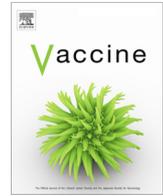




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Short communication

Modeling strategies for the allocation of SARS-CoV-2 vaccines in the United States

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ABSTRACT

The Advisory Committee on Immunization Practices (ACIP) recommended phased allocation of SARS-CoV-2 vaccines in December 2020. To support the development of this guidance, we used a mathematical model of SARS-CoV-2 transmission to evaluate the relative impact of three vaccine allocation strategies on infections, hospitalizations, and deaths. All three strategies initially prioritized healthcare personnel (HCP) for vaccination. Strategies of subsequently prioritizing adults aged ≥ 65 years, or a combination of essential workers and adults aged ≥ 75 years, prevented the most deaths. Meanwhile, prioritizing adults with high-risk medical conditions immediately after HCP prevented the most infections. All three strategies prevented a similar fraction of hospitalizations. While no model is capable of fully capturing the complex social dynamics which shape epidemics, exercises such as this one can be a useful way for policy makers to formalize their assumptions and explore the key features of a problem before making decisions.

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1. Introduction

With the expectation that early demand for SARS-CoV-2 vaccines would exceed supply for an extended period following introduction, the COVID-19 Vaccine Work Group of the ACIP began to develop a framework for evaluating phased vaccine allocation strategies in the spring of 2020, to provide guidance to federal, state, and local decision makers. Work group members considered evidence on the epidemiology of SARS-CoV-2, data on specific vaccines, vaccine program implementation issues, and ethical principles [1].

To support the development of ACIP guidance, we used a compartmental model of SARS-CoV-2 transmission in the United States to compare the relative impact of vaccination on infections, hospitalizations, and deaths across several phased allocation strategies considered by the work group. This modeling approach allowed us to simulate patterns of transmission within and between

different population groups over time, the progression of some infections to hospitalization or death, and the effect of vaccination on each of these processes. After setting up the model, we compared strategies in which the initial vaccination phases include healthcare personnel and then either prioritize vaccination for adults with high-risk medical conditions, adults aged 65 years or older, or a combination of essential workers and adults aged 75 years or older [1].

2. Methods

2.1. Model description

We used a deterministic SEPIR (Susceptible, Exposed, Pre-symptomatic infectious, symptomatic Infectious, and Recovered) compartmental model to simulate SARS-CoV-2 transmission in the US (including territories) across 6 age groups (0–4, 5–17, 18–49, 50–64, 65–74, and ≥ 75 years old). The 65–74 and ≥ 75 years old age groups were each split into 2 subgroups (those with and without a high-risk medical condition), while the 18–49 and 50–64 age groups were stratified into 4 subgroups each (essential workers and non-essential workers with and without a high-risk medical condition), for a total of 14 population strata. For the purpose of this analysis, high-risk medical conditions include chronic

Abbreviations: SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; CDC, Centers for Disease Control and Prevention; ACIP, Advisory Committee on Immunization Practices.

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obstructive pulmonary disease, heart disease, diabetes, chronic kidney disease, and body mass index ≥ 30 kg/m², consistent with the conditions identified by the CDC as having the strongest association with severe COVID-19-associated illness as of June 25, 2020 [2]. We used Behavioral Risk Factor Surveillance System data from 2019 to estimate the age-specific fraction of US adults with one or more high-risk medical conditions [3]. We also estimated that 43.5% of the population in the 18–49 and 50–64 age groups qualify as essential workers based on Bureau of Labor Statistics data for “critical industries” designated by the Department of Homeland Security [4,5]. For simplicity, we only considered essential workers in these two age groups, since this age range contains nearly all of the essential workforce, and assumed that the age-specific prevalence of high-risk medical conditions is independent of essential worker status. We account for essential workers’ elevated risk of exposure in the model by assuming that they are unable to reduce their contacts at work below a fixed level in most circumstances. Given our considerable uncertainty in the coverage and efficacy of NPI measures across industries, we explored a range of values for this contact rate “floor,” from 20% to 50% below baseline levels in sensitivity analyses, and used the midpoint of this range (35%) for our primary analysis.

