The potential public health and economic value of a hypothetical COVID-19 vaccine in the United States: use of cost-effectiveness modeling to inform vaccination prioritization

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RESEARCH IN CONTEXT

Evidence before this study: A search for economic evaluations related to COVID-19 in PubMed and Google Scholar revealed one economic analysis of treatments and vaccines for COVID-19 in the United States (US). The study found that a vaccine would be cost-saving from a societal perspective compared to no vaccination. However, the analysis did not examine the potential impact in different population subgroups nor estimate the impact of vaccine prioritization in the face of constrained vaccine supply.

Added value of this study: Our study examines the public health and economic impact of a vaccine that meets the recommended target product profile in different subgroups or tiers, assuming that a prioritization strategy will be adopted in the US. Our model combines the most recent evidence to date, including data on the morbidity and mortality of COVID-19 cases in the US from March to May and projections of future mortality over the next year. Considering the benefit to vaccinated individuals only, we estimate the incremental cost per quality-adjusted life-year gained for different prioritization strategies under a range of assumptions about SARS-CoV-2 incidence and COVID-19 treatment costs. We assess the numbers of cases and deaths prevented under a range of vaccine supply scenarios. We find that vaccination would be cost-saving in the highest-risk groups, and highly cost-effective in all but the lowest risk groups.

Implications of all the available evidence: These findings are relevant to US health care payers and public health authorities considering prioritization strategies for the vaccine. The importance of targeting the vaccine to those most at risk in to order to reduce COVID-19-related mortality increases as the vaccine supply becomes more constrained.

ABSTRACT

Background: Researchers are working at unprecedented speed to develop a SARS-CoV-2 vaccine. We aimed to assess the value of a hypothetical vaccine and its potential public health impact when prioritization is required due to supply constraints.

Methods: A Markov cohort model was used to compare COVID-19 related direct medical costs and deaths in the United States (US), with versus without implementation of a 60% efficacious vaccine. To prioritize the vaccine under constrained supply, the population was divided into tiers based on age; risk and age; and occupation and age; and outcomes were compared across one year under various supply assumptions. For each prioritization strategy, the incremental cost per quality-adjusted life-year (QALY) gained versus no vaccine was calculated overall and by tier.

Findings: Overall, the cost per QALY gained for all vaccination strategies was $8,200 versus no vaccination. For the tiers at highest risk of complications from COVID-19, vaccination was cost-saving compared to no vaccination. The cost per QALY gained increased as the risk of hospitalization and death within each tier decreased. Under the most optimistic supply scenario and the most efficient prioritization scenario, the vaccine may prevent 32% of expected deaths. As supply becomes more constrained, prioritization is required to optimize the prevention of deaths.

Interpretation: A COVID-19 vaccine is predicted to be good value for money (cost per QALY gained <$50,000). The speed at which an effective vaccine can be made available will determine how much morbidity and mortality may be prevented in the US.

Funding: Moderna, Inc.

Keywords: Coronavirus; COVID-19; cost-effectiveness analysis; economic analysis; SARS-CoV-2; vaccine

INTRODUCTION

The novel coronavirus (SARS-CoV-2) was first identified in humans in late 2019 and there have since been over 20 million cases of novel coronavirus disease 2019 (COVID-19) confirmed worldwide, with approximately 25% of these cases reported in the United States (US).[1] The health and economic consequences of COVID-19 have been staggering. As of 11 August 2020, there were over 163,000 related deaths reported in the US,[1] and a recent estimate has predicted that if 20% of the US population were to get infected, direct medical costs incurred, just during the course of the infection, could be as high as $163.4 billion.[2] This estimate does not include medical costs related to post-infection care or worsening of unrelated diseases due to postponement of preventive care and diagnosis, non-medical costs such as productivity losses due to absenteeism and premature mortality, or declines in economic activity.

In response to this global health emergency, researchers are working at unprecedented speed to find an effective vaccine and there are at least twenty potential candidates being tested in human clinical trials.[3] Three of the candidates selected by the US government's Operation Warp Speed are in Phase 3 trials: Moderna's mRNA-1273, the University of Oxford/AstraZeneca's AZD1222, and Pfizer/BioNTech's BNT162. While clinical trials will determine whether the vaccine candidates are safe and efficacious against SARS-CoV-2 infection, important questions concerning the value of such vaccines remain: what role could a successful vaccine have in reducing the substantial burden of COVID-19 and, in a world where vaccine supply may initially be much lower than demand, which target groups should be prioritized for vaccination?

In the event of limited vaccine supply in the US, a strategy to target priority groups will likely be developed to guide the roll-out of vaccination programs. Groups may be prioritized based on a variety of criteria, including health benefit to the vaccinated individual and to others who may be protected indirectly, cost-effectiveness (i.e., where can we achieve the most health benefit per dose or per dollar spent?), and social and ethical considerations such as occupational priorities and attention to vulnerable populations.[4-6]

To help address these important questions, we developed a mathematical model to assess the public health and economic impacts in the US of a hypothetical vaccine for SARS-CoV-2. Our focus was on estimating its potential value (based on cost-effectiveness) for vaccinated individuals, when distributed according to three different tier-based vaccination prioritization schemes. These include a simple age-based strategy, a risk-group-based strategy, and a strategy based on a combination of occupational groups and age. Outcomes predicted by our analysis, including estimates of clinical outcomes and vaccine cost-effectiveness by vaccination tier, should be helpful in guiding priority-setting decisions given constraints on vaccine availability as successful companies ramp up their production before and following regulatory approvals.

METHODS

Study design

We used a Markov model with five health states (Figure 1) to follow the US population for 1 year after vaccine supply is first available for use. The model compares various prioritization strategies for a hypothetical COVID-19 vaccine for adults aged 18 years and above to a no vaccine scenario.

Model structure

Individuals enter the model (Figure 1, panel A) as either susceptible to SARS-CoV-2 infection ("Susceptible"), previously infected with SARS-CoV-2 that was never detected ("Undetected Infection"), or recovered following a detected SARS-CoV-2 infection ("Recovered"). At the end of each weekly cycle, individuals can transition to other health states (e.g., become infected, recover, or die) or remain in their current health state, as indicated by the arrows in Figure 1. Patients in the "Detected Infection" health state remain there for only one cycle, during which they enter a probability tree which allocates patients through various levels of COVID-19 treatment (with or without hospitalization, +/- intensive care unit (ICU), +/- mechanical ventilation) to their ultimate resolution (recovered or dead) (Figure 1, panel B). Individuals in the "Undetected Infection" and "Recovered" states remain in these states until they die as we assume that no reinfection occurs in the 1-year period. Each week, individuals in the "Susceptible", "Undetected Infection" or "Recovered" health states may also die from non-COVID-19 causes.

We assumed that individuals in the "Recovered" state are not eligible for vaccination, while individuals in the "Susceptible" and "Undetected Infection" states can receive vaccine, even though the latter group is assumed to have developed natural immunity that persists until at least the end of the 1-year time horizon. Vaccine efficacy was modeled as reducing the probabilities of transitioning from the "Susceptible" state to the "Undetected Infection" or "Detected Infection" states.

Model parameters

Additional details on model parameters are found in the Appendix.

Population characteristics and vaccination strategies

Every adult (18 years and older) in the US is eligible to receive the vaccine, but a tier-based approach was used to create three prioritization strategies to allocate the supply of vaccine as it becomes available over the 1-year time horizon. When individuals fall within more than one defined subgroup (e.g., based on age and risk), they are assumed to be vaccinated according to their highest priority tier. For Strategy 1 (Age-based), age segments are tiered from highest to lowest risk (i.e., oldest to youngest).[5] Strategy 2 (Risk-based) is designed to give priority to high-risk groups defined by residency in nursing homes (without consideration of age), presence of medical conditions that increase the risk of COVID-19 complications, and older age. Strategy 3 (Occupational/age groups) prioritizes subgroups based on occupation and age, similar to the Centers for Disease Control and Prevention's (CDC's) 2018 influenza pandemic plan,[4] but with modifications considering the age-based mortality risk due to COVID-19.[5,6]

Within each strategy, tier groups were assumed to be vaccinated, starting with tier 1, on a weekly and uniform basis according to the weekly vaccine supply. Once the population in each tier has been vaccinated, individuals in the next tier become eligible for vaccination. Given that most of the vaccines expected to be first-to-market will involve a two-dose schedule,[7] a two-dose vaccine with the second dose given at least four weeks after administration of the first dose was assumed. In all scenarios, second doses are prioritized ahead of vaccinating new individuals. This step-wise vaccination process continues until all tiers are vaccinated according to their predicted coverage rate or until the end of the analysis time horizon, whichever occurs first. Coverage rates by age, based on 2018-19 general population influenza coverage data,[8] were applied to the first dose, and the ratio of second-dose coverage to first-dose coverage was based on data for childhood vaccinations[9] (Table 1).

