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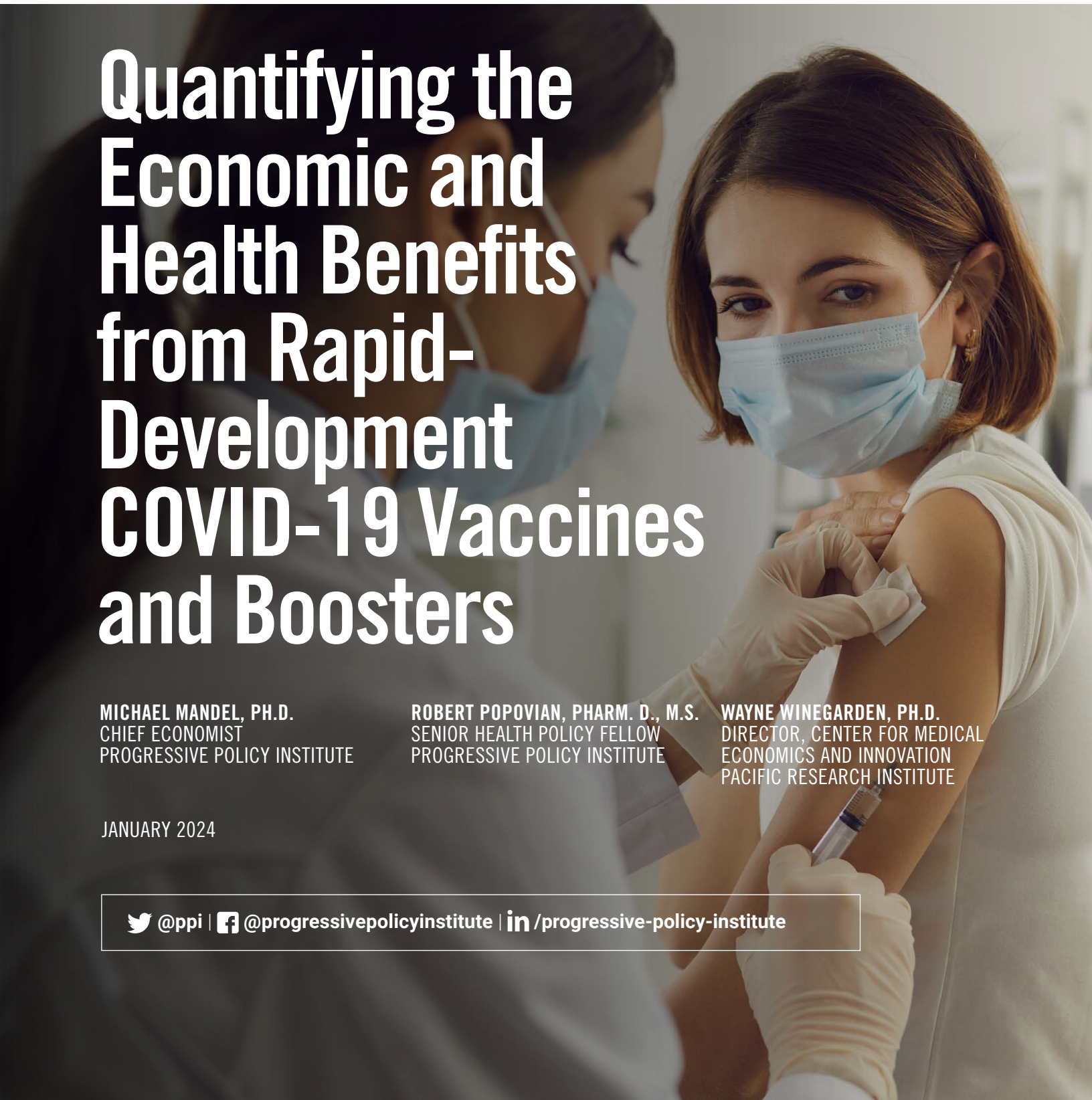

Quantifying the Economic and Health Benefits from Rapid-Development COVID-19 Vaccines and Boosters

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ABSTRACT

This paper assesses the health and economic benefits of the rapid development of COVID-19 vaccines. Using a simple framework of stylized facts, we find that the COVID-19 vaccines saved 2.9 million lives, avoided 12.5 million hospitalizations, and saved $500 billion in hospitalization costs. Importantly, these are conservative estimates, based on the assumption that successfully surviving COVID-19 infection offers protection against future severe outcomes similar to vaccination.

Using the same framework, we examine the consequences to individuals of choosing to receive or not receive new COVID-19 boosters, given the continued evolution of the virus. An illustrative calculation shows that the expected 5-year economic losses to an individual from choosing not to receive boosters rises from $654 at age 30 to more than $65,000 at age 75.

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INTRODUCTION

From the moment COVID-19 was first identified, researchers were projecting the potential economic and human cost of an unchecked major pandemic and the corresponding economic and human benefits of an effective COVID-19 vaccine. Some of these projections were exceedingly influential in guiding private and public responses to the pandemic.

The development, testing, manufacturing, and administration of COVID-19 vaccines to almost 80% of the population over the age of 12 in the United States (fully vaccinated) has been a tremendous scientific and policy achievement.[1] Globally, about 67% of the world population was fully vaccinated as of March 2023.[2]

Unfortunately, hopes that a sufficiently vaccinated population could mostly avoid initial infections have turned out to be excessively optimistic. As of November 2022, 77.5% of the population was estimated to have been infected by COVID-19 at least once.[3] In the 16- to 49- year-old age group, the percentage infected is closer to 85%.

In particular, the Omicron variant turned out to be extremely contagious in the U.S. and globally. As of April 2022, 60 to 80% of the European population was estimated to have been infected with COVID-19.[4] More recent estimates are even higher. According to one model, an estimated 95% of the European population has been infected at least once as of December 2022.[5] In Japan, the cumulative infection rate, measured by antibody tests, rose sharply from 28.6% in November 2022 to 42.3% in February 2023.[6] In Japan, an estimated 80% of the population has been infected at least once.[7] In Korea, the

cumulative infection rate was 83%.[8] Even the draconian measures applied by the Chinese government were unable to contain the wave of infections.

A related observation is that neither infection nor vaccination with the current generation of vaccines appears to offer long-lasting immunity against reinfections.[9] Past a certain point, the spread of the virus through the population could not have been prevented by a more aggressive vaccination program or other policy interventions.

However, the exceedingly good news is that vaccination appears to provide durable protection against severe outcomes such as invasive ventilation and death. Obviously, that might change as new variants arise, but for now, that's what current evidence shows.

Notably, prior infection also appears to provide durable protection against severe outcomes, even for those people who have not been vaccinated. This is no longer a "novel" pathogen attacking unprepared immune systems. Once again, this could change for a sufficiently different variant.

So now we can get a clearer picture of the benefits of COVID-19 vaccination. Vaccination provided a much lower risk path for achieving protection against severe outcomes. Without vaccines, many more people would have died or have been hospitalized.

