Alternative Dose Allocation Strategies to Increase Benefits From Constrained COVID-19 Vaccine Supply

Background: On 18 December 2020, the U.S. Food and Drug Administration issued an Emergency Use Authorization (EUA) for the Moderna COVID-19 vaccine, adding to the earlier EUA for the Pfizer-BioNTech COVID-19 vaccine. Although trial evidence for both vaccines indicates partial protection against COVID-19 illness after 1 dose (1, 2), the vaccines are authorized only as 2-dose series and have not yet been evaluated for single-dose use. In the United States, distribution plans for initial supply of vaccine doses withhold half of the available supply for second doses to be administered weeks later (3). With COVID-19 surging, there are important tradeoffs to consider between the health costs of deferring benefits of earlier protection for half of people who could be vaccinated from initial supply, weighed against risks of possible vaccine supply disruptions that could delay receipt of second doses in the absence of sufficient reserves. We used a simple model to quantify these tradeoffs.

Methods: We developed a decision analytic cohort model to estimate direct benefits of vaccination against COVID-19 under alternative strategies for dose allocation (details in the Supplement, available at Annals.org). The fixed strategy, modeled after current U.S. policy, reserves 50% of each vaccine installment for second doses to be administered 3 weeks later. The flexible strategy (an illustrative example of many possible alternatives) reserves 10% of the supply for second doses during the first 3 weeks, 90% during each of the next 3 weeks, and 50% thereafter.

Expected benefits of vaccination were computed as averted COVID-19 cases accumulated over an 8-week period, relative to no vaccination. Vaccine and programmatic characteristics were based on the Pfizer-BioNTech vaccine (1). Efficacy estimates allowed for partial protection (52.4%) after receipt of the first dose and full protection (94.8%) after the second dose (1). We assumed waning efficacy for those not receiving the

Figure 1. Model-projected outcomes of alternative vaccine allocation strategies.

A. Illustrative example of doses administered over time for the fixed and flexible strategies in a stable vaccine supply scenario (6 million doses per week). Total effective population protection represents the equivalent number of people benefiting from vaccine-associated protection against COVID-19, calculated as the number of people vaccinated with 1 or 2 doses multiplied by vaccine efficacy with 1 or 2 doses, allowing for waning protection with delayed second dose. B. Reductions in COVID-19 incidence through the fixed and flexible strategies, under the stable supply scenario and an alternative scenario with reduced supply (down from 6 million doses per week in the first 3 weeks, to 3 million doses per week afterward). Averted incidence expressed as percentage reductions in each week compared with no vaccination, which are not dependent on assumed incidence trends.
second dose within 3 weeks after the first (single-dose efficacy reduced by a factor of 0.9 each week after week 3). We computed incremental benefits of the flexible strategy as relative increases in averted COVID-19 cases compared with the fixed strategy. Across a range of simulated scenarios, we varied vaccine supply, relative protection from the first dose, and waning efficacy given delayed second dose. To consider whether the preferred strategy would depend on infection trends, we assessed results when COVID-19 incidence was stable, was steadily increasing, or was sharply rising then falling.

Results: Under a steady vaccine supply of 6 million doses per week, the flexible strategy would result in an additional 23% to 29% of COVID-19 cases averted compared with the fixed strategy (Figure 1). In both scenarios, 24 million people received at least 1 dose by the eighth week, whereas 2.4 million additional people received 2 doses of vaccine in the flexible strategy because millions more received an initial dose during the first 3 weeks; all second doses were administered on schedule (within 3 weeks of first dose) in both strategies. If vaccine supply dropped to 3 million doses per week starting in week 4, overall benefits were reduced in both strategies, and the numbers of people receiving at least 1 dose by 8 weeks, 2 doses by 8 weeks, and 2 on-schedule doses by 8 weeks were 16.5, 12, and 12 million in the fixed strategy, respectively, and 20.1, 12.9, and 6.3 million in the flexible strategy, respectively. Overall, the flexible strategy averted an additional 27% to 32% of COVID-19 cases compared with the fixed strategy in the context of this moderate supply reduction.

We examined additional scenarios that would deliberately disadvantage the flexible strategy, by assuming substantially greater declines in vaccine supply and greater waning of protection with delayed second dose (Figure 2). While numbers of fully vaccinated individuals were adversely affected by these changes, the flexible strategy continued to produce greater overall benefits than the fixed strategy even when we assumed that protection would drop to zero if the second dose was not received within 6 weeks after the first dose. In further sensitivity analyses that varied single-dose efficacy estimates over broad ranges, we found that the 2 key determinants of optimal strategy were the number of highly protected individuals at the end of the simulation and the stability of the vaccine supply. The combination of a low first-dose efficacy and a collapse in supply was the sole circumstance that favored the fixed strategy.
Discussion: In this analysis, we demonstrated the potential to improve upon current policies for deploying tightly constrained early supply of highly efficacious COVID-19 vaccines in order to maximize population health benefits. Current policies place a premium on eliminating any possible delays to delivering second doses using an allocation scheme that maintains large reserves of vaccine to guard against complete collapse of supply. The cost of this conservative approach, however, is to delay receipt of first doses in many people who could gain substantial health benefits from earlier vaccination. We find that under most plausible scenarios, a more balanced approach that withholds fewer doses during early distribution in order to vaccinate more people as soon as possible could substantially increase the benefits of vaccines, while enabling most recipients to receive second doses on schedule. Our analysis is limited by focusing only on direct benefits to vaccine recipients rather than including potential secondary benefits from avoiding transmission. Key uncertainties remain around the time course of protection afforded by the first dose of vaccine and loss of protection with extended time to the second dose. Nevertheless, we suggest a simple modification to current policy that has potential to significantly amplify urgently needed benefits from limited vaccine supply.

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See Also: Editorial comment (page 558) and related articles (pages 552 and 568).

Financial Support: Drs. Tuite and Fisman are supported by the Canadian Institutes for Health Research (2019 COVID-19 rapid research funding OVo4-170360). Drs. Zhu and Salomon are supported by the Centers for Disease Control and Prevention though the Council of State and Territorial Epidemiologists (NU38OT000297-02) and the National Institute on Drug Abuse (3R37DA015612-17S1).

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M20-8137.

Reproducible Research Statement: Study protocol, statistical code, and data set: Available at https://github.com/ashleighrt/covid19-vaccine-allocation.

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This article was published at Annals.org on 5 January 2021.