Our model simulates the process of infection as the movement between compartments. Most individuals start off in the susceptible compartment, and become infected at a rate proportional to the size of the infectious population at any given time. Once infected, individuals move sequentially between 4 compartments: exposed, pre-symptomatic infectious, (a) symptomatic infectious, and recovered. The [supplementary materials](#) contain a complete description of contact patterns between population strata and the natural history and transmission parameters which are used to calculate the rate of movement between compartments.

We derived the infection fatality rate (IFR) for each age group from *Levin et al.* [6]. We then used data on the fraction of reported COVID-19 deaths that occurred in hospitals [7] and the risk of in-hospital death following hospitalization with COVID-19 [8] to calculate the age-specific infection hospitalization rate (IHR) from the IFR. Finally, we adjusted the overall age-specific IFR and IHR to estimate these values for those with and without a high-risk medical condition, using the prevalence of individuals in each age group with a high-risk medical condition and the relative risk of progression to severe disease associated with having a high-risk medical condition. We assumed that within each age group, having a high-risk medical condition is associated with a 3x greater IFR and IHR in our primary analysis (2x and 4x in sensitivity analyses). These assumptions are consistent with published evidence on specific comorbidities and severe COVID-19 outcomes [[Supplementary Fig. 2](#)]. The [supplementary materials](#) contain a complete description of our procedures.

2.2. Epidemic scenarios

We ran our model for 731 days, corresponding to the years 2020 and 2021. After rescaling the size of the overall population from 330 million to 100 thousand, we seeded the model with 1 infection on January 25, 2020 in the non-essential worker age 18–49 age strata. This date was calibrated to produce 1% cumulative incidence by the end of March, consistent with external estimates [9]. We then gradually increased and decreased contact rates, and therefore the time-varying reproduction number R_t , between March 2020 and January 2021 in the model, in order to visually approximate the general dynamics of the SARS-CoV-2 epidemic in the US. That is, incidence peaking in the spring, summer, and winter, and approximately a third of the population experiencing infection by the end of 2020 [[Supplementary Fig. 1](#)] [9]. Finally, in our primary analysis, we tuned the contact rates to set R_t to 1

on January 15, 2021 in our primary analysis (varied between 0.9 and 1.1 in sensitivity analyses, consistent with computed estimates in the US during that time period [9,10]).

2.3. Vaccine product assumptions

We modeled two vaccine product scenarios: no vaccination (the baseline scenario), and vaccination with a product based on existing two-dose mRNA vaccines (BNT162b2 and mRNA-1273). Vaccine effectiveness against infection was assumed to be 70% after the first dose and 85% after both doses, [11] while overall vaccine effectiveness against severe disease VE_s was assumed to be 75% and 95% after the first and second doses, respectively. [12] We assumed a 14-day delay from administration of a dose to the development of its associated protection level, a 28-day delay between administration of doses, and no waning of immunity over the modeled period. Vaccines have a “leaky” protection mechanism in our model, with vaccination reducing, but not eliminating, the risk of infection in all recipients.

2.4. Vaccine Allocation Scenarios

In our model, the vaccine was introduced on January 1, 2021, with 10 million doses available weekly. We assumed 100% coverage among groups recommended for vaccination, including among those previously infected, in our primary analysis (70% in a sensitivity analysis). When the current phase includes a mix of individuals eligible for their first and second doses, administration of second doses was prioritized. This work was conducted before the specific approval data, production schedule, and administration capacity of the vaccines became known.

We modeled four sequential phases of the US vaccination campaign: 1A-C and 2 [[Fig. 1](#)]. Phase 1A includes 20 million US health-care personnel, which we define as all workers serving in a healthcare setting, not just those directly providing care to patients [4,5]. To evaluate the impact of different administration strategies, we modeled three different scenarios for the composition of Phase 1B: a) 40 million adults aged ≥ 65 , b) 40 million adults with high-risk medical conditions, or c) a combination of 20 million each of essential workers and adults aged ≥ 65 . The “combination” strategy was proposed as a potential way to balance two distinct goals of COVID-19 vaccination: prevention of morbidity and mortality, and preservation of societal functioning. [13] Phase 1C included the remaining 120 million unvaccinated essential workers, adults aged ≥ 65 , and adults with high-risk medical conditions. Finally, Phase 2 included the 150 million individuals not belonging to the target populations covered in Phases 1A–C. Starting in Phase 1B, on days in which the number of people eligible for vaccination (those who either have not received a dose or initiated the two-dose course ≥ 28 days ago) in the current phase is less than the daily vaccine supply, excess doses were instead administered to members of the next phase. This decision was consistent with our expectation (and ACIP’s recommendation) that in practice, vaccine providers would be willing to vaccinate individuals outside of the current eligibility phase when met with lapses in demand from the current phase, to minimize dose wastage.

