The impacts of COVID-19 vaccine timing, number of doses, and risk prioritization on mortality in the US

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Abstract

As COVID-19 vaccination begins worldwide, policymakers face critical trade-offs. Using a mathematical model of COVID-19 transmission, we find that timing of the rollout is expected to have a substantially greater impact on mortality than risk-based prioritization and adherence and that prioritizing first doses over second doses may be life saving.

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
In December 2020, the US Food & Drug Administration issued emergency use authorization for two different two-dose SARS-CoV-2 vaccines (1) manufactured by Moderna and Pfizer-BioNTech, both estimated to be over 94% efficacious in preventing symptomatic COVID-19 infections (2). The Advisory Committee on Immunization Practices immediately recommended the prioritization of front-line workers and high-risk subgroups (3). As of January 13, roughly 10 million of the 27.6 million doses allocated to states have been administered (4).

We used an age- and risk-structured mathematical model of COVID-19 transmission in a US city (Appendix) to evaluate the impact of vaccine timing, risk prioritization, numbers of doses administered and rates of uptake on population-level mortality.

Focusing on Austin, Texas, we project COVID-19 deaths over 8 months for both an infection-blocking vaccine that reduces susceptibility and a symptom-blocking vaccine that reduces the symptomatic ratio, assuming all vaccinated individuals enjoy a 95% reduction in susceptibility (i.e., a leaky vaccine). Vaccination begins on either January 15 or February 15, with 10M people vaccinated per week nationwide and vaccines allocated to cities pro rata. We compare three strategies: no priority groups; one of three priority groups vaccinated prior to the general public—adults over 65, adults with high-risk comorbidities, or both of these groups; ten phases that vaccinate age-risk groups sequentially, in order of risk of severe COVID-19 outcomes. Stochastic simulations are initialized assuming that 7.6% of individuals have been immunized by infection prior to January 15th.

If a perfectly risk-prioritized (ten-phase) rollout of an infection-blocking vaccine begins January 15, we estimate that 52% (95% CI: 47% - 56%) or 56% (95% CI: 51% - 60%) of the deaths would be averted relative to the baseline of no vaccines, assuming 50% or 90% uptake, respectively (Figure). If delayed by one month, 34% (95% CI: 28%-40%) or 38% (95% CI:
32%-43%) of deaths would be averted, respectively. Under low (50%) adherence, prioritization has minimal benefit. Under high adherence (90%), the ten-stage strategy is significantly better than the others, followed by prioritizing everyone over 65 and high risk young adults.

If the vaccine is only symptom-blocking, then the expected differences between the risk-based strategies are magnified. With a January 15 start and 50% uptake, the ten-phase strategy is expected to avert 40% (95% CI: 35%-45%) of deaths whereas the unprioritized rollout would avert 32% (95% CI: 25%-37%). If only a single dose with 80% efficacy (5,6) is administered under the ten-phase strategy, we would expect a greater reduction in COVID-19 mortality of 50% (95% CI: 45%-54%) for a symptom-blocking vaccine and 66% (95% CI: 63%-70%) for an infection-blocking vaccine (Tables A1.1-A1.2).

These projections validate the prioritization of high risk groups. Under a pessimistic scenario in which a symptom-blocking vaccine is not rolled out until February 2021 with only 50% uptake, prioritizing high risk adults and those over 65 is expected to avert ~17,000 (95% CI: 0-36,000) more deaths in the US than a non-prioritized campaign. However, given the alarming state of the pandemic in early 2021, with thousands dying daily in the US and across Europe, vaccine delays are expected to cost more lives than either imperfect prioritization or vaccine hesitancy. Unlike seasonal influenza vaccination campaigns, which are initiated prior to the widespread transmission of the virus, the global health community is racing to get COVID-19 vaccines to people before the virus reaches them. With the emergence of potentially more contagious variants in the UK and South Africa, this may become even more challenging.

The UK, Belgium, and some Canadian provinces have opted to prioritize first doses over second doses (7), hoping that partial immunity in more people would be advantageous over near-complete immunity in fewer people. The US has publicly resisted this approach, citing the
lack of clinical trial data validating the approach (8). We find that providing a single (80% efficacious) dose of an infection-blocking or symptom-blocking vaccine would be expected to save more lives than the corresponding two-dose strategy. However, we strongly caution that additional efficacy data and single-dose trials are needed for validation. Our model makes other assumptions about uncertain quantities, including an exponential onset and permanency of immunity and that vaccines either block infection or symptoms (whereas the reality may be a hybrid of the two). Our estimates also depend on the state of the pandemic, particularly the initial proportion susceptible and viral transmission rate. We modeled the COVID-19 pandemic in the US in early 2021, with cases surging and herd immunity likely to occur with months in the absence of substantial behavior change, expansion of testing and isolation or vaccination. We also do not account for possible behavioral relaxation due to weariness or the apparent success of the vaccination campaign.

Risk prioritization is a valid approach for maximizing the impact of vaccines, but not at the expense of vaccination speed. Our projections suggest two immediate strategies to amplify the impact of COVID-19 vaccines in the US—hybrid distributions that combine active outreach to priority groups with passive distribution to the general public and foregoing plans to hold second doses in reserve.
Figure. Projected COVID-19 mortality in the Austin-Round Rock MSA from November 8, 2020 to September 17, 2021 under various vaccine rollout scenarios. A) COVID-19 deaths averted after January 15, 2021 under combinations of: vaccine uptake, either 50% (left) or 90% (right); type of protection, either infection or symptom blocking (x-axis); rollout dates, either January 15 (circles) or February 15 (triangles); and risk prioritization, either no priority (gray), prioritize all adults over 65y (light blue), prioritize high-risk comorbidities (medium blue), or the combination of the two (dark blue), or a ten-phase risk-ordered strategy that sequentially vaccinates >65y high risk, 50-64y high risk, >65y low risk, 18-49y high risk, 50-64y low risk, 18-49y low risk, 0-4y high risk, 5-17y high risk, 0-4y low risk, 5-17y low risk. Points and whiskers indicate the median and 95% CI across 200 paired stochastic simulations. B) Weekly incident COVID-19 deaths per 100,000 assuming intermediate (70%) uptake (9) without vaccine (black) or under a ten-phase risk-based rollout of a 95% efficacious infection-blocking, starting either January 15 (orange) or February 15 (purple). The brown line assumes that only first doses are administered starting January 15. Solid lines and shading indicate the median and 95% CI across 200 stochastic simulations, respectively.
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Author Bio

Xutong Wang is a Ph.D. candidate at the University of Texas at Austin under the supervision of Dr. Lauren Ancel Meyers. Her research interest is on mathematical and statistical modeling of infectious disease dynamics.

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