone et al. (2021)
[29] Hamner et al. (2020)
[30] Gimma et al. (2022)
[31] Buckee et al. (2020)
[32] Wesolowski et al. (2016)

Data access and privacy issues should also be proactively addressed well in advance of a public health crisis.

Detailed contact tracing data can be useful for determining the level of risk associated with various types of contact. For respiratory infections, household transmission studies like the ONS Coronavirus Infection Survey in the UK[33] can be helpful for assessing the level of risk associated with close contact. For sexually transmitted infections, partnership surveys[34] can serve the same purpose. The value of such studies can be greatly enhanced by collecting pathogen genomic information, allowing researchers to distinguish direct within-household (or within-partnership) transmission from new introductions from the community.

The production and distribution of non-pharmaceutical interventions (NPIs) should be rapidly scaled up in the event of an emerging outbreak. In the early stages of an outbreak, "plausible effectiveness" should be enough to justify the use of sufficiently low-impact NPIs – for example, plausible effectiveness would justify the widespread use of masks against the early spread of SARS-CoV-2, or condoms to prevent transmission of Mpox, even in the absence of direct studies assessing the efficacy of those interventions for those specific pathogens. In tandem, the effectiveness of these NPIs should be continuously monitored so that their use can either be founded on more direct, pathogen-specific evidence or, if no effectiveness is found, their use can be phased out.

7.2 Describing the course of infection

Once infection occurs, it is critical to understand the risk of various health outcomes. Key statistics like the infection fatality rate (IFR) are subject to bias that can affect early estimates in both directions: early in an epidemic, the most severe cases are the ones that are most likely to be detected, thus skewing the IFR upward; yet, if the epidemic is spreading rapidly, a simple division of mortality by cumulative prevalence can skew the IFR downward, since recently-infected individuals have not yet had time for their cases to worsen. This underscores the need for principled studies to track the range, timing, and probability of potential health outcomes in an emerging epidemic. An understanding of the IFR and related risks of various health outcomes helps to set the appropriate level of behavioral response.

Similarly, it is important to rapidly assess how a person's infectiousness varies over time. Again, household or partnership studies can be especially helpful, especially when coupled with frequent, quantitative diagnostic testing (e.g., RT-qPCR tests to assess pathogen load) and detailed symptom reporting. A critical piece of information to gather early in an epidemic is how the timing of symptoms

[33] Pouwels et al. (2021)

[34] For example, Ueda et al. (2020)

relates to infectiousness, as this relationship plays a major role in determining how difficult it is to ultimately control a pathogen's spread.[35] If infectiousness precedes symptoms, the need to develop and deploy rapid diagnostic tests becomes paramount.

7.3 Tracking incidence and immunity

Public health response in the United States is largely coordinated at the state level, which poses major challenges for data sharing and standardization. The need for improved data collection, standardization, and dissemination is a major focus area of the new Center for Forecasting and Outbreak Analytics (CFA) based at the Centers for Disease Control and Prevention (CDC). The CFA has taken many cues from the National Weather Service,[36], and indeed a digital infrastructure for providing information on current epidemiological conditions and a near-term forecast would go a long way toward informing more targeted behavioral responses in the event of another public health crisis.

Alongside information on disease incidence, well-designed serological studies can be invaluable both for reconstructing what has happened after an outbreak ends (as we have tried to do in this report) and for informing on the dynamics of immunity. It is important to conduct ongoing serological studies so that proper baselines can be set, especially because serological tests can cross-react.[37] Serological studies can inform on the duration of immunity to infection, thus helping individuals to calibrate their behavior to better match their risk of infection.

8 Conclusion

The behavioral response to SARS-CoV-2 in 2020-2022 was highly – and unexpectedly – effective in reducing cumulative COVID-19-related mortality in the United States. We estimate that the combination of behaviorally-driven transmission reduction and vaccination resulted in roughly 800,000 lives saved during that time period, in line with other estimates. Critically, we see that both of these factors – a strong behavioral response and the relatively fast development of an effective vaccine – were needed to yield a substantial reduction in mortality. Had a vaccine not been developed, or had behavior not changed, we anticipate that much of the US population would have received their first immunological exposure to SARS-CoV-2

[35] Fraser et al. (2004)

[36] George et al. (2019)

[37] For example, serological tests for SARS-CoV-1 can turn positive based on exposure to a related common coronavirus; see Patrick et al. (2006)

from the virus itself, and thus the total mortality from the pandemic would have been much higher.

We had three main goals in writing this report: (1) we sought to provide an evidence-based estimate of the value of behavior change during the SARS-CoV-2 pandemic in terms of reduced mortality; (2) we sought to describe a straightforward modeling framework that can be adapted to assess counterfactual scenarios for SARS-CoV-2 and for infectious diseases more generally; and (3) we sought to discuss the lessons of the SARS-CoV-2 pandemic from three hypothetical perspectives: the *ex ante* perspective of a public health planner in March of 2020, with knowledge of basic parameters of the virus but no certainty about its future evolution; the *ex post* perspective, where we are today, performing an assessment of how we actually performed given our knowledge of how the pandemic actually unfolded; and the perspective of future public health planners, who will be responsible for responding to new, possibly very different, emerging infectious diseases. We now discuss each of these goals in turn.

There are many ways to estimate lives saved during the COVID-19 pandemic, some relying on sophisticated models of transmission and immunological dynamics. We pursue a simpler tack, estimating the total mortality in the scenarios with no behavioral change prior to roll-out of a vaccine in January 2021, and with behavior change but no vaccine. Based on serology data, we estimate that less than 20% of the US population – and a substantially smaller fraction of individuals over age 65 – had been infected with SARS-CoV-2 before the introduction of vaccines. Yet, other areas of the world that were impacted early, before an effective behavioral response could be mounted, saw estimated attack rates of up to 75% within a short few months, which also aligns with epidemiological models for an unmitigated epidemic with transmissibility similar to the ancestral strains of SARS-CoV-2. As such, we can attribute a mortality reduction in the roughly 55% of the population who were able to be vaccinated prior to their first infection to the transmission-reducing behavioral response. Had a successful vaccine not been developed, however, it is unclear whether behavioral response would have had a substantial impact on cumulative mortality through the present day, since immune evasion and increasingly contagious variants of the virus have rendered herd immunity moot.

By introducing a modeling framework, we were able to compare more nuanced counterfactual scenarios and to better separate the impact of behavior from that of vaccination. The framework we discuss here is completely standard, perhaps with the exception of the form of the behavior term, which reduces the transmissibility parameter β_j proportionally to an exponentially decaying function of a parameter κ_j that captures the strength of the behavioral response relative to some disease metric (e.g., total infections or the rate of increase in mortality). It is possible

to compare many counterfactual scenarios using this framework, but the main takeaway is that behavioral transmission reduction and vaccination have a powerful positive synergy, where the timing of both is paramount - that is, early behavior change, coupled with the rapid development of an effective vaccine, can pay dividends in reduced mortality.

The *ex ante* perspective of the public health planner in March of 2020 is one lacking in many critical details about the pandemic's ultimate course, and yet is perhaps the most informative perspective to consider when assessing the best course of action in future pandemics. Early modeling work during the COVID-19 pandemic, including our own, anticipated that SARS-CoV-2 would become endemic,[38] but failed to anticipate both the ratcheting transmissibility of the virus with successive variants and the relatively swift development of an effective vaccine. The *ex post* perspective is useful for determining what we might have done differently, but this has limited application for future pandemics.

Instead, rather than thinking about what we should have done differently in hindsight from a management perspective and doing that going forward, we should instead ask what types of information we would have wanted during the early days of the pandemic to make more informed, ex-post-like decisions, and determine how best to put mechanisms in place now to collect that data. For example, key elements of the natural history of infection and the route of infection – such as the frequency of asymptomatic infections, the role of pre-symptomatic transmission, and the importance of aerosols in transmission – were unclear for far longer than they should have been.

Developing protocols for rapidly identifying cases, charting their course, and determining likely routes of transmission through prospective household and contact surveys, like the ONS Coronavirus Infection Survey in the UK[39] and the European CoMix Survey,[40] are critical for future pandemics. Likewise, it is clear that behavior can change spontaneously in response to a perceived infectious threat. It is less important to have an exact model for how behavior changes in response to threat than it is to have a robust framework for measuring the relevant changes in behavior when they actually happen. This will require a robust survey-taking machinery to be rapidly deployed in the event of an emerging pathogen. Such work may be augmented by the development of secure contact tracing technologies, like the ones developed for contact notification during the COVID-19 pandemic. Regardless, we must avoid the trap of "fighting the last pandemic," recognizing that while another coronavirus pandemic could occur within our lifetimes, there are many other threats that should be carefully thought through, and incorporated

[38] See Kissler et al. (2020), Shaman and Galanti (2020) and Murray and Plot (2021)

[39] See Pouwels et al. (2021)

[40] See Gimma et al. (2022)

into the data-collecting mechanisms discussed here. That said, the experience with Mpox, and the fact that behavioral mitigation measures during the COVID-19 pandemic strongly suppressed the spread of various other pathogens,[41] suggests that behavioral mitigation can be an important tool for addressing a wide range of infectious disease threats.

Our findings are limited by a substantial degree of uncertainty in the actual number of infections that occurred during the pandemic and a lack of reliable data capturing the dynamics of behavioral change during the pandemic. Regarding the lack of behavioral data, it is unclear even what an ideal dataset would look like, given that we do not have a solid grasp on what types of interactions are necessary and sufficient for the transmission of a respiratory pathogen. See, for example Ferretti et al. (2023). Conversational encounters are often used as a proxy, but the precise dynamics of interpersonal transmission in real settings remain poorly understood. The models we use are intentionally simplified, and so gloss over much important variation in baseline risk factors, population structure, and viral attributes that can, and do, have a major impact on transmission patterns. Our goal here is to provide a scaffold to guide thinking about behavior-modulated disease transmission, rather than to faithfully recapitulate the dynamics of a particular outbreak - though we note that, under reasonable assumptions, a fairly faithful recapitulation of those dynamics is possible with a model like the one presented here.