This paper has both a backward-looking component and a forward-looking component. Based on the evidence, the backward-looking component constructs a set of stylized facts that allow us to understand the economic and health benefits of a rapid-development COVID-19 vaccine compared to reasonable counterfactuals (including no vaccine and more rapid roll-out of the vaccine at the beginning of 2021). These estimates include the mortality and hospitalization outcomes of the "worst case" counterfactual of no successful vaccine, along with the associated health-related costs.

TABLE 1: SUMMARY OF RESULTS (THROUGH MAY 2023)

	ACTUAL	WITH NO VACCINE	DIFFERENCE
ESTIMATED COVID-19 DEATHS (MILLIONS)	1.1	4.1	**2.9**
ESTIMATED COVID-19 HOSPITALIZATIONS (MILLIONS)	4.6	17.1	**12.5**
ESTIMATED COST OF COVID-19 HOSPITALIZATIONS (BILLIONS OF DOLLARS)	$182	$683	**$501**

Source: CDC, PPI estimates

Importantly, these are conservative estimates, based on the assumption that successfully surviving COVID-19 infection offers protection against future severe outcomes similar to vaccination.

Using the same framework, we examine the consequences to individuals of choosing to receive or not receive new COVID-19 boosters, given the continued evolution of the virus. The analysis assumes that existing protection against severe outcomes decays as new variants arise. Once again, there are two pathways for rebuilding protection against severe outcomes: One is receiving a booster shot, and the other is infection by the new variant. When considering the two pathways, it is important to recognize that obtaining protection through infection exposes individuals to potential health consequences that do not arise from gaining protection through vaccination.

Obviously, the benefits of the booster depends on the nature and speed of the changes in the virus. An illustrative calculation shows that the expected economic losses from not receiving boosters over the next 5 years rises from $654 at age 30 to more than $65,000 at age 75.

We acknowledge that this analysis has the benefit of information about the virus and the vaccines that were not available in 2020 and 2021, when policymakers had to make rapid decisions about nonpharmaceutical interventions, such as mandatory business closures and transportation restrictions, and measures such as vaccine mandates. As a result, we do not consider the benefits and costs of such actions.

Finally, we note that the analysis in the paper does not take into account the impact of vaccines on long COVID-19. While there is evidence that vaccinations may mitigate long COVID-19 symptoms, more research is required.

AN OVERVIEW OF PREVIOUS WORK ON THE HEALTH AND ECONOMIC VALUE OF COVID-19 VACCINES

Previous work examining the health and economic value of COVID-19 vaccines goes back to the beginning of the pandemic when the characteristics of the virus and potential vaccines were not well understood. The value of a potential COVID-19 vaccine was initially linked to the ability to avoid a "worst case" scenario, which could not be ruled out in the earliest days of the pandemic.[10] The alternative to a vaccine was assumed to be extensive and persistent imposition of nonpharmaceutical interventions (NPI) such as mobility and social gathering restrictions, business and school closures, and masking requirements.

For example, In October 2020, the RAND Corporation estimated that "As long as there is no vaccine against the disease, the global cost associated with COVID-19 and its economic impact could be $3.4 trillion a year."[11] The authors of the Rand study based their calculation on the assumption that without a vaccine, "physical distancing measures" would still be necessary.

One epidemiological modelling study from 2021 simulating the benefits of a "non-specific" vaccine showed reductions in hospital-days and mortality by more than 50%.[12] However, this study, and others at the time, assumed that one benefit of a vaccine was to achieve herd immunity. The possibility of achieving herd immunity through widespread vaccination was brought up repeatedly as late as December 2020.[13] But by March 2021, skepticism about herd immunity was growing.[14]

With the development and widespread distribution of the vaccine, research turned toward estimating the net economic and health benefits enabled by vaccines. Probably the most complete perspective on these benefits came from a series of analysis sponsored by The Commonwealth Fund.[15] Based on data from their December 2022 report,

> **[f]rom December 2020 through November 2022, we estimate that the COVID-19 vaccination program in the U.S. prevented more than 18.5 million additional hospitalizations and 3.2 million additional deaths. Without vaccination, there would have been nearly 120 million more COVID-19 infections. The vaccination program also saved the U.S. $1.15 trillion (Credible Interval: $1.10 trillion–$1.19 trillion) (data not shown) in medical costs that would otherwise have been incurred.[16]**

These analyses were carefully done and provided an excellent benchmark.

OUR FRAMEWORK

For policy purposes, it is useful to have a simple framework that provides perspective on the net economic and health benefits from the deployment of effective vaccines and boosters. To avoid the sterile vax/anti-vax debates, our framework incorporates the growing consensus that protection against severe outcomes from COVID-19 infections can be obtained through either vaccinations/boosters or previous infection. For instance, the recent meta-analysis from Stein et al. (2023) demonstrates that prior infection provides protection against severe disease similar to high-quality vaccines.[17] Based on their meta-analysis — a statistical analysis that combines the results of multiple scientific studies — they conclude that "the level of protection [against severe disease] afforded by previous infection is at least as high, if not higher than that provided by two-dose vaccination using high-quality mRNA vaccines."[18]

However, obtaining protection through infection exposes people to potential health consequences that do not arise from gaining protection through vaccination.[19] Such considerations are important for understanding the net benefits from receiving additional boosters.

Key assumptions

To provide a practical policy framework, our study starts from several stylized facts:

1. **Based on antibody tests, virtually everyone in the United States has either been vaccinated or shown signs of having been infected by one of the existing variants by the end of 2022, even if they were unaware at the time.** Combined seroprevalence was 96.7% as of the end of 2022.[20] The implication is that anyone who was not vaccinated was likely infected by the end of 2022.

2. **The pre-vaccine probability of dying from a COVID-19 infection — the infection fatality ratio (IFR) — was highly age-dependent, all other things being equal.** In particular, we base the estimates in this paper on the IFR-age curve presented by Sorensen et al. (2022), as reproduced in Figure 1, which presents fatality risk from an initial COVID-19 infection by age on a log scale.[21] This study strongly assumes that the same IFR by age curve applies to all "first exposure" unvaccinated infections in the 2020-2022 period.

3. **Vaccination prior to a "first-exposure" COVID-19 infection substantially reduced the risk of severe outcomes such as death and invasive ventilation.** For the purposes of this paper, we assume that full vaccination reduced the chances of a severe outcome by roughly 90% on average.[22]

4. **Surviving a "first-exposure" COVID-19 infection without being vaccinated gave strong and lasting protection against severe outcomes, which was similar to being vaccinated,** all other things being equal, as per Stein et al. (2023).[23]

5. **Neither vaccination nor prior infection provides lasting protection against repeat infection from the current variants.** Recent studies show a rapid waning of protection against infection or symptomatic disease.[24]

6. **Protection against severe outcomes decays over time as new variants arise.** This is true whether the protection comes from prior infection or vaccination.

