

## Surveillance report

Surveillance generated by nf-ncov-voc for Beta variant

### Date

This report is generated on 2023-03-04 using 459574 number of genomes collected between 2020-02-25 and 2023-02-16

## Pango Lineages

Pango Lineages in this report ['B.1.351']

## Indicator

This table contains key indicators identified

| Indicator                        | Sub-categories from POKAY   | Mutations   |
|----------------------------------|---|---|
| Transmissibility between humans  | transmissibility  | D614G, E484K, K417N, N501Y  |
| Infection Severity               | ACE2 receptor binding affinity, viral load, outcome hazard ratio        | A701V, D215G, D614G, D80A, E484K, H655Y, K417N, L18F, L5F, N501Y, Q677H |
| Immunity after natural infection | convalescent plasma escape, reinfection, humoral response durability    | A701V, D215G, D614G, D80A, E484K, K417N, L18F, N501Y, Q677H             |
| Vaccines                         | vaccine neutralization efficacy   | A701V, D215G, D614G, D80A, E484K, K417N, N501Y, V1176F                  |
| Monoclonal antibodies            | monoclonal antibody serial passage escape, pharmaceutical effectiveness | E484K, K417N, N501Y   |
| Diagnostics                      | clinical indicators, antigenic test failure, symptom prevalence         |   |

## Mutation Significance

This table contains key functional impacts of mutations identified

| Mutations | Sub-category                   | Function   | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| D80A      | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant combination showed no change relative to D614G.   | B.1.351  | Gong et al. (2021)       | 1108           | A                | C                | 1.0                 |
| D80A      | CD8 plus T cell response       | One individual of 30 in the study, with HLA supertype HLA*A24:02, had a linear epitope that overlaps this variant of concern.  | B.1.351  | Redd et al. (2021)       | 1108           | A                | C                | 1.0                 |
| D80A      | antibody epitope effects       | Anti-NTD CV1 mAb isolated from an early pandemic case was unable to neutralize either partial B.1.351 variant pseudovirus used (A701V or L242del). The neutralization potency of mAb CV30, which contacts K417 and N501 but not E484, was extasciitilde10-fold weaker toward both B.1.351 variants. The neutralization potency of anti-RBD mAb CV3-1 was 3-4-fold less potent against the B.1.351 variants, while anti-RBD mAb CV2-75 was modestly less effective. | B.1.351  | Stamatatos et al. (2021) | 1108           | A                | C                | 1.0                 |
| D80A      | antibody epitope effects       | Abolishes neutralizing activity of N-terminal-domain-directed mAb 4-19.  | B.1.351  | Wang et al. (2021)       | 1108           | A                | C                | 1.0                 |
| D80A      | convalescent plasma binding    | 2.11x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1108           | A                | C                | 1.0                 |

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|-----------|----------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| D80A      | convalescent plasma escape | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors   | B.1.351  | Cele et al. (2021)       | 1108           | A                | C                | 1.0                 |
| D80A      | convalescent plasma escape | Using convalescent sera from 15 early pandemic patients (Seattle Flu Study), mean 220 days post symptom onset (IQR 125-269, and three asymptomatic cases) with 27% WHO disease severity scale 3, one third (5/15) of sera neutralized this B.1.351 pseudotype and only three had ID50 titers above 100. Only two of the 15 sera achieved 80% neutralization.   | B.1.351  | Stamatatos et al. (2021) | 1108           | A                | C                | 1.0                 |
| D80A      | convalescent plasma escape | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct. Only 3 of 44 convalescent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | B.1.351  | Wibmer et al. (2021)     | 1108           | A                | C                | 1.0                 |
| D80A      | reinfection                | 4 health care workers in the 20's and 30's with no underlying conditions and seropositivity or confirmed 2020 SARS-CoV-2 infections were confirmed to have B.1.351 infection during a February 2021 hospital outbreak in Luxembourg. Symptoms were mostly mild on first infection, and milder on second infection.   | B.1.351  | Staub et al. (2021)      | 1108           | A                | C                | 1.0                 |
| D80A      | reinfection                | Hamsters re-infected with B.1.351 virus after seroconversion from previous infection with a lineage A virus did not transmit virus to naive sentinels via direct contact transmission, in contrast to the non-seroconverted animals. They had little infectious virus and no pathology in the lungs. Initial infection with SARS-CoV-2 lineage A does not prevent heterologous reinfection with B.1.351, but prevents disease and onward transmission.                       | B.1.351  | Yinda et al. (2021)      | 1108           | A                | C                | 1.0                 |

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|-----------|---------------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| D80A      | symptom prevalence              | Inoculation with the B.1.351 isolate resulted in lower clinical scores in 6 rhesus macaques that correlated with lower virus titers in the lungs, less severe histologic lung lesions and less viral antigen detected in the lungs. Our comparative pathogenicity study suggests that ongoing circulation under diverse evolutionary pressure favors transmissibility and immune evasion rather than an increase in intrinsic pathogenicity.  | B.1.351  | Munster et al. (2021)    | 1108           | A                | C                | 1.0                 |
| D80A      | trafficking                     | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing mild decrease in infection rate amongst the cells, suggesting that this mutation does not contributing to cell entry fitness.   | B.1.351  | Tada et al. (2021)       | 1108           | A                | C                | 1.0                 |
| D80A      | vaccine neutralization efficacy | Using B.1.351 defining mutations for Spike, observed 4x average decrease in neutralization efficiency (but still relevant titres) for sera from 10 BNT162b2 vaccinees 12 days after second dose, but only one relevant titre 12 days after first dose. Compares unfavorably to wild type or B.1.1.7 titres.   | B.1.351  | Alenquer et al. (2021)   | 1108           | A                | C                | 1.0                 |
| D80A      | vaccine neutralization efficacy | In sera collected from 15 early pandemic patients (Seattle Flu Study), mean 16 days post first dose with either Pfizer/BioNTech or Moderna vaccines, the median ID50 titers were extasciitilde3-fold lower against this B.1.351 pseudotyped virus relative to wild type. A single asymptomatic patient, who had no detectable RBD-specific IgG memory before vaccination, also did not elicit nAbs against the B.1.351 variant. [compare to extasciitilde10 fold with L242del] ID50 titres in non-infected mRNA vaccines more than two weeks post-booster were significant, but >100x weaker than in previously infected patients after first dose. | B.1.351  | Stamatatos et al. (2021) | 1108           | A                | C                | 1.0                 |
| D80A      | vaccinee plasma binding         | 1.64x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.35x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.  | B.1.351  | Gong et al. (2021)       | 1108           | A                | C                | 1.0                 |
| D80A      | virion structure                | Estimated that there is no free energy change (ddG) for this variant (i.e. same stability as wild type)   | B.1.351  | Spratt et al. (2021)     | 1108           | A                | C                | 1.0                 |

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|-----------|--------------------------------|--|----------|-----------------------|----------------|------------------|------------------|---------------------|
| N501Y     | ACE2 receptor binding affinity | The N501Y mutation had the biggest effect on ACE2 affinity of any VOC mutation tested, increasing the affinity extasciitilde10 fold to KD extasciitilde7 nM, by increasing the k(on) extasciitilde1.8 fold and decreasing the k(off) by extasciitilde 7 fold as measured by surface plasmon resonance.   | B.1.351  | Barton et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | In the case of VOC B.1.1.7+E484K, the addition of the E484K mutation to N501Y further increased the affinity, to extasciitilde15 fold higher than WT RBD (KD extasciitilde5 nM), by further increasing the k(on) as measured by surface plasmon resonance. Because the higher k(on) could result in mass transfer limiting binding, we confirmed that the kinetic measurement for this variant was not substantially affected by varying levels of immobilization. | B.1.351  | Barton et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | The affinity of the B.1.351 RBD variants for ACE2 increased by 3.7 fold as measured by surface plasmon resonance relative to wild type RBD by increasing the k(on) and decreasing the k(off) rate constants.   | B.1.351  | Barton et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | This combination showed extasciitilde3x increase binding to ACE2 vs wild type, about half that of the B.1.1.7 lineage, suggesting that the K417N mutation is slightly detrimental to ACE2 binding, probably as a result of disrupting the salt bridge formed with ACE2 residue D30   | B.1.351  | Collier et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | The most frequent RBM mutation N501Y (165,519 instances) makes defective the atypical N-glycosylation sequon NGV 501-503, becoming a key RBM position for the interaction with hACE2-binding hotspot 353.  | B.1.351  | Gamez et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 2.52x increase in binding (KD) relative to D614G, mostly due to decreased in "off-rate" a.k.a. dissociation rate (Kdis). Compare to full Spike variant complements for major lineages containing this variant subset: 5.43x (B.1.1.7 aka Alpha), 3.56x (B.1.351 aka Beta), 4.24x (P.1 aka Gamma).  | B.1.351  | Gong et al. (2021)    | 1027           | A                | T                | 1.0                 |

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| N501Y     | ACE2 receptor binding affinity | RBD containing the N501Y mutation results in 9-fold stronger binding to the hACE2 receptor than wild type RBD. The E484K mutation does not significantly influence the affinity for the receptor, while K417N attenuates affinity. As a result, RBD from B.1.351 containing all three mutations binds 3-fold stronger to hACE2 than wild type RBD but 3-fold weaker than N501Y.  | B.1.351  | Laffeber et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Reported 10-fold increase in ACE2 binding vs wild-type (Kd)  | B.1.351  | Liu et al. (2021)        | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Studying the key covariants in lineage of concern 501Y.V2, observed about 2-fold increase in ACE2 binding vs wildtype, but greatly decreased mAb binding, suggesting evolutionary optimum tension between immune evasion and ACE2 binding affinity as the N501Y variant alone has 10x increase in affinity but no effect on tested mAb binding.  | B.1.351  | Liu et al. (2021)        | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | extasciitilde4-fold increase in binding affinity vs wild type.   | B.1.351  | Motozono et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Using Microscale Thermophoresis, this variant binds ACE2 at nearly two-fold greater affinity than the original SARS-COV-2 RBD (203.7 nM vs 402.5 nM).  | B.1.351  | Ramanathan et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Using Mircoscale Thermophoresis, the B.1.351 variant harboring three mutations, binds ACE2 at nearly five-fold greater affinity than the original SARS-COV-2 RBD (Kd 87.6, vs 402.5 nM).   | B.1.351  | Ramanathan et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | In silico methods (PyMOL and PDBePISA) involving mutagenesis (N501Y mutation) and interface analysis focusing on the Spike RDB-ACE2 interaction showed that the SARS-CoV-2 N501Y mutant (lineage B.1.1.7) establishes a more significant number of interactions relating to the mutant residue Y501 (Spike RDB) with residues Y41 and K353 (ACE2). This finding shows that the increased infectivity of SARS-CoV-2 lineage B.1.1.7 is associated with the interaction force between the Spike RBD Y501 mutant residue with the ACE2 receptor, which in this strain is increased. | B.1.351  | Santos and Passos (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Experimentally, ACE2 binding affinity increased 0.24 fold  | B.1.351  | Starr et al. (2020)      | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | This single mutation causes major increase in binding affinity vs. wild type as measured by IC50 vs pseudotyped lentivirus, but combined with the complete set of B.1.1.7 lineage variants no major change vs wild type affinity is observed.  | B.1.351  | Tada et al. (2021)       | 1027           | A                | T                | 1.0                 |