[41] See Koutsakos et al. (2021)

A Model Appendix

This appendix presents the model and parameters used in this paper. This model is an update of the model presented in the appendix to "Behavior and the Dynamics of Epidemics" by Andrew Atkeson for the Brookings Panel on Economic Activity Spring 2021 and in "The Impact of Behavior and Vaccines on U.S. Cumulative Deaths from COVID-19" by Andrew Atkeson available as NBER Working Paper 31525. This model is based closely on that presented in "A Parsimonious Behavioral SEIR Model of the 2020 COVID Epidemic in the United States and United Kingdom" which is available as NBER working paper 28434 and as Federal Reserve Bank of Minneapolis Staff Report 619. This appendix discusses the model extended to include vaccines and the potential for waning immunity, as well as the arrival of the Delta and Omicron variants. It is applied to the United States.

This appendix has three parts. In section A.1, we present the equations of the model. We also compare the structure of this model with that of a simpler behavioral SIRD model as analyzed in Atkeson, Kopecky, and Zha (2021)[42] and Droste and Stock (2021)[43] .

In section A.2, we discuss the values of the parameters and the rationale behind the choice of these parameters. The model is fit to US data on daily deaths from COVID as well as the serology estimates of the cumulative portion of the population infected and vaccinated prior to infection. Several parameters are set to match recommendations from the Center for Disease Control for modeling of COVID-19.

A full version of the MATLAB codes to run this model will be forthcoming for the conference draft.

A.1 Model

The model is as follows.

The SEIHR model extends the SIR model by adding both the exposed state E and the hospitalized state H. In this version of the model the total population N is given by the sum of susceptible agents in state S, exposed in state E, infected in I, hospitalized in H, recovered in R, and dead in D. We do not consider population growth in the model.

The compartments E and I are further broken down by variant i, where i

[42] Atkeson, Kopecky, and Zha "Behavior and the Transmission of COVID-19" forthcoming, *American Economic Review Papers and Proceedings* with the longer version available here `https://www.minneapolisfed.org/research/staff-reports/behavior-and-the-transmission-of-covid19`

[43] Droste and Stock "Adapting to the COVID-19 Pandemic" (2021) *American Economic Review Papers and Proceedings*

indexes the original variant, and the Alpha, Delta, and Omicron variants. The rate at which agents leave the E_i compartmenst for both the normal and more transmissible variants is σ and the rate at which agents leave the I_i compartments for all variants is γ. We also include compartments E_i and I_i corresponding to those experiencing breakthrough Omicron infections. These individuals are modeled as having immunity to previous variants but not to Omicron. The mean generation time for the model is then $1/\sigma + 1/\gamma$. As discussed below, the choice of these parameters is guided by CDC recommendations for these disease parameters.

As agents leave the I_i compartment, fraction η_i go into the hospitalized compartment H and $1 - \eta_i$ transition directly to the recovered compartment R_i. The rate at which agents leave the H compartment is ζ. We assume that all agents leaving the H compartment die. Thus, the overall infection fatality rate for variants is given by η_i and the mean time in the H compartment corresponding to illness and delays in reporting deaths is $1/\zeta$. Note that with these assumptions, it is not appropriate to compare the model's predictions for hospitalizations to data. Instead, this H compartment simply serves to introduce a delay between infection and death.

Those who recover from an infection with the original variant or the Alpha or Delta variants flow into compartment R and are immune from a second infection with these variants. This immunity wanes at rate ξ. They are also susceptible to breakthrough infections with Omicron as discussed below. There is a compartment V introduced to count those who have protection from vaccination prior to a first infection with COVID. Agents flow into this compartment from the compartment S as they are vaccinated and flow out with waning immunity (at rate ξ) and breakthrough infections from Omicron. There is a separate recovered compartment R_O for those recovered from an infection with Omicron. This is introduced to allow for faster waning immunity from an Omicron infection at rate ξ_o.

To introduce breakthrough infections for the Omicron variant, We assume that those infected with Omicron transmit their infection to those in the removed compartment R (those recovered from an infection with a prior variant) and the vaccinated prior to first infection compartment V at a fraction ν_O of the rate at which they transmit their infection to those in the susceptible compartment S. The infection fatality rate from Omicron for those with no prior infection or vaccination is η_O while that for those infected with Omicron but with prior immunity (i.e. coming out of the R or V compartments) is η_{OR}. We include separate compartments for those exposed to and infected with Omicron depending on whether they came out of the S compartment or the R compartment to allow for these separate infection fatality rates. We assume that those infected with Omicron who do not die transit to a separate compartment removed compartment R_O indicating immunity from prior infection with Omicron. We assume that this protection against a second Omicron infection and serious disease wanes at the

rate ξ_0.

The transmission rate of the original variant is denoted by $\beta(t)$. Those for the new variants are denoted by $\beta_i(t)$. New variants are introduced by setting $\bar{E}_i(t) = 1/population$ in the equations below for several days around a specified date t_i and equal to zero otherwise. This allows for a discrete jump from zero exposed to particular variant to a positive number. The window of days for this introduction needs to be chosen so that the differential equation solver (which samples on discrete dates) picks up the introduction of the variant.

The dynamics of the model are given by

$$\frac{dS(t)}{dt} = -\left(\beta(t)I(t) + \sum_{i=A,D}\beta_i(t)I_i(t) + \beta_O(I_O(t) + I_{OO}(t))\right)S(t) - \lambda(t)S(t) + \xi(R(t)+V(t)) + \xi_O R_O($$

Here the original variant is denoted without a subscript, $i = A, D$ refers to Alpha and Delta, $i = O$ refers to Omicron, and $I_{OO}(t)$ refers to those with a breakthrough Omicron infection. The parameter $\lambda(t)$ is the vaccination rate. The inflows $\xi(R(t) + V(t))$ are $\xi_O R_O(t)$ are due to waning immunity. Note that these individuals are also susceptible to severe disease and death in a manner equivalent to a completely naive individual.

The outflows from the S compartment are distributed as follows.

$$\frac{dE(t)}{dt} = \beta(t)I(t)S(t) - \sigma E(t)$$

For $i = A, D$

$$\frac{dE_i(t)}{dt} = \beta_i(t)I_i(t)S(t) - \sigma E_i(t) + \bar{E}_i(t)$$

For $i = O$

$$\frac{dE_O(t)}{dt} = \beta_O\nu_O(I_O(t) + I_{OO}(t))(R(t) + V(t)) - \sigma E_O(t) + \bar{E}_O(t)$$

Here the terms $\bar{E}_i(t)$ are used to introduce agents infected with new variants on particular dates. In the code, these terms are zero except for a window of several days in which the new variant is introduced with this term equal to 1/332,000,000 in this two-day time window. For $i = OO$ representing breakthrough Omicron infections we have

$$\frac{dE_{OO}(t)}{dt} = \beta_O(t)(I_O(t) + I_{OO}(t))\nu_O(R(t) + V(t)) - \sigma E_{OR}(t)$$

Outflows from the exposed states move to corresponding infectious states as follows

$$\frac{dI(t)}{dt} = \sigma E(t) - \gamma I(t),$$

For $i = A, D, O, OO$

$$\frac{dI_i(t)}{dt} = \sigma E_i(t) - \gamma I_i(t)$$

Infection leads to hospitalization (and death) as follows. Infection fatality rates are denoted by η_i.

$$\frac{dH(t)}{dt} = \eta(t)\gamma(I(t) + \sum_{i=A,D} I_i(t)) + \eta_O \gamma I_O + \eta_{OO}\gamma I_{OO} - \zeta H(t)$$

The infection fatality rate for the original, Alpha, and Delta variants, denoted by $\eta(t)$ is allowed to vary by time to reflect the apparent decline in the infection fatality rate from 2020 to 2021 implied by the serology data. The infection fatality rates for an initial infection with Omicron η_O and a breakthrough infection with Omicron η_{OO} are assumed to be constant over time.

Deaths are recorded as agents flow out of the H compartment

$$\frac{dD(t)}{dt} = \zeta H(t)$$

Those who do not die from their infection with the original, Alpha, or Delta variants flow direclty into the recovered compartment

$$\frac{dR(t)}{dt} = (1-\eta)\gamma(I(t) + \sum_{i=A,D} I_i(t)) - \beta_O \nu_O (I_O(t) + I_{OO}(t))R(t) - \xi R(t)$$

Note the two outflows from this compartment are due to breakthrough infections with Omicron and waning immunity.

$$\frac{dR_O(t)}{dt} = (1-\eta_O)\gamma I_O + (1-\eta_{OO})\gamma I_{OO} - \xi_O R_O(t)$$

All those who do not die of Omicron flow into the recovered from Omicron compartment. The evolution of those vaccinated prior to their first COVID infection is given by

$$\frac{dV(t)}{dt} = \lambda(t)S(t) - \beta_O(t)(I_O(t) + I_{OO}(t))\nu_O V(t) - \xi V(t)$$

To measure cumulative first infections (corresponding to the serology data) we introduce a compartment $CI(t)$ that evolves as follows

$$\frac{dCI(t)}{dt} = \left(\beta(t)I(t) + \sum_{i=A,D} \beta_i(t) I_i(t)\right) +$$

$$\beta_O\left(I_O(t) + I_{OO}(t)\right)\Big) S(t) + \beta_O(t)(I_O(t) + I_{OO}(t))\nu_O V(t) - \xi CI(t)$$

The reduced-form for the behavioral response of the transmission rate to the level of daily deaths is given by

$$\beta(t) = \bar{\beta} \exp(-\kappa(t)\frac{dD(t)}{dt} + \psi(t)) \tag{1}$$

and for variants

$$\beta_i(t) = \bar{\beta}_i \exp(-\kappa(t)\frac{dD(t)}{dt} + \psi(t))$$

where the parameters $\bar{\beta}$ and $\bar{\beta}_i$ control the baseline transmissibility of the original and subsequent variants of COVID, the parameter $\psi(t)$ is used to introduce seasonality in transmission, and $\kappa(t)$ is the semi-elasticity of transmission with respect to the level of daily deaths. Note that the relative transmissibility of each variant for any level of daily deaths and point in the seasonal cycle is given by $\bar{\beta}_i/\bar{\beta}$.