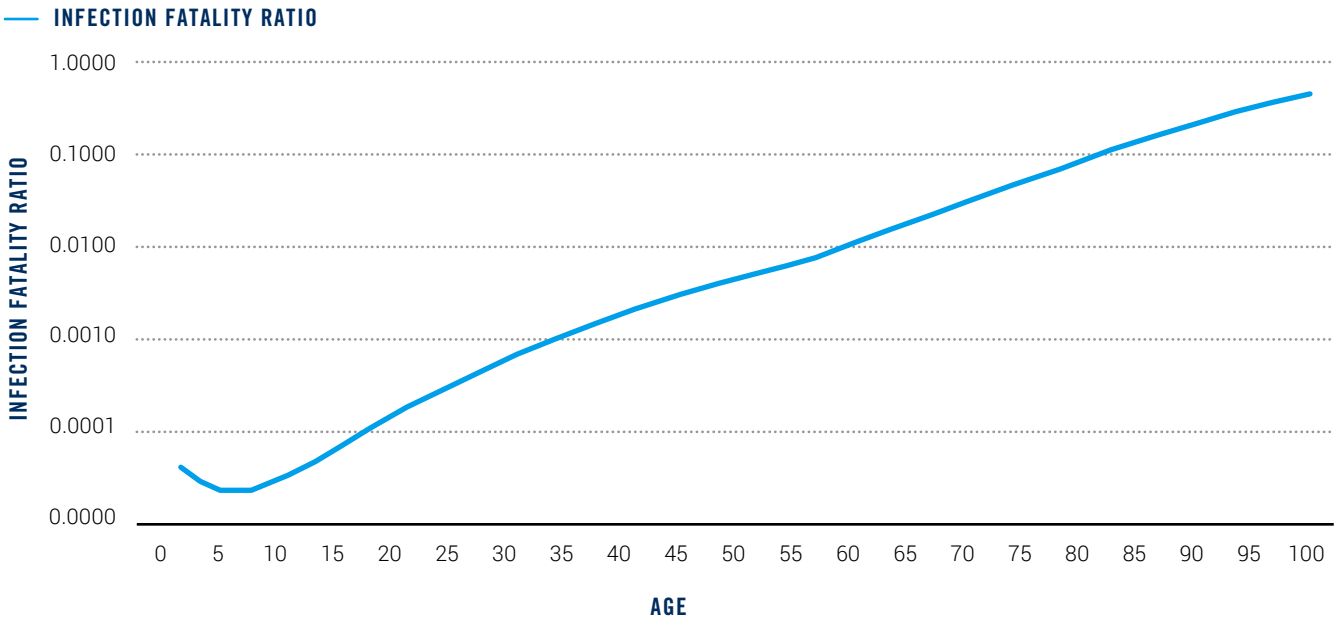
For policy purposes, it is important to discuss assumption 4, the similarity of prior infection and vaccination for achieving protection against severe outcomes. This assumption, combined with assumption 1, suggests that we shouldn't necessarily expect to see higher COVID-19 death rates in states with low vaccination rates as long as the variants don't drift much, since most unvaccinated people in those states will have acquired protection against severe outcomes through previous infection.

To put it another way, assumption 4 implies a low correlation between current state vaccination rates and current short-term COVID-19 death rates. To illustrate this point, we constructed a short-term COVID-19 death rate by state by annualizing the number of COVID-19 deaths reported to the CDC for the first 13 weeks of 2023 and dividing by the state's population.[25] We compared that to the percentage of the population 18+ with a completed primary series in early 2023 by state.[26]

Table 2 shows that there is virtually no correlation between current short-term COVID-19 death rates and current vaccination rates by state. By comparison, cumulative COVID-19 death rates and vaccination have a strong negative correlation.

This table has very important policy implications. It suggests that low vaccination states are not currently suffering health consequences from their low vaccination rates in the short run. But it also suggests that if the COVID-19 virus undergoes a shift that significantly reduces acquired protection against severe outcomes, there could be a noticeable difference in health consequences for states with low booster rates.

FIGURE 1: INFECTION FATALITY RATIO BY AGE



(Based on data from Sorensen et al. 2022)

TABLE 2. CORRELATION OF SHORT-TERM AND CUMULATIVE COVID-19 DEATH RATES WITH STATE VACCINATION RATES*

	CORRELATION WITH STATE VACCINATION RATE
SHORT-TERM COVID-19 DEATH RATE	-.06
CUMULATIVE COVID-19 DEATH RATE	-.57

**Annualized COVID-19 deaths for first 13 weeks of 2023, divided by state population. Florida data based on last week of 2022 and first 12 weeks of 2023. State vaccination rate based on percent of 18+ population having completed primary series.*

Data: CDC, Census, PPI calculations

VACCINES AND COVID-19 FATALITIES

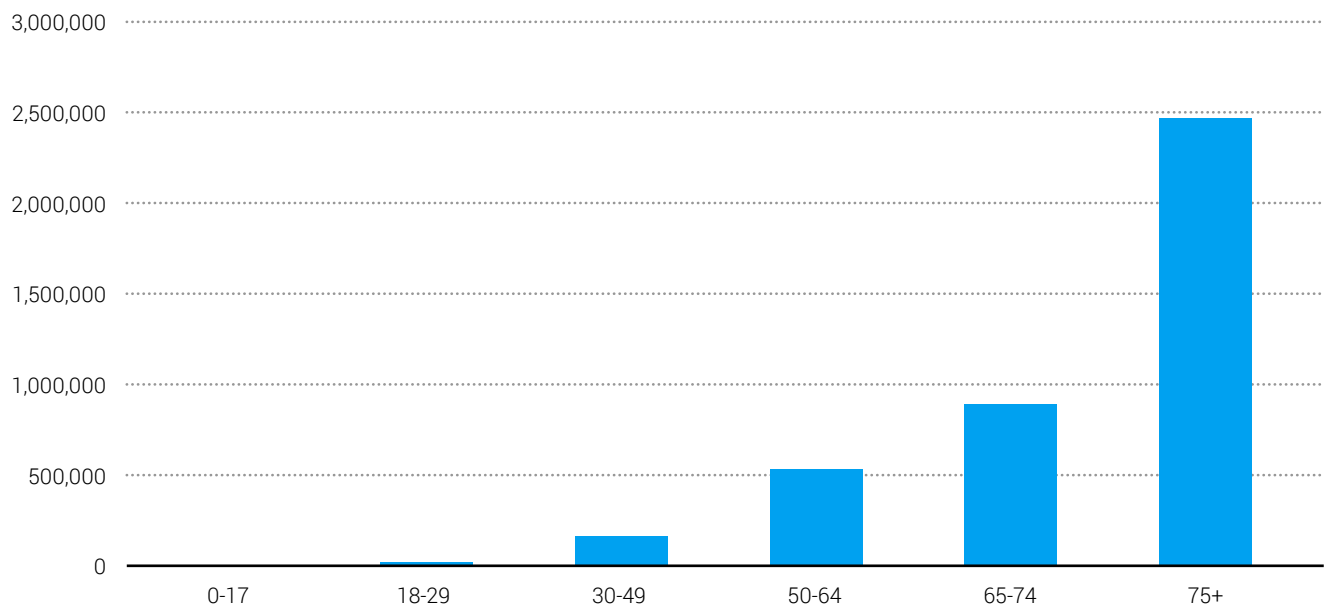
A key fatality benchmark — the hypothetical mortality from COVID-19 by age if no vaccine had been developed — can be constructed based on the IFR curve in Figure 1 and the stylized facts listed above. This benchmark is estimated by multiplying the infection fatality ratio that prevailed for each age by the 2021 population count for the age as measured by the U.S. Census (see Figure 2 and Table 3).[27] We note that these calculations do not take into account the immuno-compromised population.

