LETTER

REPLY TO DUSHOFF ET AL. AND PIFARRÉ I AROLAS ET AL.:

Age prioritization for COVID-19 vaccination does save lives and years of life

Joshua R. Goldstein[a,1], Thomas Cassidy[b], and Kenneth W. Wachter[a]

In our PNAS brief report about COVID-19 vaccination priorities (1), we present a demographic analysis of characteristic age-specific schedules of COVID-19 death rates and show, contrary to widespread intuition, that the goals of maximizing lives saved per vaccination and of maximizing years of future life saved per vaccination are not in conflict.

In our report, we take pains to emphasize that effects beyond the direct age-based effects that we model deserve consideration, including transmission dynamics—"indirect effects"—and wider ethical and biomedical implications. In their letter entitled "Transmission dynamics are crucial to COVID-19 vaccination policy" (2), Dushoff et al. reemphasize our point: Indirect effects deserve consideration.

However, the word "crucial" in the letter title sounds like overstatement. The simulation study (3) cited by ref. 2 takes account of indirect as well as direct effects. Most of the optimal allocation strategies calculated there for minimizing deaths turn out to include priority for the oldest old (ref. 3, figures 9 and 10). In the even more comprehensive simulation study which we cited, Bubar et al. (4) state, "we conclude that for mortality reduction, prioritization of older adults is a robust strategy that will be optimal or close to optimal to minimize mortality for virtually all plausible vaccine characteristics" (ref. 4, p. 919).

As for years of life saved, the simulation studies do not report them. However, no argument is being made in ref. 2 (nor elsewhere, to our knowledge) that the implications of indirect effects with respect to years of life saved run contrary to the implications for lives saved. In short, the cited studies give no basis for thinking that indirect effects would sideline our findings for direct effects.

A recent study by some of us (5) quantifies the direct effects of lives saved by age-prioritized vaccination. Gains from more strenuous targeting of older people look very substantial. Across US states, in early stages of vaccine rollout, eligibility rules were largely designed to realize these gains. Recently, eligibility has been rapidly widening, while coverage at older ages has remained incomplete (6). As of the time we are writing, in mid-May, the reservoir of unvaccinated high-risk elderly continues to be a cause for concern.

Our analysis in ref. 1 was built around empirical findings that COVID-19 mortality rates tend to rise with age more or less proportionally to all-other-cause mortality. We illustrated this pattern with high-quality schedules from the United States, Germany, and South Korea. Castro and Singer (7) found that the same pattern also applied to Brazil. In their letter (8), Pifarré i Arolas et al. broaden the empirical analysis to 40 countries. They find that the pattern of proportionality and the concordance between lives saved and years of life saved that we present continues to hold in the large majority of cases in their wider sample. They also identify several apparent exceptions.

COVID-19 mortality rates reflect the combined action of the infection fatality rate and the population rate of infection. Biological pathways that drive the age-specific response of infection fatality rates are likely similar across countries, especially before the advent of new viral variants. However, population rates of infection by age may be expected to reflect the histories of epidemic spread country by country, especially in early stages. For example, the societal balance between the elderly living with their families and living in institutions could show up in age-specific infection rates. For these reasons, we would not find it surprising to encounter some exceptions to the general pattern we studied.

On the other hand, we are not convinced of the reliability of the data behind all of the exceptions presented in ref. 8. Of the three cases in figure 1 in ref.8, bad mismatch in figure 1*B* for Peru between the line based on confirmed COVID-19 deaths and the line based on estimated excess deaths suggests

[a]Department of Demography, University of California, Berkeley, CA 94720; and [b]Department of Mathematics, Bucknell University, Lewisburg PA 17837

Author contributions: J.R.G., T.C., and K.W.W. wrote the paper.

The authors declare no competing interest.

[1]To whom correspondence may be addressed. Email: josh.goldstein@berkeley.edu.

Published July 6, 2021.

something wrong with the data. A smaller discrepancy in the opposite direction stands out in figure 1*B* in ref. 8 for Chile. In figure 2 in ref. 8, it appears that none of the exceptions has crossover ages that agree for excess deaths and reported COVID-19 deaths. Aligning the curves in figure 1*A* in ref. 8 to join together at the least precisely measured oldest age group has drawbacks. Without local knowledge of conditions and data collection systems, which we do not possess for these countries, we keep an open mind as to how many of the apparent exceptions are real. Still, full uniformity is not to be expected, and we are grateful to the writers of the letter for expanding our empirical purview and crystallizing discussion.

As the writers of ref. 8 say, our report (1) contains mathematical results on life table functions that apply to settings beyond COVID-19, in the context of demographically realistic schedules of mortality. We are presently working to extend our formal investigation to broader classes of schedules that may arise in more general applications of survival analysis. We second the hope expressed in ref. 9 in PNAS that research stimulated by COVID-19 will have value that lasts beyond the pandemic's ardently desired end.

1 J. R. Goldstein, T. Cassidy, K. W. Wachter, Vaccinating the oldest against COVID-19 saves both the most lives and the most years of life. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2026322118 (2021).

2 J. Dushoff, C. Colijn, D. J. D. Earn, B. M. Bolker, Transmission dynamics are crucial to COVID-19 vaccination policy. *Proc. Natl. Acad. Sci. U.S.A.*, 10.1073/pnas.2105878118 (2021).

3 L. Matrajt, J. Eaton, T. Leung, E. R. Brown, Vaccine optimization for COVID-19: Who to vaccinate first? *Sci. Adv.* **7**, eabf1374 (2020).

4 K. M. Bubar *et al.*, Model-informed COVID-19 vaccine prioritization strategies by age and serostatus. *Science* **371**, 916–921 (2021).

5 J. R. Goldstein., T. Cassidy, A. S. Mahmud, Lives saved from age-prioritized Covid-19 vaccination. *medRxiv* [Preprint] (2021). https://doi.org/10.1101/2021.03.19.21253991. Accessed 15 May 2021.

6 Centers for Disease Control, Demographic trends of people receiving COVID-19 vaccinations in the United States. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends. Accessed 18 May 2021.

7 M. C. Castro, B. Singer, Prioritizing COVID-19 vaccination by age. *Proc. Natl. Acad. Sci. U.S.A.* **118**, 1–2 (2021).

8 H. Pifarré i Arolas, E. Acosta, M. Myrskylä, Optimal vaccination age varies across countries. *Proc. Natl. Acad. Sci. U.S.A.* **118**, 10.1073/pnas.2105987118 (2021).

9 D. Conley, T. Johnson, Opinion: Past is future for the era of COVID-19 research in the social sciences. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2104155118 (2021).