Vaccine supply

A hypothetical vaccine supply over time was estimated based on the scale and timing of four manufacturers' public disclosures.[10-13] Exponential regression models were fit to each manufacturer's disclosed estimate of US cumulative stock availability starting at launch to estimate weekly supply forecasts in the first year. For the "high supply" scenario, four vaccines are successfully launched and supply is fulfilled on time. For a "medium supply" scenario, manufacturers' estimated supply is delayed by one quarter, while for the "low supply" scenario, supply is delayed by two quarters. The resultant curves, shown in the Appendix (Figure A1), predict that a stockpile of doses will be available at launch within the US with a total of 529·2, 413·3, and 413·3 million doses available respectively after one year (i.e., sufficient to vaccinate 264·6, 206·7, and 206·7 million persons). In addition, a hypothetical "immediate supply" scenario wherein sufficient doses are available to vaccinate all individuals in the first week following launch was created in order to compare strategies without regard for delayed access.

Transition probabilities

COVID-19-related transition probabilities were estimated using a two-stage calibration process. First, the age-specific risks of COVID-19-related hospitalization, admission to ICU with or without ventilation, and death from any location for individuals in a "Detected Infection" state were estimated separately for those with serious medical conditions versus those without, using data from the CDC case surveillance from January to May,[14] the COVID-NET hospital surveillance system,[15] and US studies of the outcomes of hospitalized COVID-19 patients.[16,17] Second, the SARS-CoV-2 attack rates were estimated by calibrating to mortality targets generated using forecasts from the Institute for Health

Metrics and Evaluation (IHME) model available on July 22, 2020.[18] Based on IHME's estimates of total and detected infections, the attack rate for undetected infections was assumed to be 1·05 times that for detected infections (i.e., 2·05 true infections per detected infection). IHME's projections were also used to estimate the proportion of people in the "Recovered" and "Undetected Infection" health states at the start of the model (Table 1). Finally, all-cause mortality from the "Susceptible", "Recovered" or "Undetected Infection" states was applied.[19]

Vaccine efficacy

Vaccine efficacy was modeled as the proportional reduction in the probability of SARS-CoV-2 infection (both detected and undetected). The World Health Organization (WHO) and the Food and Drug Administration (FDA) require a minimum efficacy of 50% for a COVID-19 vaccine, but the WHO prefers an efficacy of 70%.[20,21] Therefore, two-dose efficacy was assumed to be 60% in the base-case and varied between 50% and 70% in sensitivity analyses. Single-dose efficacy was assumed to be 40% and 25% of two-dose efficacy for those aged 18 – 54 years and 55 years and above, respectively, based on preliminary immunogenicity data[22] (Table 1). It was assumed that vaccine efficacy does not wane during the 1-year time horizon of the analysis.

Resource use, costs and health state utilities

A US health care system perspective was used and all costs are reported in 2020 US dollars [USD]. The base-case cost of the hypothetical vaccine was assumed to be $35 per dose ($70 per course),[23] while the cost per administration was $14·44.[24] A single "toll" cost was applied to each patient with a new detected infection, dependent on their highest level of care, based on the potential estimated Medicare costs as shown in Table 1.[25] Disutility tolls (disutility weights and event durations), reflecting

impaired health-related quality-of-life during infection, were applied for those experiencing morbidity due to COVID-19 (Table 1). The expected quality-adjusted life-years (QALYs) lost due to death attributable to COVID-19 include both years of life lost and disutility owing to morbidity over a lifetime horizon and were discounted at an annual rate of 3%.

Analyses

For estimation of the base-case cost-effectiveness results, the "immediate supply" vaccination scenario was modeled to allow for a full year of benefits to be captured for all vaccinated individuals, regardless of when, in reality, they would have received their vaccination throughout the year. Given the uncertainty in estimating the model, a series of deterministic sensitivity analyses were conducted to explore the impact of alternative inputs and assumptions, including alternative sets of attack rates consistent with available data, and treatment costs for commercial payers versus Medicare (see Appendix). A second set of analyses was conducted to compare the deaths, hospitalizations, infections and costs across one year in the US population under the age-based, risk-based, and occupational prioritization strategies compared to no prioritization under the various vaccine-supply conditions.

Role of the Sponsor

The study sponsor conceived of the study, provided references for data inputs and commented on the report. The funder was not involved in study design, data analysis, or data interpretation. The corresponding author had full access to all the data used in the study and had final responsibility for the decision to submit for publication.

RESULTS

For the age-based and risk-based prioritization strategies, vaccination is less costly and more effective than no vaccination for the highest risk individuals (tier 1; Table 2). For both strategies, the incremental cost per QALY gained increases as tiers with lower risk of hospitalization and death due to COVID-19 are vaccinated. For the occupation-based strategy, the incremental cost per QALY gained for Tier 1 (priority and critical occupations) was $20,000, while vaccination is cost-saving for Tier 2 (65 years and above). Cost savings are not seen in Tier 1 because the overall risks of hospitalization and deaths are lower in the younger age groups that comprise these occupations. In addition, the attack rate for the priority occupations (i.e., health care workers) was assumed to be the same as the general population. In this scenario, which assumes immediate supply, the overall cost per QALY gained of vaccination, including all tiers, would be $8,200. This result is consistent for all prioritization strategies (Table 2) because all eligible and covered persons are vaccinated immediately under this scenario.

The incremental cost per QALY gained was most sensitive to changes in the attack rate, the vaccine price, and the costs of hospitalizations, but changes in the amount of disutility experienced by patients due to the morbidity associated with COVID-19 has minimal effect (Figure 2). Varying the expected age-specific baseline utility has more impact on this outcome as this affects the QALY loss assigned to deaths from COVID-19. The detailed results in the Appendix (Table A7) show that the cost per QALY for the lowest risk individuals (ages 18-49 years) is high but, importantly, the incremental cost-effectiveness ratio (ICER) decreases if the incidence pattern shifts and the predicted proportion of deaths seen in those under 50 years increases. Under base-case assumptions, the vaccine would have to be priced at over $150 per dose ($300 per course) in order to exceed an incremental cost per QALY of over $50,000 (Appendix, Table A8).

As expected, as vaccine availability is accelerated and people are vaccinated more quickly, additional infections, hospitalizations, deaths and costs are prevented (Table 3). Prioritization increases the number of deaths averted compared to no prioritization for the low and medium supply scenarios (20-23% versus 16% and 25-27% versus 22%, respectively). The occupational strategy is expected to prevent fewer COVID-19-related outcomes because of the younger ages reflected in the Tier 1 critical occupations subgroup in the model (20% versus 23% and 25% versus 27% for low and medium supply, respectively).

DISCUSSION

Our analysis, based on available data, suggests that a COVID-19 vaccine that meets the target product profile of the WHO and the FDA has the potential to be good value for money. This conclusion holds even though the model considers only the benefits to vaccinated individuals (and not secondary benefits due to reduced transmission) and direct health care system costs (and not the value of economic productivity). Vaccination of persons over age 65 appears to be cost-saving because of the high cost and higher incidence of ICU care and ventilation. Except in the lowest-priority tier of each strategy, the ICERs are well under standard willingness-to-pay thresholds cited in the US, which range from $50,000 to $150,000 per QALY gained.[26] The results are consistent with an analysis that found vaccination ($100 per course; 90% efficacy) to be cost-saving overall considering societal costs.[27]

One of the largest influencers of value is the attack rate for the year following the launch of the vaccine. Current models predict mortality only several months into the future, as changes in policy and individual behaviour may affect the course of the disease such that longer-term estimates are highly uncertain. In all three incidence scenarios considered in this analysis, the overall ICER for the hypothetical vaccine falls below $50,000 per QALY.

The ICERs for the different tiers in the prioritization strategies are primarily driven by the risk of hospitalization (which increases costs) and the risk of death (which leads to substantial loss of QALYs due to early death). For this reason, the value associated with the vaccination of priority occupations is lower than other tiers in our analysis. The WHO[5] and the CDC[6] are discussing ethical principles that will not be reflected in the ICER but should be considered when allocating vaccines during a pandemic, including the idea that those putting themselves at risk to serve others during the pandemic may be considered as high priority. Furthermore, our model does not estimate the impact of vaccination on the transmission of infection between individuals. As individuals in priority occupations are frequently in contact with COVID-19-infected persons and others at work, they may be at increased risk of infection or of spreading the disease if infected. Therefore, the value associated with vaccinating these individuals may be underestimated.

Our analysis predicts that the value associated with vaccinating individuals in the lower risk groups, primarily those under 50 years of age, is much lower than the value of vaccinating the older age groups. If a greater portion of the deaths occur in this age group due to shifting incidence patterns, then the cost per QALY of vaccinating these age groups will be lower. Furthermore, while these younger age groups are at low risk of developing more severe complications from COVID-19, they have been shown to be responsible for spreading the disease within the community.[28] The value of vaccinating these individuals is likely underestimated; an analysis with a transmission model that includes the impact of herd immunity is required to understand the value of vaccinating younger persons to prevent community spread.

As data on COVID-19 are still emerging, assumptions were made to combine the sources of evolving data to create this model. The data on the risk of hospitalization and mortality used in this model were based on early experience with the pandemic. As many of the cases reported to the CDC were missing data on death and hospitalization status, Stokes[14] suggests there may be under-reporting of symptoms. On the other hand, as testing capabilities increase and the proportion of detected asymptomatic cases increases, the proportion of severe disease in detected cases will correspondingly decrease. We attempted to control for this by calibrating to predictions of mortality rather than to predictions of the number of detected infections when estimating the future SARS-CoV-2 attack rate. Furthermore, as the pandemic progresses, emerging therapeutics may decrease the mortality and morbidity of COVID-19. As the use and effectiveness of future therapies is uncertain, we conducted sensitivity analyses on incidence, mortality and cost of hospitalization rather than explicitly incorporating these therapies into the model.