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| N501Y     | ACE2 receptor binding affinity | Lentiviral pseudotyped with the key mutations from COH.20G/677H lineage was tested on ACE2.293T cells for ACE2 affinity changes vs D614G alone, showing a 70% drop in IC <sub>50</sub> (i.e. increased affinity).   | B.1.351  | Tada et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Reported 4-fold increase in affinity compared to wild-type RBD on the cell surface (Kd  | B.1.351  | Tian et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Reported slight increase in affinity compared to wild-type RBD on the cell surface (Kd  | B.1.351  | Tian et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | The affinity of ACE2 for this mutation combination was twice as high as for wild type. Having in mind that the affinity of SARS-CoV-2 for ACE2 is only 4-fold higher compared to SARS-CoV-1, this factor of 2 is expected to be biologically significant.                               | B.1.351  | Vogel et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | Among the first selected and fixed variants in an in vitro evolution experiment for ACE2 binding. Calculated disassociation constant for this variant is nearly four fold lower than wild type (Kd  | B.1.351  | Zahradnik et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | ACE2 receptor binding affinity | N501Y residue inserts into a cavity at the binding interface near Y41 of ACE2. The additional interactions result in increased affinity of ACE2 for the N501Y mutant, accounting for its increased infectivity.   | B.1.351  | Zhu et al. (2021)       | 1027           | A                | T                | 1.0                 |
| N501Y     | T cell evasion                 | Vaccinated, but not post-infection sera, show decreased average T cell response to an N501Y peptide. When we primed transgenic mice expressing human HLA-DRB1*0401 with the Wuhan Hu-1 peptide pool, T cell responses to the B.1.1.7 variant peptide pool were significantly reduced (p | B.1.351  | Reynolds et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects       | Ablates Class 3 N-terminal domain targeting antibody COV2-2489, diminishes COV2-2676.   | B.1.351  | Chen et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects       | Ablates Class 1 receptor-binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384, and S2H58. Ablates Class 3 N-terminal domain targeting antibody COV2-2489, diminishes COV2-2676.  | B.1.351  | Chen et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects       | Ablates Class 1 receptor-binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384, and S2H58.  | B.1.351  | Chen et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects       | Of 50 mAbs tested, major loss of neutralization observed for S2X128, S2D8, S2X192, S2D19, S2H14, S2H19.   | B.1.351  | Collier et al. (2021)   | 1027           | A                | T                | 1.0                 |

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| N501Y     | antibody epitope effects | Wildtype elicits immune response, COVID-19 cohort epitope score > 99th percentile of the 497 pre-pandemic controls, mutant drops PIWAS epitope score from 3% to 1.2% (poorer immune recognition) Together with other B.1.1.7 lineage mutational changes (Spike: Y144del, A570D, P681H, Nucleoprotein: D3L, S235F) resulted in only 2 or 579 individuals (0.3% of the population) having a dramatic reduction in PIWAS antigen scores, which reflects the peak epitope signal along the entire antigen. | B.1.351  | Haynes et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects | Abolished neutralization by mAbs CQ026 and CQ038, greatly diminished neutralization by CQ012 and CQ046.  | B.1.351  | Hu et al. (2021)         | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects | Contrary to other reports on N501Y containing lineages (i.e. with additional mutations), N501Y alone may have an even greater affinity for a human monoclonal antibody specific for wild type. These results suggest that the individual N501Y mutation does not contribute to altered viral properties by itself, but may contribute to a collective conformational shift produced by multiple mutations.   | B.1.351  | Klegerman et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects | Lowered the neutralization potency of mAb COVA1-12 to the limit of the assay. Decrease in potency was observed against the N501Y pseudotype for the cluster IX mAb COVA2-17.   | B.1.351  | Rees-Spear et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects | Reduction in neutralization by mAbs COVA1-18 ( extasciitilde4x), COVA2-15 ( extasciitilde9x), S309 ( extasciitilde3x)  | B.1.351  | Shen et al. (2021)       | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects | Anti-NTD CV1 mAb isolated from an early pandemic case was unable to neutralize either partial B.1.351 variant pseudovirus used (A701V or L242del). The neutralization potency of mAb CV30, which contacts K417 and N501 but not E484, was extasciitilde10-fold weaker toward both B.1.351 variants. The neutralization potency of anti-RBD mAb CV3-1 was 3-4-fold less potent against the B.1.351 variants, while anti-RBD mAb CV2-75 was modestly less effective.                                     | B.1.351  | Stamatatos et al. (2021) | 1027           | A                | T                | 1.0                 |

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|-----------|-----------------------------|--|----------|------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | antibody epitope effects    | Complete loss of binding in ELISA by the variant against monoclonal antibodies ab8 and IgG1 ab1. Complete loss for the same antibodies was also observed against S1 pseudotyped and full Spike protein trimers with both B.1.351 and P.1 lineage variants, with slight binding signal for P.1 against IgG1 at the highest concentration tested (1uM). Complete loss of neutralization by these two antibodies was also observed.   | B.1.351  | Sun et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects    | 4 antibodies tested were less potent against K417N by ten-fold or more, in both mAb classes 1 and 3  | B.1.351  | Wang et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | antibody epitope effects    | Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody CA1 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody LyCoV016 (also known as CB6 or JS016) on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody CC12.1 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody BD23 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody C119 (also known as CB6 or JS016) on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody P2B-2F6 on 501Y.V2 ("South African") lineage background | B.1.351  | Wibmer et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma binding | 1.65x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape  | Average extasciitilde10-fold reduction in neutralization efficacy in convalescent sera of 16 health workers infected in Spring 2020.   | B.1.351  | Alenquer et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape  | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors   | B.1.351  | Cele et al. (2021)     | 1027           | A                | T                | 1.0                 |



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|-----------|----------------------------|--|----------|----------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | convalescent plasma escape | In 19 convalescent human sera extasciitilde1mo post infection had mild to moderate resistance against all samples.   | B.1.351  | Chen et al. (2021)         | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | In 19 convalescent human sera extasciitilde1mo post infection had mild to moderate resistance against most samples   | B.1.351  | Chen et al. (2021)         | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | Neutralizing antibody titers of 18 samples (90%) decreased against this B.1.351 pseudotyped virus below an ID50 threshold of 40 (sera collected extasciitilde8mo post Jan 2020 first wave in China).   | B.1.351  | Hu et al. (2021)           | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | 0.7x reduction in neutralization by key variant in several variants of concern in sera collected from cohort of 10 with severe disease 21 to 63 days post-onset.   | B.1.351  | Kuzmina et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | extasciitilde7x reduction in neutralization by key B.1.351 lineage RBD variant combination in sera collected from cohort of 10 with severe disease 21 to 63 days post-onset. Two of the cohort showed no neutralization against this variant.  | B.1.351  | Kuzmina et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | In 30 samples collected 111 to 260 days post onset of symptoms, the convalescent plasma can neutralize both the reference USA-WA1/2020 strain and the mouse adapted strain that contains the N501Y spike mutation with similar efficiency.   | B.1.351  | Rathnasinghe et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | Neutralization activity of convalescent sera tested decreased extasciitilde2x with this B.1.1.7 pseudotyped virus.   | B.1.351  | Shen et al. (2021)         | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | Using convalescent sera from 15 early pandemic patients (Seattle Flu Study), mean 220 days post symptom onset (IQR 125-269, and three asymptomatic cases) with 27% WHO disease severity scale 3, one third (5/15) of sera neutralized this B.1.351 pseudotype and only three had ID50 titers above 100. Only two of the 15 sera achieved 80% neutralization. | B.1.351  | Stamatatos et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | Viruses containing the point mutations of B.1.1.7 showed that the single point mutations ( $\Delta$ 69-70 and N501Y) were neutralized as efficiently as D614G across 10 convalescent sera from April 2020 infectees.   | B.1.351  | Tada et al. (2021)         | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape | Lentiviral pseudotyped with the key mutations from COH.20G/677H ("Ohio") lineage was neutralized similarly to D614G in 10 convalescent sera from April 2020 infectees.   | B.1.351  | Tada et al. (2021)         | 1027           | A                | T                | 1.0                 |

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|-----------|---|--|----------|-----------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | convalescent plasma escape                | As measured by surface plasmon resonance, RBD with the N501Y mutation alone showed a mean 2.1x decrease in binding affinity for six batches of hyper-immune immunoglobulin (hCoV-2IG) preparations generated from SARS-CoV-2 convalescent plasma.  | B.1.351  | Tang et al. (2021)          | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape                | Demonstrate (via competitive assays in human and mouse) immune escape from polyclonal antibodies induced by vaccination or infection, comparable to what was previously shown with monoclonal antibodies for N501Y and more importantly for E484K. Even though viral mutations may more strongly affect monoclonal antibodies than sera activity, the latter may also be reduced as confirmed here.  | B.1.351  | Vogel et al. (2021)         | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape                | 27% of 44 early pandemic exposure convalescent plasma/sera lose all activity against a RBD triple mutant pseudovirus (RBD mutants of the 501Y.V2 "South African" lineage), while only 23% retained high titres   | B.1.351  | Wibmer et al. (2021)        | 1027           | A                | T                | 1.0                 |
| N501Y     | convalescent plasma escape                | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct. Only 3 of 44 convalescent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | B.1.351  | Wibmer et al. (2021)        | 1027           | A                | T                | 1.0                 |
| N501Y     | environmental condition stability         | Relative to D614G, this mutation demonstrated significant increase in infectivity (i.e. heat stability) after incubation at 50C after 30 minutes or 1 hour   | B.1.351  | Tada et al. (2021)          | 1027           | A                | T                | 1.0                 |
| N501Y     | homoplasmy                                | Variant within the six key residues in the receptor binding domain (RBD). Independently reported in UK, Australia (same origin as UK), and South Africa (independent origin).  | B.1.351  | Flores-Alanis et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | immunosuppression variant emergence       | Appeared (day 128) and persisted in chronic (152 day) SARS-CoV-2 infection of immunocompromised patient with severe antiphospholipid syndrome  | B.1.351  | Choi et al. (2020)          | 1027           | A                | T                | 1.0                 |
| N501Y     | monoclonal antibody serial passage escape | In vitro selection against class 1 (Spike 'up' conformation) monoclonal antibody C663, and to a lesser extent C613.  | B.1.351  | Wang et al. (2021)          | 1027           | A                | T                | 1.0                 |
| N501Y     | pharmaceutical effectiveness              | COR-101 lost extascitilde8x binding against this isolated mutation. Regdanvimab lost extascitilde6x binding against this isolated mutation.  | B.1.351  | Engelhart et al. (2021)     | 1027           | A                | T                | 1.0                 |