To model seasonality in the transmission of the virus, we set

$$\psi(t) = seasonalsize * (\cos((t + seasonalposition) * 2\pi/365) - 1)/2$$

where $seasonalsize$ controls the magnitude of the seasonal fluctuations in transmissibility holding behavior fixed and $seasonalposition$ controls the location of the seasonal peak in transmission. Note that t is indexed to $t = 0$ on February 15, 2020.

To model the change in $\kappa(t)$, I set

$$\kappa(t) = \bar{\kappa} * (1 - normcdf(t, fatiguemean, fatiguesig))+$$

$$fatiguesize * \bar{\kappa} * normcdf(t, fatiguemean, fatiguesig)$$

where $\bar{\kappa}$ sets the initial semi-elasticity of transmission with respect to daily deaths, $fatiguesize$ sets the percentage reduction in this semi-elasticity in the long run, $normcdf$ is the normal CDF, $fatiguemean$ sets the date at which the transition in $\kappa(t)$ from its initial to new long run level is halfway complete, and $fatiguesig$ sets the speed with which that transition occurs.

Initial conditions for all simulations are $E(0) > 0$, $E_i(0) = I(0) = I_i(0) = R(0) = R_O(0) = V(0) = H(0) = D(0) = CI(0) = 0$, $S(0) = 1 - E(0)$. For the United States, $E(0) = 33$ on February 15, 2020 out of a population of 332 million. The model is simulated for four years after its starting date.

A.2 Parameters

In this section we discuss the choice of parameters of the model.

The four variants of COVID-19 considered in the model are the original variant, and the Alpha, Delta, and Omicron Variants. We assume that for all four variants, the rate at which agents flow from exposed (E) to infectious (I) compartments

is given by $\sigma = 0.425$ and the rate at which they flow out of the infectious compartment is $\gamma = 0.4$. The parameter σ corresponds to an expected time before an exposed agent becomes infectious of 2.35 days and the parameter γ corresponds to an expected time for which an infected individual is infectious of 2.5 days. The generation time is defined as the average time between which one infected individual shows symptoms and a person infected by that individual shows symptoms. These two parameters together imply an average generation time of $1/\sigma + 1/\gamma = 4.85$ days.[44] As mentioned above, this generation time sets the time-scale of the epidemic implied by the model.

The rate at which agents flow out of the hospitalized compartment is $\zeta = 1/30$, corresponding to a mean time between infection and reported death of 30 days. The rates at which immunity wanes (so agents from from the R or RO compartments back to the S compartment) are set at $\xi = \xi_O = 1/(3 \times 365)$ corresponding to a mean time in these compartments (and thus with protection from severe disease) of three years.

The baseline transmission rates β_i for the four variants are given by $\bar{\beta} = 3\gamma$ for the original variant, $\bar{\beta}_A = 4\gamma$ for Alpha, $\bar{\beta}_D = 8\gamma$ for Delta, and $\bar{\beta}_O = 15.3\gamma$. The scalar in front of γ corresponds in the model to the basic reproduction number for each variant. Omicron is also assumed to breakthrough to infect those in the R compartment. The parameter ν_O governing the rate of these breakthrough infections is set to 1/10.

The infection fatality rate for the original variant is set to $\eta(t) = 0.01$ from February 15 through mid December 2020. After that time, the infection fatality rate for the original variant, Alpha, and Delta is $\eta(t) = 0.05$. This pattern of declining IFRs is required to simultaneously match the estimates of cumulative COVID deaths and COVID infections from the serology data. The infection fatality rate for someone infected with Omicron out of the S compartment (and thus either with no prior infection or vaccination or whose protection against severe disease has waned) is $\eta_O(t) = 0.0015$ corresponding to 30% of the IFR of the Delta variant that it displaced. This infection fatality rate declines gradually through 2022 and 2023. The infection fatality rate for breakthrough infections with Omicron is set at $\eta_{OO} = 2.25 \times 10^{-5}$ or 1.5% of that of first infections with Omicron.

The Alpha variant is introduced on November 30, 2020. The Delta variant is introduced on April 25, 2021. The Omicron variant is introduced on November 13, 2021

Note that our parameter choices for variant transmissibility $\bar{\beta}_i$ and infection

[44] See `https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html`. On that webpage, the CDC notes a mean time of approximately six days between symptom onset in one person to symptom onset in another person infected by that individual.

fatality rates are chosen to match the time patterns of growth rates of infections (from the serology data) and deaths. As is standard for models of this kind, a number of additional parameters impact the model implications for growth rates of infections and deaths, including the parameters σ and γ impacting the generation interval and the parameter ν_O governing the probability of breakthrough infections. Further work is required to reconcile these parameters and our model specification with other data measuring the timing and speed of the emergence of new variants measured with testing data. The model implications for the prevalence of each variant at each moment in time is given by the vector of $I_i(t)$.

The initial semi-elasticity of transmission with respect to daily deaths (measured as a fraction of the population) for the United States is $\bar{\kappa} = 250000$. To model the onset of pandemic fatigue in the United States, We set $fatiguesize = 0.375$ and $fatiguemean = 285$ and $fatiguesig = 15$. These parameters imply that $\kappa(t)$ falls from its original value of $\bar{\kappa}$ to 35% of that value in mid to late November of 2020. This behavioral parameter then remains constant for the remainder of the simulation.

To model seasonality of transmission in the United States, we set $seasonalsize = 0.35$ (line 74) and $seasonalposition = 20$ (line 77). This seasonal variation in the parameter $\psi(t)$ leads to variation over time in the basic reproduction number of the virus as discussed in the Spring 2021 version of this paper.

To model the impact of vaccines, we set $\lambda(t) = 0.0065$ starting on January 1, 2021 and zero before that date. Vaccines are administered at this rate for the first 185 days of 2021. The rate of vaccination then drops to $\lambda(t) = 0.0065/5$ until the end of 2022 and then $\lambda(t)$ is set to zero after that. In our model, agents in compartment $V(t)$ enjoy full protection from infection by the Alpha and Delta variants and substantial protection against death from Omicron. Thus, we regard the number of agents in this compartment as representing the population that is both vaccinated prior to a first COVID infection and that gained protection from that vaccination. We assume that this is 75% of the total vaccinated. Thus, when we compare the model implications for $V(t)$ to the measures from the serology data on those vaccinated but not infected in Figure 6, we plot $V(t)/0.75$ as a measure of the total population vaccinated.

Table 1: Model Implied Cumulative COVID Deaths:
Baseline and Alternative Scenarios

Baseline behavior and vaccines	1,180,000
Baseline behavior no vaccines	1,975,000
No mitigation with vaccines	3,341,000

Table 2: Model Implied Cumulative COVID Deaths:
Alternative Scenarios For Comparison with Other Estimates

Baseline behavior and vaccines	1,180,000
Baseline behavior and faster vaccines	907,000
Baseline behavior and vaccines through Sep 15 2021	659,000
Baseline behavior no vaccines through Sep 15 2021	1,107,000

Table 3: Model Implied Cumulative COVID Deaths:
Alternative Scenarios Capturing Cross-State Outcomes

Weaker behavior ($0.5 \times \kappa_t$), baseline transmission, with vaccines	1,581,000
Stronger behavior ($2 \times \kappa_t$), baseline transmission, with vaccines	863,000
Faster transmission ($1.5 \times \bar{\beta}_i$), baseline behavior, with vaccines	1,558,000
Slower transmission ($0.66 \times \bar{\beta}_i$), baseline behavior, with vaccines	764,000

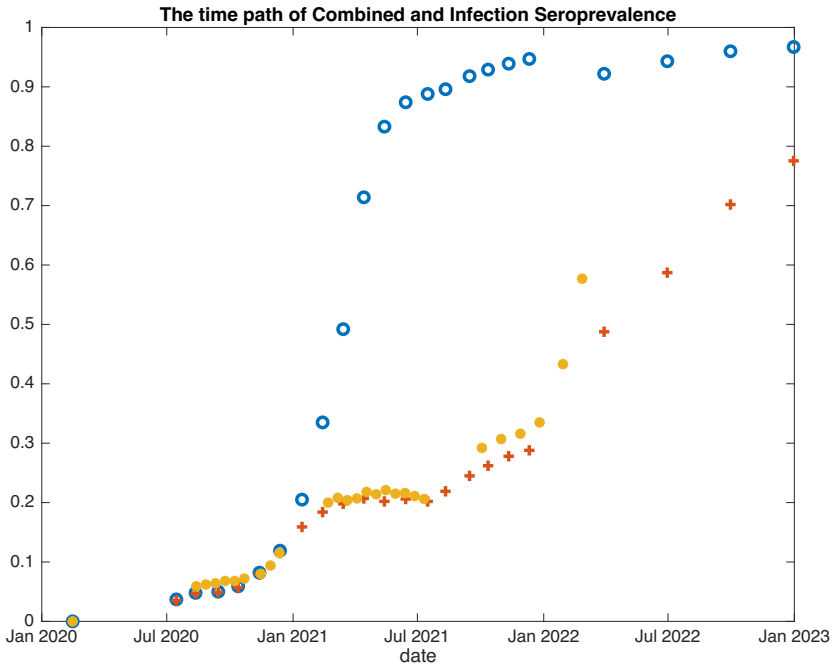

Figure 1: Combined Seroprevalence from Blood Donor Surveys in blue and Seroprevalence from Infection
(Blood Donor Survey in red, Commercial Lab Survey in Yellow) Overall Population