TABLE 3: HYPOTHETICAL FATALITIES FROM COVID-19- WITH NO VACCINE BY AGE CATEGORY

	DEATHS BY AGE (NO VACCINE)		
	DEATHS (THOUSANDS)	POPULATION (THOUSANDS)	DEATHS % OF POPULATION
0-17	3	73,416	0.00%
18-29	14	53,954	0.03%
30-49	160	85,803	0.19%
50-64	529	63,512	0.83%
65+	3,348	54,827	6.11%
65-74	891	32,372	2.75%
75+	2,457	22,455	10.94%
TOTAL	**4,054**	**331,512**	**1.22%**

Data: Author calculations

FIGURE 2. TOTAL EXPECTED DEATHS, NO VACCINE



Data: Author calculations

The benchmark provides an important perspective on COVID-19's fatality before developing effective vaccines. Based on the assumptions that the entire population would eventually be exposed to COVID-19 and that the infection fatality ratio for each age would remain constant, in total, there was the potential for over four million fatalities from COVID-19, more than three-quarters of whom were in the 65 and older age category. This skewing of the hypothetical fatalities is evident in Figure 2. Overall, total fatalities would have equaled 1.22% of the entire population.

The estimated greater than 4.1 million fatalities under the no-vaccine benchmark are significantly higher than the actual number of cumulative fatalities attributed to COVID-19 through May 6, 2023, which was 1.1 million.[28] These numbers indicate that the total fatalities were 2.9 million lower than the fatality pathway that existed before the introduction of the vaccines (see Table 4). Note that this number is consistent with the Commonwealth Fund study.

TABLE 4: HYPOTHETICAL FATALITIES FROM COVID-19 WITH NO VACCINE COMPARED TO ACTUAL FATALITIES AS OF MAY 6, 2023

	TOTAL CUMULATIVE FATALITIES (THOUSANDS)
NO VACCINE BENCHMARK	4,054
ACTUAL AS OF MAY 6, 2023	1,128
REDUCTION IN FATALITIES	**2,927**

Data: Author calculations

HYPOTHETICAL BENEFITS OF IMMEDIATE DISTRIBUTION

Our simple framework allows us to examine some interesting policy questions. For example, the actual vaccine roll-out was rapid but not instantaneous, exposing some unprotected Americans to COVID-19 during the lag. How many additional lives could have been saved under the unrealistic assumption that the two-dose regimen was available to all adults as soon as the FDA emergency use authorization was issued?

Making this calculation requires two numbers. First, we need to know how many people had already been infected by COVID-19, by age, at the time of the vaccines' introduction. Table 5 shows estimated seroprevalence levels by age as of December 2020, according to data from the NIH COVID-19 Serohub.[29] The more prior exposure in an age group, the less benefit from immediate administration of the vaccine.

The second number is the effectiveness of the vaccines. As noted earlier, we're assuming that the vaccines available for use in early 2021 reduced severe outcomes by 90%. And as noted before, this would include a small number of Janssen vaccine doses with somewhat lower efficacy.

Based on this data, the maximum reduction in fatalities is estimated as the number of deaths as of December 19, 2020, plus the additional fatalities that would have still occurred even with immediate vaccination. The additional fatalities are estimated relative to the number of deaths avoided for each age relative to the estimated fatalities without a vaccine. The additional COVID-19 fatalities following immediate vaccination were calculated by multiplying the total fatalities for each age category by one minus the seroprevalence rate, which is an estimate for the share of each age category that had not yet obtained antibodies to COVID-19 from a previous infection.

Multiplying this "at-risk" group by one minus the vaccine effectiveness estimates the number of fatalities that will still occur even with immediate vaccination. Across all age categories, these calculations indicate that an additional 393,000 deaths would have occurred even had the vaccines been immediately dispensed upon approval. These figures indicate that the minimum number of COVID-19 fatalities, assuming 100% of the population would become infected, is 737,000 (see Table 6). Immediate vaccination would have led to 3.3 million fewer fatalities compared to the no vaccine benchmark.

While irrelevant to the past, the potential decrease in fatalities from the faster vaccination benchmark indicates potentially important benefits gained from rapid vaccination administration against future COVID-19 variants.

TABLE 5: APPROXIMATE SEROPREVALENCE RATES AS OF DECEMBER 2020 BY AGE CATEGORY

AGE CATEGORY	APPROXIMATE SEROPREVALENCE AS OF 12/2020
0-17	20%
18-49	13%
50-64	10%
65+	6%
OVERALL	**15%**

Data: NIH COVID-19 Serohub

TABLE 6: HYPOTHETICAL FATALITIES FROM COVID-19 WITH NO VACCINE COMPARED TO THEORETICAL MINIMUM FATALITIES

	TOTAL CUMULATIVE FATALITIES (THOUSANDS)
NO VACCINE BENCHMARK	4,054
THEORETICAL MINIMUM	737
IMMEDIATE VACCINATION ADDITIONAL FATALITIES	393
PRE-VACCINE FATALITIES (AS OF 12/19/2020)	344
REDUCTION IN FATALITIES	**3,318**

Data: Author calculations

VACCINES AND THE REDUCTION OF COVID-19 HOSPITALIZATIONS

Just as with the fatality calculations, the analysis begins by establishing a benchmark hospitalization scenario. The benchmarks estimate the total hospitalizations that would have occurred without any vaccinations. Applying the benchmark scenario to actual hospitalization rates demonstrates that the COVID-19 vaccines created cost and health benefits due to reduced hospitalizations.

Estimating these benchmarks requires an estimate of the infection hospitalization rate (IHR) for the population, by age category, for those individuals who were infected with the COVID-19 virus before introducing the vaccines.

This measure is calculated in three stages, summarized in Table 7. The first stage estimates the cumulative number of people infected with COVID-19 at the time of the vaccine's approval by multiplying COVID-19's seroprevalence as of December 2020 for each age category by the population of each age category. The second stage estimates the cumulative number of people hospitalized with COVID-19 by age category by multiplying the cumulative hospitalization rate as of January 2021 by the population of each age category. The third stage divides the cumulative number of people hospitalized with COVID-19 by the cumulative number of infected to estimate the infection hospitalization rate before the vaccine.

