

for the same period in 2019, a rise secondary to an increase in the number of offers as other transplant centres have closed. Follow-up times for these 38 transplants are 1–58 days; we have at least 7 days of follow-up for 31 cases. Initial results are reported here and summarised in the appendix. Median length of hospital stay was 5 days. 9 (29%) of 31 patients had delayed graft function, defined as any use of postoperative dialysis. All discharged patients are no longer dialysis dependent. During this short-term follow-up period none of these recipients have contracted SARS-CoV-2. Three were readmitted to hospital—one for peritoneal dialysis catheter related peritonitis, and two for management of diabetes.

COVID-19 appears to be more prevalent in the UK haemodialysis population than the UK transplant population (8.6% vs 1.1%) with comparable mortality risk (22.5% vs 25.1%)—summarised in the appendix (p 5).<sup>3</sup> Our early results support the notion that a continued (albeit radically altered) transplant programme helps minimise pandemic risk in a highly vulnerable population. Soon transplant services might need to coexist with COVID-19 and, much as previous generations did in an earlier era of infectious disease, we will need to learn to segregate patients who are at risk.

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- 1 Loupy A, Aubert O, Reese PP, Bastien O, Bayer F, Jacquelinet C. Organ procurement and transplantation during the COVID-19 pandemic. *Lancet* 2020; **395**: e95–96.
- 2 NHS Blood and Transplant. COVID-19 bulletin number 7: organ and tissue donation and transplantation directorate. April 16, 2020. <https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/18296/covid-19-bulletin-7-16-04-2020.pdf> (accessed May 13, 2020).
- 3 The Renal Association. COVID-19 surveillance report for renal centres in the UK. All regions and centres – up to 6 May 2020. Bristol: The Renal Association, 2020.

## Host or pathogen-related factors in COVID-19 severity?

Lucy Okell and colleagues<sup>1</sup> observed that the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently in marked decline in many countries. Okell and colleagues suggest two possible explanations for this decline, namely the effect of lockdowns, physical distancing, and other interventions; or, alternatively, herd immunity. After analysing trends in cumulative deaths over time in many European countries that went into lockdown at different stages of their epidemic, and data obtained from serology studies on the proportion of the population that had the infection previously, Okell and colleagues found few data to support an explanation that relies on herd immunity.

In the first explanation, there is a high risk of renewed transmission if interventions or behavioural modifications are relaxed. In the explanation regarding herd immunity, further declines in cases and deaths are to be expected even in the absence of interventions or behavioural modifications. We support Okell and colleagues for stating that identifying

the most probable explanation is key to any future plans to lift physical distancing and travel restrictions. However, we would like to suggest a third explanation linked to changes in the pathogen, and hence in disease severity.

SARS-CoV-2 has mutated.<sup>2,3</sup> This observation coincides with reports of a lower disease severity (measured in the number of days with symptoms and degree of pneumonia severity) in newer patients compared with those who contracted the disease earlier.<sup>4</sup> If changes in population susceptibility or pathogen virulence are associated with a decline in disease severity, then less aggressive control interventions will be enough for future COVID-19 management.

We encourage future epidemiological studies to include indicators of disease severity as predictor variables. Analyses that do not account for host-related or pathogen-related changes in disease severity should be interpreted with caution.

We declare no competing interests.

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- 1 Okell LC, Verity R, Watson OJ, et al. Have deaths from COVID-19 in Europe plateaued due to herd immunity? *Lancet* 2020; **395**: e110–11.
- 2 Kim JS, Jang JH, Kim JM, Chung YS, Yoo CK, Han MG. Genome-wide identification and characterization of point mutations in the SARS-CoV-2 genome. *Osong Public Health Res Perspect* 2020; **11**: 101–11.
- 3 Zhang L, Jackson CB, Mou H, et al. The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity. *bioRxiv* 2020; published online June 12. <https://doi.org/10.1101/2020.06.12.148726> (preprint).

- 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,<sup>1</sup> 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,<sup>2,3</sup> alongside their own report arguing that the severity of COVID-19 has decreased over time.<sup>4</sup> 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,<sup>3</sup> but large, well powered studies have not detected a link between this genetic variant and COVID-19 mortality.<sup>5</sup> 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.<sup>6</sup> 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. Treatment<sup>7</sup> 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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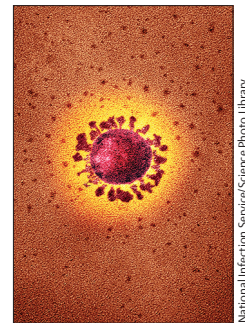
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- Okell LC, Verity R, Watson OJ, et al. Have deaths from COVID-19 in Europe plateaued due to herd immunity? *Lancet* 2020; **395**: e110–11.
- Kim JS, Jang JH, Kim JM, Chung YS, Yoo CK, Han MG. Genome-wide identification and characterization of point mutations in the SARS-CoV-2 genome. *Osong Public Health Res Perspect* 2020; **11**: 101–11.
- Zhang L, Jackson CB, Mou H, et al. The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity. *bioRxiv* 2020; published online June 12. <https://doi.org/10.1101/2020.06.12.148726> (preprint).
- 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).
- Volz EM, Hill V, McCrone JT, et al. Evaluating the effects of SARS-CoV-2 Spike mutation D614G on transmissibility and pathogenicity. *medRxiv* 2020; published online August 4. <https://doi.org/10.1101/2020.07.31.20166082> (preprint).
- Young BE, Fong S-W, Chan Y-H, et al. Effects of a major deletion in the SARS-CoV-2 genome on the severity of infection and the inflammatory response: an observational cohort study. *Lancet* 2020; **396**: 603–11.
- Horby P, Lim WS, Emberson J, et al. Effect of dexamethasone in hospitalized patients with COVID-19: preliminary report. *medRxiv* 2020; published online June 22. <https://doi.org/10.1101/2020.06.22.20137273> (preprint).

### 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>