| Mutations | Sub-category                 | Function  | Lineages | Citation                | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|------------------------------|---|----------|-------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | pharmaceutical effectiveness | Tixagevimab, Regdanvimab and COR-101 display reduced binding affinity to virus pseudotyped as RBD from B.1.351.   | B.1.351  | Engelhart et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | pharmaceutical effectiveness | Bamlanivimab (LY-CoV555) lost extasci-tilde64x binding against this double mutation. COR-101 lost extasci-tilde50x binding against this double mutation. Casirivimab lost extasci-tilde250x binding against this double mutation. Estesevimab lost extasci-tilde16x binding against this double mutation. Regdanvimab lost extasci-tilde32x binding against this double mutation. Tixagevimab lost extasci-tilde10x binding against this double mutation. | B.1.351  | Engelhart et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | pharmaceutical effectiveness | COR-101 lost extasci-tilde20x binding against this double mutation. Estesevimab lost extasci-tilde16x binding against this double mutation. Regdanvimab lost extasci-tilde6x binding against this double mutation. M396 lost extasci-tilde10x binding against this double mutation.   | B.1.351  | Engelhart et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | pharmaceutical effectiveness | This mutated version of RBD completely abolishes the binding to a therapeutic antibody, Bamlanivimab, in vitro.   | B.1.351  | Liu et al. (2021)       | 1027           | A                | T                | 1.0                 |
| N501Y     | reinfection                  | 4 health care workers in the 20's and 30's with no underlying conditions and seropositivity or confirmed 2020 SARS-CoV-2 infections were confirmed to have B.1.351 infection during a February 2021 hospital outbreak in Luxembourg. Symptoms were mostly mild on first infection, and milder on second infection.  | B.1.351  | Staub et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | reinfection                  | Hamsters re-infected with B.1.351 virus after seroconversion from previous infection with a lineage A virus did not transmit virus to naive sentinels via direct contact transmission, in contrast to the non-seroconverted animals. They had little infectious virus and no pathology in the lungs. Initial infection with SARS-CoV-2 lineage A does not prevent heterologous reinfection with B.1.351, but prevents disease and onward transmission.    | B.1.351  | Yinda et al. (2021)     | 1027           | A                | T                | 1.0                 |

| Mutations | Sub-category        | Function   | Lineages | Citation              | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------|--|----------|-----------------------|----------------|------------------|------------------|---------------------|
| N501Y     | symptom prevalence  | Inoculation with the B.1.351 isolate resulted in lower clinical scores in 6 rhesus macaques that correlated with lower virus titers in the lungs, less severe histologic lung lesions and less viral antigen detected in the lungs. Our comparative pathogenicity study suggests that ongoing circulation under diverse evolutionary pressure favors transmissibility and immune evasion rather than an increase in intrinsic pathogenicity. | B.1.351  | Munster et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | syncytium formation | Slight increase in Vero cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, no change relative to D614G.  | B.1.351  | Kim et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | syncytium formation | extasciitilde50% Vero cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, significantly higher than D614G.  | B.1.351  | Kim et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking         | The entry efficiencies of Spike pseudotyped viruses bearing N501Y Variant 2 (B.1.351) mutant were about 3 to 4.4 times higher than that of the WT pseudovirus when viral input was normalized, suggesting that these spike variants promote the infectivity of SARS-CoV-2.   | B.1.351  | Hu et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking         | More efficient infectivity (24h) compared to wild type, in Caco-2 cells extasciitilde9x, Vero extasciitilde8x, and Calu-3 extasciitilde8x. Compare to wild type at extasciitilde5x across cell types.  | B.1.351  | Kim et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking         | extasciitilde4x more efficient S2 domain cleavage compared to wild type, no change relative to D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3).   | B.1.351  | Kim et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking         | More efficient infectivity (24h) compared to wild type, in Caco-2 cells extasciitilde11x, Vero extasciitilde10x, and Calu-3 extasciitilde11x. Compare to wild type at extasciitilde5x across cell types.   | B.1.351  | Kim et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking         | extasciitilde6x more efficient S2 domain cleavage compared to wild type, compared to 4x by D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3). [N501Y+D614G does not show an increase in cleavage, therefore a synergistic effect of the trio is implied]  | B.1.351  | Kim et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking         | 9x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.  | B.1.351  | Kuzmina et al. (2021) | 2054           | A                | T                | 1.0                 |
| N501Y     | trafficking         | extasciitilde12x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction ( extasciitildeadditive effects of 501 and 484).  | B.1.351  | Kuzmina et al. (2021) | 1027           | A                | T                | 1.0                 |

| Mutations | Sub-category     | Function   | Lineages | Citation                | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|------------------|--|----------|-------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | trafficking      | extasciitilde13x more infective as D614G alone in HEK293T-ACE2 cells 48h post-transduction.  | B.1.351  | Kuzmina et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking      | extasciitilde9x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction (no synergy as level approx. that of N501Y alone).   | B.1.351  | Kuzmina et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking      | Decreased stability of RBD expression in yeast, suggesting decreased Spike protein stability.  | B.1.351  | Motozono et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking      | Lentiviral pseudotyped with this individual mutation from B.1.1.7 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing slightly increased infection rate amongst the cells. [in what is essentially a replicate experiment in the same paper, because each B.1.351 lineage variant was independently evaluated and N501 is in both lineages, a significant decrease was observed, therefore the error bars described in this paper should be interpreted carefully] | B.1.351  | Tada et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | trafficking      | Lentiviral pseudotyped with the key mutations from COH.20G/677H lineage was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing no significant change in infection rate amongst the cells, suggesting that this mutation does not contributing to cell entry fitness.  | B.1.351  | Tada et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | transmissibility | Assuming complete cross-protection, we estimate 501Y.V2/B.1.351 was 1.50 (95% CrI: 1.20-2.13) times as transmissible than previously circulating variants. Assuming instead that 501Y.V2 is identically transmissible, the new variant evades 21% (95% CrI: 11-36%) of previously acquired immunity. Reality may lie between these extremes, with an intermediate increase in transmissibility and mildly imperfect cross-protection from past exposure.   | B.1.351  | Pearson et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | transmissibility | 36,590 variant-specific RT-PCR tests were performed on samples collected between April 12 and May 7, 2021 in France to compare variant spread. Compared to January to March 2021, B.1.351 variant had a significant transmission advantage over B.1.1.7 in some regions (15.1 to 16.1% in Île-de-France and 16.1 to 18.8% in Hauts-de-France). This shift in transmission advantage is consistent with the immune evasion abilities of B.1.351 and the high levels of immunization in these regions.           | B.1.351  | Roquebert et al. (2021) | 1027           | A                | T                | 1.0                 |

| Mutations | Sub-category                    | Function   | Lineages | Citation               | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|--|----------|------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | vaccine neutralization efficacy | Using B.1.351 defining mutations for Spike, observed 4x average decrease in neutralization efficiency (but still relevant titres) for sera from 10 BNT162b2 vaccinees 12 days after second dose, but only one relevant titre 12 days after first dose. Compares unfavorably to wild type or B.1.1.7 titres.  | B.1.351  | Alenquer et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | Observed 1.3-fold reduction in neutralization efficiency of Pfizer vaccinee sera (collected 14 days after second dose) against pseudotype B.1.1.7 key variant lentivirus. Compare to 2.6-fold reduction against cultured B.1.1.7 virus.  | B.1.351  | Bates et al. (2021)    | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | Observed 1.4-fold reduction in neutralization efficiency of Pfizer vaccinee sera (collected 14 days after second dose) against pseudotype B.1.351 key variants lentivirus. Compare to 8.8-fold reduction against cultured B.1.351 virus.   | B.1.351  | Bates et al. (2021)    | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | The neutralizing activity of vaccine was slightly to significantly lower against this variant combination in sera from all 24 patients with the BNT162b2 mRNA vaccine. (Fig. 4) [In stark contrast to this combination plus K417N, which had no effect (P<0.0001 vs. P   | B.1.351  | Chen et al. (2021)     | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | 1.2x drop in neutralization using sera collected from 14 healthy adult participants that received two injections of the mRNA-1273 (Moderna) vaccine at a dose of 100 µg (18-55 years: day 1 and day 14 post-2nd dose) against a recombinant single variant virus (modified replicating WA-1 cDNA clone) relative to contemporary circulating D614G variant (USA/GA-EHC-083E/2020) using a live-virus Focus Reduction Neutralization Test (FRNT) assay. | B.1.351  | Edara et al. (2021)    | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | The presence of this variant in 189 post-mRNA-vaccination COVID-19 cases was proportionally in line with lineage prevalence in Northern California during the study period, suggesting no effect of these variants on immune escape.   | B.1.351  | Jacobson et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | This variant showed no change in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).   | B.1.351  | Kuzmina et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | This variant showed >5x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | This variant showed >5x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021)  | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | In post-vaccination sera from individuals who received one (3 weeks post-first dose: n   | B.1.351  | Kuzmina et al. (2021)  | 1027           | A                | T                | 1.0                 |

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|-----------|---------------------------------|---|----------|----------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | vaccine neutralization efficacy | This variant of key B.1.351 lineage mutations showed extasciitilde10x decrease in Pfizer sera (3 weeks post-first dose: n   | B.1.351  | Kuzmina et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | In a multicenter, double-blind, randomized, controlled trial to assess the safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) with enrollment June 24 and November 9, 2020 from extasciitilde2000 HIV-negative 18-64 year olds (1:1 placebo to treatment), incidence of serious adverse events 14 or more days post- 2nd dose was balanced between the vaccine and placebo groups. A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant. Serum samples obtained from 13 ChAdOx1 nCoV-19 vaccine recipients without SARS-CoV-2 infection through 41 days after vaccination showed 3.5x reduction in neutralization (ID50) for B.1.351 RBD pseudotype HIB-1 virus compared to D614G alone. This RBD variant combination's neutralization by a placebo control group of 6 naturally infected patients showed a similar 3.2x drop (though with D614G starting at a 1.7x higher titre than vaccinee sera). | B.1.351  | Madhi et al. (2021)        | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | Human sera from 6 two-dose Pfizer vaccinated individuals (47-68 days post 1st-dose) can neutralize both the reference USA-WA1/2020 strain and the mouse adapted SARS-CoV-2 strain that contains the N501Y spike mutation with similar efficiency.   | B.1.351  | Rathnasinghe et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | In sera collected from 15 early pandemic patients (Seattle Flu Study), mean 16 days post first dose with either Pfizer/BioNTech or Moderna vaccines, the median ID50 titers were extasciitilde3-fold lower against this B.1.351 pseudotyped virus relative to wild type. A single asymptomatic patient, who had no detectable RBD-specific IgG memory before vaccination, also did not elicit nAbs against the B.1.351 variant. [compare to extasciitilde10 fold with L242del] ID50 titres in non-infected mRNA vaccines more than two weeks post-booster were significant, but >100x weaker than in previously infected patients after first dose.   | B.1.351  | Stamatatos et al. (2021)   | 1027           | A                | T                | 1.0                 |