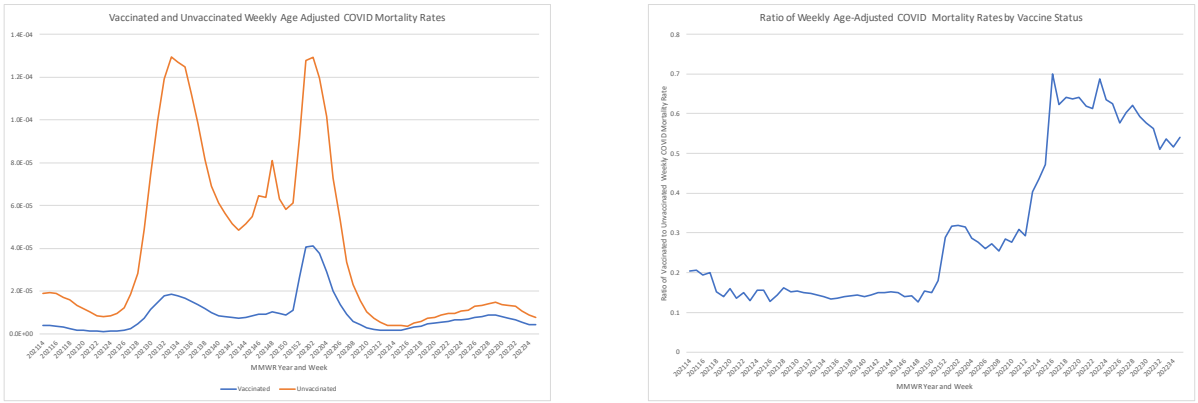

Figure 2: Left Panel: Weekly COVID Age-Adjusted Death Rates per 100K population by vaccination status. These series are a count of weekly COVID deaths for those who had received at least the two primary doses of the original vaccine 14 days prior to death and those that had not, each divided by the corresponding population of those vaccinated and not vaccinated.
Right Panel: the ratio of these weekly mortality rates.

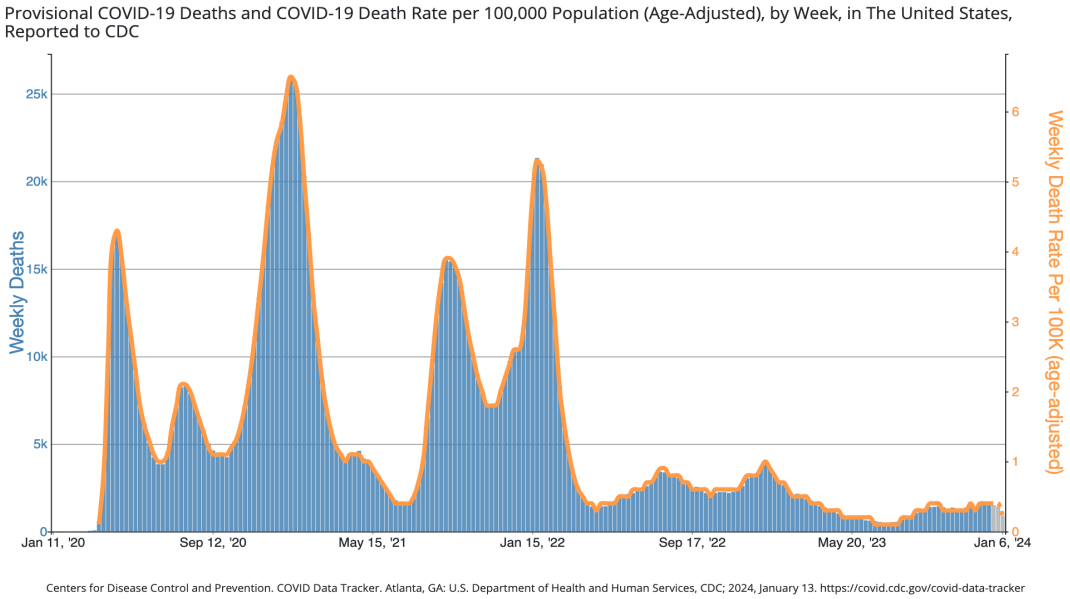

Figure 3: Weekly COVID deaths in the United States. Left Axis total number. Right Axis Cumulative death rate per 100K population age-adjusted.

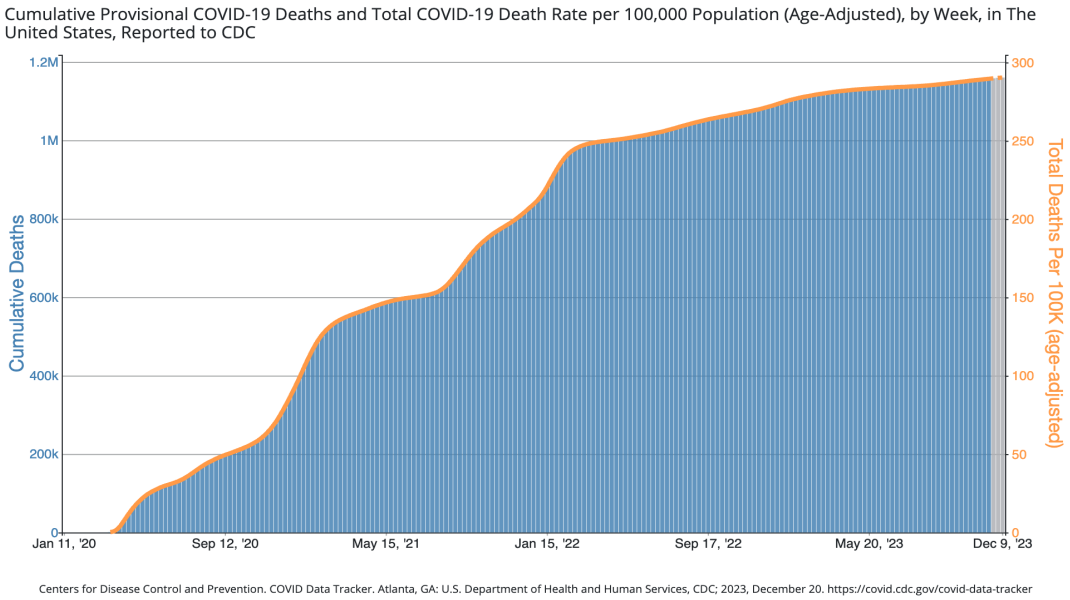

Figure 4: Cumulative COVID deaths in the United States. Left Axis total number. Right Axis Cumulative death rate per 100K population age-adjusted.

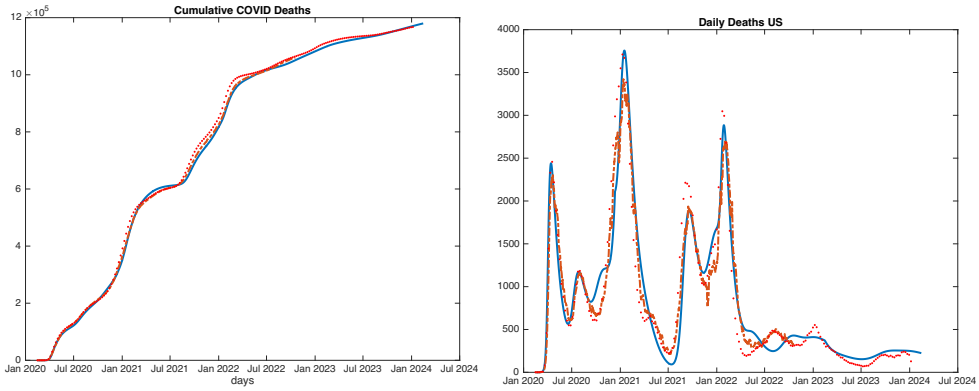

Figure 5: Left Panel: Baseline Model Cumulative COVID deaths in blue and data in red. Right Panel: Baseline Model Weekly COVID deaths in blue and data in red

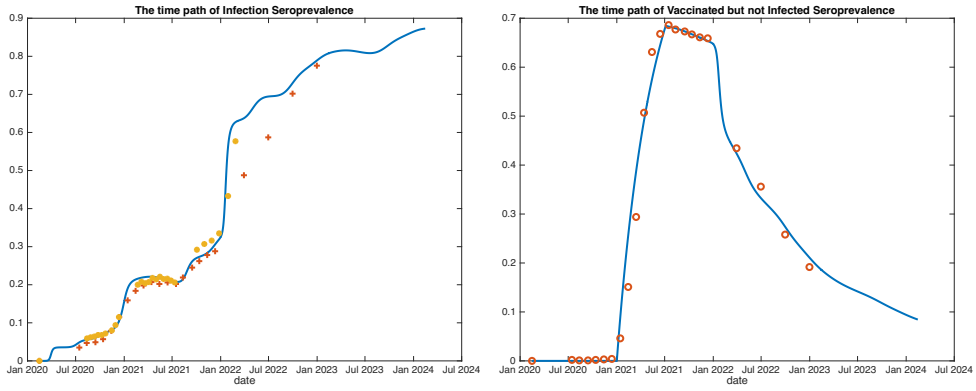

Figure 6: Left panel: Model implied percent infected in blue. Blood donor survey percent infected in red crosses. Commercial lab survey percent infected in yellow stars. Right panel: Model implied percent vaccinated in blue (equal to $V(t)/0.75$ where $V(t)$ is the portion of the population with effective protection after vaccination in the model). Blood donor survey estimate of those vaccinated but not infected seroprevalence in red circles.

