

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Comment

deaths associated with the Delta variant of concern, June–July, 2021 We previously reported on the speed with which the

Predicted COVID-19 positive cases, hospitalisations, and

Delta variant of concern (VOC) took hold in Scotland.¹ The Delta VOC has subsequently established itself in many other parts of the world and has emerged as the dominant strain internationally.² Recent data have shown that the Delta VOC is more transmissible,³ associated with higher rates of hospitalisation than other variants, and that vaccines might be less effective in preventing infection than they are with the Alpha VOC.^{1,4} Consequently, there are concerns about the extent to which lockdown restrictions can safely be lifted, even in countries with high vaccination coverage.⁵

The Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) national-level surveillance system links multiple datasets in near realtime providing access to individual-level data.⁶ We have used EAVE II to build data driven models to describe and forecast the epidemiological and clinical profile of the COVID-19 pandemic. Building on methods previously described in the context of the first and second waves in largely unvaccinated individuals,6 we developed a prediction model that estimates the likelihood of hospitalisation and deaths of people currently positive, and people predicted to be positive, with COVID-19 over a 4-week time horizon (appendix p 1). Specific advances are that we have trained the model on the Delta VOC and that it now also incorporates time varying vaccination status, school closures, and the effect of the surge in cases around the time of the 2020 UEFA European football tournament.

For forecasting, we fitted a spline model to the daily number of positive cases in the past 10 weeks and then took the number of cases from an over-dispersed Poisson distribution (appendix p 2). We computed the age and clinical risk group distribution of all patients who tested positive in the most recent week (beginning June 12, 2021; appendix p 2), and then drew a stratified random sample of individuals from the entire database who had not previously tested positive. The risk of hospitalisation or death was based on 26 clinical characteristics (comorbidities such as diabetes and

chronic kidney disease) identified from primary care records that are known to increase the risk of serious COVID-19 outcomes.⁸ We thus obtained a forecasted cohort of individuals who were simulated to test positive over the ensuing 4-week time horizon.

We used a Cox regression model that took demographics, clinical characteristics, and vaccination status as inputs, and yielded probabilities of hospitalisation within the next 14 days and death within 28 days of testing positive. For each day during the projected 4-week time horizon, we applied the model to all positive cases to estimate the daily numbers of hospitalisations and deaths. To account for the changing dynamics of the pandemic-in particular, the rapid spreading of the Delta VOC-we retrained our model so that it was based on all positive cases from March 16 to June 7, 2021. This date range corresponds to the period during which the Delta VOC became the dominant strain in Scotland.¹ Further, we have now included the ratio of Delta to Alpha variant to model the effect of the Delta VOC on risks of hospitalisation and death in addition to the temporal trend term to allow for additional temporal factors not explicitly modelled.

Our initial model, based upon all data on cases in Scotland up to June 19, 2021, predicted that the number See Online for appendix of daily positive cases could rise to 3349 (exceeding the maximum of 3146 cases during the second wave), leading to 105 daily COVID-19 hospitalisations (44% of the maximum 240 during the second wave; appendix p 3) and 7 daily COVID-19 deaths (9% of the 76 maximum during the second wave; appendix p 3) by July 19, 2021, the cutoff date when most of the lockdown restrictions in Scotland were lifted. However, after factoring in summer holiday school closures from June 25, and the assumed 50% growth reduction in the increase of new cases from July 2, our adjusted model suggests that, by July 19, the daily cases could rise to 2751 cases, lead to 97 daily COVID-19 hospitalisations, and seven daily COVID-19 deaths. We subsequently observed daily cases exceeding 2500, daily hospitalisations reaching 100, and daily deaths reaching 10 during our projections



oa 🜔



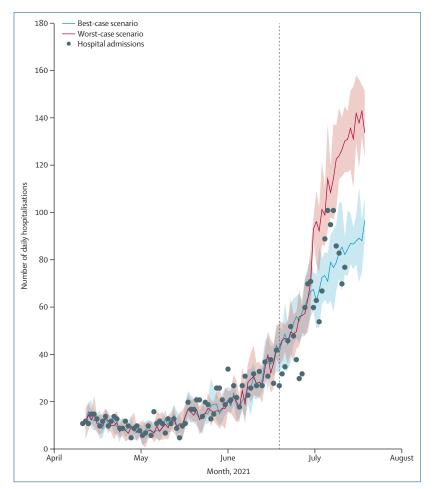


Figure: Number of daily hospitalisations forecasted in the near future illustrating the impact of the recent surge in positive COVID-19 cases suspected to be triggered by UEFA EURO 2020 Championship The purple vertical represents June 20, 2021; the beginning of our projections window in which we have forecasted COVID-19 positive cases, hospitalisations, and deaths. The best-case scenario represents the adjusted model that factors in school closure, and the worst-case scenario represents the model including excess cases due to the football championship. Note that the hospitalisation data in the last few days is incomplete as there is some lag before all data is curated at Public Health Scotland.

window. On July 19, though, there were 1908 daily cases, 75 hospitalisations, and 8 daily deaths.

