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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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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-bioinformatics-sop.html

For **Pangolin** see https://cov-lineages.org/resources/pangolin.html

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

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 (NAb) 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

2020 cohort), or April–May, 2021 (hereafter denoted the natural infection 2021 cohort). We used a live-virus microneutralisation assay for NAb titre quantification. Details regarding cohort demographics, methods, and statistical analyses can be found in the appendix (pp 4, 6–8).

We found that 100% of participants in all cohorts were seropositive for virus-specific IgG. We next assessed NAb-afforded protection against WT and VOCs in our cohorts. Overall, the percentage of participants with quantifiable NAb titres (≥20 units) was highest against the WT strain, followed by much lower titres against the alpha, beta, and delta variants (appendix p 5). This pattern was consistently observed in all cohorts, and notably, the percentages of individuals with detectable NAbs were lower in CoronaVac recipients than in the naturally infected cohorts (appendix p 5). In adjusted analyses, we observed that, in all cohorts, geometric mean NAb titres were significantly lower against all VOCs than against WT (appendix p 2). NAb titres against the alpha and beta variants were not significantly different from each other, and NAb titres against the delta variant were the lowest and significantly different from the rest (appendix p 2).

We further found that WT was best neutralised by natural infection 2020 sera and the alpha variant was best neutralised by natural infection 2021 sera (appendix p 2). These results are consistent with the predominant strains circulating in Thailand in early to mid-2020 and mid-2021 at the time of sample collection for each respective cohort. The beta variant was neutralised equally well by natural infection 2020 and 2021 sera, with geometric mean NAb titres that were higher than those elicited by CoronaVac (appendix p 2). Similarly, the delta variant was neutralised equally well by natural infection 2020 and 2021 sera, but with markedly lower NAb titres than those obtained with the beta variant. Titres against the delta variant in CoronaVac recipients were lower still, almost at the limit of detection (appendix p 2). Together, these results highlight the relatively low NAb titres elicited by CoronaVac compared with natural infection.

Although NAb titres are not an exclusive immune correlate of protection, they are highly predictive of immune protection from symptomatic SARS-CoV-2 infection.[3] Based on our data, although there was robust production of S1-RBD-binding IgG and 100% seropositivity across the board, NAb-mediated protection was markedly reduced (and in many cases undetectable) against the three VOCs compared with WT in sera from all groups. Furthermore, NAb potency against alpha and beta VOCs was comparable in our CoronaVac vaccinee sera; this finding is inconsistent with a previous report showing that the beta variant is more resistant to neutralisation than the alpha variant with sera from CoronaVac recipients collected 14 days after the second dose when tested using a pseudovirus neutralisation assay.[4] Worryingly, the delta variant, which is the most transmissible, possibly among the most virulent of all VOCs identified to date,[5] and a dominant variant in many countries, appears to be most refractory to neutralisation. Lastly, our study highlights a low degree of neutralisation-afforded protection mounted by CoronaVac when compared with natural infection. Further booster doses, heterologous or otherwise, beyond the conventional two-dose regimen might be needed for recipients of CoronaVac to maintain a long-term anamnestic response. Amid steady NAb decay over time[3] and the continued emergence of divergent SARS-CoV-2 variants, it is imperative to maintain effective mitigation strategies and to continue monitoring vaccine efficiency in areas with circulating VOCs.

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See **Online** for appendix

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See **Online** for appendix 2

Performance of saliva and mid-turbinate swabs for detection of the beta variant in South Africa

In December, 2020, South Africa faced an exponential surge in COVID-19 cases, which was associated with replacement of circulating lineages with a novel variant of concern (VOC), the beta variant (B.1.351 lineage).[1] Preliminary analyses suggested that this variant, defined by three mutations at key sites in the receptor-binding domain, might have functional significance, including increased transmissibility.[1] We compared the performance of saliva and mid-turbinate sampling, as non-aerosol-generating procedures, with nasopharyngeal samples for confirmation of SARS-CoV-2 infection[2] before and after replacement with the beta VOC.

Between Aug 1, 2020, and Jan 16, 2021, we enrolled 410 eligible ambulatory participants who presented to Groote Schuur Hospital in Cape Town, South Africa, for SARS-CoV-2 testing. Of these, 300 were enrolled before, and 110 after, replacement of wild-type virus with the beta VOC. All participants provided a supervised, self-collected saliva and mid-turbinate swab, in addition to the standard nasopharyngeal swab collected by health-care workers; all samples were tested with RT-PCR not targeting the S gene.[3] Whole-genome sequencing of specimens with a cycle threshold (Ct) value of less than 30 was done. Individual participant results are available in appendix 1.

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See **Online** for appendix 1

Differences between before and after beta VOC replacement were assessed for the following parameters: diagnostic validity of saliva and mid-turbinate sampling relative to nasopharyngeal swabs, mean Ct differences, pre-test probability of having SARS-CoV-2, and Nextstrain clades (appendix 2).[4]

Before beta VOC replacement, 21 (7%) of 300 participants tested positive on saliva swabs, 27 (9%) on mid-turbinate swabs, and 33 (11%) on nasopharyngeal swabs. After beta VOC replacement, 30 (28%) of 107 participants tested positive on saliva swabs, 31 (29%) on mid-turbinate swabs, and 40 (37%) on nasopharyngeal swabs.

The positive percentage agreement (PPA) of saliva swabs with nasopharyngeal swabs increased by 21 percentage points (from 51·5% to 72·5%) from before to after variant replacement, whereas the PPA for mid-turbinate swabs relative to nasopharyngeal swabs remained similar (75·8% before replacement and 77·5% after). The negative percentage agreement with nasopharyngeal swabs was greater than 98% for both saliva and mid-turbinate swabs at both timepoints.

The reasons for the significant improvement in PPA for saliva but not mid-turbinate samples are currently unclear but could include changes in tissue tropism[5] associated with the beta VOC. However, increased viral replication in salivary glands would be expected to decrease the mean Ct value to a greater extent for saliva swabs than for nasopharyngeal swabs, which was not observed (appendix 2). Another explanation could be the presence of increased quantities of beta virus RNA, reflected by decreased mean Ct values (appendix 2), for all sample types, which might support the preliminary modelling-based finding of increased transmissibility.[1] Further investigation of the respiratory viral load kinetics is needed to establish whether prolonged elevation or greater peak values primarily explain our findings. Although altered test-seeking behaviour in the study population related to prevalence cannot be excluded, the inclusion criteria remained the same throughout the study.

Regardless of the underlying causes, our findings suggest that established diagnostic methods might require re-validation with the emergence of novel variants. Further whole-genome sequencing analysis and other studies are underway to determine whether the beta VOC is associated with compartmentalised replication, distinct oral shedding dynamics, increased viral burden, and increased infectious duration.

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Vaccinating children: fairness and childism

A recent Editorial in this journal argued that, despite mixed reactions to the news that Pfizer-BioNTech's mRNA BNT162b2 vaccine was efficacious,