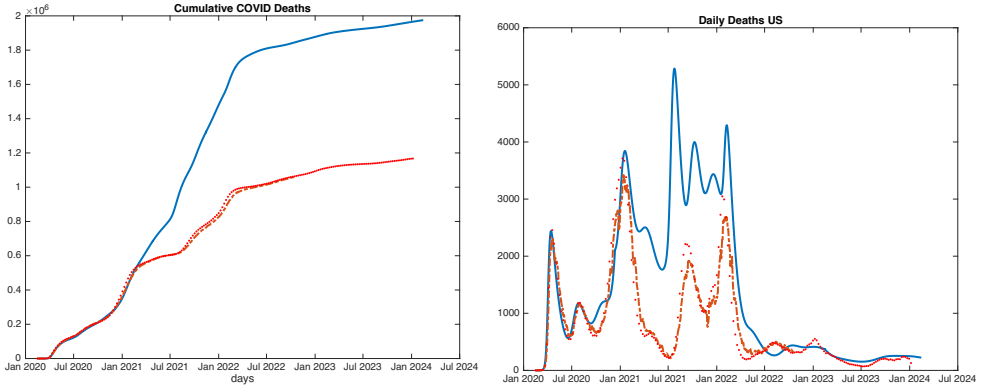

Figure 7: Baseline Model behavior but no vaccines. Left Panel: Cumulative COVID deaths in blue and data in red. Right Panel: Weekly COVID deaths in blue and data in red

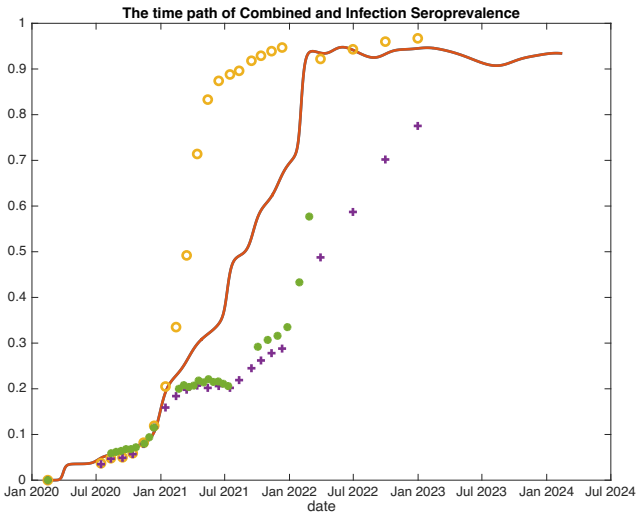

Figure 8: Model implied percent infected in red with baseline behavior and no vaccines. Blood donor survey percent infected in purple crosses. Commercial lab survey percent infected in green. Blood donor survey combined seroprevalence in yellow circles.

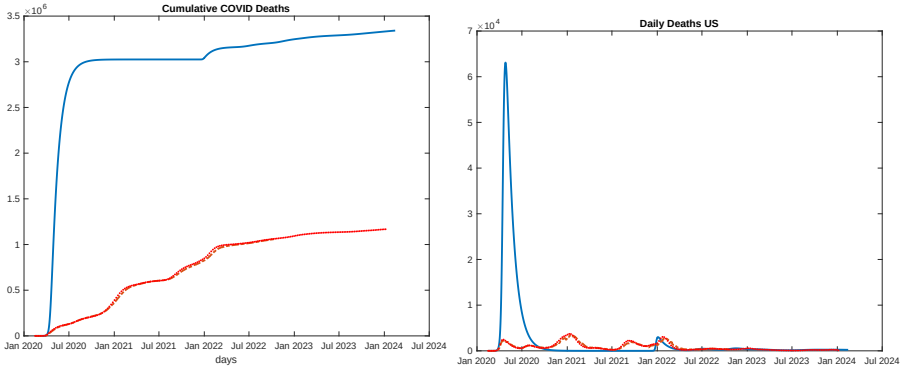

Figure 9: Model with no behavioral response Left Panel: Cumulative COVID deaths in blue and data in red. Right Panel: Weekly COVID deaths in blue and data in red

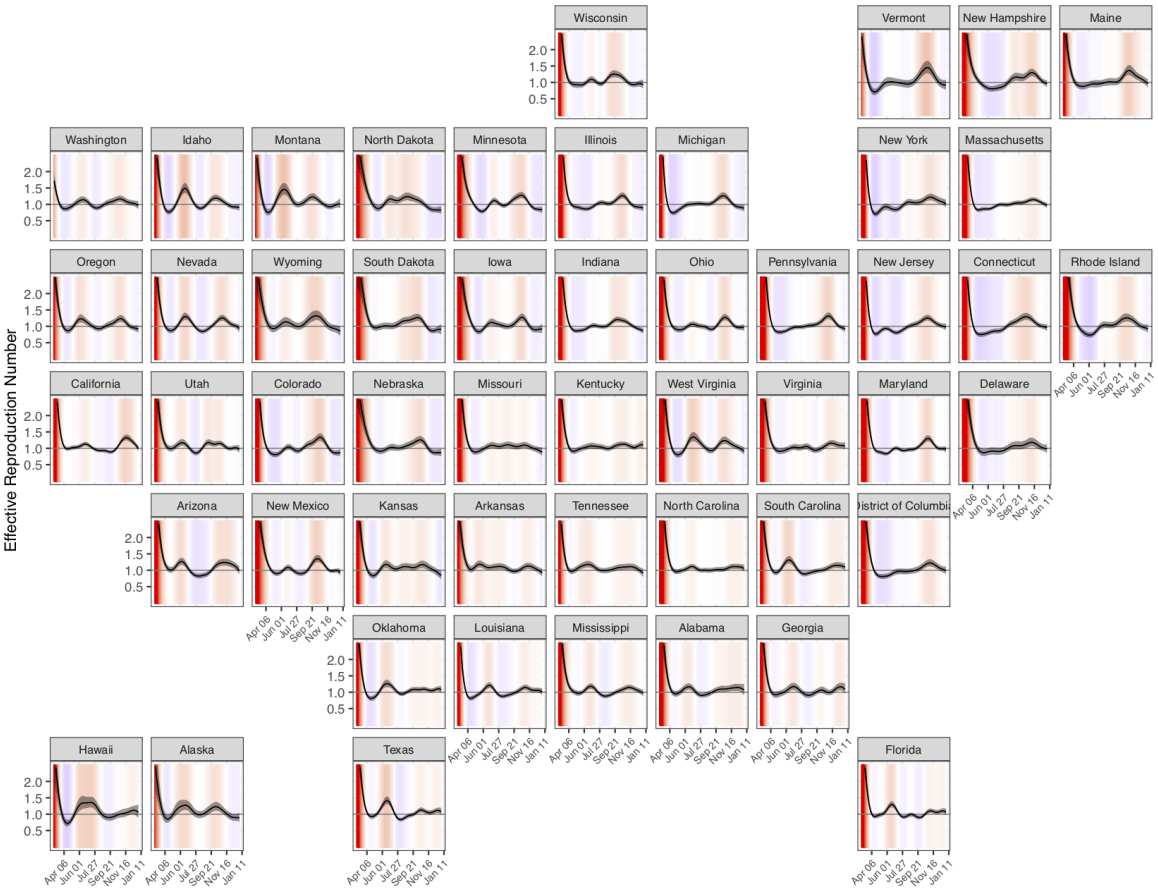

Figure 10: Dynamics of the Effective Reproduction Number by State. This is Figure 4 from Chitwood et al. (2022). $\mathcal{R}_t$ estimates for each US state from March 1, 2020 to January 1, 2021. Background colors indicate whether $\mathcal{R}_t$ is substantially greater than 1 (red), close to 1 (white), or substantially less than 1 (blue). Grey line indicates $\mathcal{R}_t = 1$. Shaded areas represent 95% credible intervals.