Hospitalization for COVID-19 is another important driver of the value of the vaccine as the cost of ICU care and ventilation is expected to be high. These estimates were based on the current billing rules for COVID-19 patients,[25] but the true cost of COVID-19 treatment will not be known until empirical health economic studies are conducted. We did not include the cost associated with diagnostic testing, as we assumed that testing behaviours will not change with vaccination but will continue until it is clear that the epidemic is controlled. When estimating the amount of QALYs lost due to death from COVID-19, we assigned a toll based on average expected QALYs and did not adjust for presence or absence of comorbid conditions. To be conservative, we did not include the health system costs that may be unrelated to SARS-CoV-2 itself, such as mental illness, or of conditions that are exacerbated because care is delayed due to the pandemic. Our analysis does not consider the broader societal costs

such as the productivity costs and patient out-of-pocket costs associated with the pandemic. Nor does it include the less tangible costs such as the value of reducing fear of contagion, the value of protecting against future productivity loss due to illness (insurance value), and improving equity, all of which have been proposed as part of future frameworks for cost-effectiveness analyses.[29]

We have created hypothetical vaccine supply scenarios by assuming that vaccine will not get to market as quickly as currently predicted by manufacturers. Other challenges, including failure of products during clinical trials, may arise to reduce or delay the vaccine supply. During the H1N1 pandemic, supply was not sufficient to meet the demand from the identified priority groups.[30] Decisions were then made at the local level to prioritize vaccines further and the range of recommendations led to public confusion as to who was eligible for vaccination. In any prioritization system, there may be challenges in identifying and targeting high priority individuals; we have not considered those costs and challenges in our analysis and made simplifying assumptions to model allocation of vaccination by tiers.

Given the lack of data, we did not consider the long-term sequalae that may occur following COVID-19. For an infectious disease, it is typical that symptoms for acute infections have a small impact on cost-effectiveness because of their short durations, while any long-term consequences have a more significant impact. Finally, we examined the impact of vaccination only in a 1-year time horizon. If the vaccine provides protection for a longer time frame, its benefits will increase.

Despite the uncertainties, our analyses demonstrate that a hypothetical COVID-19 vaccine would be a cost-effective health care intervention compared to no vaccine. Under the base-case conditions, the

vaccine would have to be priced as high as $150 per dose to exceed an ICER of $50,000 per QALY gained. The speed at which an effective vaccine can be made available over the course of a year will determine the amount of morbidity and mortality that may be prevented.

CONTRIBUTORS: MK, MM, and MCW designed the study. MM programmed the model with quality assurance and validation conducted by MK, DB, and MCW. Data collection and parameterization were completed by MK, MM, and DB. MM and MK conducted the analysis. DB and MK wrote the initial draft of the manuscript, and all remaining co-authors critically revised the manuscript and approved the final version.

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DECLARATION OF INTERESTS:

MK and DB are shareholders in Quadrant Health Economics Inc. Quadrant Health Economics Inc. was contracted by Moderna, Inc. to conduct this study. MM and MCW are consultants at Quadrant Health Economics Inc.

TABLE AND FIGURE LEGENDS

Figure 1. Structure of the model of SARS-CoV-2 infection and COVID-19 progression. (A) Markov health states showing allowed transitions. (B) Probability tree linking transitions from the "Detected Infection" state in the Markov model. Arrows represent the movements between the health states. Death from "Detected infection" is due to COVID-19 while death from all other health states is due to other causes.

Table 1. Model parameters

Table 2. Base-case cost-effectiveness analysis results

Figure 2. Tornado diagram showing the impact of the sensitivity analyses on the overall incremental cost per quality-adjusted life-year gained of vaccination compared to no vaccination

Table 3. Base-case population-level outcomes under various vaccine supply scenarios

FIGURES AND TABLES

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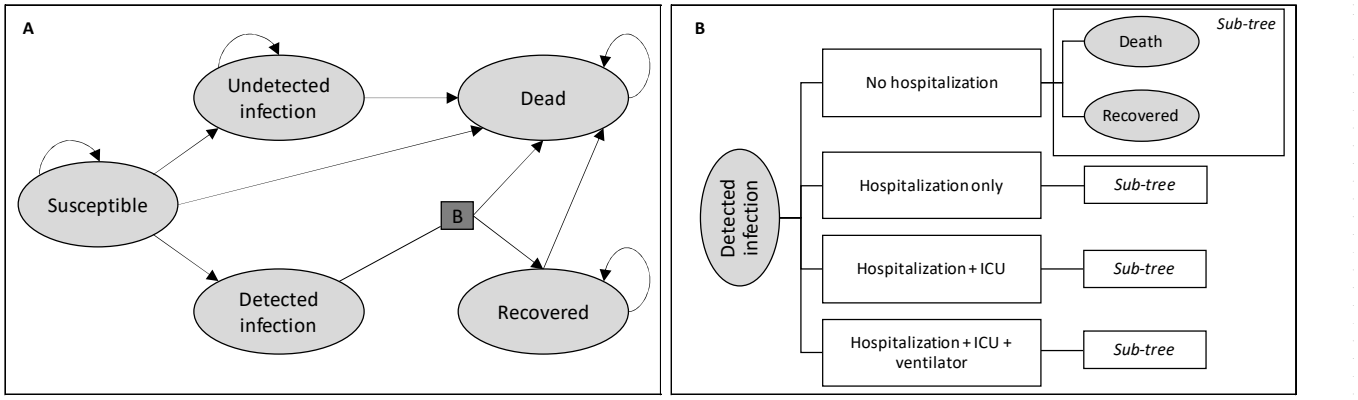


ICU, intensive care unit.

Table 1. Model parameters

Parameter	Base-case value	Source
Vaccine coverage rates		
First dose		
18 to 49 years	34·9%	[8]
50 to 64 years	47·3%	[8]
65+ years	68·1%	[8]
Second dose (all ages)	87·5% of proportion receiving first dose	[9]
Population distribution at baseline		
Susceptible	92·7%	
Undetected Infection	5·2%	Estimated from IHME data[18]
Recovered	2·1%	Estimated from IHME data[18]
SARS-CoV-2 incidence		
Detected infection	Appendix Table A4	Described in Appendix
Undetected infection	1·05 times detected infection rates	Described in Appendix
Decision tree transition probabilities	Appendix Table A2	Described in Appendix
Non-COVID-19 mortality rates	Appendix Table A2	[19]
Vaccine efficacy (against detected and undetected SARS-CoV-2 infection)		
First dose, age 18-49 years	24·0%	Assumption
First dose, age 50-59 years	19·5%	Assumption
First dose, age 60+ years	15·0%	Assumption
Second dose, all ages	60·0%	Assumption
Costs		
Vaccine (per dose)	$35·00	Assumption
Vaccine administration (per dose)	$14·44	Code CPT90471[24]
COVID-19 treatment: ambulatory care only (per event)	$228·98	Physician visit ($112) + ED visit ($582 x 20.1% with visit*)[25]
COVID-19 treatment: hospitalization without ICU or ventilator (per event)	$16,924·00	Physician visit ($112) + hospitalization ($16,812)[25]
COVID-19 treatment: hospitalization with ICU as highest level of care (per event)	$37,429·00	Physician visit ($112) + midpoint of hospitalization and hospitalization with ventilator ($37,317)[25]
COVID-19 treatment: hospitalization with ICU + ventilator as highest level of care (per event)	$57,934·00	Physician visit ($112) + hospitalization with ventilator ($57,822)[25]
Health state utility parameters		
Detected infection symptoms disutility weight	0·19	Described in Appendix
Detected infection hospitalization as highest setting disutility weight	0·30	Described in Appendix
Detected infection hospitalization with ICU as highest setting disutility weight	0·50	Described in Appendix
Detected infection hospitalization with ICU + ventilator as highest setting disutility weight	0·60	Described in Appendix
Event durations		
COVID-19 symptoms among all confirmed infections	14 days	Described in Appendix
Hospitalization among detected infections not requiring ICU or ventilator	6 days	Described in Appendix

Hospitalization among detected infections with ICU as highest level of care	15 days	Described in Appendix
Hospitalization among detected infections with ventilator as highest level of care	15 days	Described in Appendix

