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- 4 Gortazar C, Rodríguez del Río F, Hervás D, Domínguez L, de la Fuente J. COVID-19 severity declines over time. *Authorea* 2020; published online June 10. <https://doi.org/10.22541/au.15918113778287140> (preprint).

Authors' reply

Christian Gortázar and colleagues, in their response to our Correspondence about herd immunity in COVID-19,¹ suggest that the mutation of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might provide an alternative explanation for the observed decline in deaths in Europe. As evidence, they highlight the observation that the SARS-CoV-2 virus has mutated,^{2,3} alongside their own report arguing that the severity of COVID-19 has decreased over time.⁴ Unfortunately, their own study appears to have ended before many recoveries could have occurred, severely undermining the main conclusion. There are, however, other data that could be interpreted as declining severity—for example, in Europe and parts of the USA from August to September, 2020, the number of cases have been rising without the expected spike in deaths shortly thereafter. The question is whether mutation can provide a parsimonious explanation for these trends.

When thinking about viral evolution it is useful to make a distinction between transmissibility (chance of onward infection) and virulence (severity of disease). The D614G mutation, noted by Gortázar and colleagues, has been found to increase transmissibility,³ but large, well powered studies have not detected a link between this genetic variant and COVID-19 mortality.⁵ Furthermore, the increasing prevalence of the D614G variant largely predates the observed changes in COVID-19 mortality. Other SARS-CoV-2 mutations, such as Δ382, have been found to confer reduced virulence, but with no data showing increased transmissibility.⁶ Crucially, neither of these mutations,

nor any other mutation identified to date, can explain the sudden and large scale drop in deaths observed in many European countries following lockdown. Furthermore, the mutation hypothesis still offers no explanation as to why countries that enforced lockdown earlier should have had fewer deaths in subsequent weeks. Hence, we strongly disagree that mutation offers an alternative explanation for the trends described in our original Correspondence.

What about the current trend of increasing cases without subsequent deaths? We think it is less plausible to be because of genetic factors, and basic epidemiological explanations should be first ruled out. Foremost among these explanations is that testing has increased, and might have been applied to a previously under-represented subset of the population. Cases might be concentrated in young people who are known to have a better prognosis. Treatment⁷ and clinical management have improved, alongside increased hospital capacity and response speed.

SARS-CoV-2 will continue to evolve, and a gradual change in disease severity and transmissibility should be anticipated, but there is currently no evidence to support an evolutionary trend towards greater or lesser virulence. Competing epidemiological data must first be dismissed alongside more genetic evidence before it can be concluded that mutation has rendered COVID-19 a reduced threat to public health.

We declare no competing interests. LCO, RV, NMF, and SB contributed equally.

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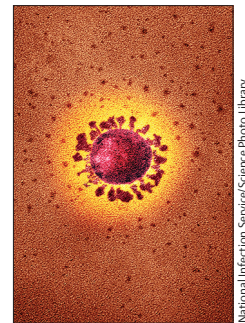
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Nursing's seat at the research roundtable

WHO's Year of the Nurse and Midwife 2020 began as an unforeseen global health-care crisis quietly gained traction. With no disease-specific prevention, treatment or cure for COVID-19, public health measures and supportive care—interventions developed and delivered largely by nurses—were the first and remain the only unequivocally effective defences against severe acute respiratory syndrome coronavirus 2.

Nurses have earned well deserved recognition for their essential roles in providing skilled, compassionate care for patients throughout this pandemic. What has been left out of the conversation is that, in addition



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For more on the **Year of the Nurse and Midwife 2020** see <https://www.who.int/campaigns/year-of-the-nurse-and-the-midwife-2020>