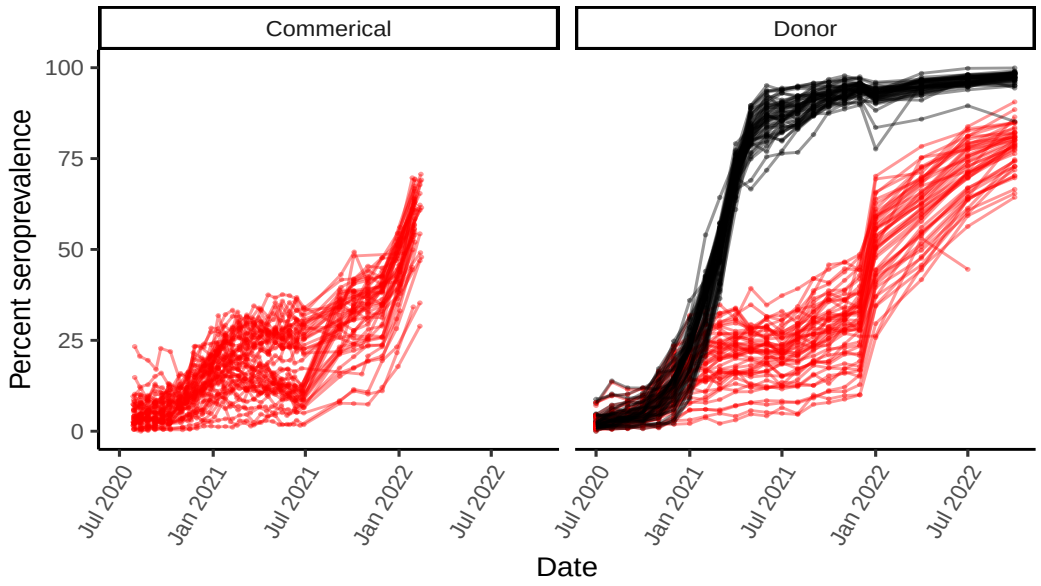

Figure 11: Dynamics of Blood Serology Estimates of Cumulative Infections (red) and Combined Vaccinated and/or Infected (black). Left Panel: Commercial Lab Survey Right Panel: Blood Donor Surveys

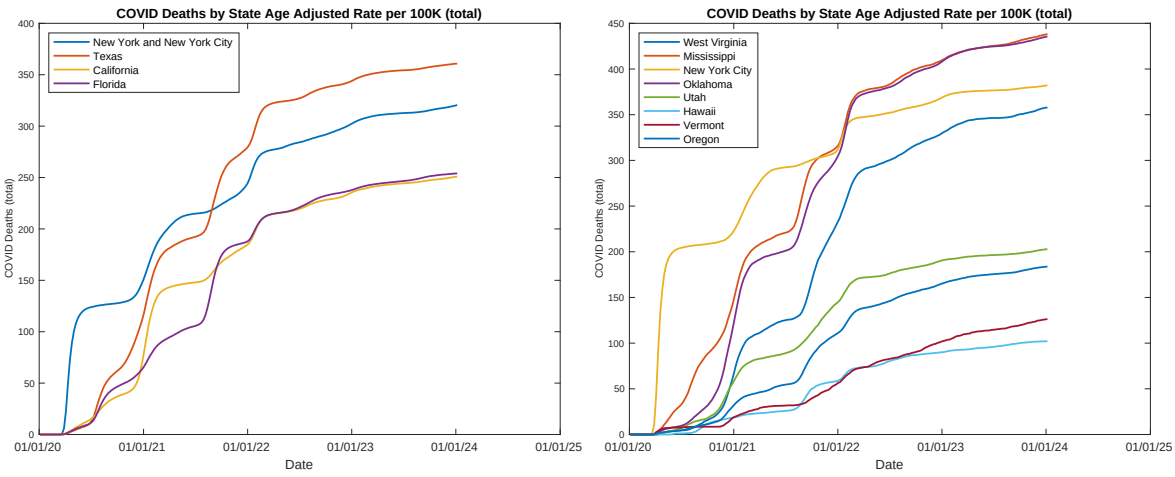

Figure 12: Dynamics of Cumulative COVID Deaths by State Rate per 100K population age-adjusted. Left Panel: Four big states Right Panel: High and Low Outcomes

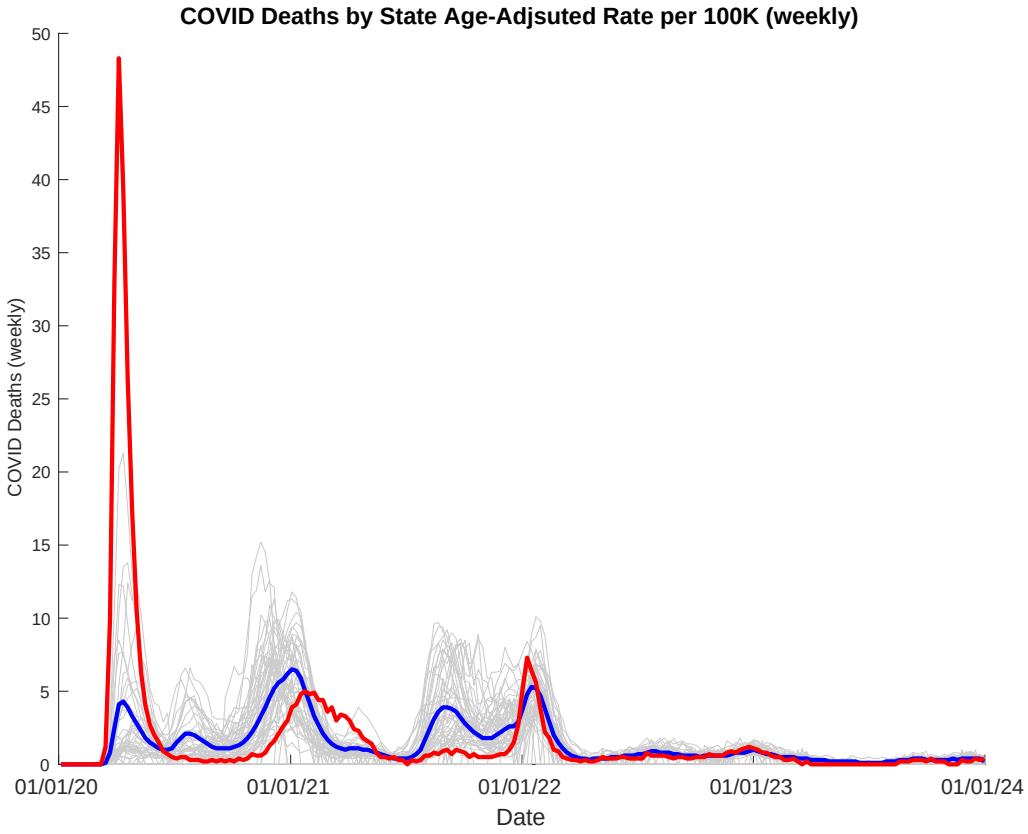

Figure 13: Dynamics of Weekly COVID Deaths by State Rate per 100K population age-adjusted. Red: New York City Blue: United States

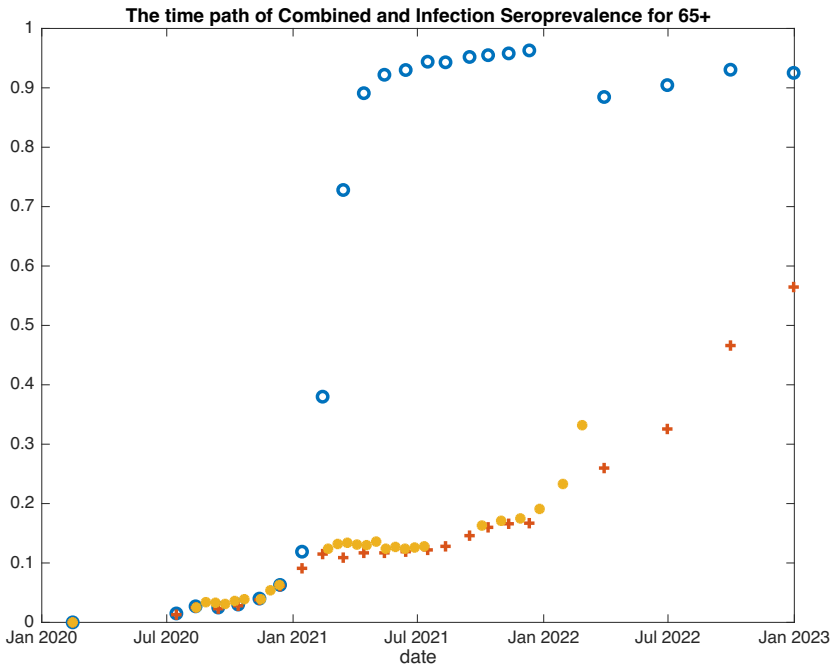

Figure 14: Combined Seroprevalence from Blood Donor Surveys in blue and Seroprevalence from Infection
(Blood Donor Survey in red, Commercial Lab Survey in Yellow) Population 65 and over

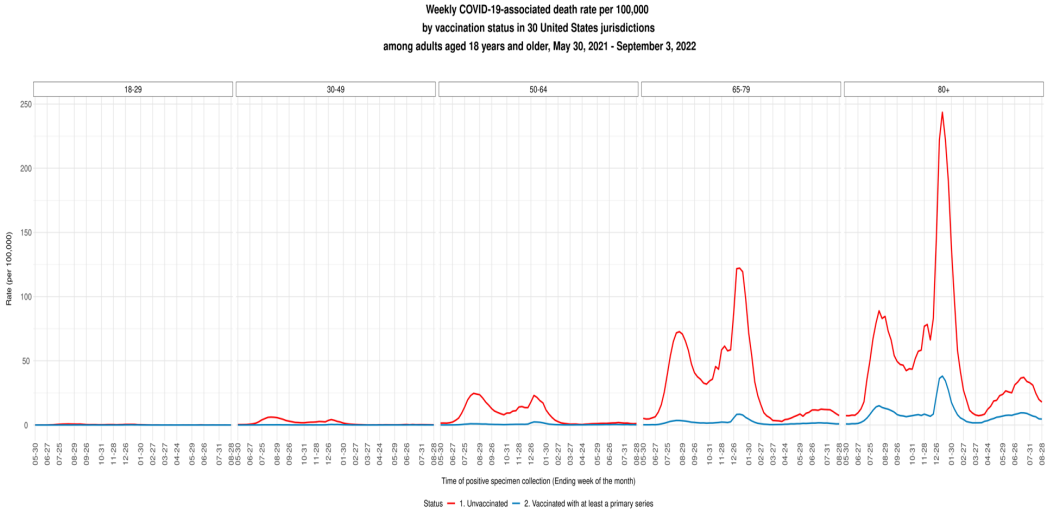

Figure 15: Weekly Mortality by Vaccine Status and Age May 2021 to Sept 2022 from Jia et al. (2023) figure S3. Mortality rates for the unvaccinated are shown in red. Those for the vaccinated in blue.