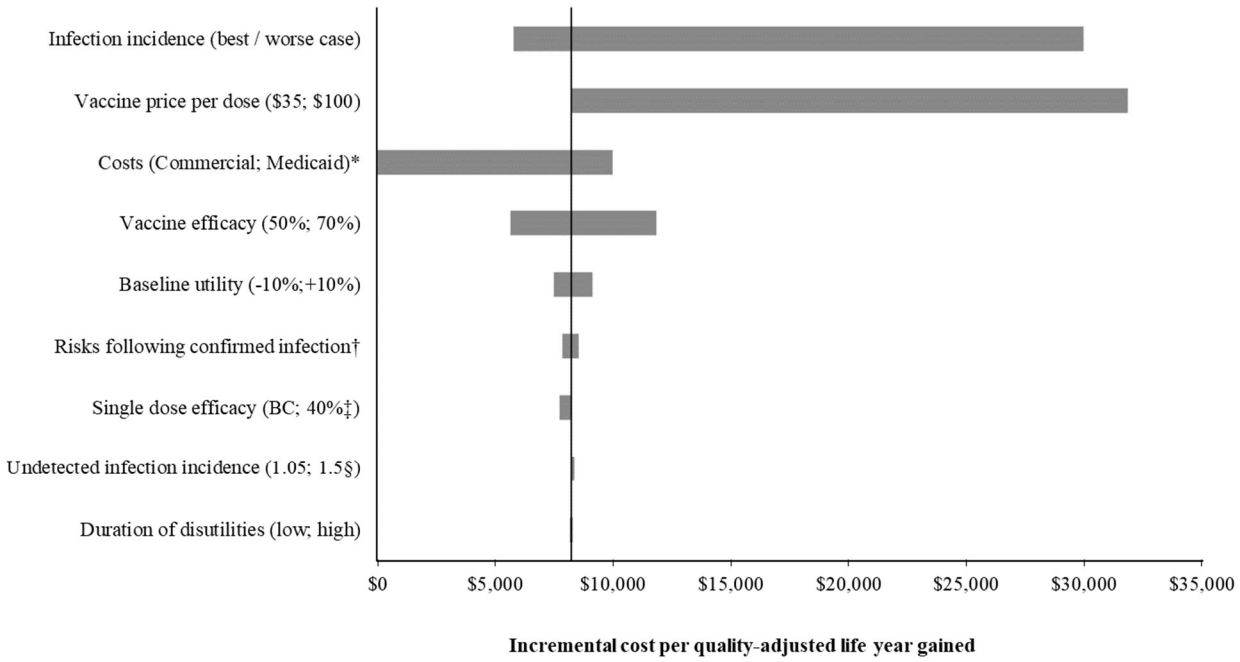
ED, emergency department; ICU, intensive care unit; IHME, Institute for Health Metrics and Evaluation.
*Proportion of patients who have an ED visit is assumed to be equal to 20·1% which is the average rate of hospitalization observed in our model, consistent with the approach utilized by Fiedler and Song, 2020.[25]

Table 2. Base-case cost-effectiveness analysis results

Strategy	Vaccination tier ICER ($/QALY gained)				Overall strategy
	1	2	3	4	ICER ($/QALY gained)**
1. Age-based					
*Subgroup**	*65+ yrs*	*50-64 yrs*	*18-49 yrs*	*n/a*	
# eligible for vaccination	*56,051,566*	*63,292,950*	*139,327,967*	-	
Base-case	**Vaccination Dominates†**	**$8,000**	**$94,000**	**n/a**	**$8,200**
2. Risk-group-based					
*Subgroup**	*Nursing homes; serious medical condition, 65+ yrs with or without serious medical condition*	*Serious medical condition, 18-64 years; no serious medical condition, 50-64 yrs*	*No serious medical condition, 18-49 yrs*	*n/a*	
# eligible for vaccination	*56,282,700*	*92,599,345*	*109,790,438*	-	
Base-case	**Vaccination Dominates†**	**$10,000**	**$340,000**	**n/a**	**$8,200**
3. **Occupational/age groups**					
*Subgroup**	*Priority‡ and other critical occupations§*	*65+ yrs*	*50-64 yrs*	*18-49 yrs*	
# eligible for vaccination	*21,700,000*	*54,706,166*	*57,390,550*	*124,875,767*	
Base-case	**$20,000**	**Vaccination Dominates†**	**$8,000**	**$94,000**	**$8,200**

ICER, incremental cost-effectiveness ratio; n/a, not applicable; QALY, quality-adjusted life-year; yrs, years.
*Individuals are assigned to one subgroup only; those qualifying for more than one subgroup are assigned to their highest tier. While those aged <18 years are included in the model, they are not targeted for vaccination as current clinical trials target only those 18+ years.
†Vaccination dominates: the vaccine is less costly and more effective than no vaccination.
‡Includes: public health personnel; inpatient health care providers; outpatient and home health providers; health care providers in long-term care facilities; pharmacists and pharmacy technicians; community support and emergency management; and mortuary services personnel.[4]
§Includes: other health care personnel; emergency services and public safety sector personnel; manufacturers of pandemic vaccine and antiviral drugs; communications/information technology, electricity, nuclear, oil and gas, water sector personnel, and financial clearing and settlement personnel; critical government personnel; and other critical government personnel.[4]
**Overall ICER is consistent across all prioritization strategies because all eligible and covered persons are vaccinated immediately under all strategies. Base-case vaccine cost is $35 per dose ($70 per course).

Figure 2. Tornado diagram showing the impact of the sensitivity analyses on the overall incremental cost per quality-adjusted life-year gained of vaccination compared to no vaccination[**]



BC, base-case
*Vaccination dominates no vaccination (it is less costly and more effective) when estimates of commercial costs are used as inputs.
[†]Alternative values were used for the calibrated probabilities of hospitalization and death following detected infection as described in the Appendix.
[‡]For the base-case, single dose efficacy was assumed to be 40% and 25% of full efficacy for those under 55 years and those 55+ years, respectively. This was increased to 40% of full efficacy for everyone in the sensitivity analysis.
[§]Undetected infection incidence was assumed to be 1·05 times the incidence of detected infection in the base-case. This was increased to 1·5 for the sensitivity analysis.
[**]The results are the same for all strategies because all eligible and covered persons are vaccinated immediately under all strategies.

Table 3. Base-case population-level outcomes under various vaccine supply scenarios

Vaccine supply scenario	Vaccination strategy	Deaths		Hospitalizations		Detected infections		Costs (millions)		
		Total	Difference from base-case	Total	Difference from base-case	Total	Difference from base-case	Hospitali-zations	Vacci-nation	Total
No vaccine	**n/a**	**264,602**		**726,115**		**3,601,719**		**$20,628**	**$0**	**$20,628**
Low	Age-based	204,253	-23%	595,040	-18%	3,149,627	-13%	$16,895	$10,823	$27,718
Low	Risk-group-based	204,298	-23%	594,838	-18%	3,153,147	-12%	$16,895	$10,823	$27,718
Low	Occupational/age-based	210,668	-20%	604,383	-17%	3,156,372	-12%	$17,161	$10,823	$27,984
Low	No priority	221,785	-16%	621,556	-14%	3,171,221	-12%	$17,653	$10,823	$28,476
Medium	Age-based	194,092	-27%	566,570	-22%	3,011,973	-16%	$16,085	$10,823	$26,908
Medium	Risk-group-based	194,131	-27%	566,463	-22%	3,014,785	-16%	$16,087	$10,823	$26,910
Medium	Occupational/age-based	198,237	-25%	572,768	-21%	3,017,299	-16%	$16,263	$10,823	$27,086
Medium	No priority	207,305	-22%	586,539	-19%	3,028,438	-16%	$16,657	$10,823	$27,480
High	Age-based	181,526	-31%	528,585	-27%	2,819,933	-22%	$15,002	$10,823	$25,825
High	Risk-group-based	181,412	-31%	527,716	-27%	2,821,040	-22%	$14,983	$10,823	$25,806
High	Occupational/age-based	182,097	-31%	529,569	-27%	2,821,455	-22%	$15,030	$10,823	$25,854
High	No priority	187,591	-29%	539,108	-26%	2,835,583	-21%	$15,307	$10,823	$26,130
Immediate	Age-based	179,775	-32%	520,452	-28%	2,760,399	-23%	$14,776	$10,823	$25,599
Immediate	Risk-group-based	179,775	-32%	520,452	-28%	2,760,399	-23%	$14,776	$10,823	$25,599
Immediate	Occupational/age-based	179,775	-32%	520,452	-28%	2,760,399	-23%	$14,776	$10,823	$25,599

n/a, not applicable

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TECHNICAL APPENDIX

Prioritization Strategies

For strategy 1 (age-based), it was assumed that the overarching goal of vaccination is to reduce mortality; therefore age segments were tiered from highest to lowest risk (i.e., oldest to youngest).[1] The age ranges, with their corresponding population estimates,[2] are shown in Table A1.

Strategy 2 (risk-based) was designed to give priority to high-risk groups defined by residency in nursing homes (without consideration of age), presence of medical conditions that increase the risk of COVID-19 complications, and age. Estimates of the proportions of the United States (US) adult population falling within each subgroup were obtained from a National Center for Health Statistics report on long-term care providers and services users in the US[3] and from a publication by the Henry J. Kaiser Family Foundation using data from the 2018 Behavioral Risk Factor Surveillance System. We assumed that all individuals in nursing homes had at least one condition that put them at increased risk of complications from a COVID-19 infection. Tiers were again assigned based on overall risk of mortality (Table A1).