2.5. Quantifying vaccine impact

For each modeling scenario, we derived the total number of infections, hospitalizations, and deaths over the first 6 months of 2021. We then calculated the percent of these outcomes that are averted by vaccination under each set of assumptions and finally compared the percent of infections, hospitalizations, and deaths averted in the entire population across vaccination strategies [[Figs. 2 and 3](#) and [Supplementary Fig. 3](#)].

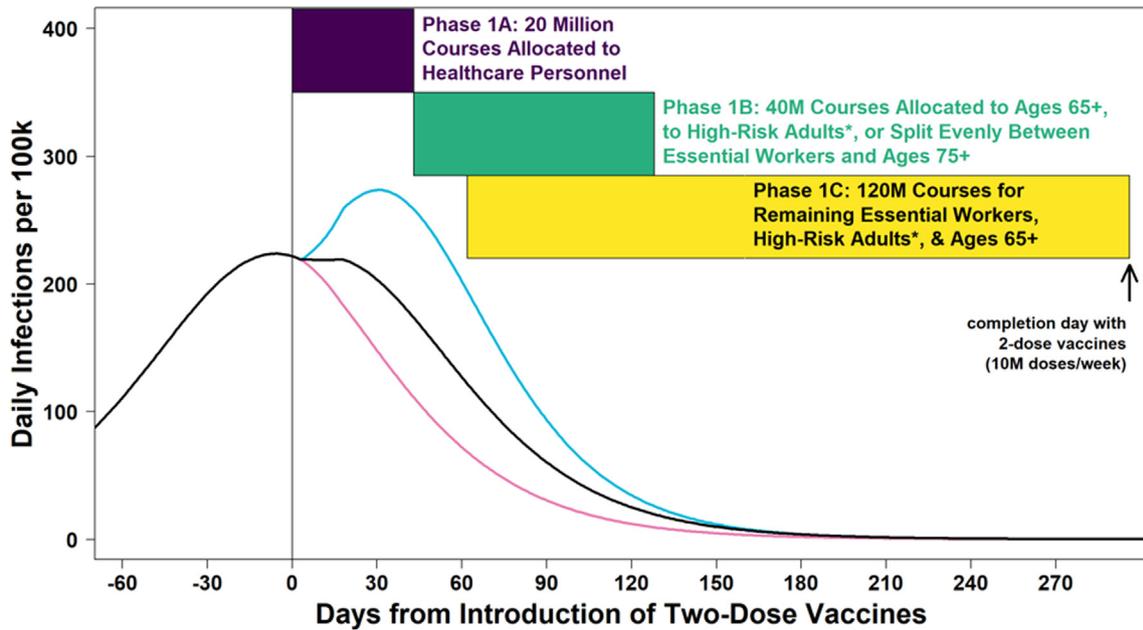


Fig. 1. Timing of Modeled Vaccine Rollout. The width and position (relative to the x-axis) of the purple, green, and yellow boxes indicate the period during which vaccination phases 1A, 1B, and 1C occur, respectively. For reference, the y-axis shows the modeled daily incidence of SARS-CoV-2 infection without vaccination when R_t on January 1st, 2021 is set to 1.0 (black), 1.1 (blue), and 0.9 (pink). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

We implemented this analysis using the ‘flumodels’ R package [14], which we modified to support changes in contact rates over time, and the simultaneous rollout of single- and two-dose vaccines. Code for replicating this analysis is available at github.com/cdcepi/ACIP-SARS-CoV-2-Vaccine-Modeling.