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|-----------|---------------------------------|--|----------|-------------------------|----------------|------------------|------------------|---------------------|
| N501Y     | vaccine neutralization efficacy | In a cohort of 20 patients 8+ weeks after second vaccine dose of Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines, a modest decrease in neutralization by vaccine plasma was observed.   | B.1.351  | Wang et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | In a cohort of 20 patients 8+ weeks after second vaccine dose of Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines, a significant (0.5 to 20-fold, but average extasciitilde2x) decrease in neutralization by vaccine plasma was observed.  | B.1.351  | Wang et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | In Moderna vaccinee sera, 2.7x reduction in neutralization, and 6.4 for the full B.1.351 Spike mutation complement, but despite the observed decreases, titers in human vaccinee sera against the B.1.351 variant remained at clinically significant level of extasciitilde1/300.  | B.1.351  | Wu et al. (2021)        | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccine neutralization efficacy | In 20 sera from BNT162b2 mRNA vaccine inoculated participants, 6 displayed mild (2x) reductions in neutralization. This variant combination showed the highest reduction, but the magnitude of the differences was small compared to the >4x differences in HA-inhibition titers that have been used to signal potential need for a strain change in influenza vaccines. | B.1.351  | Xie et al. (2021)       | 1027           | A                | T                | 1.0                 |
| N501Y     | vaccinee plasma binding         | 1.17x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.09x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.             | B.1.351  | Gong et al. (2021)      | 1027           | A                | T                | 1.0                 |
| N501Y     | viral load                      | B.1.351 and P.1 samples showed average Ct cycle threshold of 22.2 vs 23 for wildtype (i.e. extasciitilde60% higher viral load) comparing 3360 and 22535 samples respectively.  | B.1.351  | Roquebert et al. (2021) | 1027           | A                | T                | 1.0                 |
| N501Y     | viral load                      | The 62 B.1.351 (a.k.a. N501Y.V2) variant cases in three Paris hospital labs had a extasciitilde2-fold viral load increase ( extasciitilde1 Ct drop in both N and ORF1ab probes) compared to 332 ancestral lineage cases from the same time frame (2020-12-20 to 2021-02-26).   | B.1.351  | Teyssou et al. (2021)   | 1027           | A                | T                | 1.0                 |
| N501Y     | virion structure                | Estimated free energy change (ddG) for this variant is 0.69 kcal/mol (i.e. stabilizing relative to wild type)  | B.1.351  | Spratt et al. (2021)    | 1027           | A                | T                | 1.0                 |



| Mutations | Sub-category                   | Function   | Lineages | Citation               | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|----------|------------------------|----------------|------------------|------------------|---------------------|
| L18F      | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.07x decrease in binding (KD) relative to D614G. Compare to increased binding in full Spike variant complements for major lineages containing this variant subset: 3.56x (B.1.351 aka Beta), 4.24x (P.1 aka Gamma).   | B.1.351  | Gong et al. (2021)     | 1138           | C                | T                | 0.57                |
| L18F      | antibody epitope effects       | Massive reduction in S2L28 monoclonal antibody EC50 (i.e. ablated recognition), within antigenic supersite "i", but no effect on other mAbs within that supersite  | B.1.351  | McCallum et al. (2021) | 1138           | C                | T                | 0.57                |
| L18F      | antibody epitope effects       | Ablates neutralization by N-terminal-domain-targeting mAbs 4-19. Impairs neutralization by N-terminal-domain-targeting mAbs 4A8 and 2-17.  | B.1.351  | Wang et al. (2021)     | 1138           | C                | T                | 0.57                |
| L18F      | convalescent plasma binding    | 1.66x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset. Compare to decreased binding in full Spike variant complements for major lineages containing this variant subset: 0.96x (B.1.351 aka Beta), 0.77x (P.1 aka Gamma).  | B.1.351  | Gong et al. (2021)     | 1138           | C                | T                | 0.57                |
| L18F      | convalescent plasma escape     | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors   | B.1.351  | Cele et al. (2021)     | 1138           | C                | T                | 0.57                |
| L18F      | convalescent plasma escape     | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct. Only 3 of 44 convalescent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | B.1.351  | Wibmer et al. (2021)   | 1138           | C                | T                | 0.57                |
| L18F      | trafficking                    | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing mild decrease in infection rate amongst the cells, suggesting that this mutation does not contribute to cell entry fitness.  | B.1.351  | Tada et al. (2021)     | 1138           | C                | T                | 0.57                |

| Mutations | Sub-category                   | Function   | Lineages | Citation               | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|----------|------------------------|----------------|------------------|------------------|---------------------|
| L18F      | vaccinee plasma binding        | 1.30x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. Compare to varied binding in full Spike variant complements for major lineages containing this variant subset: 1.28x increase (B.1.351 aka Beta), and 1.14x decrease (P.1 aka Gamma). 1.47x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. Compare to varied binding in full Spike variant complements for major lineages containing this variant subset: 1.17x increase (B.1.351 aka Beta), and 1.47x decrease (P.1 aka Gamma). | B.1.351  | Gong et al. (2021)     | 1138           | C                | T                | 0.57                |
| K417N     | ACE2 receptor binding affinity | The K417N mutation decreased the affinity extasciitilde4 fold, mainly by decreasing the k(on) but also by increasing the k(off) as measured by surface plasmon resonance.  | B.1.351  | Barton et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | The affinity of the B.1.351 RBD variants for ACE2 increased by 3.7 fold as measured by surface plasmon resonance relative to wild type RBD by increasing the k(on) and decreasing the k(off) rate constants.   | B.1.351  | Barton et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | This combination showed extasciitilde3x increase binding to ACE2 vs wild type, about half that of the B.1.1.7 lineage, suggesting that the K417N mutation is slightly detrimental to ACE2 binding, probably as a result of disrupting the salt bridge formed with ACE2 residue D30   | B.1.351  | Collier et al. (2021)  | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.5x decrease in binding (KD) relative to D614G.   | B.1.351  | Gong et al. (2021)     | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | RBD containing the N501Y mutation results in 9-fold stronger binding to the hACE2 receptor than wild type RBD. The E484K mutation does not significantly influence the affinity for the receptor, while K417N attenuates affinity. As a result, RBD from B.1.351 containing all three mutations binds 3-fold stronger to hACE2 than wild type RBD but 3-fold weaker than N501Y.  | B.1.351  | Laffeber et al. (2021) | 1096           | G                | T                | 1.0                 |

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|-----------|--------------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| K417N     | ACE2 receptor binding affinity | Studying the key covariants in lineage of concern 501Y.V2, observed about 2-fold increase in ACE2 binding vs wildtype, but greatly decreased mAb binding, suggesting evolutionary optimum tension between immune evasion and ACE2 binding affinity as the N501Y variant alone has 10x increase in affinity but no effect on tested mAb binding.  | B.1.351  | Liu et al. (2021)        | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | Using Microscale Thermophoresis, the B.1.351 variant harboring three mutations, binds ACE2 at nearly five-fold greater affinity than the original SARS-COV-2 RBD (Kd 87.6, vs 402.5 nM).   | B.1.351  | Ramanathan et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | Reported 3-fold decrease in affinity compared to wild-type RBD on the cell surface (Kd   | B.1.351  | Tian et al. (2021)       | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | Reported slight increase in affinity compared to wild-type RBD on the cell surface (Kd   | B.1.351  | Tian et al. (2021)       | 1096           | G                | T                | 1.0                 |
| K417N     | ACE2 receptor binding affinity | The affinity of ACE2 for this mutation combination was twice as high as for wild type. Having in mind that the affinity of SARS-CoV-2 for ACE2 is only 4-fold higher compared to SARS-CoV-1, this factor of 2 is expected to be biologically significant.  | B.1.351  | Vogel et al. (2021)      | 1096           | G                | T                | 1.0                 |
| K417N     | antibody epitope effects       | Ablates Class 1 receptor-binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384, and S2H58.   | B.1.351  | Chen et al. (2021)       | 1096           | G                | T                | 1.0                 |
| K417N     | antibody epitope effects       | Abolished neutralization by mAbs CQ026 and CQ038, greatly diminished neutralization by CQ012 and CQ046.  | B.1.351  | Hu et al. (2021)         | 1096           | G                | T                | 1.0                 |
| K417N     | antibody epitope effects       | Anti-NTD CV1 mAb isolated from an early pandemic case was unable to neutralize either partial B.1.351 variant pseudovirus used (A701V or L242del). The neutralization potency of mAb CV30, which contacts K417 and N501 but not E484, was extasciilde10-fold weaker toward both B.1.351 variants. The neutralization potency of anti-RBD mAb CV3-1 was 3-4-fold less potent against the B.1.351 variants, while anti-RBD mAb CV2-75 was modestly less effective. | B.1.351  | Stamatatos et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | antibody epitope effects       | >20% (ELISA significance threshold) drop in antibody binding (ELISA) by this variant against IgG1 monoclonal antibody ab1.   | B.1.351  | Sun et al. (2021)        | 1096           | G                | T                | 1.0                 |

| Mutations | Sub-category                | Function   | Lineages | Citation               | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|-----------------------------|--|----------|------------------------|----------------|------------------|------------------|---------------------|
| K417N     | antibody epitope effects    | Complete loss of binding in ELISA by the variant against monoclonal antibodies ab8 and IgG1 ab1. Complete loss for the same antibodies was also observed against S1 pseudotyped and full Spike protein trimers with both B.1.351 and P.1 lineage variants, with slight binding signal for P.1 against IgG1 at the highest concentration tested (1uM). Complete loss of neutralization by these two antibodies was also observed.   | B.1.351  | Sun et al. (2021)      | 1096           | G                | T                | 1.0                 |
| K417N     | antibody epitope effects    | 5 antibodies tested were less potent against K417N by ten-fold or more (class 1 mAbs)  | B.1.351  | Wang et al. (2021)     | 1096           | G                | T                | 1.0                 |
| K417N     | antibody epitope effects    | Pseudotyped virus model ablates binding by RBD-directed mAbs CB6 and 910-30 (targeting the inner side of the RBD). Pseudotyped virus model impairs binding by RBD-directed mAbs 4-20 and REGN10933.  | B.1.351  | Wang et al. (2021)     | 1096           | G                | T                | 1.0                 |
| K417N     | antibody epitope effects    | Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody CA1 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody LyCoV016 (also known as CB6 or JS016) on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody CC12.1 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody BD23 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody C119 (also known as CB6 or JS016) on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody P2B-2F6 on 501Y.V2 ("South African") lineage background | B.1.351  | Wibmer et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma binding | 2.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)     | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape  | Average extasciitilde10-fold reduction in neutralization efficacy in convalescent sera of 16 health workers infected in Spring 2020.   | B.1.351  | Alenquer et al. (2021) | 1096           | G                | T                | 1.0                 |

| Mutations | Sub-category               | Function  | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|----------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| K417N     | convalescent plasma escape | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors  | B.1.351  | Cele et al. (2021)       | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape | In 19 convalescent human sera extasciitilde1mo post infection, Two-tailed Wilcoxon matched-pairs signed-rank test shows mild resistance P   | B.1.351  | Chen et al. (2021)       | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape | In 19 convalescent human sera extasciitilde1mo post infection had mild to moderate resistance against most samples  | B.1.351  | Chen et al. (2021)       | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape | Neutralizing antibody titers of 18 samples (90%) decreased against this B.1.351 pseudotyped virus below an ID50 threshold of 40 (sera collected extasciitilde8mo post Jan 2020 first wave in China).  | B.1.351  | Hu et al. (2021)         | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape | extasciitilde7x reduction in neutralization by key B.1.351 lineage RBD variant combination in sera collected from cohort of 10 with severe disease 21 to 63 days post-onset. Two of the cohort showed no neutralization against this variant.   | B.1.351  | Kuzmina et al. (2021)    | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape | Using convalescent sera from 15 early pandemic patients (Seattle Flu Study), mean 220 days post symptom onset (IQR 125-269, and three asymptomatic cases) with 27% WHO disease severity scale 3, one third (5/15) of sera neutralized this B.1.351 pseudotype and only three had ID50 titers above 100. Only two of the 15 sera achieved 80% neutralization.  | B.1.351  | Stamatatos et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape | Demonstrate (via competitive assays in human and mouse) immune escape from polyclonal antibodies induced by vaccination or infection, comparable to what was previously shown with monoclonal antibodies for N501Y and more importantly for E484K. Even though viral mutations may more strongly affect monoclonal antibodies than sera activity, the latter may also be reduced as confirmed here. | B.1.351  | Vogel et al. (2021)      | 1096           | G                | T                | 1.0                 |
| K417N     | convalescent plasma escape | 27% of 44 early pandemic exposure convalescent plasma/sera lose all activity against a RBD triple mutant pseudovirus (RBD mutants of the 501Y.V2 "South African" lineage), while only 23% retained high titres  | B.1.351  | Wibmer et al. (2021)     | 1096           | G                | T                | 1.0                 |

