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Hospitalisation associated with SARS-CoV-2 delta variant in Denmark

The SARS-CoV-2 B.1.617.2 (delta) variant was first reported in India in December, 2020, and by July, 2021, was predominant over the B.1.1.7 (alpha) variant in most of Europe due to its higher transmissibility.^{1,2} Infections with the alpha variant have been shown to be more severe than preceding SARS-CoV-2 strains,^{3,4} and a similar concern has now been raised for infections with the delta variant, particularly among unvaccinated people, although vaccination is effective against COVID-19 hospitalisation.

Katherine Twohig and colleagues² reported an increased hospitalisation risk for delta variant infections (hazard ratio 2.26 [95% CI 1.32–3.89]) compared with alpha variant infections in England between March 29 and May 23, 2021. The study included 196 patients admitted to hospital with the delta variant, 47 (24%) of whom were admitted more than 21 days after first vaccination. To corroborate these results, we updated our Danish national analysis of hospitalisation risk associated with the alpha variant between Jan 1 and March 28, 2021,⁴ with cases until June 27, 2021, including patients with the delta lineage. We found a similarly increased risk of hospitalisation associated with the delta variant (risk ratio 2.83 [95% CI 2.02–3.98]; appendix p 2). Our analysis included 44 patients admitted to hospital with the delta variant, only four (9%) of whom were admitted more than 14 days after first vaccination. The risk of hospitalisation was only significantly increased among non-vaccinated people and among those who tested positive within

14 days after the first vaccine dose (appendix p 2). We consider the two study findings comparable (because the underlying populations had similar COVID-19 vaccine coverage and rollout for doses one and two, and despite the Oxford-AstraZeneca ChAdOx1 vaccine comprising approximately 3% of administered vaccine doses by June 23, 2021, in Denmark, which is lower than in England). In addition, there were only minor differences between the analyses in regression method and adjustment factors.

The observed hospitalisation risk for delta variant infections might, as Twohig and colleagues² suggest, be key for resource planning to mitigate the impact of the delta variant in countries with rapid spread, despite vaccination. However, it could be argued that it is increasingly difficult to determine causality of the relative severity across emerging variants using surveillance data as the pandemic is constantly changing with respect to testing patterns, age distribution, and social behaviour with the rollout of the vaccination programme. In addition, the vaccine effectiveness against infection and hospitalisations might also vary depending on circulating variants.⁵

We declare no competing interests. The datasets analysed during the current study are located in the Danish national COVID-19 surveillance system database at Statens Serum Institut, and the data are becoming or are already available for research upon request and with permission from the Danish Data Protection Agency and Danish Health Authority (<https://sundhedsdatastyrelsen.dk/da/forskerservice>).

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Rapid genome sequencing in hospitals to identify potential vaccine-escape SARS-CoV-2 variants



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SARS-CoV-2 genome sequencing is embedded in academic and public health laboratories, but whether there are benefits to rapid sequencing in front-line hospital laboratories is unclear. We did rapid genome sequencing of SARS-CoV-2-positive nose and throat swabs from patients admitted to our hospital since July 7, 2021, to identify potential SARS-CoV-2 vaccine-escape variants for infection control and public health purposes. In addition, we did PCR-based genotyping of all new SARS-CoV-2 cases for three south London hospitals (Guy's and St Thomas', King's College, and Princess Royal University) using the AusDiagnostics SARS-CoV-2 Typing Panel (16-well) on the AusDiagnostics HighPlex, sequencing any non-typeable results.

We identified two cases of a potential vaccine-escape variant from the B.1.621 lineage. This variant of interest,¹ first identified in Colombia, has lineage-associated spike mutations R346K, E484K, and

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For distribution of lineages over time in the UK see <https://microreact.org/project/COGconsortium/f85f1a27>

For the ARTIC Network SARS-CoV-2 bioinformatic platform see <https://artic.network/ncov-2019/ncov2019-bioinformatic-sop.html>

For Pangolin see <https://covid-lineages.org/resources/pangolin.html>

For type-variant tools see https://github.com/cov-ert/type_variants

P681H, which have been reported to show reduced neutralisation by antibodies.²⁻⁴ In addition, the variant we detected harbours a K417N spike mutation, which is associated with vaccine escape in the beta variant first identified in South Africa.^{5,6} We first identified this variant on July 12, 2021, and since then more cases have been reported by public health authorities.⁷ The presence of mutations associated with vaccine escape might warrant reclassification of this variant to a variant of concern and deployment of additional public health resources to contain spread.

These two community cases with identical genomes (GISAID accession numbers EPI_ISL_2993635 and EPI_ISL_2993634) presented to different hospitals; both individuals were unvaccinated, lived 5 miles apart, and had no known epidemiological contact or recent travel. This finding indicates ongoing community transmission of this variant even in a setting where, as of writing, the delta variant accounts for 99% of cases, further suggesting that this variant has a fitness advantage, perhaps through the potential to escape vaccination.

Our sequencing workflow uses Oxford Nanopore technology with rapid barcoding kits (SQK-RBK004) and the ARTIC Network SARS-CoV-2 bioinformatic pipeline with Pango nomenclature and type-variant tools. Previous studies have shown the ability of this technology to provide sequencing data in 24 h.⁸ This workflow can complete in 8 h, allowing whole-genome sequencing and variant reporting to be completed on the same day as sample positivity. By contrast, the average turnaround time from our offsite reference sequencing laboratory is around 10 working days.

For both cases, the variant was reported to Public Health England within 72 h of sampling. Our experience suggests that using rapid workflows in hospitals, close to where samples are tested, could

improve public health surveillance efforts and expedite identification of new variants. This is particularly important as physical-distancing measures are lifted in the context of ongoing high rates of community transmission in a partially vaccinated population. This will undoubtedly lead to the emergence of vaccine-escape variants, however, the frequency at which they will arise and their capacity for sustained transmission are unknown. Further work is ongoing to characterise this variant and assess escape from neutralisation by antibodies generated from past infection and vaccination.

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CoronaVac induces lower neutralising activity against variants of concern than natural infection

The inactivated whole-virus CoronaVac vaccine (Sinovac Biotech, Beijing, China) has been approved for emergency use in mass vaccination programmes in Thailand and is widely available in many low-income countries. Results from a phase 1-2 clinical trial of CoronaVac were recently published in this journal,¹ and a large, observational study in Chile further estimated that two doses of CoronaVac had vaccine effectiveness of 65.9% against COVID-19, 87.5% against hospitalisation, 90.3% against intensive care unit admission, and 86.3% against death, with values adjusted for potential effects of age and sex.² Variants of concern (VOCs) circulating in Thailand as of writing include B.1.1.7 (alpha), B.1.351 (beta), and B.1.617.2 (delta). To assess the impact of SARS-CoV-2 variants on vaccine-induced and infection-induced antibodies, we evaluated titres of SARS-CoV-2 S1-receptor-binding domain (RBD)-binding IgG, as well as neutralising antibody (NAbs) titres against the SARS-CoV-2 prototypic vaccine strain (wild-type [WT]) and VOCs in sera from health-care workers who had received two doses of CoronaVac; we compared these with sera from unvaccinated, naturally infected patients who had been hospitalised in March-May, 2020 (hereafter denoted the natural infection