TABLE 7: ESTIMATING THE PRE-VACCINE INFECTION-HOSPITALIZATION RATE BY AGE CATEGORY

	POPULATION (THOUSANDS)	ESTIMATED SEROPREVALENCE AS OF 12/2020	ESTIMATED CUMULATIVE NUMBER OF INFECTED, PRE-VACCINE (THOUSANDS)	CUMULATIVE HOSPITALIZATION RATE / 100,000 JAN-21	CUMULATIVE NUMBER HOSPITALIZED, PRE-VACCINE (THOUSANDS)	INFECTION HOSPITALIZATION RATE (IHR) BEFORE VACCINE
0-17	73,416	20%	14,683	26.6	19	0.1%
18-49	139,757	13%	18,168	228.5	319	1.8%
50-64	63,512	10%	6,351	567.9	361	5.7%
65-74	32,372	6%	1,942	858.8	278	14.3%
75-84	15,972	6%	958	1,465.7	234	24.4%
85+	6,483	6%	389	2,219.0	144	37.0%
TOTAL	**331,512**		**42,492**		**1,356**	**3.2%**

Data: Author Calculations, NIH COVID-19 Serohub, CDC

These calculations demonstrate that, before introducing the vaccine, 3.2% of all people infected with COVID-19 were hospitalized. As with the fatality data, the hospitalization rate varied significantly across different categories, with the older age categories experiencing much higher hospitalization rates than younger ones.

The cumulative number of hospitalizations under the no vaccine benchmark is estimated by applying the infection hospitalization rates for each age category to the category's total population, assuming that everyone would eventually have been infected with COVID-19. This analysis's actual number of hospitalizations applies the cumulative hospitalization rates as of January 2023 for each age category (see Table 8) to the category's total population.

TABLE 8: CUMULATIVE HOSPITALIZATION RATES AS OF JANUARY 2023 BY AGE CATEGORY

	CUMULATIVE HOSPITALIZATION RATE / 100,000
0-17	184.8
18-49	791.6
50-64	1,748.0
65-74	2,764.0
75-84	4,975.0
85+	7,954.0

Data: CDC

TABLE 9: TOTAL HOSPITALIZATIONS: NO VACCINE BENCHMARK AND ACTUAL, BY AGE CATEGORY

	HOSPITALIZATIONS ASSUMING NO EFFECTIVE VACCINE AND EVERYONE EVENTUALLY INFECTED (THOUSANDS)	ACTUAL HOSPITALIZATIONS (THOUSANDS)
18-49	2,456	1,106
50-64	3,607	1,110
65-74	4,633	895
75-84	3,902	796
85+	2,398	516
TOTAL (INCLUDING CHILDREN)	**17,094**	**4,557**

Data: CDC, Author calculations

Given the significant costs associated with the average COVID-19 hospitalization, these reductions indicate that vaccinations have enabled large reductions in hospitalization costs. Table 9 illustrates that, compared to the no-vaccine benchmark of 17.1 million hospitalizations, the introduction of vaccinations helped reduce the actual number of hospitalizations by more than 12.5 million people.

According to one 2022 study from KFF, the average cost of a COVID-19 hospitalization in 2020 for patients with large employer coverage was $41,611.[30] Another source estimated the average allowed cost of a complex COVID-19 in-patient stay in 2021 as $98,139, and the average allowed cost of a "noncomplex" COVID-19 hospitalization as $33,525.[31] Other estimates fall into the same range.

Using an assumption of an average $40,000 in cost for a COVID-19 hospitalization, the 17.1 million hospitalizations that would have occurred under the no-vaccine benchmark would have led to $683.7 billion in hospitalization costs. This is 275% higher ($501.4 billion) than the estimated total costs that occurred, which are $182.3 billion. Vaccinations, consequently, helped avert these $501.4 billion in hospital expenditures. (Table 10).

THE NEED FOR COVID-19 BOOSTERS

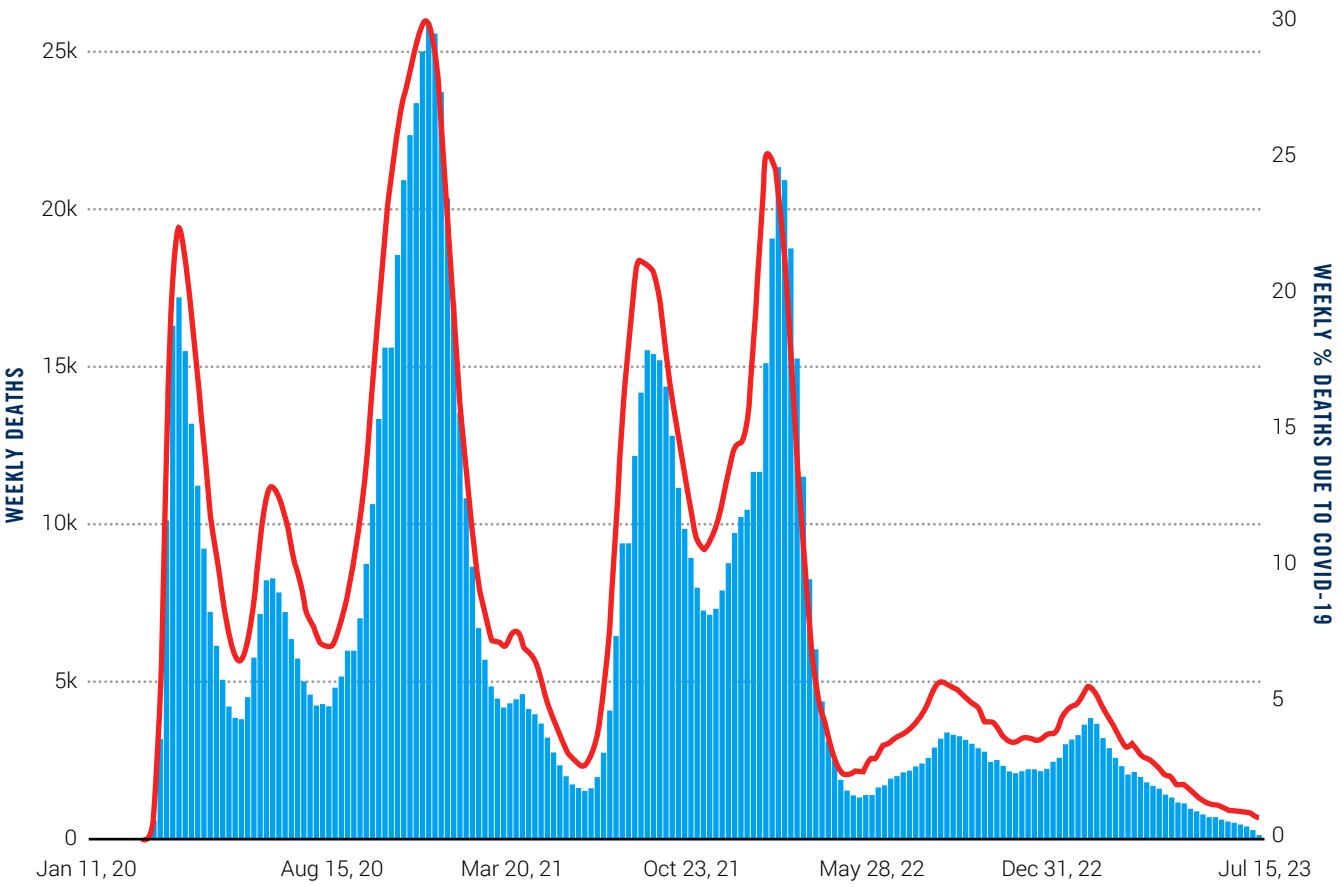
We apply this analytic framework to understanding the benefits and choices around the rapid development of COVID-19 boosters. As of July 2023, the CDC is reporting that the number of COVID-19 deaths and the percentage of reported deaths from COVID-19 are down to their lowest levels since the pandemic started (the latter figure is less affected by incomplete data reporting).[32] The death rate is highest for the oldest Americans, but even that has been falling, as most Americans have high-quality protection against severe outcomes from current variants, either from vaccination or prior infections. (See Figure 3).