| Mutations | Sub-category                              | Function   | Lineages | Citation                | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---|--|----------|-------------------------|----------------|------------------|------------------|---------------------|
| K417N     | convalescent plasma escape                | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct. Only 3 of 44 convalescent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | B.1.351  | Wibmer et al. (2021)    | 1096           | G                | T                | 1.0                 |
| K417N     | gene expression increase                  | Experimentally, Spike gene expression increased 0.1 fold   | B.1.351  | Starr et al. (2020)     | 1096           | G                | T                | 1.0                 |
| K417N     | monoclonal antibody serial passage escape | Escape mutation against monoclonal antibody LY-CoV016  | B.1.351  | Starr et al. (2021)     | 1096           | G                | T                | 1.0                 |
| K417N     | monoclonal antibody serial passage escape | In vitro selection against class 1 (Spike 'up' conformation) monoclonal antibody C682, and to a lesser extent C614 and C660  | B.1.351  | Wang et al. (2021)      | 1096           | G                | T                | 1.0                 |
| K417N     | pharmaceutical effectiveness              | COR-101 lost extasci-tilde6x binding against this isolated mutation. Estesevimab lost extasci-tilde100x binding against this isolated mutation.  | B.1.351  | Engelhart et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | pharmaceutical effectiveness              | Tixagevimab, Regdanvimab and COR-101 display reduced binding affinity to virus pseudotyped as RBD from B.1.351.  | B.1.351  | Engelhart et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | pharmaceutical effectiveness              | Bamlanivimab (LY-CoV555) lost extasci-tilde32x binding against this double mutation. COR-101 lost extasci-tilde160x binding against this double mutation. Casirivimab lost extasci-tilde16x binding against this double mutation. Estesevimab lost extasci-tilde32x binding against this double mutation. Regdanvimab lost extasci-tilde4x binding against this double mutation. Tixagevimab lost extasci-tilde12x binding against this double mutation.                     | B.1.351  | Engelhart et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | pharmaceutical effectiveness              | COR-101 lost extasci-tilde20x binding against this double mutation. Estesevimab lost extasci-tilde16x binding against this double mutation. Regdanvimab lost extasci-tilde6x binding against this double mutation. M396 lost extasci-tilde10x binding against this double mutation.  | B.1.351  | Engelhart et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | pharmaceutical effectiveness              | This mutated version of RBD completely abolishes the binding to a therapeutic antibody, Bamlanivimab, in vitro.  | B.1.351  | Liu et al. (2021)       | 1096           | G                | T                | 1.0                 |

| Mutations | Sub-category       | Function   | Lineages | Citation              | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------|--|----------|-----------------------|----------------|------------------|------------------|---------------------|
| K417N     | reinfection        | 4 health care workers in the 20's and 30's with no underlying conditions and seropositivity or confirmed 2020 SARS-CoV-2 infections were confirmed to have B.1.351 infection during a February 2021 hospital outbreak in Luxembourg. Symptoms were mostly mild on first infection, and milder on second infection.   | B.1.351  | Staub et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | reinfection        | Hamsters re-infected with B.1.351 virus after seroconversion from previous infection with a lineage A virus did not transmit virus to naive sentinels via direct contact transmission, in contrast to the non-seroconverted animals. They had little infectious virus and no pathology in the lungs. Initial infection with SARS-CoV-2 lineage A does not prevent heterologous reinfection with B.1.351, but prevents disease and onward transmission. | B.1.351  | Yinda et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | symptom prevalence | Inoculation with the B.1.351 isolate resulted in lower clinical scores in 6 rhesus macaques that correlated with lower virus titers in the lungs, less severe histologic lung lesions and less viral antigen detected in the lungs. Our comparative pathogenicity study suggests that ongoing circulation under diverse evolutionary pressure favors transmissibility and immune evasion rather than an increase in intrinsic pathogenicity.           | B.1.351  | Munster et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | trafficking        | The entry efficiencies of Spike pseudotyped viruses bearing N501Y Variant 2 (B.1.351) mutant were about 3 to 4.4 times higher than that of the WT pseudovirus when viral input was normalized, suggesting that these spike variants promote the infectivity of SARS-CoV-2.   | B.1.351  | Hu et al. (2021)      | 1096           | G                | T                | 1.0                 |
| K417N     | trafficking        | extasciitilde2x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.   | B.1.351  | Kuzmina et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | trafficking        | Approximately as infective as D614G alone in HEK293T-ACE2 cells 48h post-transduction (extasciitildeadditive effects of the individual variants).  | B.1.351  | Kuzmina et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | trafficking        | extasciitilde13x more infective as D614G alone in HEK293T-ACE2 cells 48h post-transduction.  | B.1.351  | Kuzmina et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | trafficking        | extasciitilde9x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction (no synergy as level approx. that of N501Y alone).   | B.1.351  | Kuzmina et al. (2021) | 1096           | G                | T                | 1.0                 |

| Mutations | Sub-category                    | Function   | Lineages | Citation                | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|--|----------|-------------------------|----------------|------------------|------------------|---------------------|
| K417N     | trafficking                     | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing mild decrease in infection rate amongst the cells, suggesting that this mutation does not contributing to cell entry fitness.  | B.1.351  | Tada et al. (2021)      | 1096           | G                | T                | 1.0                 |
| K417N     | transmissibility                | Assuming complete cross-protection, we estimate 501Y.V2/B.1.351 was 1.50 (95% CrI: 1.20-2.13) times as transmissible than previously circulating variants. Assuming instead that 501Y.V2 is identically transmissible, the new variant evades 21% (95% CrI: 11-36%) of previously acquired immunity. Reality may lie between these extremes, with an intermediate increase in transmissibility and mildly imperfect cross-protection from past exposure.   | B.1.351  | Pearson et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | transmissibility                | 36,590 variant-specific RT-PCR tests were performed on samples collected between April 12 and May 7, 2021 in France to compare variant spread. Compared to January to March 2021, B.1.351 variant had a significant transmission advantage over B.1.1.7 in some regions (15.1 to 16.1% in Île-de-France and 16.1 to 18.8% in Hauts-de-France). This shift in transmission advantage is consistent with the immune evasion abilities of B.1.351 and the high levels of immunization in these regions. | B.1.351  | Roquebert et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | Using B.1.351 defining mutations for Spike, observed 4x average decrease in neutralization efficiency (but still relevant titres) for sera from 10 BNT162b2 vaccinees 12 days after second dose, but only one relevant titre 12 days after first dose. Compares unfavorably to wild type or B.1.1.7 titres.  | B.1.351  | Alenquer et al. (2021)  | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | Observed 1.4-fold reduction in neutralization efficiency of Pfizer vaccinee sera (collected 14 days after second dose) against pseudotype B.1.351 key variants lentivirus. Compare to 8.8-fold reduction against cultured B.1.351 virus.   | B.1.351  | Bates et al. (2021)     | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).  | B.1.351  | Kuzmina et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | This variant showed extasciitilde10x decrease in Pfizer sera (3 weeks post-first dose: n   | B.1.351  | Kuzmina et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | This variant of key B.1.351 lineage mutations showed extasciitilde10x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021)   | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | This variant showed >5x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021)   | 1096           | G                | T                | 1.0                 |



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|-----------|---------------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| K417N     | vaccine neutralization efficacy | In post-vaccination sera from individuals who received one (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021)    | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | In a multicenter, double-blind, randomized, controlled trial to assess the safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) with enrollment June 24 and November 9, 2020 from extasciitilde2000 HIV-negative 18-64 year olds (1:1 placebo to treatment), incidence of serious adverse events 14 or more days post- 2nd dose was balanced between the vaccine and placebo groups. A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant. Serum samples obtained from 13 ChAdOx1 nCoV-19 vaccine recipients without SARS-CoV-2 infection through 41 days after vaccination showed 3.5x reduction in neutralization (ID50) for B.1.351 RBD pseudotype HIB-1 virus compared to D614G alone. This RBD variant combination's neutralization by a placebo control group of 6 naturally infected patients showed a similar 3.2x drop (though with D614G starting at a 1.7x higher titre than vaccinee sera). | B.1.351  | Madhi et al. (2021)      | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | In sera collected from 15 early pandemic patients (Seattle Flu Study), mean 16 days post first dose with either Pfizer/BioNTech or Moderna vaccines, the median ID50 titers were extasciitilde3-fold lower against this B.1.351 pseudotyped virus relative to wild type. A single asymptomatic patient, who had no detectable RBD-specific IgG memory before vaccination, also did not elicit nAbs against the B.1.351 variant. [compare to extasciitilde10 fold with L242del] ID50 titres in non-infected mRNA vaccines more than two weeks post-booster were significant, but >100x weaker than in previously infected patients after first dose.   | B.1.351  | Stamatatos et al. (2021) | 1096           | G                | T                | 1.0                 |
| K417N     | vaccine neutralization efficacy | In a cohort of 20 patients 8+ weeks after second vaccine dose of Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines, a significant (0.5 to 20-fold, but average extasciitilde2x) decrease in neutralization by vaccine plasma was observed.   | B.1.351  | Wang et al. (2021)       | 1096           | G                | T                | 1.0                 |

