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

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See Online for appendix 2

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 infection² 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.

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 tropism⁵ 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,



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