TABLE 10: TOTAL HOSPITALIZATION COSTS INCURRED: NO VACCINE BENCHMARK AND ESTIMATED CURRENT (ASSUMING AN AVERAGE $40,000 IN COST PER HOSPITALIZATION)

	TOTAL HOSPITALIZATION COSTS (BILLIONS OF DOLLARS)
NO VACCINE BENCHMARK	$683.7
ESTIMATED ACTUAL COSTS	$182.3
REDUCTION	$501.4

Data: Author calculations

FIGURE 3: PROVISIONAL COVID-19 DEATHS AND PERCENTAGE OF DEATHS DUE TO COVID-19 BY WEEK IN THE UNITED STATES REPORTED TO CDC



Data: CDC, downloaded July 2023

Nevertheless, the COVID-19 virus has already given rise to several important new variants and subvariants over its relatively short-recorded history. That suggests there's a good chance that the virus will continue to drift or shift over time, either slowly or rapidly. Possible sources of new variants include animal reservoirs such as deer, which may have accelerated rates of mutation compared to human hosts.[33] Chronic infections in immunocompromised people can give the virus "an extended period of time during which it can acquire rare combinations of mutations."[34, 35]

These changes in the virus can potentially evade the immunity acquired via infection or vaccination, raising the odds of hospitalization or death from COVID-19. You can think of the current level of protection against severe outcomes being degraded, at a highly uncertain rate.

The response of private and public actors in the health care ecosystem to new variants will be to develop, approve, manufacture, and distribute targeted boosters. This effort includes vaccine manufacturers, the FDA, the CDC, health insurers, and retail pharmacies. There are no

guarantees, but based on the performance of the current vaccines and boosters, we will assume in this paper that receiving a COVID-19 booster will restore durable protection against severe outcomes back to the 90% level, as well as temporarily protecting against infection.

THE BOOSTER CHOICE

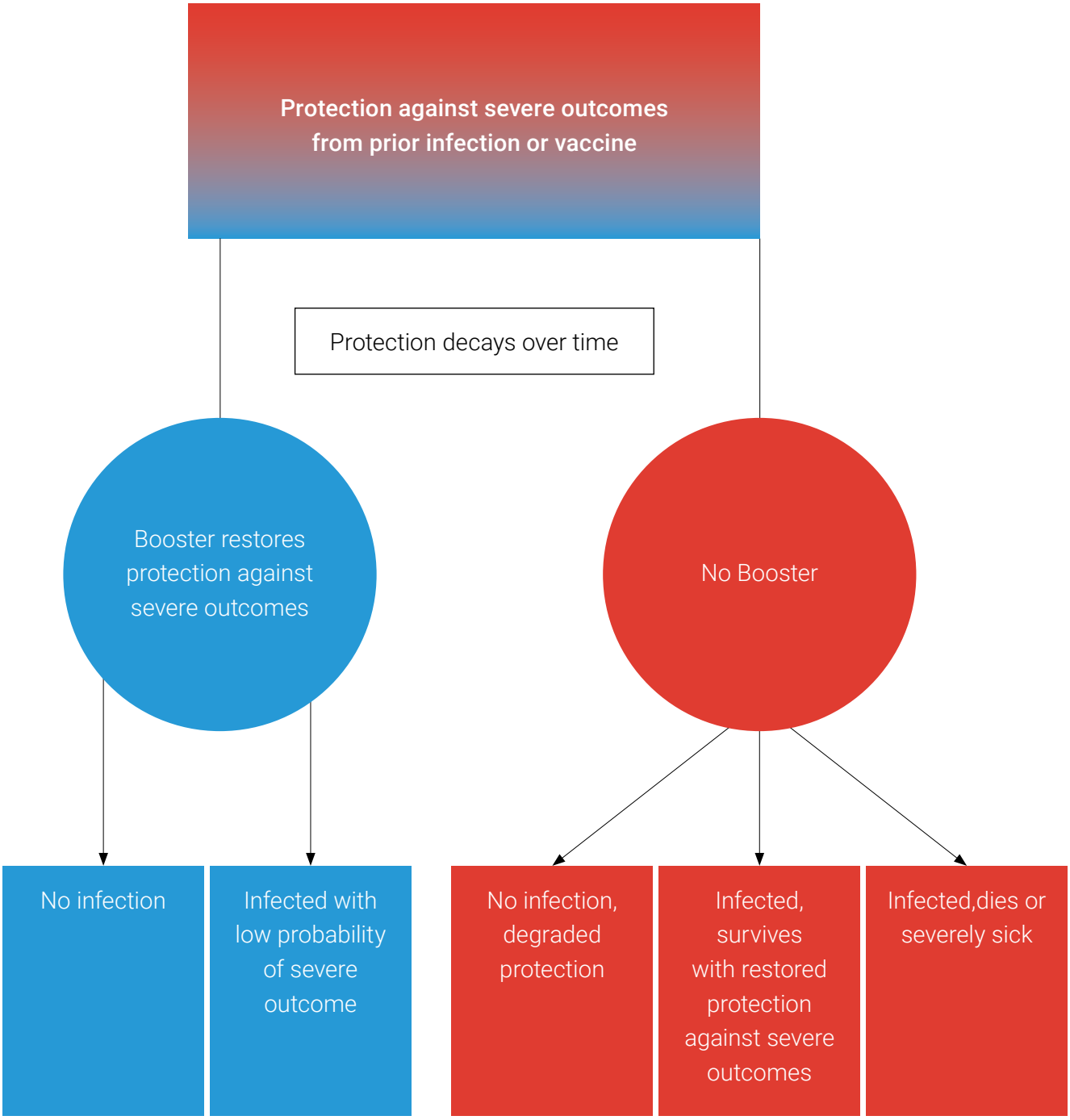
Booster uptake is not expected to be universal — far from it. Based on interviews conducted from November to December 2022, only 27.1% of adults and 18.5% of adolescents who had completed a COVID-19 primary series received a bivalent booster.[36] Based on our analytic framework, how can we understand the choice to take or not take the booster?

Figure 4 lays out a model of the decision process. If an individual takes the booster, we will assume that it restores the original level of protection against severe outcomes. Then either the individual avoids infection, or gets infected with a low probability of a severe outcome.

The decision tree associated with the choice not to get a booster has three branches rather than two. First, the individual can avoid infection. Second, the individual can get infected and survive with restored protection against severe outcomes. Third, the individual can get infected and experience a severe outcome such as death.

It's important to note that people who choose to not get a COVID-19 booster over time risk becoming infected down the road, after their protection against severe outcomes has begun to wane. That in turn exposes them to a higher chance of experiencing severe outcomes. The exact probability depends on how long it's been since protection was acquired through infection and how fast it decays.