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|-----------|---------------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| K417N     | vaccine neutralization efficacy | In Moderna vaccinee sera, 2.7x reduction in neutralization, and 6.4 for the full B.1.351 Spike mutation complement, but despite the observed decreases, titers in human vaccinee sera against the B.1.351 variant remained at clinically significant level of extasciitilde1/300.  | B.1.351  | Wu et al. (2021)         | 1096           | G                | T                | 1.0                 |
| K417N     | vaccinee plasma binding         | 1.76x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.75x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.   | B.1.351  | Gong et al. (2021)       | 1096           | G                | T                | 1.0                 |
| K417N     | viral load                      | B.1.351 and P.1 samples showed average Ct cycle threshold of 22.2 vs 23 for wildtype (i.e. extasciitilde60% higher viral load) comparing 3360 and 22535 samples respectively.  | B.1.351  | Roquebert et al. (2021)  | 1096           | G                | T                | 1.0                 |
| K417N     | viral load                      | The 62 B.1.351 (a.k.a. N501Y.V2) variant cases in three Paris hospital labs had a extasciitilde2-fold viral load increase ( extasciitilde1 Ct drop in both N and ORF1ab probes) compared to 332 ancestral lineage cases from the same time frame (2020-12-20 to 2021-02-26).   | B.1.351  | Teyssou et al. (2021)    | 1096           | G                | T                | 1.0                 |
| K417N     | virion structure                | Estimated free energy change (ddG) for this variant is -0.86 kcal/mol (i.e. destabilizing relative to wild type)   | B.1.351  | Spratt et al. (2021)     | 1096           | G                | T                | 1.0                 |
| A701V     | ACE2 receptor binding affinity  | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed essentially no change in binding (KD) relative to D614G.   | B.1.351  | Gong et al. (2021)       | 1140           | C                | T                | 1.0                 |
| A701V     | antibody epitope effects        | Anti-NTD CV1 mAb isolated from an early pandemic case was unable to neutralize either partial B.1.351 variant pseudovirus used (A701V or L242del). The neutralization potency of mAb CV30, which contacts K417 and N501 but not E484, was extasciitilde10-fold weaker toward both B.1.351 variants. The neutralization potency of anti-RBD mAb CV3-1 was 3-4-fold less potent against the B.1.351 variants, while anti-RBD mAb CV2-75 was modestly less effective. | B.1.351  | Stamatatos et al. (2021) | 1140           | C                | T                | 1.0                 |
| A701V     | convalescent plasma binding     | 1.11x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1140           | C                | T                | 1.0                 |

| Mutations | Sub-category                    | Function   | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| A701V     | convalescent plasma escape      | Using convalescent sera from 15 early pandemic patients (Seattle Flu Study), mean 220 days post symptom onset (IQR 125-269, and three asymptomatic cases) with 27% WHO disease severity scale 3, one third (5/15) of sera neutralized this B.1.351 pseudotype and only three had ID50 titers above 100. Only two of the 15 sera achieved 80% neutralization.   | B.1.351  | Stamatatos et al. (2021) | 1140           | C                | T                | 1.0                 |
| A701V     | reinfection                     | 4 health care workers in the 20's and 30's with no underlying conditions and seropositivity or confirmed 2020 SARS-CoV-2 infections were confirmed to have B.1.351 infection during a February 2021 hospital outbreak in Luxembourg. Symptoms were mostly mild on first infection, and milder on second infection.   | B.1.351  | Staub et al. (2021)      | 1140           | C                | T                | 1.0                 |
| A701V     | reinfection                     | Hamsters re-infected with B.1.351 virus after seroconversion from previous infection with a lineage A virus did not transmit virus to naive sentinels via direct contact transmission, in contrast to the non-seroconverted animals. They had little infectious virus and no pathology in the lungs. Initial infection with SARS-CoV-2 lineage A does not prevent heterologous reinfection with B.1.351, but prevents disease and onward transmission. | B.1.351  | Yinda et al. (2021)      | 1140           | C                | T                | 1.0                 |
| A701V     | symptom prevalence              | Inoculation with the B.1.351 isolate resulted in lower clinical scores in 6 rhesus macaques that correlated with lower virus titers in the lungs, less severe histologic lung lesions and less viral antigen detected in the lungs. Our comparative pathogenicity study suggests that ongoing circulation under diverse evolutionary pressure favors transmissibility and immune evasion rather than an increase in intrinsic pathogenicity.           | B.1.351  | Munster et al. (2021)    | 1140           | C                | T                | 1.0                 |
| A701V     | trafficking                     | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing mild decrease in infection rate amongst the cells, suggesting that this mutation does not contribute to cell entry fitness.  | B.1.351  | Tada et al. (2021)       | 1140           | C                | T                | 1.0                 |
| A701V     | vaccine neutralization efficacy | Using B.1.351 defining mutations for Spike, observed 4x average decrease in neutralization efficiency (but still relevant titres) for sera from 10 BNT162b2 vaccinees 12 days after second dose, but only one relevant titre 12 days after first dose. Compares unfavorably to wild type or B.1.1.7 titres.  | B.1.351  | Alenquer et al. (2021)   | 1140           | C                | T                | 1.0                 |

| Mutations | Sub-category                    | Function  | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| A701V     | vaccine neutralization efficacy | In sera collected from 15 early pandemic patients (Seattle Flu Study), mean 16 days post first dose with either Pfizer/BioNTech or Moderna vaccines, the median ID50 titers were extasciitilde3-fold lower against this B.1.351 pseudotyped virus relative to wild type. A single asymptomatic patient, who had no detectable RBD-specific IgG memory before vaccination, also did not elicit nAbs against the B.1.351 variant. [compare to extasciitilde10 fold with L242del] ID50 titres in non-infected mRNA vaccines more than two weeks post-booster were significant, but >100x weaker than in previously infected patients after first dose. | B.1.351  | Stamatatos et al. (2021) | 1140           | C                | T                | 1.0                 |
| A701V     | vaccinee plasma binding         | 1.19x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.   | B.1.351  | Gong et al. (2021)       | 1140           | C                | T                | 1.0                 |
| A701V     | virion structure                | Estimated free energy change (ddG) for this variant is -0.33 kcal/mol (i.e. destabilizing relative to wild type)  | B.1.351  | Spratt et al. (2021)     | 1140           | C                | T                | 1.0                 |
| D614G     | ACE2 receptor binding affinity  | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed essentially no change in binding (KD) relative to D614G.  | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity  | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.19x increase in binding (KD) relative to D614G.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity  | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant combination showed no change relative to D614G.  | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity  | This variant appears twice in the experiments, with slightly different affinities (both extasciitilde1.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex.  | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity  | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.21x increase in binding (KD) relative to D614G.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity  | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.5x decrease in binding (KD) relative to D614G.  | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |

| Mutations | Sub-category                   | Function   | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| D614G     | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.07x decrease in binding (KD) relative to D614G. Compare to increased binding in full Spike variant complements for major lineages containing this variant subset: 3.56x (B.1.351 aka Beta), 4.24x (P.1 aka Gamma).   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.1x decrease in binding (KD) relative to D614G.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 2.52x increase in binding (KD) relative to D614G, mostly due to decreased in "off-rate" a.k.a. dissociation rate (Kdis). Compare to full Spike variant complements for major lineages containing this variant subset: 5.43x (B.1.1.7 aka Alpha), 3.56x (B.1.351 aka Beta), 4.24x (P.1 aka Gamma).  | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity | In four cell lines (including 293T-hACE2 cells), this mutation combination increases infectivity vs D614G alone  | B.1.351  | Li et al. (2020)         | 1104           | A                | G                | 1.0                 |
| D614G     | ACE2 receptor binding affinity | Lentiviral pseudotyped with the key mutations from COH.20G/677H lineage was tested on ACE2.293T cells for ACE2 affinity changes vs D614G alone, showing a extasciilde70% drop in IC50 (i.e. increased affinity).   | B.1.351  | Tada et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | antibody epitope effects       | Abolished neutralization by mAbs CQ026 and CQ038, greatly diminished neutralization by CQ012 and CQ046.  | B.1.351  | Hu et al. (2021)         | 1104           | A                | G                | 1.0                 |
| D614G     | antibody epitope effects       | Anti-NTD CV1 mAb isolated from an early pandemic case was unable to neutralize either partial B.1.351 variant pseudovirus used (A701V or L242del). The neutralization potency of mAb CV30, which contacts K417 and N501 but not E484, was extasciilde10-fold weaker toward both B.1.351 variants. The neutralization potency of anti-RBD mAb CV3-1 was 3-4-fold less potent against the B.1.351 variants, while anti-RBD mAb CV2-75 was modestly less effective. | B.1.351  | Stamatatos et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding    | 1.11x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding    | 2.29x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding    | 2.11x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |

| Mutations | Sub-category                | Function   | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|-----------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| D614G     | convalescent plasma binding | 1.42x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding | 1.48x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding | 2.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding | 1.66x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset. Compare to decreased binding in full Spike variant complements for major lineages containing this variant subset: 0.96x (B.1.351 aka Beta), 0.77x (P.1 aka Gamma).  | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding | No change in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.  | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma binding | 1.65x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma escape  | Average extasciitilde10-fold reduction in neutralization efficacy in convalescent sera of 16 health workers infected in Spring 2020.   | B.1.351  | Alenquer et al. (2021)   | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma escape  | Neutralizing antibody titers of 18 samples (90%) decreased against this B.1.351 pseudotyped virus below an ID50 threshold of 40 (sera collected extasciitilde8mo post Jan 2020 first wave in China).   | B.1.351  | Hu et al. (2021)         | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma escape  | Using convalescent sera from 15 early pandemic patients (Seattle Flu Study), mean 220 days post symptom onset (IQR 125-269, and three asymptomatic cases) with 27% WHO disease severity scale 3, one third (5/15) of sera neutralized this B.1.351 pseudotype and only three had ID50 titers above 100. Only two of the 15 sera achieved 80% neutralization.   | B.1.351  | Stamatatos et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | convalescent plasma escape  | Pseudotyped viruses for B.1.618 was 2.5-fold resistant to neutralization by convalescent sera compared to wild type - a finding that was similar to that of the 3-fold resistance of the South Africa B.1.351 variant using the same assay. The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618. [details on the convalescent patient sera collection are not abundantly clear in the preprint] | B.1.351  | Tada et al. (2021)       | 1104           | A                | G                | 1.0                 |

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|-----------|-------------------------------------|---|----------|----------------------|----------------|------------------|------------------|---------------------|
| D614G     | convalescent plasma escape          | Lentiviral pseudotyped with the key mutations from COH.20G/677H ("Ohio") lineage was neutralized similarly to D614G in 10 convalescent sera from April 2020 infectees.  | B.1.351  | Tada et al. (2021)   | 1104           | A                | G                | 1.0                 |
| D614G     | humoral response durability         | 27yo female nurse reinfectd in December 2020 (B.1.177) after initial infection in March 2020 (B.3), i.e. with a 9 month interval. Both cases were mild. No significant differences in the neutralizing capacity of the two linages were observed in 4 sera taken (1 pre-reinfection, three post-reinfection). Neutralizing antibody titres (IC50) before and immediately after re-infection were <300 against both strains, and jumped >7x upon re-infection. Viral titres were also higher in the second case. Second case also includes N:p.A220V | B.1.351  | Brehm et al. (2021)  | 1104           | A                | G                | 1.0                 |
| D614G     | immunosuppression variant emergence | Studying 94 COVID-19 extended infection cases with genomics April 1 to October 17, 2020, one case developed 23 mutations in a 19 day period, including this combination in Spike.   | B.1.351  | Landis et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | reinfection                         | 27yo female nurse reinfectd in December 2020 (B.1.177) after initial infection in March 2020 (B.3). Both cases were mild. Second case also includes N:p.A220V   | B.1.351  | Brehm et al. (2021)  | 1104           | A                | G                | 1.0                 |
| D614G     | syncytium formation                 | Slight increase in Vero cell membrane fusion assay under infection with VSV pseudotyped virus.  | B.1.351  | Kim et al. (2021)    | 1104           | A                | G                | 1.0                 |
| D614G     | syncytium formation                 | extasciitilde50% Vero cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, significantly higher than D614G.   | B.1.351  | Kim et al. (2021)    | 1104           | A                | G                | 1.0                 |
| D614G     | syncytium formation                 | Slight increase in Vero cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, no change relative to D614G.   | B.1.351  | Kim et al. (2021)    | 1104           | A                | G                | 1.0                 |
| D614G     | syncytium formation                 | Slight increase in Vero cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, no change relative to D614G.   | B.1.351  | Kim et al. (2021)    | 1104           | A                | G                | 1.0                 |