Strategy 3 (occupational/age groups) utilized a combination of subgroups based on occupation and age, similar in nature to the Centers for Disease Control and Prevention's (CDC's) 2018 pandemic plan,[4] but with modifications to reflect prioritization of those at highest mortality risk due to COVID-19 as well as those in occupations dedicated to delivery of health care and national security (Table A1). "Priority occupations" included those involved in health care and community support services, while the "other critical occupations" subgroup included those identified by the CDC as responsible for homeland and national security as well as other critical infrastructure.[4] The age-specific proportions of each group within the US population were estimated using 2018 labor force projections from the US Bureau of Labor Statistics in combination with the CDC estimates,[4] and the resulting estimates are shown in Table A1.

Vaccine Supply

Hypothetical vaccine supply scenarios were estimated across one year using exponential regression models as shown in Figure A1.

Calibration Methods

COVID-19-related transition probabilities were estimated using a two-stage calibration process.[5]

Risk of hospitalization and death due to SARS-CoV-2

In order to calibrate the probability of hospitalization and death following infection, a separate model which isolated the probability tree shown in Panel B of Figure 1 of the main article was created. The probability of hospitalization by age and risk group, which was based upon the CDC case surveillance data, was used to calculate the probability of not being hospitalized for use in the probability tree. Data from the CDC COVID-NET hospital surveillance data were used to determine age-specific probabilities of being admitted to an intensive care unit (ICU) and of being placed on a ventilator. Ranges were defined for these inputs based on 95% confidence intervals generated using the sample sizes of the source data and assuming the data followed a beta distribution. The probability of being admitted to the hospital without ICU admission was calculated so that all of the probabilities of treatment locations in the probability tree summed to 1. The probability of death on ventilation was allowed to range from 36% to 79% based on published studies of hospitalized patients in the US,[6,7] but this range was extended downwards to 10% for the younger age groups. Broad ranges for the relative risk (RR) for deaths were defined for the different treatment locations (i.e., RR death on ventilation: ICU only; RR death in ICU: hospitalization without ICU; RR death with hospitalization only: no hospitalization), as age-specific data ranges were not available for these probabilities.

The calibration target was defined as the overall age- and risk-group-specific probability of death, from any location, based on the CDC case surveillance data. Ranges for this target were calculated based on 95% confidence intervals generated using the sample sizes of the data and assuming that the data followed a beta distribution.

Latin hypercube sampling[5] was used to create 10,000 parameter sets. For each set, probability inputs for the probability tree were calculated using sampled values from a uniform distribution. The parameter sets were run through the probability tree in order to calculate the overall probability of death and the overall proportion of deaths in hospital. Parameter sets were excluded if they either (a) resulted in an overall probability of death outside the calculated target range, or (b) predicted a proportion of death within the hospital[8] outside of the range of 50% to 90%. The parameter set that had the closest goodness-of-fit, measured by least squares, was chosen for use in the base-case analysis.

The base-case inputs are shown in Table A2 and have been graphed in Figure A2; Panel A illustrates the probability of being admitted to hospital only; being admitted to hospital and ICU; and being admitted to hospital and ICU and placed on a ventilator. With the exception of the youngest age groups, these probabilities increase with age and are consistently higher in individuals with conditions. Panel B illustrates the probabilities of death for those treated outside of hospital and those treated in the different locations in hospital. Probability of death is lowest for those treated outside of hospital and highest for those placed on ventilators. Once again, age is a strong determinant of mortality in all treatment locations, and mortality is higher in those with conditions compared to those without conditions.

In order to conduct a multi-way sensitivity analysis involving mortality and probability of ventilator use, four sets of parameters, in which inputs for all age / risk groups were varied at once, were generated. From the non-excluded parameter sets, of the five with the lowest probabilities of deaths, the two sets with the lowest and the highest values for the probability of ventilator were identified. Similarly, two parameters sets were identified from the five with the highest probabilities of deaths.

SARS-CoV-2 Attack Rate

Mortality projections from the Institute for Health Metrics and Evaluation (IHME) were used to estimate the potential number of deaths due to COVID-19 in a 1-year period. Their reference scenario, which assumes that social distancing mandates are re-imposed for 6 weeks whenever daily deaths reach 8 per million, was used for the base-case analysis. Sensitivity analyses were generated using their worst and best scenarios. Their worst scenario assumes that mandated social distancing will not be re-imposed. Their best scenario assumes that there will be 95% mask usage in every public location.

The IHME plots for the projected mean cumulative deaths from COVID-19 up until November 1, 2020 were examined. While a variety of models were considered, a linear model provided good fit without producing inconsistent forecasts such as decreasing cumulative deaths. Using the linear model, deaths for a 1-year period were predicted to be 264,602, 307,542 and 118,910 using IHME's reference, worst, and best scenarios. As shown in Table A3, these deaths were allocated across age groups using the distribution of deaths from the CDC case surveillance data for March to May.[9] For one additional

sensitivity analyses, the calibration was altered so that a higher proportion of deaths occurred in those under 50 years of age. A constant incidence rate was assumed over time and for those with and without conditions in the same age group.

For each age group, the weekly attack rates are a function of the proportion of the age group with and without serious medical conditions. We assumed that the prevalence of conditions that increased the risk of COVID-19 was age-dependent: prevalence rates of 2·5%, 21·2%, and 55·2% were assumed for individuals aged under 18 years,[10] 18-64 years, and aged 65 years and over, respectively. For each age group, the weekly attack rate run through the model was varied using the Excel Solver function until the mortality targets (Table A3) were met. Base-case attack rates are shown in Table A4.

Estimation of the Rate of Undetected Infection

The CDC has reported initial results of a seroprevalence study of antibody testing of samples from two labs serving ten areas in the United States.[11] Blood samples from several weeks for each area were tested, and the testing periods ranged from March 23 - April 1 to April 30 – May 12. While the seroprevalence varied widely by region, average seroprevalence across samples was 3·4%. The CDC compared the number of infections, as measured by seroprevalence, to the number of detected infections reported by the end of the testing dates in each region. On average, the ratio of detected infections to infections measured by seroprevalence was 10·7.

The IHME model includes measures of detected infection and actual infections in the US. In the first months of the pandemic, which corresponds to the period during which testing capacity was being increased in the US, the majority of infections were undetected. On May 12th, the IHME model estimates that, cumulatively, 1,269,287 detected infections and 11,759,045 total infections occurred in the US. On that date, the ratio of cumulative detected to cumulative total infections in the model was estimated at 9·3, and the crude seroprevalence was estimated at 3·54%. As time progresses, a higher portion of infections are becoming detected. In the model, from June 8 to July 14, the ratio of total to detected infections was estimated at 2·05, which gives a ratio of undetected to detected infections of 1·05. For this analysis, we assumed that the ratio of undetected to detected infections would remain at 1·05 moving forward.

All-cause mortality

All-cause mortality from the “Susceptible”, “Recovered” or “Undetected Infection” states was applied based on US life expectancy tables, assuming a 50:50 male to female ratio (Table A2).[12]

Health State Utilities

The expected number of life years lost due to early deaths from COVID-19 were calculated using expected survival by age as predicted by the National Center for Health Statistics [2017].[12] Age-specific utility values for individuals without detected infection, obtained using the EuroQol-5D (EQ-5D) in a group of US adults,[13] were used to calculate the present value of the quality-adjusted life-years (QALYs) lost at the point of death assuming a 3% discount rate.[14]

A QALY decrement, or a disutility weighted by the time spent with COVID-19 symptoms and being treated in hospital, was applied to anyone experiencing a detected infection. Disutility weights were obtained from a recent report on pricing models for COVID-19 treatments published by the Institute for Clinical and Economic Review, in which the disutility weights were derived from data collected in patients experiencing influenza and *Clostridium difficile* infection. In our analysis these weights were applied for each day a patient experienced symptoms and was treated in hospital for COVID-19, dependent on their level of care (Main Article Table 1). COVID-19 symptoms were assumed to persist for 14 days in all patients, representing the median time from onset to clinical recovery for mild cases reported by the World Health Organization (WHO)-China Joint Mission on COVID-19. For individuals hospitalized (without ICU) for COVID-19, a length of stay (LOS) of 6 days was assumed, representing the median LOS among 1,305 inpatients hospitalized with COVID-19 in Michigan between March 1 and April 1, 2020. Longer estimates of 15 days were assumed for patients in ICU (with or without ventilation), reflecting the median LOS observed among 217 critically ill patients admitted to COVID-19-designated ICUs in Atlanta between March 6 and April 17, 2020.[7] Although evidence of long-term damage to the heart,[15] lungs,[16] and brain[17] following COVID-19 is beginning to emerge, we did not include these in the model to be conservative.

Sensitivity Analyses

Parameters that were explored in sensitivity analyses included:

i) vaccine cost ($50/dose; $100/dose);

ii) infection incidence (worst-case; best-case; increased death in those 50 years and under) as described in the calibration methods above;

iii) number of patients at baseline starting in the “Never detected infection” and “Recovered” states (ratio of undetected to detected infection increased from 1·05 in the base-case to 1·5);

iv) vaccine efficacy (50%; 70%);

v) QALY decrements due to infection (increased and decreased time with symptoms; see Appendix Table A5 for values);

vi) alternative COVID-19 treatment costs (Table A6)[18];

vii) alternative values for risk of COVID-19 hospitalization and death as described in the Calibration methods;

viii) Alternative baseline utility values: In assigning QALY-tolls for early death, we used average age-specific values and did not adjust the values for those with conditions and those without. Those with chronic conditions may experience lower lifetime QALYs, however, given the range of conditions that increase risk of COVID-19 complications, it was not possible to estimate what the difference may be. Therefore, we increased and decreased baseline age-specific utility values that affect this calculation by 10% overall to determine the potential effect of over- or under-estimating the impact.