FIGURE 4: DECISION TREE AND IMPLICATIONS OF RECEIVING BOOSTER OR DECLINING BOOSTER



QUANTIFYING THE BENEFITS OF A COVID-19 BOOSTER

In the Appendix, we show how to quantify the benefits of taking an annual COVID-19 booster versus not taking one. More precisely, we look at the benefits of taking a booster each year versus refraining from taking a booster every year. We'll call this the "repeat booster strategy" compared to the "no booster strategy."

To demonstrate the benefits of receiving a booster, we perform several illustrative calculations. First, we estimate the *relative fatality probability* between the no-booster scenario and the repeated booster scenario. The relative fatality probability is the increased odds of an individual dying from COVID-19 in period j by choosing not to take the booster, compared to that same individual taking the booster every year. This is a useful calculation because it is age-independent.

For this illustrative calculation, we assume that initial protection for everyone starts at 90%, and decays linearly over 10 years without boosting. With a well-timed booster, protection stays at 90%. Obviously, the real-world evolution of protection may differ. For example, the shift from the Delta variant to the Omicron dramatically increased the transmissibility of the virus, without necessarily degrading protection against severe outcomes. However, these values provide a reasonable case to benchmark the relative benefits of receiving COVID-19 boosters.

We also assume the probability of getting infected with COVID-19 each year without the booster is 10%, or roughly the probability of contracting the annual flu.[37] Table 11 lays out two alternative scenarios. In scenario 1, the booster provides no additional protection against infection, so the odds of infection are 10%.

In scenario 2, the booster reduces the odds of infection to 7.5%.

Under scenario 1, an individual who does not take the booster faces odds of dying from COVID-19 that are 1.9 times higher than the odds of mortality with a booster (which might be quite low, depending on age). The difference increases over time as the immunity protection degrades over time without a booster. By year 5, the expected annual COVID-19 fatality rate for the no-booster strategy is 4.7 times that for the repeat booster strategy.

Under scenario 2, in the first year an individual who does not take the booster faces odds of dying from COVID-19 in the first year that are 2.5 times higher than the odds of mortality with a booster (which might be quite low, depending on age). The difference increases over time as the protection against severe outcomes degrades over time without a booster. By year 5, the expected annual COVID-19 fatality rate for the no-booster strategy is 6.2 times that for the repeat booster strategy.

Note that these calculations are tied closely to the rate at which protection against severe outcomes degrades over time. However, we assume that both natural immunity and vaccine-mediated immunity follow the same time paths.

This framework allows us to compare 5-year cumulative COVID-19 fatalities for the no booster and the repeat booster strategies. For a range of "no immunity" infection fatality ratio, Table 12 shows the expected cumulative fatality ratio per 100,000 people.

TABLE 11: ILLUSTRATIVE SCENARIOS: RELATIVE FATALITY PROBABILITY BY YEAR (NO BOOSTER VERSUS REPEAT BOOSTER)

	YEAR BEGINNING FALL OF				
	2023	2024	2025	2026	2027
ILLUSTRATIVE SCENARIO 1: ANNUAL PROBABILITY OF INFECTION IS 10% FOR BOTH NO-BOOSTER AND BOOSTER INDIVIDUALS	1.9	2.7	3.4	4.1	4.7
ILLUSTRATIVE SCENARIO 2: ANNUAL PROBABILITY OF INFECTION IS 10% FOR NO-BOOSTER INDIVIDUALS AND 7.5% FOR BOOSTER INDIVIDUALS	2.5	3.6	4.6	5.5	6.2

Relative fatality probability is the ratio of the annual COVID-19 death rate for a no booster individual versus that same individual taking a booster every year. Assumes linear decay of protection over 10 years, starting from 90%

TABLE 12: COMPARING CUMULATIVE COVID-19 FATALITY RATES BETWEEN PEOPLE NOT RECEIVING BOOSTERS VERSUS PEOPLE RECEIVING REPEATED BOOSTERS

	CUMULATIVE COVID-19 FATALITIES PER 100,000 AFTER 5 YEARS	
UNDERLYING INFECTION FATALITY RATIO (WITHOUT NATURAL OR VACCINE-MEDIATED IMMUNITY)	NO BOOSTERS	REPEATED BOOSTERS
0.05%	8	2
0.1%	17	4
0.5%	84	19
1.0%	168	37
5.0%	840	187

Assumptions: linear decay of protection over 10 years, starting from 90%. Based on scenario 2, annual probability of infection is 10% for no booster individuals versus 7.5% for individuals who receive boosters.

TABLE 13: EXPECTED ECONOMIC GAINS FROM RECEIVING BOOSTERS: 10-YEAR DECAY OF PROTECTION

AGE	EXPECTED ECONOMIC GAINS FROM RECEIVING BOOSTERS ANNUALLY OVER FIVE YEARS, COMPARED TO NO BOOSTERS (DOLLARS)
30	$654
35	$1,308
52	$6,538
60	$13,074
75	$65,255

Assumptions: Linear decay of protection over 10 years, starting from 90%. No booster annual probability of infection= 10%. Booster annual probability of infection = 7.5%. Assuming $10 million statistical value of a human life, not including hospitalization or productivity losses

Table 13 associates a "no immunity" IFR with an age group, based on the IFR-age curve shown in Figure 1. We assume the statistical value of a human life is $10 million, consistent with federal government estimates.[38] Based on this assumption, we see that the benefit of the repeat booster strategy rises from $654 for 30-year-olds to $65,000 for 75-year-olds.

We make several important caveats here. First, this illustrative example is based on several assumptions, including the decay rate of protection and infection rate. Second, if we push the analysis past five years, we would have to consider putting a floor on how low Protection[i] can drop.

Importantly, a faster decay rate of protection, which is likely should the virus experience large mutations, would significantly increase the dollar benefits enabled by the repeat booster strategy. For example, as Table 14 illustrates, a 20% decay in the protection enabled by past infection or past vaccination would lead to significant increases in the dollar benefits across all age groups. Given the large mutation experiences that have already occurred with respect to this virus, there are sound reasons to believe that the potential benefits estimated in Table 13 are conservative lower-bound estimates.

TABLE 14: EXPECTED ECONOMIC GAINS FROM RECEIVING BOOSTERS: 5-YEAR DECAY OF PROTECTION

AGE	EXPECTED ECONOMIC GAINS FROM RECEIVING BOOSTERS ANNUALLY OVER FIVE YEARS, COMPARED TO NO BOOSTERS (DOLLARS)
30	$1,254
35	$2,489
52	$12,446
60	$24,893
75	$124,464

Assumptions: Linear decay of protection over 5 years, starting from 90%. No booster annual probability of infection= 10%. Booster annual probability of infection = 7.5%. Assuming $10 million statistical value of a human life, not including hospitalization or productivity losses.

However, even if the quantitative results change, the above illustrative example demonstrates the trade-offs facing people of all ages when considering getting COVID-19 boosters. Gaining protection from new variants through infection exposes people of all age categories to significantly higher fatality risks compared to the fatality risks associated with an effective booster shot that raises protection back to the 90% level. While there is a positive gain for all adult age categories for the vaccine compared to obtaining immunity through infection, the expected gain from taking the booster is significantly higher for the older age categories.