Our adjusted model also assessed the effect of the sudden surge in cases that likely resulted from widespread socialisation and mobility during the 2020 UEFA European championship.⁹ During the surge in cases over 11 days (June 20–30), there were a median of 1349 excess positive cases over the originally forecasted positive cases (appendix p 2). In the worstcase scenario, assuming that this surge would lead to an excess of 1349 cases per day in addition to those originally forecasted until July 19, we estimated that daily COVID-19 hospitalisations could potentially rise to 134 (56% of the maximum during the second peak) and the deaths to 10 (13% of the maximum during the second peak). Figure illustrates the daily hospitalisations expected on the basis of these projections with school closure and with (worst case) and without (best case) the excess cases due to the football tournament during the entire projection period. The most recent daily hospitalisation data are also superimposed on figure (data available until July 12) and this suggests that the worst-case scenario is unlikely to occur as the most recent hospitalisations are below the worst case projections in line with the observed reduction in cases since July 1 (appendix p 2). The appendix (p 4) summarises these three scenarios projected to July 19. The age distribution of all cases predicted to be hospitalised is also provided (appendix p 4).

There are limitations to our approach. Our forecasting approach assumes short-term exponential growth, which is not based on a transmission dynamic model, and that the current restrictions and associated mobility patterns will continue until July 19, 2021. Further, we have assumed that excess positive cases due to the football surge will not trigger additional exponential increases.

In summary, we have forecasted the number of COVID-19 cases, hospitalisations, and deaths in Scotland driven by the Delta VOC while factoring age, sex, comorbidities, vaccinations, school holidays, and potential scenarios resulting from the surge in cases related to UEFA EURO 2020 Championship. The number of daily hospitalisations forecasted during July 2021, is expected to increase to around 100 per day. Consequently, we recommend caution when proceeding to lift lockdown restrictions until a higher proportion of the population is double vaccinated than currently stands.

AS, JM, and CR are members of the Scottish Government's Chief Medical Officer COVID-19 Advisory Group. AS and CR are members of the New and Emerging Respiratory Virus Threats (NERVTAG) risk stratification subgroup. JM is a member of NERVTAG. CR is a member of Scientific Pandemic Influenza Group on Modelling. AS is a member of AstraZeneca's Thrombotic Thrombocytopenic Advisory Group. SVK is co-chair of the Scottish Government's Expert Reference Group on ethnicity and COVID-19. All roles are unremunerated. All other co-authors report no competing interests.

Our thanks to the Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) patient advisory group for their support. EAVE II is funded by the Medical Research Council (MR/R008345/1) with the support of BREATHE - The Health Data Research Hub for Respiratory Health [MC_PC_9004], which is funded through the UK Research and Innovation Industrial Strategy Challenge Fund and delivered through Public Health Data Research UK. Additional support has been provided through Public Health Scotland and Scottish Government DG Health and Social Care and the Data and Connectivity National Core Study, led by Health Data Research UK in partnership with the Office for National

Statistics and funded by UK Research and Innovation. SVK is funded by a NHS Research Scotland Senior Clinical Fellowship (SCAF/15/02), the Medical Research Council (MC_UU_00022/2), and the Scottish Government Chief Scientist Office (SPHSU17).

Copyright @ 2021 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY-NC-ND 4.0 license.

Syed Ahmar Shah, Emily Moore, Chris Robertson, Jim McMenamin, Srinivasa Vittal Katikireddi, Colin R Simpson, Ting Shi, Uktarsh Agrawal, Colin McCowan, Sarah Stock, Lewis D Ritchie, *Aziz Sheikh, on behalf of Public Health Scotland and the EAVE II Collaborators aziz.sheikh@ed.ac.uk

Usher Institute, University of Edinburgh, Edinburgh, UK (SAS, AS, TS, SS); Public Health Scotland, Glasgow, UK (EM, JM, CR); University of Glasgow, Glasgow, UK (SVK); Academic Primary Care, University of Aberdeen, Aberdeen, UK (LDR); Victoria University of Wellington, Wellington, New Zealand (CRS); School of Medicine, University of St Andrews, St Andrews, UK (UA, CM)

- 1 Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. *Lancet* 2021; **397**: 2461–62.
- 2 Campbell F, Archer B, Laurenson-Schafer H, et al. Increased transmissibility and global spread of SARS-CoV-2 variants of concern as at June 2021. *Euro Surveill* 2021; **26:** 2100509.

- 3 Callaway E. Delta coronavirus variant: scientists brace for impact. June 22, 2021. https://www.nature.com/articles/d41586-021-01696-3 (accessed July 12, 2021).
- 4 Vasileiou E, Simpson CR, Shi T, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. Lancet 2021; 397: 1646–57.
 - Day M. Covid-19: Israel advises against foreign travel after recording 125 new cases. BMJ 2021; **373:** n1617.

5

- 6 Simpson CR, Robertson C, Vasileiou E, et al. Temporal trends and forecasting of COVID-19 hospitalisations and deaths in Scotland using a national real-time patient level data platform. *Lancet Digit Health* 2021; 3: e517–25.
- 7 Moore S, Hill EM, Tildesley MJ, Dyson L, Keeling MJ. Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study. *Lancet Infect Dis* 2021; 21: 793–802.
- 8 Clift AK, Coupland CAC, Keogh RH, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 2020; 371: m3731.
- 9 Scotland BBC. Football linked to 2000 Scottish Covid cases. June 30, 2021. https://www.bbc.co.uk/news/uk-scotland-57667163 (accessed July 12, 2021).