The results of the sensitivity analyses for each of the prioritization strategies, by tier and overall are shown in Table A7. The unit price per dose required for the incremental cost-effectiveness ratio (ICER) to equal $50,000 per QALY gained versus no vaccination is shown in Table A8.

APPENDIX FIGURES AND TABLES

Table A1. Summary of population eligible for vaccination by tier*

Strategy	Vaccination tier			
	1	2	3	4
1. Age-based				
Subgroup	65+ years	50-64 years	18-49 years	n/a
# eligible for vaccination[2]	56,051,566	63,292,950	139,327,967	-
2. Risk-group-based				
Subgroup	Nursing homes; 65+ years with or without serious medical conditions	Serious medical condition, 18-64 years and no serious medical condition, 50-64 years	No serious medical condition, 18-49 years	n/a
# eligible for vaccination[2,3,19]	56,282,700	92,599,345	109,790,438	-
3. Occupational/age groups				
Subgroup	Priority† and other critical occupations‡	65+ years	50-64 years	18-49 years
# eligible for vaccination[2,4,20]	21,700,000	54,706,166	57,390,550	124,875,767

n/a, not applicable.

*Individuals are assigned to one subgroup only; those qualifying for more than one subgroup are assigned to their highest tier. While those aged under 18 years are included in the model, they are not targeted for vaccination as current clinical trials target only those 18 years and above.

†Includes: public health personnel; inpatient health care providers; outpatient and home health providers; health care providers in long-term care facilities; pharmacists and pharmacy technicians; community support and emergency management; and mortuary services personnel.[4]

‡Includes: other health care personnel; emergency services and public safety sector personnel; manufacturers of pandemic vaccine and antiviral; communications/information technology, electricity, nuclear, oil and gas, water sector personnel, and financial clearing and settlement personnel; critical government personnel; and other critical government personnel.[4]

Figure A1. Cumulative estimated weekly vaccine supply curve

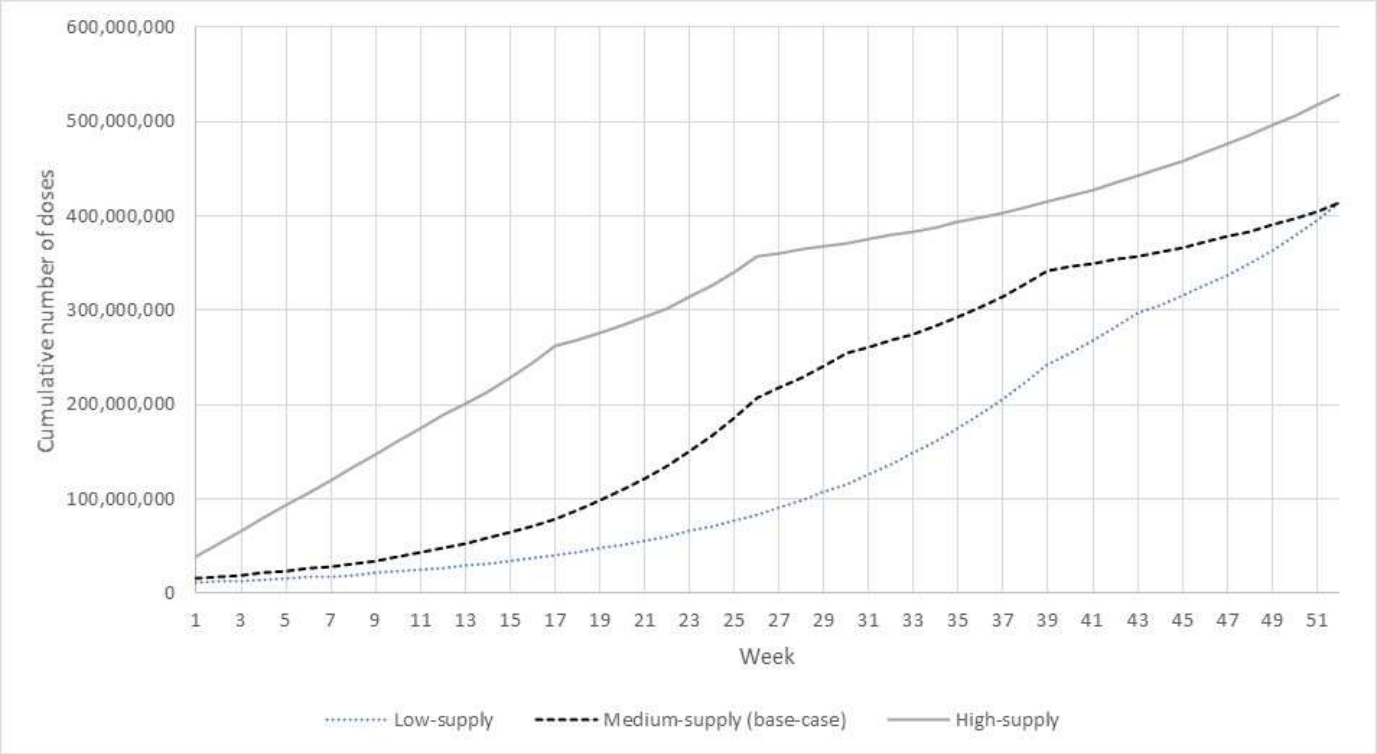


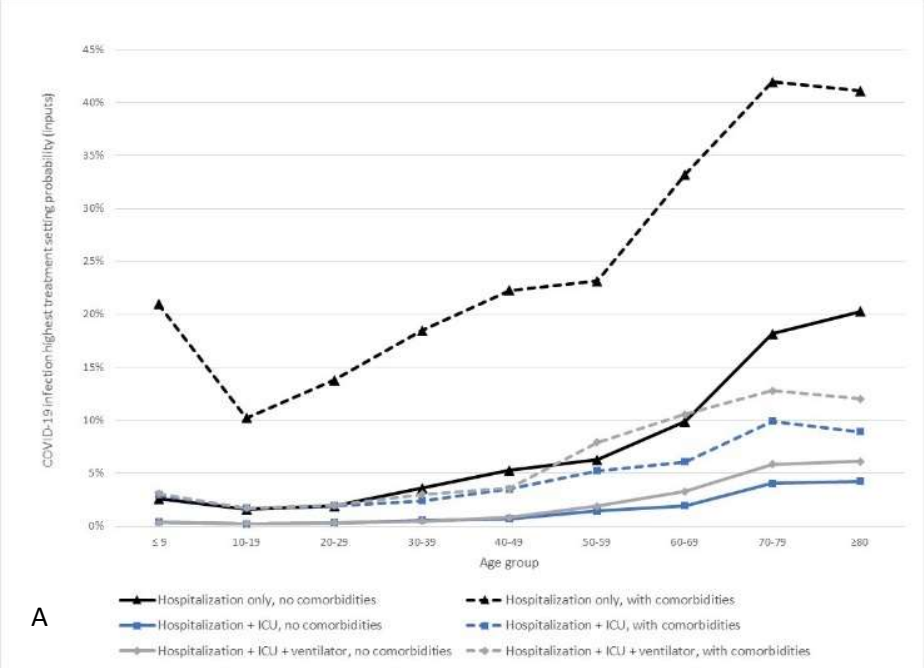
Table A2. Model transition probabilities: mortality and individuals with detected COVID-19 infection