This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.²

3. Results

Fig. 2 depicts the percent of infections, hospitalizations, and deaths averted by vaccination under each unique target population and product-usage strategy, given our primary assumptions that $R_t = 1$ in mid-January, high-risk medical conditions are associated with a 3x higher risk of severe disease if infected, and essential workers can generally only eliminate 35% of their workplace contact rates. Vaccinating both essential workers and adults aged ≥ 75 in Phase 1B, and exclusively targeting adults aged ≥ 65 , were comparably effective strategies for reducing expected mortality (22.6% and 22.8% of deaths averted, respectively), while targeting adults with high-risk medical conditions in Phase 1B prevented fewer deaths (18.5% of deaths averted). Vaccinating adults with high-risk medical conditions in Phase 1B was the most effective strategy for preventing infections (19.7% of infections averted in the first six months of vaccination, compared to a no-vaccination scenario), followed by the strategy of targeting essential workers and adults aged ≥ 75 simultaneously (18.6% of infections averted), and targeting adults aged ≥ 65 exclusively (17% of infections averted). All three strategies were similarly effective at preventing hospitalizations (between 20.6% and 21.1% of hospitalizations averted).

Sensitivity analyses showed that varying the value of R_t in mid-January, the relative risk of severe disease associated with high-risk medical conditions, and the level of distancing that essential workers are able to practice affected the absolute fraction of

SARS-CoV-2 outcomes that can be averted through vaccination, although the relative performance of the three modeled strategies remained largely robust [Fig. 3]. A separate sensitivity analysis demonstrated that gradually increasing contact rates over the course of the vaccine rollout period, rather than holding them constant, did not alter the rank ordering of vaccine strategies, but did increase the fraction of SARS-CoV-2 outcomes that vaccination prevents, as this shifts incidence later in the spring when vaccine coverage was higher [Supplementary Fig. 3B]. Varying the pace of vaccination from 5 million to 20 million doses per week demonstrated that the overall effectiveness of vaccination was directly proportional to the speed at which doses are administered, although the relative effectiveness of the modeled strategies was generally consistent between scenarios [Supplementary Fig. 3C/D]. At the fastest modeled rollout pace, targeting adults aged ≥ 65 years in Phase 1B became slightly more effective at preventing deaths than targeting a combination of essential workers and adults aged ≥ 75 years (28% vs 27.3% of deaths averted, respectively): at slower rollout speeds, the effectiveness of these strategies at preventing deaths was nearly identical.

4. Discussion

To support the ACIP’s development of recommendations for the phased allocation of SARS-CoV-2 vaccines, we used a dynamic transmission model to evaluate the impact of prioritizing three different populations for vaccination following healthcare personnel: adults aged ≥ 65 , adults with high-risk medical conditions, and a combination of essential workers and adults aged ≥ 75 in equal proportions. Of these strategies, we found that targeting adults aged ≥ 65 , or both essential workers and adults aged ≥ 75 , prevented the most deaths, while targeting adults with high-risk medical conditions prevented the most infections. All three strategies prevented a similar fraction of hospitalizations. These results are consistent with other modeling analyses, [15–17] which suggest that the most effective strategies for preventing infections involve prioritizing groups with the highest contact rates, usually younger adults, while vaccination strategies which initially prioritize older

