OBSERVATION: BRIEF RESEARCH REPORT

Speed Versus Efficacy: Quantifying Potential Tradeoffs in COVID-19 Vaccine Deployment

Background: The global effort to develop a vaccine for coronavirus disease 2019 (COVID-19) has already produced 2 candidates, each requiring 2 doses, with reported efficacies exceeding 90% (1). The U.S. Food and Drug Administration (FDA) has granted Emergency Use Authorization for both vaccines (Pfizer-BioNTech and Moderna). Their reported efficacies greatly exceed the 50% threshold the FDA cited in a June 2020 guidance document (2). Additional vaccine candidates at earlier stages of development hold the promise of single dosing, simpler storage requirements, and more rapid immunity after vaccination (3).

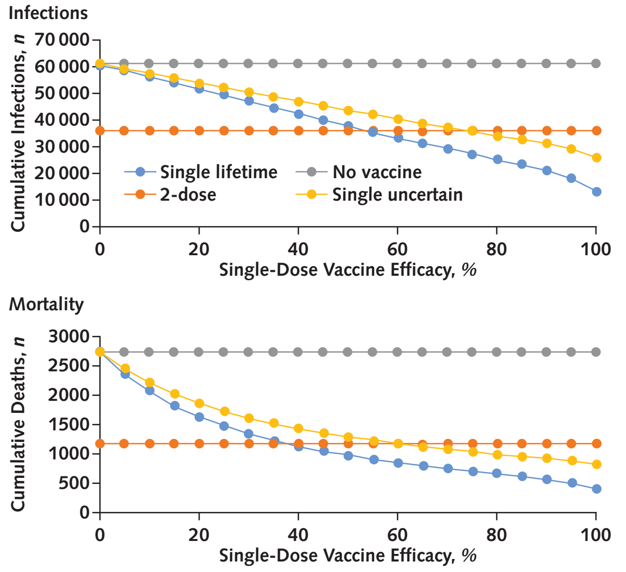
The availability of multiple vaccine options would be a welcome development but would create policy dilemmas. How do we define the "best" vaccine, and which populations should receive it? Should the FDA expect all candidates to meet or exceed the 90% efficacy benchmark established by the 2 front-runners? From a population perspective, how good is "good enough"? Given that some portion of the population will inevitably fail to return for a second dose, might a single-dose vaccine that is 75% effective and takes 2 weeks to achieve protection better contain the pandemic than a 95%-effective vaccine requiring 2 doses and a 4-week lag before full efficacy?

Objective: To quantify the speed-versus-efficacy tradeoff using a previously published model of a COVID-19 vaccination program (4). The model accounts for transmission of severe acute respiratory syndrome coronavirus 2, COVID-19 disease severity, and recovery or vaccination leading to protective immunity. Modifying parameters related to vaccine efficacy, vaccination program scale-up and coverage, and the time to vaccine benefits, we compared the likely performance of 1- and 2-dose vaccine candidates over a 6-month horizon on outcomes of cumulative infections, deaths, and peak hospitalizations.

Methods and Findings: Consistent with the FDA efficacy definition, we assumed that a 2-dose vaccine produced a 95% decrease in rates of progression to symptomatic disease, to severe or critical disease from mild disease, and to COVID-19–related death, as well as a nearly 3-fold increase in rates of disease recovery. We further assumed that this vaccine had a 0.5% daily uptake, double the observed peak rate for influenza vaccination in the United States (4), and took 4 weeks to achieve lifetime protection, allowing for partial immunity after the first dose. We compared this vaccine with 2 hypothetical, single-dose alternatives, one conferring lifetime protection and the other with stable efficacy of uncertain duration (exponentially distributed with a mean duration of 6 months). Both of these single-dose vaccines were assumed to achieve more rapid daily uptake (0.75%) and to take effect 14 days after administration. We considered efficacies for both single-dose vaccines ranging from 0% to 100%.

We did the base analysis in the context of an epidemic with an effective reproduction number (R_t) of 1.8. Other inputs were obtained from published sources, particularly the guidance for COVID-19 model parameterization from the Centers for Disease Control and Prevention and the Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response (4, 5).

Figure. Comparison of vaccine performance.



The figures illustrate the performance of 4 vaccination strategies in 100 000 persons with 0.1% infected and 9000 recovered in a susceptible-exposed–infectious–recovered model: 1) no vaccination (*gray line*); 2) a 95%-effective, 2-dose vaccine (*orange line*); 3) a single-dose vaccine conferring lifetime protection (*blue line*); and 4) a single-dose vaccine conferring an uncertain duration of protection that is exponentially distributed with a mean of 6 mo (*yellow line*). The vertical axes represent the outcome of interest (cumulative infections [*top*] and deaths [*bottom*]). The horizontal axes denote the efficacy of the single-dose vaccine. The crossing point of the blue line with the orange and yellow lines denotes the efficacy levels at which the 2 single-dose vaccines match the performance of the 95%-effective, 2-dose comparator.

In this model, a single-dose vaccine conferring lifetime protection need only attain an efficacy of 55% to avert as many infections as a 2-dose vaccine with 95% efficacy (**Figure** [*top*], *blue crossing orange line*). However, the single-dose vaccine with an uncertain duration of protection (mean, 6 months; *yellow line*), would need to attain 75% efficacy to avert the same number of infections. Similar mortality outcomes (**Figure**, *bottom*) can be achieved at single-dose efficacy levels of 40% (lifetime) and 60% (uncertain). Under more severe epidemic assumptions (R_t = 2.1), the single-dose vaccine at lower efficacy levels of 50% (lifetime) and 70% (uncertain) would prevent as many infections as a 2-dose vaccine with 95% effectiveness. Parity of mortality outcomes would be achieved at single-dose efficacy levels of 30% (lifetime) and 45% (uncertain). The single-dose vaccine could also achieve outcome parity at lower efficacy if the challenges of administering a 2-dose vaccination series reduced coverage.

Discussion: Prior work has shown that the success of a COVID-19 vaccination program will depend more on the speed and reach of its implementation than on the efficacy of the vaccine itself (4). The analysis presented here highlights the steep clinical and epidemiologic costs imposed by a 2-dose vaccination series in the context of ongoing pandemic response. Depending on the duration of protection conferred—and, of note, considering only a 6-month time horizon—a single-dose

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vaccine with 55% effectiveness may confer greater population benefit than a 95%-effective vaccine requiring 2 doses. This suggests that now that a highly effective, 2-dose vaccine for COVID-19 has been authorized and vaccination programs have begun, sustained and aggressive investment in pursuit of faster-acting, more convenient, 1-dose vaccine candidates remains justified.

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Reproducible Research Statement: *Study protocol and data set:* Not available. *Statistical code:* The underlying model that we adapted to produce these results is available in the appendix of reference 4.

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