Transition probability	0-9 yrs	10-17 yrs	18-29 yrs	30-39 yrs	40-49 yrs	50-59 yrs	60-64 yrs	65-69 yrs	70-79 yrs	80+ yrs
Detected infections with no serious medical conditions										
Detected infection → No hospitalization	96·62%	97·95%	97·46%	95·40%	93·21%	90·39%	84·87%	84·87%	71·95%	69·39%
Detected infection → Hospitalization	2·58%	1·59%	1·90%	3·58%	5·26%	6·29%	9·89%	9·89%	18·15%	20·27%
Detected infection → Hospitalization with ICU	0·42%	0·20%	0·31%	0·55%	0·70%	1·42%	1·96%	1·96%	4·04%	4·24%
Detected infection → Hospitalization with ICU + ventilator	0·38%	0·27%	0·33%	0·47%	0·84%	1·90%	3·29%	3·29%	5·86%	6·10%
No hospitalization → Dead	0·04%	0·04%	0·06%	0·04%	0·04%	0·11%	0·12%	0·12%	2·29%	19·57%
Hospitalization → Dead	0·27%	0·32%	0·34%	0·20%	0·41%	0·67%	0·93%	0·93%	17·71%	43·02%
Hospitalization with ICU → Dead	1·84%	2·94%	2·69%	1·72%	4·11%	4·93%	6·49%	6·49%	34·56%	65·77%
Hospitalization with ICU + ventilator → Dead	10·40%	12·12%	16·08%	12·41%	31·47%	36·69%	62·16%	62·16%	67·58%	76·12%
Detected infections with serious medical conditions*										
Detected infection → No hospitalization	73·01%	86·37%	82·30%	76·11%	70·62%	63·72%	50·16%	50·16%	35·32%	37·95%
Detected infection → Hospitalization	20·96%	10·24%	13·79%	18·48%	22·28%	23·14%	33·19%	33·19%	41·97%	41·10%
Detected infection → Hospitalization with ICU	2·94%	1·70%	1·95%	2·41%	3·53%	5·22%	6·07%	6·07%	9·91%	8·92%
Detected infection → Hospitalization with ICU + ventilator	3·09%	1·69%	1·96%	3·00%	3·57%	7·92%	10·58%	10·58%	12·81%	12·03%
No hospitalization → Dead	0·12%	0·22%	0·34%	0·41%	0·77%	1·33%	4·60%	4·60%	12·94%	33·12%
Hospitalization → Dead	0·24%	0·99%	0·99%	1·87%	4·46%	2·96%	16·10%	16·10%	31·69%	49·18%
Hospitalization with ICU → Dead	1·75%	5·74%	6·04%	11·32%	10·80%	13·24%	31·91%	31·91%	49·58%	72·33%
Hospitalization with ICU + ventilator → Dead	14·87%	22·50%	42·67%	61·23%	71·16%	70·86%	67·28%	67·28%	69·47%	86·74%
All individuals[12]										
Susceptible → Dead Never detected infection → Dead Recovered → Dead	0·00142%	0·00049%	0·00196%	0·00306%	0·00510%	0·01184%	0·02021%	0·02842%	0·05343%	0·19912%

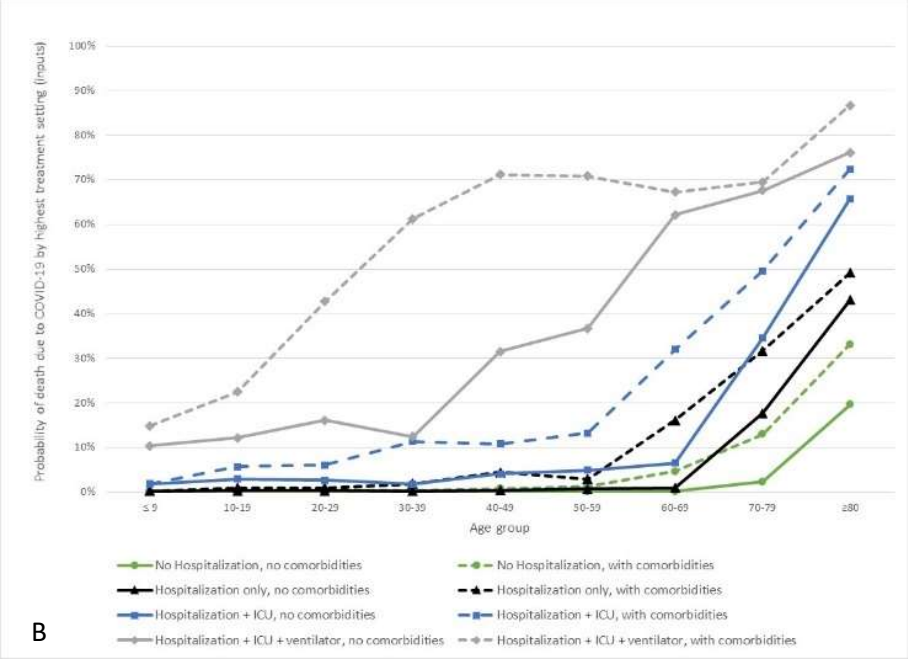
ICU, intensive care unit; yrs, years.

*Serious medical conditions assumed to be prevalent in 100% of individuals in nursing homes, 100% of individuals in "serious medical conditions" subgroups, 0% in "no serious medical conditions" subgroups, and 2·5%, 21·2%, and 55·2% in individuals age 0-17, 18-64 and 65+ years in remaining subgroups, respectively.[19]

Figure A2. Calibration results: COVID-19 infection treatment location and death probabilities for those with and without conditions. (A) the probability of being admitted to hospital by highest level of care received (hospital only; hospital + ICU; hospital + ICU + ventilator). (B) probabilities of death by treatment location (out of hospital; hospital by level of care).



A



B

ICU, intensive care unit

Table A3. Expected* number of deaths in a 1-year period compared to the model predicted* number of deaths following calibration of the SARS-CoV-2 attack rates

Age group	Base-case scenario		Worst scenario		Best scenario		Base-case scenario (additional deaths in under 50 years)	
	Expected	Predicted	Expected	Predicted	Expected	Predicted	Expected	Predicted
0 to 9 years	39	39	46	46	18	18	158	158
10 to 17 years	132	132	153	153	59	59	526	526
18 to 29 years	960	960	1,116	1,116	431	431	3,840	3,840
30 to 39 years	2,840	2,840	3,301	3,301	1,276	1,276	11,362	11,362
40 to 49 years	7,463	7,463	8,674	8,674	3,354	3,354	14,925	14,925
50 to 59 years	21,626	21,626	25,135	25,135	9,718	9,718	21,626	21,626
60 to 69 years	47,584	47,584	55,306	55,306	21,384	21,384	47,584	47,584
70 to 79 years	67,684	67,684	78,668	78,668	30,417	30,417	59,935	59,935
80+ years	116,274	116,274	135,143	135,143	52,253	52,253	104,647	104,647
Total	**264,602**	**264,602**	**307,542**	**307,542**	**118,910**	**118,910**	**264,602**	**264,602**

*Expected number of deaths were the calibration targets generated using the IHME predictions as described in the text. The predicted numbers were generated by our model after calibration of the age-specific attack rate for SARS-CoV-2.

Table A4. Weekly attack rates for SARS-CoV-2 by age group used for the base-case and sensitivity analyses

Age group	Base-case scenario	Worst scenario	Best scenario	Base-case scenario (additional deaths in under 50 years)
0 to 9 years	0·0020%	0·0023%	0·0009%	0·0079%
10 to 17 years	0·0085%	0·0099%	0·0038%	0·0345%
18 to 29 years	0·0095%	0·0110%	0·0042%	0·0384%
30 to 39 years	0·0197%	0·0229%	0·0088%	0·0812%
40 to 49 years	0·0318%	0·0370%	0·0145%	0·0646%
50 to 59 years	0·0458%	0·0534%	0·0203%	0·0458%
60 to 64 years	0·0401%	0·0500%	0·0182%	0·0401%
65 to 69 years	0·0300%	0·0330%	0·0132%	0·0300%
70 to 79 years	0·0264%	0·0307%	0·0118%	0·0233%
80+ years	0·0483%	0·0564%	0·0214%	0·0434%

Table A5. Duration of symptoms assumed to calculate disutility decrement for each severity of symptoms in the base-case and in sensitivity analyses

Event	Estimated duration (days)			
	Base-case	Lower values for sensitivity analysis	Higher values for sensitivity analysis	Source
COVID-19 symptoms among all detected infections	14	7	21	[21]
Hospitalization among detected infections not requiring ICU or ventilator*	6	3	10	[22]
Hospitalization among detected infections with ICU as highest level of care*	15	9	15	[7]
Hospitalization among detected infections with ventilator as highest level of care*	15	9	15	[7]

*Values for the sensitivity analyses are based on the inter-quartile range for length of stay reported in the cited studies.

Table A6. Summary of costs used in the base-case and sensitivity analyses

Resource	Medicare costs*	Medicaid costs	Commercial costs
Physician visit	$112	$80	$129
Emergency department visit	$582	$540	$1,312
Hospitalization without ventilator	$16,812	$13,780	$34,890
Hospitalization with ICU	$37,317	$30,588	$74,866
Hospitalization with ICU/ventilator	$57,822	$47,396	$114,842

ICU, intensive care unit

*For the base-case analysis, Medicare costs as estimated by Fiedler and Song[18] were used assuming that the cost of hospitalization with ICU is the midpoint of costs of hospitalization and hospitalization with ventilator.