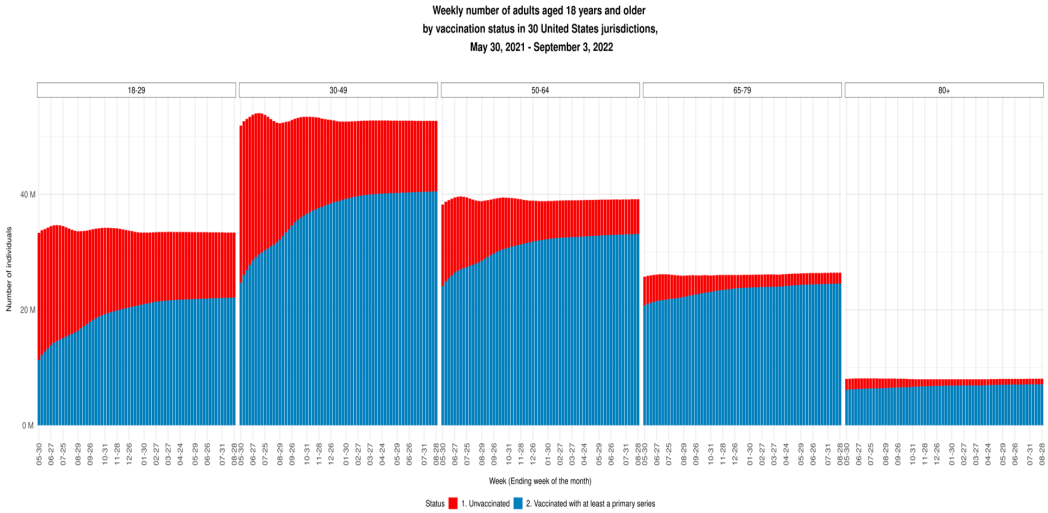

Figure 16: Population by Vaccine Status and Age May 2021 to Sept 2022 from Jia et al. (2023) figure S2, The number of unvaccinated people in each age category is shown in red and the number of vaccinated in blue.

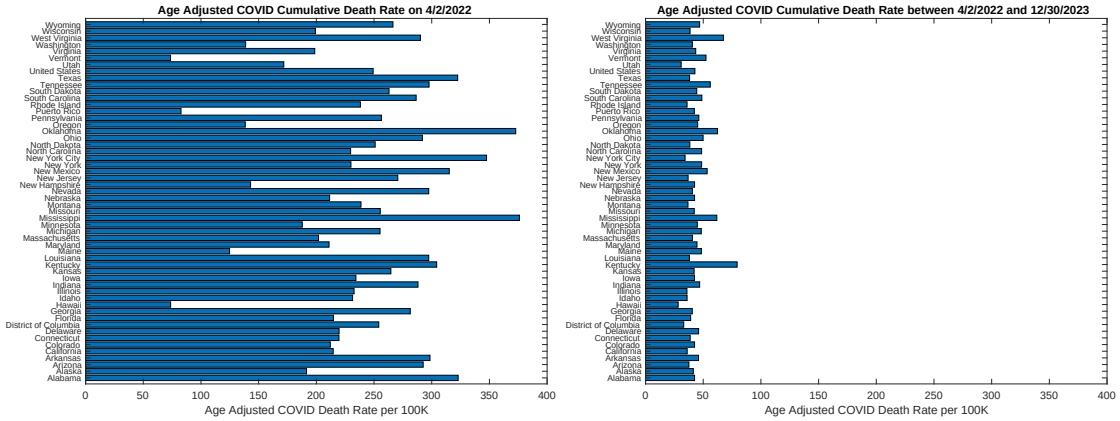

Figure 17: Cumulative COVID Deaths by State Rate per 100K population age-adjusted. Left Panel: January 2020 - April 2, 2022 Right Panel: April 2, 2020 - December 30, 2023

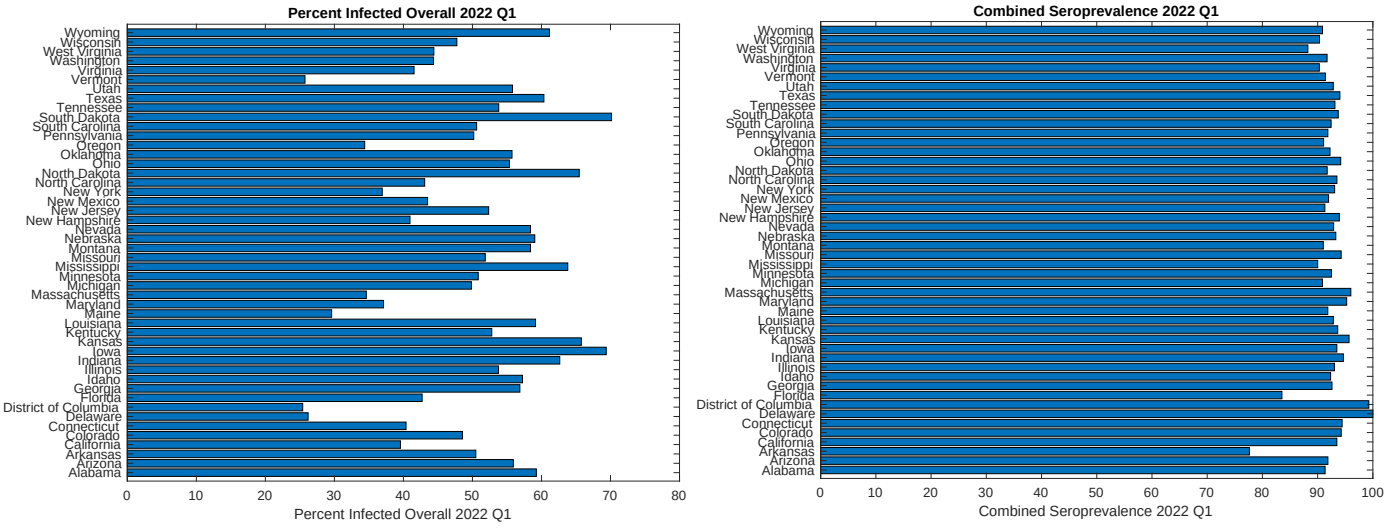

Figure 18: Left Panel: State-level measures of percent infected in Blood Donor Serology Survey First Quarter 2022
Right Panel: State-level measures of Combined seroprevalence in Blood Donor Serology Survey First Quarter 2022

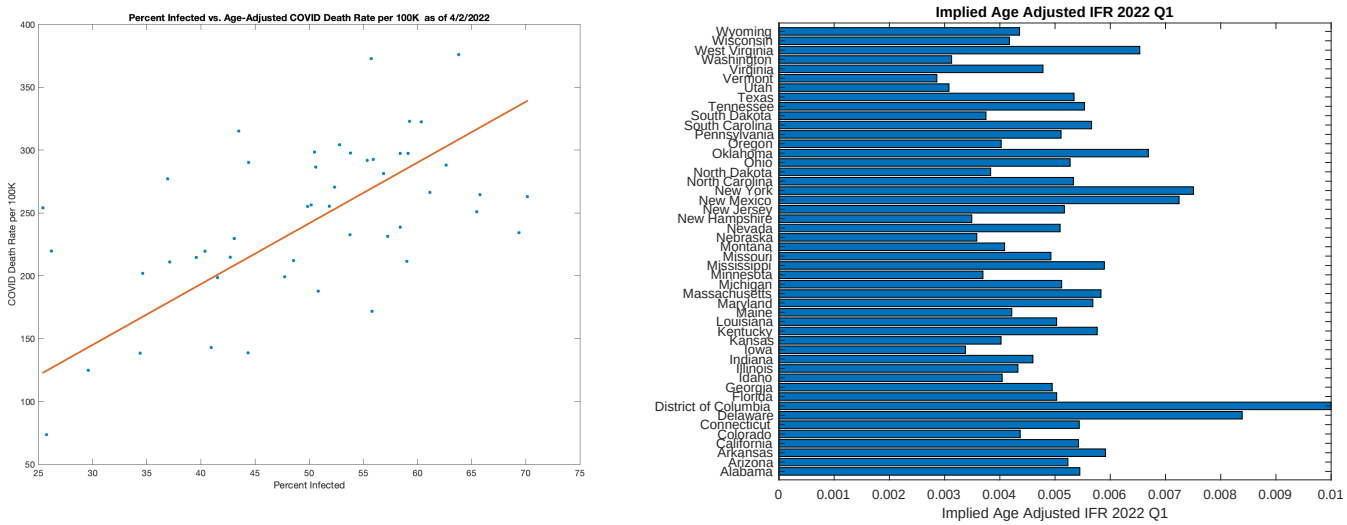

Figure 19: Left Panel: Scatter plot of state-level cumulative COVID mortality as of April 2, 2022 vs. percent infected in Blood Donor Serology Survey First Quarter 2022

Right Panel: State level Infection Fatality Rates implied by these serology and deaths data.