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|-----------|--------------------------------|---|----------|-------------------------|----------------|------------------|------------------|---------------------|
| D614G     | tissue specific neutralization | The nasal mucosa of Pfizer vaccinees with time course collection was evaluated against VSV pseudotypes: results (only one nasal swab from different previously infected vaccinee neutralizing at weeks 3 and 6 against B.1.1.7 and D614G) suggest that vaccinees probably do not elicit an early humoral response detectable at mucosal surfaces even though sera neutralization was observed. They strengthen the hypothesis that some vaccines may not protect against viral acquisition and infection of the oral-nasal region, but may prevent severe disease associated with viral dissemination in the lower respiratory tract. | B.1.351  | Planas et al. (2021)    | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking                    | Circulating variant shown in vitro to not have major defects or enhancement of cell surface protein trafficking (i.e. Spike cleavage or fusion required for cell entry)   | B.1.351  | Barrett et al. (2021)   | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking                    | The increased transduction with Spike D614G ranged from 1.3- to 2.4-fold in Caco-2 and Calu-3 cells expressing endogenous ACE2 and from 1.5- to 7.7-fold in A549ACE2 and Huh7.5ACE2 overexpressing ACE2. Although there is minimal difference in ACE2 receptor binding between the D614 and G614 Spike variants, the G614 variant is more resistant to proteolytic cleavage, suggesting a possible mechanism for the increased transduction.  | B.1.351  | Daniloski et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking                    | The entry efficiencies of Spike pseudotyped viruses bearing N501Y Variant 2 (B.1.351) mutant were about 3 to 4.4 times higher than that of the WT pseudovirus when viral input was normalized, suggesting that these spike variants promote the infectivity of SARS-CoV-2.  | B.1.351  | Hu et al. (2021)        | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking                    | No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3.   | B.1.351  | Kim et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking                    | extasciitilde4x more efficient S2 domain cleavage compared to wild type in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3).   | B.1.351  | Kim et al. (2021)       | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking                    | More efficient infectivity (24h) compared to wild type, in Caco-2 cells extasciitilde11x, Vero extasciitilde10x, and Calu-3 extasciitilde11x. Compare to wild type at extasciitilde5x across cell types.  | B.1.351  | Kim et al. (2021)       | 1104           | A                | G                | 1.0                 |



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|-----------|--------------|---|----------|-----------------------|----------------|------------------|------------------|---------------------|
| D614G     | trafficking  | extasciitilde6x more efficient S2 domain cleavage compared to wild type, compared to 4x by D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3). [N501Y+D614G does not show an increase in cleavage, therefore a synergistic effect of the trio is implied] | B.1.351  | Kim et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | More efficient infectivity (24h) compared to wild type, in Caco-2 cells extasciitilde9x, Vero extasciitilde8x, and Calu-3 extasciitilde8x. Compare to wild type at extasciitilde5x across cell types.   | B.1.351  | Kim et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | extasciitilde4x more efficient S2 domain cleavage compared to wild type, no change relative to D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3).  | B.1.351  | Kim et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | No change in infectivity (24h) relative to D614G alone in Caco-2 cells, Vero or Calu-3.   | B.1.351  | Kim et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | extasciitilde4x more efficient S2 domain cleavage compared to wild type, no change relative to D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3).  | B.1.351  | Kim et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | extasciitilde2x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | Approximately as infective as D614G alone in HEK293T-ACE2 cells 48h post-transduction ( extasciitildeadditive effects of the individual variants).  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | extasciitilde13x more infective as D614G alone in HEK293T-ACE2 cells 48h post-transduction.   | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | extasciitilde12x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction ( extasciitildeadditive effects of 501 and 484).   | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | extasciitilde2x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | extasciitilde9x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction (no synergy as level approx. that of N501Y alone).  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking  | 9x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.   | B.1.351  | Kuzmina et al. (2021) | 2208           | A                | G                | 1.0                 |
| D614G     | trafficking  | Among S variants tested, the D614G mutant shows the highest cell entry ( extasciitilde3.5x wild type), as supported by structural and binding analyses.   | B.1.351  | Ozono et al. (2020)   | 1104           | A                | G                | 1.0                 |

| Mutations | Sub-category                    | Function   | Lineages | Citation                     | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|--|----------|------------------------------|----------------|------------------|------------------|---------------------|
| D614G     | trafficking                     | Lentiviral pseudotyped with the key mutations from COH.20G/677H lineage was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing no significant change in infection rate amongst the cells, suggesting that this mutation does not contribute to cell entry fitness.  | B.1.351  | Tada et al. (2021)           | 1104           | A                | G                | 1.0                 |
| D614G     | trafficking                     | We report here pseudoviruses carrying SG614 enter ACE2-expressing cells more efficiently than wild type (extending 9-fold). This increased entry correlates with less S1-domain shedding and higher S-protein incorporation into the virion. D614G does not alter S-protein binding to ACE2 or neutralization sensitivity of pseudoviruses. Thus, D614G may increase infectivity by assembling more functional S protein into the virion.  | B.1.351  | Zhang et al. (2020)          | 1104           | A                | G                | 1.0                 |
| D614G     | transmissibility                | Assuming complete cross-protection, we estimate 501Y.V2/B.1.351 was 1.50 (95% CrI: 1.20-2.13) times as transmissible than previously circulating variants. Assuming instead that 501Y.V2 is identically transmissible, the new variant evades 21% (95% CrI: 11-36%) of previously acquired immunity. Reality may lie between these extremes, with an intermediate increase in transmissibility and mildly imperfect cross-protection from past exposure.   | B.1.351  | Pearson et al. (2021)        | 1104           | A                | G                | 1.0                 |
| D614G     | transmissibility                | 36,590 variant-specific RT-PCR tests were performed on samples collected between April 12 and May 7, 2021 in France to compare variant spread. Compared to January to March 2021, B.1.351 variant had a significant transmission advantage over B.1.1.7 in some regions (15.1 to 16.1% in Île-de-France and 16.1 to 18.8% in Hauts-de-France). This shift in transmission advantage is consistent with the immune evasion abilities of B.1.351 and the high levels of immunization in these regions. | B.1.351  | Roquebert et al. (2021)      | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | Pseudotyped D614G virus has reduced neutralization activity vs wild type: 1.2x (37 sera Pfizer median 9 days post 2nd dose, 37 sera Moderna median 18 days post 2nd dose). This was NOT significant by ANOVA.  | B.1.351  | Garcia-Beltran et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | Pseudotyped P.2 virus has reduced neutralization activity vs wild type: 5.8x (30 sera Pfizer median 9 days post 2nd dose) and 2.9x (35 sera Moderna median 18 days post 2nd dose). This was significant by ANOVA.  | B.1.351  | Garcia-Beltran et al. (2021) | 1104           | A                | G                | 1.0                 |

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|-----------|---------------------------------|--|----------|-----------------------|----------------|------------------|------------------|---------------------|
| D614G     | vaccine neutralization efficacy | Using a lentivirus virus pseudotyped with D614G Spike, sera from vaccinated individuals who received the second dose (9–11 days post-second dose of Pfizer) exhibited a robust neutralizing potential, with a mean NT50 value of 99,000. This was an average of a 2-fold increase, relative to sera drawn from the individuals who received one dose of vaccination—mean NT50 dilution of 51,300. Importantly, a 6-fold increase in mean NT50 dilution was obtained when sera from the first vaccination dose was compared to convalescent sera from cohort with severe disease (NT50 51,000 vs 8,700) 21 to 63 days post-onset. | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | This variant showed >5x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | This variant showed extasciitilde10x decrease in Pfizer sera (3 weeks post-first dose: n   | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | This variant of key B.1.351 lineage mutations showed extasciitilde10x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | This variant showed >5x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | This variant showed no change in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).   | B.1.351  | Kuzmina et al. (2021) | 1104           | A                | G                | 1.0                 |

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|-----------|---------------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| D614G     | vaccine neutralization efficacy | In a multicenter, double-blind, randomized, controlled trial to assess the safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) with enrollment June 24 and November 9, 2020 from extasciitilde2000 HIV-negative 18-64 year olds (1:1 placebo to treatment), incidence of serious adverse events 14 or more days post- 2nd dose was balanced between the vaccine and placebo groups. A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant. Serum samples obtained from 13 ChAdOx1 nCoV-19 vaccine recipients without SARS-CoV-2 infection through 41 days after vaccination showed 3.5x reduction in neutralization (ID50) for B.1.351 RBD pseudotype HIB-1 virus compared to D614G alone. This RBD variant combination's neutralization by a placebo control group of 6 naturally infected patients showed a similar 3.2x drop (though with D614G starting at a 1.7x higher titre than vaccinee sera). | B.1.351  | Madhi et al. (2021)      | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | In sera collected from 15 early pandemic patients (Seattle Flu Study), mean 16 days post first dose with either Pfizer/BioNTech or Moderna vaccines, the median ID50 titers were extasciitilde3-fold lower against this B.1.351 pseudotyped virus relative to wild type. A single asymptomatic patient, who had no detectable RBD-specific IgG memory before vaccination, also did not elicit nAbs against the B.1.351 variant. [compare to extasciitilde10 fold with L242del] ID50 titres in non-infected mRNA vaccines more than two weeks post-booster were significant, but >100x weaker than in previously infected patients after first dose.   | B.1.351  | Stamatatos et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccine neutralization efficacy | Pseudotyped viruses for B.1.618 was 2.7-fold resistant to neutralization by 6 BNT162b2 vaccine sera 28 days post-booster compared to wild type - a finding that was similar to that of the 3.4-fold resistance of the South Africa B.1.351 variant using the same assay. Neutralization by 3 Moderna vaccine sera 28 days post-booster was 3-fold resistant (vs. 2.2-fold for B.1.351). The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618.   | B.1.351  | Tada et al. (2021)       | 1104           | A                | G                | 1.0                 |

| Mutations | Sub-category            | Function   | Lineages | Citation           | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|-------------------------|--|----------|--------------------|----------------|------------------|------------------|---------------------|
| D614G     | vaccinee plasma binding | 1.19x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.  | B.1.351  | Gong et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccinee plasma binding | 1.79x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.3x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.  | B.1.351  | Gong et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccinee plasma binding | 1.64x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.35x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | B.1.351  | Gong et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccinee plasma binding | 1.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.06x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | B.1.351  | Gong et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccinee plasma binding | 1.04x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.09x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | B.1.351  | Gong et al. (2021) | 1104           | A                | G                | 1.0                 |
| D614G     | vaccinee plasma binding | 1.76x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.75x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. | B.1.351  | Gong et al. (2021) | 1104           | A                | G                | 1.0                 |