² See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

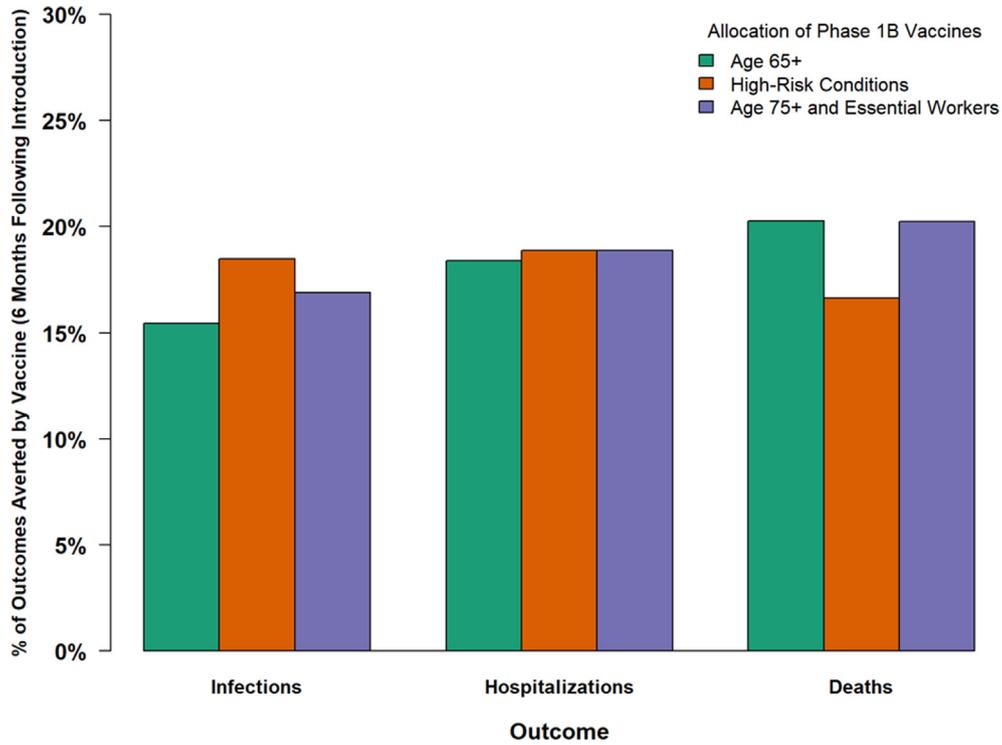


Fig. 2. Population-Wide SARS-CoV-2 Outcomes Prevented by Vaccination in the Six Months Following Introduction. Bars indicate the modeled % of infections, hospitalizations, and deaths prevented by vaccination across the entire population in the 6 months after vaccination begins. This averted burden is shown for scenarios in which Phase 1B of vaccination (following healthcare workers) includes adults aged 65+ years old (green), adults with high-risk medical conditions (orange), and a combination of essential workers and adults aged 75+ years old (purple). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