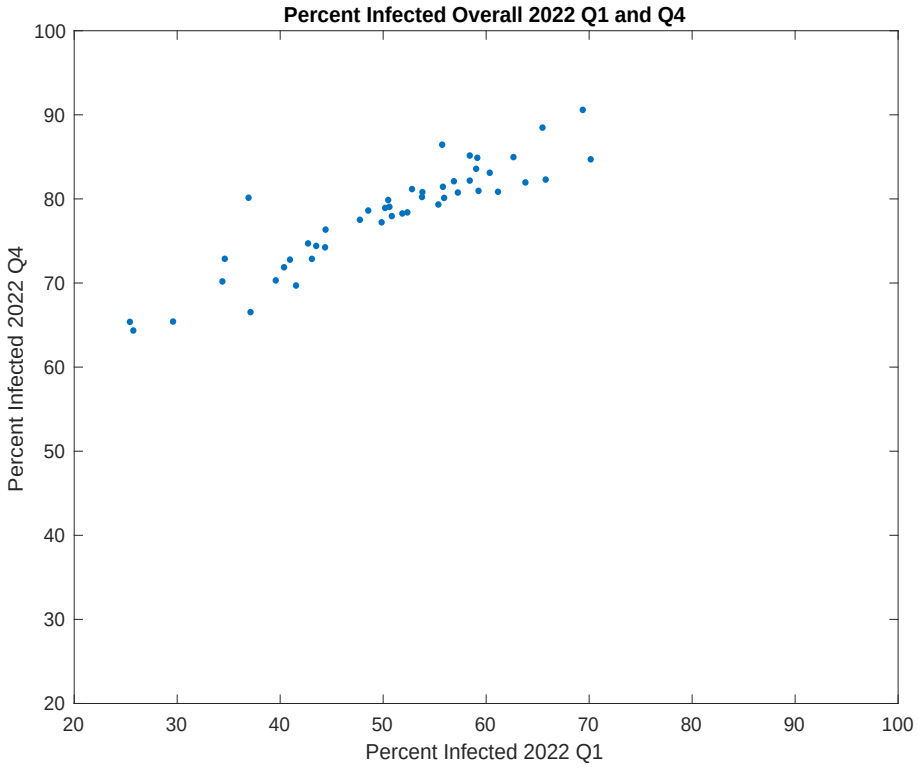

Figure 20: Scatter plot of Blood Donor serology data on percent infected by state in the fourth quarter of 2022 vs. percent infected by state in the first quarter of 2022

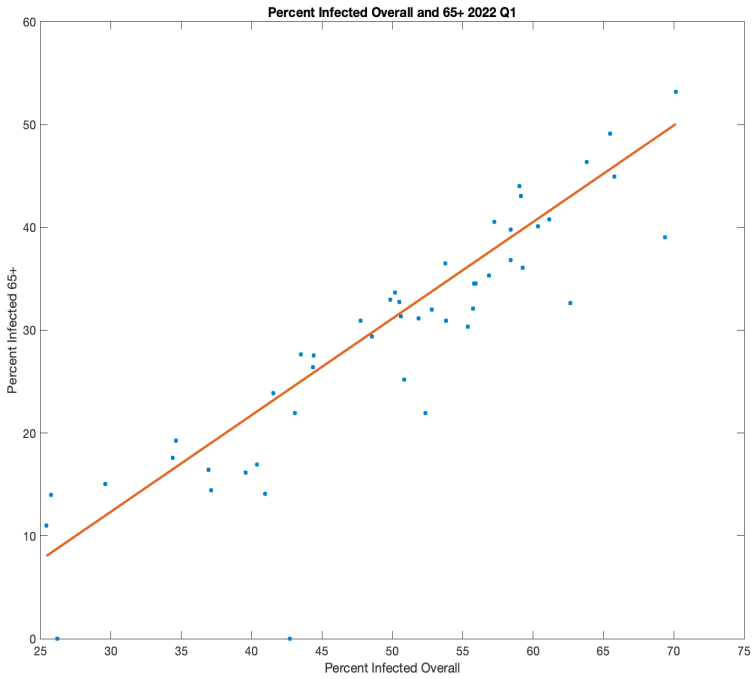

Figure 21: Scatter plot of Blood Donor serology data on percent of those over 65 infected by state in the first quarter of 2022 vs. overall percent infected in the same survey. These data show that the elderly consistently avoided infection relative to the general population across states

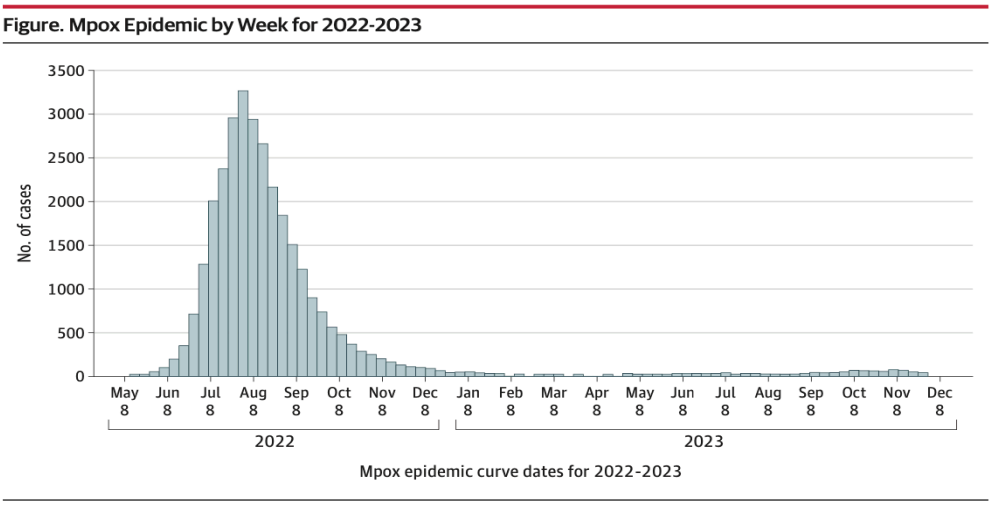

Figure 22: Weekly Mpox cases in the United States 2022 and 2023. This chart is from Daskalakis, Romanik, and Jha (2024)

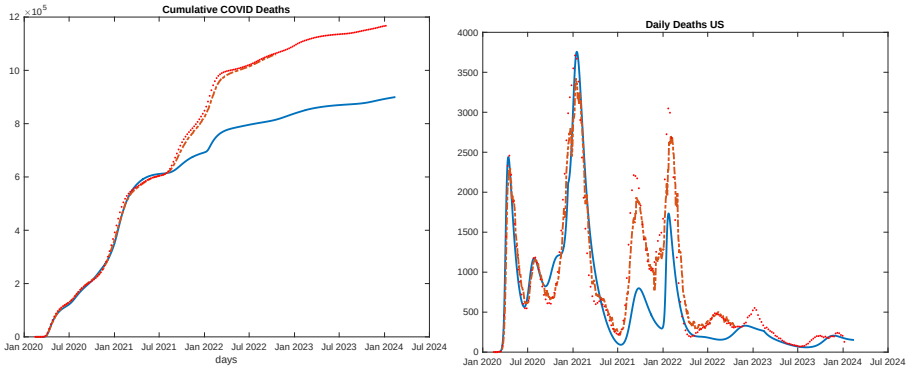

Figure 23: Model baseline behavior with faster vaccines. Left Panel: Cumulative COVID deaths in blue and data in red. Right Panel: Weekly COVID deaths in blue and data in red

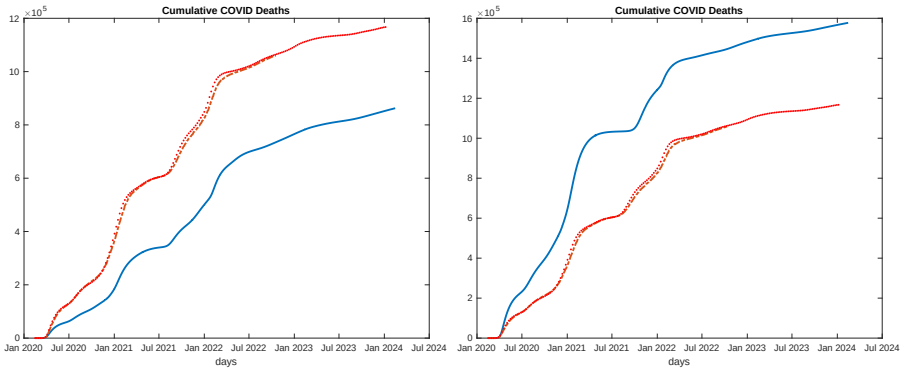

Figure 24: Model with strong and weak behavioral response Left Panel: Strong behavior Cumulative COVID deaths in blue and data in red. Right Panel: Weak behavior Cumulative COVID deaths in blue and data in red

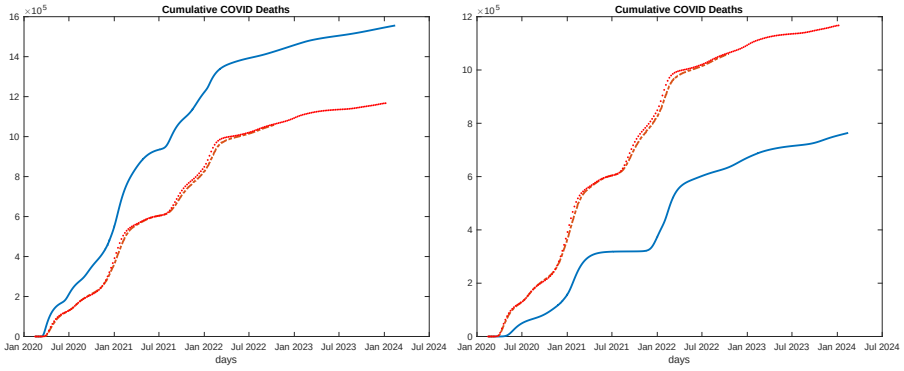

Figure 25: Model with fast and slow transmission Left Panel: Fast Transmission Cumulative COVID deaths in blue and data in red. Right Panel: Slow Transmission Cumulative COVID deaths in blue and data in red

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