CONCLUSION

Leveraging a set of stylized facts, this paper created an analytical framework to evaluate the net benefits from the rapid development and deployment of the COVID-19 vaccines. This framework illustrated that the COVID-19 vaccines enabled significant economic and health benefits including reduced mortality and hospitalization rates, along with the associated health-related costs. Importantly, these are conservative estimates, based on the assumption that successfully surviving COVID-19 infection offers similar protection against future severe outcomes.

Given the continued evolution of the virus, the analysis then leveraged the same framework to examine the consequences to individuals when choosing to receive or not receive new COVID-19 boosters. The analysis assumed that existing protection against severe outcomes decayed due to the rise of new variants. Similar to the original pathogen, protection against severe outcomes from the new variants can be gained through two pathways: One is receiving a booster shot, and the other is infection by the new variant. While the two pathways are similar in the final outcome, obtaining protection through infection exposes individuals to potential health consequences that include higher rates of hospitalization and mortality that do not arise from gaining protection through vaccination.

The benchmarks evaluated above provide a critical perspective regarding the value enabled by the efficacious mRNA vaccines. While the data demonstrate that both prior infection and vaccination provide similar protection against future infections, there are consequences from obtaining protection through prior infection compared to vaccination. Based on the changes in the fatality and hospitality rates, protection gained through prior infection comes with significantly higher risks of hospitalization and death. However, this risk is the most pronounced for people in the 65 and older age categories.

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Appendix

This appendix lays out an illustrative calculation for determining the value of taking a booster. Our model assumes that as of today, all individuals of the same age have the same probability of dying if infected with COVID-19. That probability can be written as

(1) IFR (AGE)* (1-Protection)

The IFR is the "infection fatality ratio" mentioned earlier in the paper, which links the age of the individual to the odds of dying if infected. "Protection" is a number between 0 and 1 that represents the degree of protection against severe outcomes such as death.

In our analysis, the parameter Protection has the same value today for everyone, acquired through either vaccination or prior infection. Then the parameter Protection can fall over time, because immunity decays naturally and new variants arise that evade existing immunity; The parameter Protection is also affected by boosters and by new infections, both of which tend to push Protection back to its initial value.

In our model, an individual who follows the "repeat booster strategy" will always have Protection equal to the initial value. So the probability of dying each year is equal to the probability of dying if infected, multiplied by the probability of getting infected when boosted. That translates into

(2) IFR (AGE)* (1-Protection$_{Initial}$) * ProbInfectBoost

where -Protection$_{Initial}$ is the initial level of protection, and ProbInfectBoost is the probability of getting infected in the year after getting a booster. In other words, with the repeat-booster strategy, individuals start out with a high level of protection against severe outcomes, which the booster maintains.

How does this compare to individuals who choose the "no-booster" strategy? In the no-booster strategy, we assume that individuals start out with the same high level of protection against severe outcomes from either prior infection or being vaccinated. That protection declines over time unless/until the individual gets infected again, which either returns protection against severe outcomes to its original level, or leads to a severe outcome.

The exact calculation is complicated, and depends on how fast protection drop and on the probability of getting infected without a booster. In the no booster scenario, the fatality odds in period j are.

(3) Fatality Odds with no booster

= IFR (AGE) * ProbInfectNoBoost *Σi Prob(j,i)*(1-Protection[i]);

where,

ProbInfectNoBoost: the probability of getting infected by COVID-19 in a year without a booster

Prob (J, i): probability in period j that it has been i periods since the last infection or vaccination. This is a function of Prob_Infect_No_Boost and Protection[i]

Protection[i]: efficacy of protection, i periods after the most recent infection or vaccination.

Three points in this comparison. First, we do not assume that an individual's choice to take the booster or not affects the overall spread of infection. Too few people are getting boosters to create herd immunity.

Second, the experience thus far has been that the protection against infection from COVID-19 boosters is not durable. For that reason, the timing of the booster and whether there is a seasonal surge in COVID-19 infections like the seasonal surge in the flu are important.

Third, the process of developing an mRNA booster against a new variant would take about 100 days, not including time for regulatory approval.[39] As noted in previous sections, faster approval leads to decreased adverse outcomes.

The relative fatality probability between the no-booster scenario and the repeated booster scenario can be estimated by dividing equation (3) by equation (2)

(4) Relative Fatality Probability in period j = (ProbInfectNoBoost / ProbInfectBoost) * (Σi Prob(j,i)*(1-Protection[i])) / (1-Protection)

The relative fatality probability is the increased odds of an individual dying from COVID-19 in period j by choosing not to take the booster, compared to that same individual taking the booster every year. This is a useful calculation because it is age-independent.

For this illustrative calculation, we assume that initial protection for everyone starts at 90%, and decays linearly over 10 years without boosting. With a well-timed booster, protection stays at 90%. Obviously, the real-world evolution of protection may differ. For example, the shift from the Delta variant to the Omicron dramatically increased the transmissibility of the virus, without necessarily degrading protection against severe outcomes. However, these values provide a reasonable case to benchmark the relative benefits of receiving COVID-19 boosters.

We also assume the probability of getting infected with COVID-19 each year without the booster is 10% or roughly the probability of contracting the annual flu.[40] Table 11 lays out two alternative scenarios. In scenario 1, the booster provides no additional protection against infection, so the odds of infection are 10%. In scenario 2, the booster reduces the odds of infection to 7.5%.

Under scenario 1, an individual who does not take the booster faces odds of dying from COVID-19 that are 1.9 times higher than the odds of mortality with a booster (which might be quite low, depending on age). The difference increases over time as the immunity protection degrades over time without a booster. By year 5, the expected annual COVID-19 fatality rate for the no-booster strategy is 4.7 times that for the repeat booster strategy.

Under scenario 2, in the first year an individual who does not take the booster faces odds of dying from COVID-19 in the first year that are 2.5 times higher than the odds of mortality with a booster (which might be quite low, depending on age). The difference increases over time as the protection against severe outcomes degrades over time without a booster. By year 5, the expected annual COVID-19 fatality rate for the no-booster strategy is 6.2 times that for the repeat booster strategy.

Note that these calculations are tied closely to the rate at which protection against severe outcomes degrades over time. However, we assume that both natural immunity and vaccine-

mediated immunity follow the same time paths. This framework allows us to compare 5-year cumulative COVID-19 fatalities for the no booster and the repeat booster strategies.

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Over 350 million mRNA vaccines were given during the study period and CDC scientists found that rates of myocarditis were highest following the second dose of an mRNA vaccine among males in the following age categories:
- 12–15 years (70.7 cases per one million doses of Pfizer-BioNTech)
- 16–17 years (105.9 cases per one million doses of Pfizer-BioNTech)
- 18–24 years (52.4 cases and 56.3 cases per million doses of Pfizer-BioNTech and Moderna, respectively)

Multiple studies and reviews of data from vaccine safety monitoring systems continue to show that vaccines are safe. As a result, the agency will refocus enhanced surveillance and safety monitoring efforts toward children and adolescents.
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