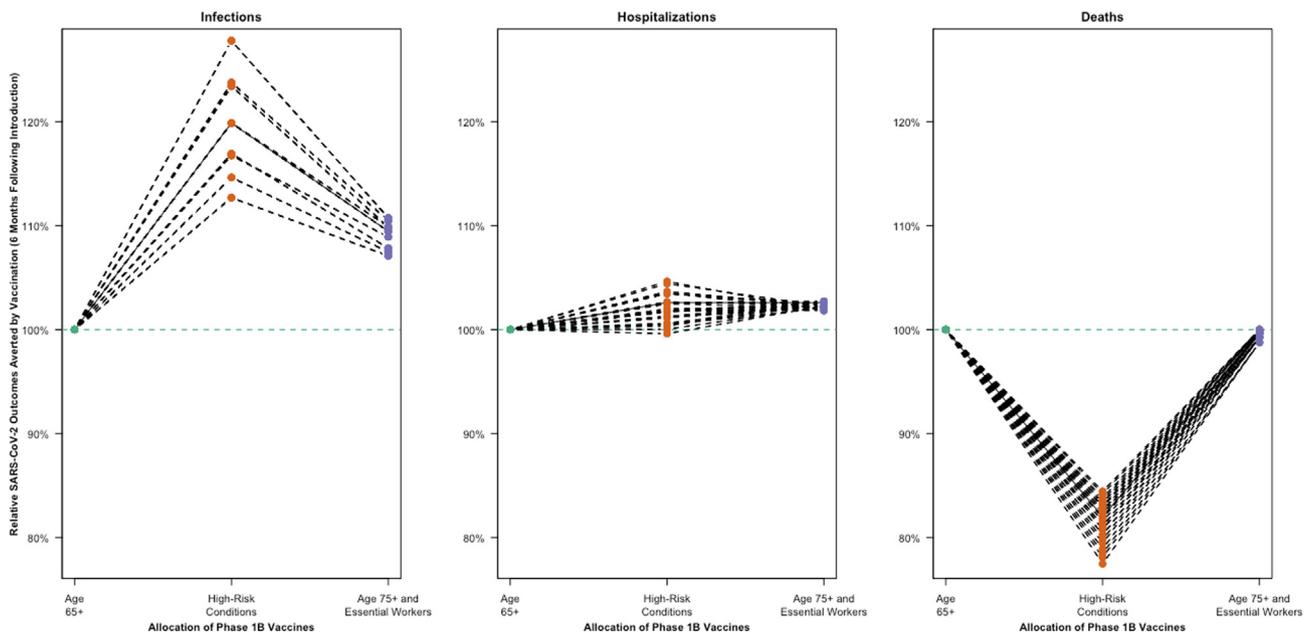


Fig. 3. Relative Number of SARS-CoV-2 Outcomes Prevented Across Vaccination Strategies and Scenarios. Each set of three points connected by black lines (solid for the primary analysis, dashed for sensitivity analyses) represents a unique combination of values for the time-varying reproduction number (R_t) in January 2021, the level of essential worker distancing, and the relative risk of severe disease for those with underlying medical conditions (see methods for the specific values considered). Within each unique parameter set, points represent the number of SARS-CoV-2 infections, hospitalizations, or deaths prevented by a given vaccination strategy, standardized as a percent of the outcomes averted by vaccination by the strategy of targeting adults aged ≥ 65 years in Phase 1B. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

adults prevent the most deaths, due to the strong relationship between age and COVID-19 disease severity. While our analysis is focused on the overall US population, variation in certain conditions may affect the optimal vaccination strategy at the local level. For instance, Matrajt et al. found that when a high fraction of the population has already been infected, prioritizing younger populations with high contact rates for vaccination can be optimal for minimizing deaths, as this strategy achieves herd immunity relatively quickly. [15] Meanwhile, results in this analysis were robust to the prevalence of acute infection at the time of vaccination. Similarly, Bubar et al. found that in populations with much younger age distributions than the US, prioritizing older adults for vaccination is not necessarily the optimal strategy for reducing mortality, although the optimal strategy was robust to seroprevalence at the time of vaccination. [17]

This analysis is subject to several limitations. Residents of long-term care facilities (LTCF), a population that ACIP recommended be included in Phase 1A, were not explicitly modeled as a distinct population in this analysis. Accurately representing transmission within both LTCFs and the community in a single model is challenging, given variability in the rate of movement between these settings, the stochastic nature of outbreaks in congregate settings, limited data on contact patterns and the effectiveness of interventions within LTCFs, and uncertainty in the relative risk of severe disease following infection between LTCF residents and community dwellers. We developed a series of models of LTCF transmission and mitigation measures to support decision making in this setting. [18–20] We did not explicitly stratify the population by sex or race/ethnicity, as this would have significantly increased the complexity of the model, with limited available data for parameterization. As a result, our model does not fully capture the complex relationships between demographics, social vulnerability, and disease risk. Similarly, we made a simplifying assumption that equal fractions of the 18–49 and 50–64 age groups were essential workers. Future analyses may be able to use a variety of data sources, such as the American Community Survey, to make more precise assumptions. Due to a paucity of high-quality data on the relative contact rates of essential workers and other adults, we were also forced to make certain assumptions in this area. While our results were largely robust across sensitivity analyses, more precise estimates of contact rates by occupational status, perhaps based on surveys or mobility data, could be useful for future modeling exercises. We also did not consider the impact of reinfection, waning immunity, or novel variants with different profiles of transmissibility, disease severity, or vaccine effectiveness. At the time this analysis was performed, neither the CDC nor the World Health Organization had designated any SARS-CoV-2 lineage as a variant of concern (VOC), and no recognized VOC had been detected in the US. For simplicity, our primary estimates assumed that all Americans would eventually be vaccinated, and therefore did not account for vaccine hesitancy. However, the relative impact of our modeled strategies was unchanged in a sensitivity analysis that assumed 70% final vaccination coverage in all population groups [Supplementary Fig. 3A]. More broadly, our primary objective was to compare the relative impact of different vaccination strategies, rather than the specific number of SARS-CoV-2 outcomes that would be averted by vaccination, as the latter is sensitive to the specific epidemic trajectory and pace of vaccine rollout. The scope of this analysis was limited to evaluating strategies for the phased allocation of vaccines across population groups, and does not include other important questions (e.g., the optimal timing of vaccine doses in a series).

Results from this analysis were used alongside other forms of evidence to guide the development of COVID-19 vaccination strategies. Our overall findings informed and are aligned with

ACIP's recommendation that persons aged ≥ 75 years and non-healthcare frontline essential workers be offered vaccination in Phase 1B [13].

All authors attest they meet the ICMJE criteria for authorship.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official views of the U.S. Centers for Disease Control and Prevention.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2022.02.015>.

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