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instrument-dependent, and of limited deployability. We agree with Larremore and colleagues⁵ that test sensitivity is secondary to frequency of screening and time to result.

Finally, the excellent negative predictive value of Ag-RDTs is a mathematical computation of probability based on test sensitivity and prevalence of infection in the population. It is not misleading as long as one is clear about the purpose of testing and how the sensitivity of a test is derived.

We declare no competing interests.

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(ACE2) receptor to facilitate viral entry.¹ Such variants represent a public health challenge during the COVID-19 pandemic because they increase viral transmission and disease severity.² The B.1.351 variant, first identified in South Africa, has three notable mutations in the spike receptor-binding domain (RBD)—namely, K417N, E484K, and N501Y³—whereas the B.1.1.7 variant, first identified in the UK, carries the N501Y mutation (appendix pp 2–4). B.1.351 is of particular concern for its potential resistance to antibodies elicited by previous SARS-CoV-2 infection and vaccination.⁴

Several mechanisms might account for increased variant transmissibility, such as increased spike protein density, greater furin cleavage accessibility, and enhanced spike protein binding affinity for the ACE2 receptor.⁵ To test whether the B.1.351 and B.1.1.7 variants bind ACE2 with increased affinity, binding of purified recombinant B.1.351 and B.1.1.7 RBD was compared with binding of the Hu-1 RBD, which was originally identified in Wuhan (SCoV2) using microscale thermophoresis. The B.1.1.7 RBD bound ACE2 with 1.98-times greater affinity than the SCoV2 RBD (mean equilibrium dissociation constant [Kd] 203.7 nM [SD 57.1] vs 402.5 nM [112.1]; $p=0.0521$; appendix p 5). The B.1.351 RBD bound ACE2 with 4.62-times greater affinity than the SCoV2 RBD (mean Kd 87.6 nM [SD 25.5] vs 402.5 nM [112.1]; $p=0.0009$; appendix p 5). These data are consistent with a model in which variant spike proteins mediate increased transmissibility of the B.1.1.7 and B.1.351 variants, at least in part, by enhancing ACE2 binding affinity in line with in-silico predictions.⁶

In the initial stage of infection, virions bind lung airway epithelial cells with kinetics governed in part by spike-ACE2 binding affinities. Enhanced affinity likely mediates increased infectivity by lowering the effective concentration of

virions required for cell entry and is a convergent feature in more transmissible SARS-CoV-2 variants arising in multiple geographical regions. Finally, characterisation of binding between variant spike proteins and cognate human receptor ACE2 on the basis of microscale thermophoresis represents a potential surveillance strategy for predicting enhanced transmissibility of emerging SARS-CoV-2 variants harbouring novel spike mutations.

We declare no competing interests.

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What chikungunya teaches us about COVID-19

Since December, 2019, the COVID-19 pandemic has generated huge challenges, numerous breakthroughs in research and care, and innovations in public health. 1 year after its emergence, the world is discovering

See Online for appendix



SARS-CoV-2 B.1.1.7 and B.1.351 spike variants bind human ACE2 with increased affinity

Genomic surveillance efforts have uncovered SARS-CoV-2 variants with mutations in the viral spike glycoprotein, which binds the human angiotensin-converting enzyme 2

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