Table A7. Detailed cost-effectiveness analysis results

Strategy / Sensitivity analysis	Vaccination tier ICER ($/QALY gained)				Overall strategy	
	1	2	3	4	ICER ($/QALY gained)	Change from base-case ICER
1. Age-based						
Subgroup[*]	*65+ yrs*	*50-64 yrs*	*18-49 yrs*	*n/a*		
# eligible for vaccination[2]	*56,051,566*	*63,292,950*	*139,327,967*	-		
Base-case	**Vaccination Dominates**[†]	**$8,000**	**$94,000**	**n/a**	**$8,200**	**-**
Vaccine cost $50/dose	$2,300	$14,000	$130,000	n/a	$14,000	71%
Vaccine cost $100/dose	$11,000	$33,000	$240,000	n/a	$32,000	290%
Infection incidence: worst case, mandates easing	Vaccination Dominates[†]	$4,900	$79,000	n/a	$5,800	-29%
Infection incidence: best case, universal masks	$10,000	$31,000	$220,000	n/a	$30,000	266%
Higher death rates in <50 years	$490	$8,000	$25,000	n/a	$6,600	-20%
Higher undetected infection incidence (1.5x)	Vaccination Dominates[†]	$8,200	$94,000	n/a	$8,400	2%
2nd dose vaccine efficacy: 50%	$1,400	$12,000	$120,000	n/a	$12,000	46%
2nd dose vaccine efficacy: 70%	Vaccination Dominates[†]	$5,300	$78,000	n/a	$5,700	-30%
Vaccine efficacy: single dose efficacy 40%, all ages	Vaccination Dominates[†]	$7,600	$94,000	n/a	$7,700	-6%
Duration of disutilities: low	Vaccination Dominates[†]	$8,100	$96,000	n/a	$8,300	1%
Duration of disutilities: high	Vaccination Dominates[†]	$7,900	$92,000	n/a	$8,200	0%
Unit costs: commercial[18]	Vaccination Dominates[†]	Vaccination Dominates[†]	$80,000	n/a	Vaccination Dominates[†]	n/a
Unit costs: Medicaid[18]	$1,300	$10,000	$96,000	n/a	$10,000	22%
Low mortality, low ventilator use	Vaccination Dominates[†]	$8,500	$110,000	n/a	$8,500	4%
Low mortality, high ventilator use	Vaccination Dominates[†]	$8,400	$110,000	n/a	$8,500	4%
High mortality, low ventilator use	Vaccination Dominates[†]	$7,300	$83,000	n/a	$7,900	-4%
High mortality, high ventilator use	Vaccination Dominates[†]	$7,300	$83,000	n/a	$7,900	-4%
Baseline utility -10%	Vaccination Dominates[†]	$8,900	$100,000	n/a	$9,100	11%
Baseline utility +10%	Vaccination Dominates[†]	$7,300	$86,000	n/a	$7,500	-9%
2. Risk-group-based						
Subgroup[*]	*Nursing homes; serious medical condition, 65+ yrs with or without serious medical condition*	*Serious medical condition, 18-64 years; no serious medical condition, 50-64 yrs*	*No serious medical condition, 18-49 yrs*	*n/a*		
# eligible for vaccination[2,3,19]	*56,282,700*	*92,599,345*	*109,790,438*	-		
Base-case	**Vaccination Dominates**[†]	**$10,000**	**$340,000**	**n/a**	**$8,200**	**-**
Vaccine cost $50/dose	$2,300	$17,000	$450,000	n/a	$14,000	71%
Vaccine cost $100/dose	$11,000	$38,000	$830,000	n/a	$32,000	290%
Infection incidence: worst case, mandates easing	Vaccination Dominates[†]	$7,000	$290,000	n/a	$5,800	-29%

Infection incidence: best case, universal masks	$10,000	$36,000	$790,000	n/a	$30,000	266%
Higher death rates in <50 years	$480	$5,300	$110,000	n/a	$6,600	-20%
Higher undetected infection incidence (1.5x)	Vaccination Dominates†	$10,000	$340,000	n/a	$8,400	2%
2nd dose vaccine efficacy: 50%	$1,400	$15,000	$420,000	n/a	$12,000	46%
2nd dose vaccine efficacy: 70%	Vaccination Dominates†	$7,300	$290,000	n/a	$5,700	-30%
Vaccine efficacy: single dose efficacy 40%, all ages	Vaccination Dominates†	$9,900	$340,000	n/a	$7,700	-6%
Duration of disutilities: low	Vaccination Dominates†	$10,000	$370,000	n/a	$8,300	1%
Duration of disutilities: high	Vaccination Dominates†	$10,000	$320,000	n/a	$8,200	0%
Unit costs: commercial[18]	Vaccination Dominates†	Vaccination Dominates†	$310,000	n/a	Vaccination Dominates†	n/a
Unit costs: Medicaid[18]	$1,300	$12,000	$350,000	n/a	$10,000	22%
Low mortality, low ventilator use	Vaccination Dominates†	$11,000	$440,000	n/a	$8,500	4%
Low mortality, high ventilator use	Vaccination Dominates†	$11,000	$450,000	n/a	$8,500	4%
High mortality, low ventilator use	Vaccination Dominates†	$9,500	$270,000	n/a	$7,900	-4%
High mortality, high ventilator use	Vaccination Dominates†	$9,400	$270,000	n/a	$7,900	-4%
Baseline utility -10%	Vaccination Dominates†	$11,000	$370,000	n/a	$9,100	11%
Baseline utility +10%	Vaccination Dominates†	$9,400	$320,000	n/a	$7,500	-9%
3. Occupational/age groups						
*Subgroup**	*Priority‡ and other critical occupations§*	*65+ yrs*	*50-64 yrs*	*18-49 yrs*		
# eligible for vaccination[2,4,20]	*21,700,000*	*54,706,166*	*57,390,550*	*124,875,767*		
Base-case	**$20,000**	**Vaccination Dominates†**	**$8,000**	**$94,000**	**$8,200**	**-**
Vaccine cost $50/dose	$29,000	$2,300	$14,000	$130,000	$14,000	71%
Vaccine cost $100/dose	$60,000	$11,000	$33,000	$240,000	$32,000	290%
Infection incidence: worst case, mandates easing	$15,000	Vaccination Dominates†	$4,900	$79,000	$5,800	-29%
Infection incidence: best case, universal masks	$56,000	$10,000	$31,000	$230,000	$30,000	266%
Higher death rates in <50 years	$12,000	$450	$8,000	$25,000	$6,600	-20%
Higher undetected infection incidence (1.5x)	$20,000	Vaccination Dominates†	$8,200	$95,000	$8,400	2%
2nd dose vaccine efficacy: 50%	$26,000	$1,400	$12,000	$120,000	$12,000	46%
2nd dose vaccine efficacy: 70%	$15,000	Vaccination Dominates†	$5,200	$79,000	$5,700	-30%
Vaccine efficacy: single dose efficacy 40%, all ages	$19,000	Vaccination Dominates†	$7,600	$94,000	$7,700	-6%
Duration of disutilities: low	$20,000	Vaccination Dominates†	$8,100	$96,000	$8,300	1%
Duration of disutilities: high	$19,000	Vaccination Dominates†	$7,900	$92,000	$8,200	0%
Unit costs: commercial[18]	$8,800	Vaccination Dominates†	Vaccination Dominates†	$80,000	Vaccination Dominates†	n/a
Unit costs: Medicaid[18]	$22,000	$1,300	$10,000	$97,000	$10,000	22%
Low mortality, low ventilator use	$21,000	Vaccination Dominates†	$8,500	$110,000	$8,500	4%
Low mortality, high ventilator use	$21,000	Vaccination Dominates†	$8,400	$110,000	$8,500	4%
High mortality, low ventilator use	$18,000	Vaccination Dominates†	$7,300	$84,000	$7,900	-4%

High mortality, high ventilator use	$18,000	Vaccination Dominates†	$7,300	$84,000	$7,900	-4%
Baseline utility -10%	$22,000	Vaccination Dominates†	$8,900	$100,000	$9,100	11%
Baseline utility +10%	$18,000	Vaccination Dominates†	$7,300	$86,000	$7,500	-9%

ICER, incremental cost-effectiveness ratio; n/a, not applicable; QALY, quality-adjusted life-year; yrs, years.
*Individuals are assigned to one subgroup only; those qualifying for more than one subgroup are assigned to their highest tier. While those aged <18 years are included in the model, they are not targeted for vaccination as current clinical trials target only those 18+ years.
†Vaccination dominates: the vaccine is less costly and more effective than no vaccination.
‡Includes: public health personnel; inpatient health care providers; outpatient and home health providers; health care providers in long-term care facilities; pharmacists and pharmacy technicians; community support and emergency management; and mortuary services personnel.[4]
§Includes: other health care personnel; emergency services and public safety sector personnel; manufacturers of pandemic vaccine and antiviral; communications/information technology, electricity, nuclear, oil and gas, water sector personnel, and financial clearing and settlement personnel; critical government personnel; and other critical government personnel.[4]

Table A8. The vaccine unit price required so that the cost per quality-adjusted life-year gained equals at least $50,000, by tier and overall, under base-case assumptions

Strategy	Vaccine price per dose to achieve a cost per QALY ≥ $50,000 vs no vaccination				
	Tier 1	Tier 2	Tier 3	Tier 4	Overall*
Base-case incidence					
1. Age-based	$328	$143	$15	n/a	$150
2. Risk-group-based	$328	$127	Not possible†	n/a	$150
3. Occupational/age groups	$84	$329	$143	$15	$150
Worst-case incidence					
1. Age-based	$378	$174	$20	n/a	$176
2. Risk-group-based	$378	$154	Not possible†	n/a	$176
3. Occupational/age groups	$101	$379	$174	$19	$176
Best-case incidence					
1. Age-based	$140	$58	Not possible†	n/a	$60
2. Risk-group-based	$140	$50	Not possible†	n/a	$60
3. Occupational/age groups	$31	$141	$58	Not possible†	$60

QALY, quality-adjusted life-year; n/a not applicable
*Unit price of $150 per dose or $300 per course.
†As the cost per administration is $14·44, there is no unit price where the vaccine achieves a cost per QALY of ≥ $50,000.

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