| Mutations | Sub-category            | Function   | Lineages | Citation               | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|-------------------------|--|----------|------------------------|----------------|------------------|------------------|---------------------|
| D614G     | vaccinee plasma binding | 1.30x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. Compare to varied binding in full Spike variant complements for major lineages containing this variant subset: 1.28x increase (B.1.351 aka Beta), and 1.14x decrease (P.1 aka Gamma). 1.47x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees. Compare to varied binding in full Spike variant complements for major lineages containing this variant subset: 1.17x increase (B.1.351 aka Beta), and 1.47x decrease (P.1 aka Gamma). | B.1.351  | Gong et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | vaccinee plasma binding | 1.23x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.1x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.  | B.1.351  | Gong et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | vaccinee plasma binding | 1.17x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.09x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.   | B.1.351  | Gong et al. (2021)     | 1104           | A                | G                | 1.0                 |
| D614G     | viral load              | Hamsters infected with SARS-CoV-2 expressing spike(D614G) (G614 virus) produced higher infectious titres in nasal washes and the trachea, but not in the lungs, supporting clinical evidence showing that the mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increase transmission.   | B.1.351  | Plante et al. (2020)   | 1104           | A                | G                | 1.0                 |
| D614G     | virion structure        | Estimated free energy change (ddG) for this variant is 2.5 kcal/mol (i.e. stabilizing relative to wild type)   | B.1.351  | Spratt et al. (2021)   | 1104           | A                | G                | 1.0                 |
| D614G     | virion structure        | Negative stain EM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2.  | B.1.351  | Weissman et al. (2020) | 1104           | A                | G                | 1.0                 |

| Mutations | Sub-category                   | Function   | Lineages | Citation                   | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|--|----------|----------------------------|----------------|------------------|------------------|---------------------|
| D614G     | virion structure               | CryoEM shows increased proportion of "one-up" trimer conformation of Spike proteins on the surface of virions, where the up conformation is presumed to be more likely to bind ACE2.   | B.1.351  | Yurkovetskiy et al. (2020) | 1104           | A                | G                | 1.0                 |
| D614G     | virion structure               | Based on pseudotyped virus experiments, D614G may increase infectivity by assembling more functional S protein into the virion.  | B.1.351  | Zhang et al. (2020)        | 1104           | A                | G                | 1.0                 |
| D215G     | ACE2 receptor binding affinity | Using flow cytometry and ACE2 ectodomains-Fc portion IgG complex, this variant showed a 1.19x increase in binding (KD) relative to D614G.  | B.1.351  | Gong et al. (2021)         | 1142           | A                | G                | 1.0                 |
| D215G     | antibody epitope effects       | Anti-NTD CV1 mAb isolated from an early pandemic case was unable to neutralize either partial B.1.351 variant pseudovirus used (A701V or L242del). The neutralization potency of mAb CV30, which contacts K417 and N501 but not E484, was extasciitilde10-fold weaker toward both B.1.351 variants. The neutralization potency of anti-RBD mAb CV3-1 was 3-4-fold less potent against the B.1.351 variants, while anti-RBD mAb CV2-75 was modestly less effective. | B.1.351  | Stamatatos et al. (2021)   | 1142           | A                | G                | 1.0                 |
| D215G     | convalescent plasma binding    | 2.29x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)         | 1142           | A                | G                | 1.0                 |
| D215G     | convalescent plasma escape     | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors   | B.1.351  | Cele et al. (2021)         | 1142           | A                | G                | 1.0                 |
| D215G     | convalescent plasma escape     | Using convalescent sera from 15 early pandemic patients (Seattle Flu Study), mean 220 days post symptom onset (IQR 125-269, and three asymptomatic cases) with 27% WHO disease severity scale 3, one third (5/15) of sera neutralized this B.1.351 pseudotype and only three had ID50 titers above 100. Only two of the 15 sera achieved 80% neutralization.   | B.1.351  | Stamatatos et al. (2021)   | 1142           | A                | G                | 1.0                 |

| Mutations | Sub-category               | Function   | Lineages | Citation              | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|----------------------------|--|----------|-----------------------|----------------|------------------|------------------|---------------------|
| D215G     | convalescent plasma escape | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct. Only 3 of 44 convalescent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | B.1.351  | Wibmer et al. (2021)  | 1142           | A                | G                | 1.0                 |
| D215G     | homoplasy                  | In experimental models of SARS-CoV-2 mutational evolution (without immune pressure), this mutation in the N terminal domain appears convergent.  | B.1.351  | Borges et al. (2021)  | 1142           | A                | G                | 1.0                 |
| D215G     | reinfection                | 4 health care workers in the 20's and 30's with no underlying conditions and seropositivity or confirmed 2020 SARS-CoV-2 infections were confirmed to have B.1.351 infection during a February 2021 hospital outbreak in Luxembourg. Symptoms were mostly mild on first infection, and milder on second infection.   | B.1.351  | Staub et al. (2021)   | 1142           | A                | G                | 1.0                 |
| D215G     | reinfection                | Hamsters re-infected with B.1.351 virus after seroconversion from previous infection with a lineage A virus did not transmit virus to naive sentinels via direct contact transmission, in contrast to the non-seroconverted animals. They had little infectious virus and no pathology in the lungs. Initial infection with SARS-CoV-2 lineage A does not prevent heterologous reinfection with B.1.351, but prevents disease and onward transmission.                       | B.1.351  | Yinda et al. (2021)   | 1142           | A                | G                | 1.0                 |
| D215G     | symptom prevalence         | Inoculation with the B.1.351 isolate resulted in lower clinical scores in 6 rhesus macaques that correlated with lower virus titers in the lungs, less severe histologic lung lesions and less viral antigen detected in the lungs. Our comparative pathogenicity study suggests that ongoing circulation under diverse evolutionary pressure favors transmissibility and immune evasion rather than an increase in intrinsic pathogenicity.                                 | B.1.351  | Munster et al. (2021) | 1142           | A                | G                | 1.0                 |
| D215G     | trafficking                | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing mild decrease in infection rate amongst the cells, suggesting that this mutation does not contribute to cell entry fitness.  | B.1.351  | Tada et al. (2021)    | 1142           | A                | G                | 1.0                 |



| Mutations | Sub-category                    | Function  | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| D215G     | vaccine neutralization efficacy | Using B.1.351 defining mutations for Spike, observed 4x average decrease in neutralization efficiency (but still relevant titres) for sera from 10 BNT162b2 vaccinees 12 days after second dose, but only one relevant titre 12 days after first dose. Compares unfavorably to wild type or B.1.1.7 titres.   | B.1.351  | Alenquer et al. (2021)   | 1142           | A                | G                | 1.0                 |
| D215G     | vaccine neutralization efficacy | In sera collected from 15 early pandemic patients (Seattle Flu Study), mean 16 days post first dose with either Pfizer/BioNTech or Moderna vaccines, the median ID50 titers were extasciitilde3-fold lower against this B.1.351 pseudotyped virus relative to wild type. A single asymptomatic patient, who had no detectable RBD-specific IgG memory before vaccination, also did not elicit nAbs against the B.1.351 variant. [compare to extasciitilde10 fold with L242del] ID50 titres in non-infected mRNA vaccines more than two weeks post-booster were significant, but >100x weaker than in previously infected patients after first dose. | B.1.351  | Stamatatos et al. (2021) | 1142           | A                | G                | 1.0                 |
| D215G     | vaccinee plasma binding         | 1.79x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.3x decrease in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.   | B.1.351  | Gong et al. (2021)       | 1142           | A                | G                | 1.0                 |
| D215G     | virion structure                | Estimated free energy change (ddG) for this variant is 0.98 kcal/mol (i.e. stabilizing relative to wild type)   | B.1.351  | Spratt et al. (2021)     | 1142           | A                | G                | 1.0                 |
| E484K     | ACE2 receptor binding affinity  | The affinity of the B.1.351 RBD variants for ACE2 increased by 3.7 fold as measured by surface plasmon resonance relative to wild type RBD by increasing the k(on) and decreasing the k(off) rate constants.  | B.1.351  | Barton et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity  | In the case of VOC B.1.1.7+E484K, the addition of the E484K mutation to N501Y further increased the affinity, to extasciitilde15 fold higher than WT RBD (KD extasciitilde5 nM), by further increasing the k(on) as measured by surface plasmon resonance. Because the higher k(on) could result in mass transfer limiting binding, we confirmed that the kinetic measurement for this variant was not substantially affected by varying levels of immobilization.  | B.1.351  | Barton et al. (2021)     | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category                   | Function  | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| E484K     | ACE2 receptor binding affinity | This combination showed extasciitilde3x increase binding to ACE2 vs wild type, about half that of the B.1.1.7 lineage, suggesting that the K417N mutation is slightly detrimental to ACE2 binding, probably as a result of disrupting the salt bridge formed with ACE2 residue D30  | B.1.351  | Collier et al. (2021)    | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | This variant appears twice in the experiments, with slightly different affinities (both extasciitilde1.2x decrease in binding relative to D614G) using flow cytometry and ACE2 ectodomains-Fc portion IgG complex.  | B.1.351  | Gong et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | RBD containing the N501Y mutation results in 9-fold stronger binding to the hACE2 receptor than wild type RBD. The E484K mutation does not significantly influence the affinity for the receptor, while K417N attenuates affinity. As a result, RBD from B.1.351 containing all three mutations binds 3-fold stronger to hACE2 than wild type RBD but 3-fold weaker than N501Y. | B.1.351  | Laffeber et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | Studying the key covariants in lineage of concern 501Y.V2, observed about 2-fold increase in ACE2 binding vs wildtype, but greatly decreased mAb binding, suggesting evolutionary optimum tension between immune evasion and ACE2 binding affinity as the N501Y variant alone has 10x increase in affinity but no effect on tested mAb binding.                                 | B.1.351  | Liu et al. (2021)        | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | Using Microscale Thermophoresis, the B.1.351 variant harboring three mutations, binds ACE2 at nearly five-fold greater affinity than the original SARS-CoV-2 RBD (Kd 87.6, vs 402.5 nM).  | B.1.351  | Ramanathan et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | Experimentally, ACE2 binding affinity increased 0.06 fold   | B.1.351  | Starr et al. (2020)      | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | Reported moderate increase in affinity compared to wild-type RBD on the cell surface (Kd  | B.1.351  | Tian et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | Reported slight increase in affinity compared to wild-type RBD on the cell surface (Kd  | B.1.351  | Tian et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | The affinity of ACE2 for this mutation combination was twice as high as for wild type. Having in mind that the affinity of SARS-CoV-2 for ACE2 is only 4-fold higher compared to SARS-CoV-1, this factor of 2 is expected to be biologically significant.   | B.1.351  | Vogel et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | ACE2 receptor binding affinity | Among the first selected variants in an in vitro evolution experiment for ACE2 binding.   | B.1.351  | Zahradnik et al. (2021)  | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category             | Function   | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| E484K     | T cell evasion           | Analyzing responses to the E484K mutation seen in B.1.351 and P.1 variants, we noted that it did not fall in a region predicted to bind the HLAII alleles tested (table S4). The mutation appeared to have no substantial or differential impact on T cell responses.  | B.1.351  | Reynolds et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Ablates Class 1 receptor-binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384 and S2H58.  | B.1.351  | Chen et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Ablates Class 1 receptor-binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384, and S2H58.   | B.1.351  | Chen et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Ablates Class 1 receptor-binding-motif targeting antibodies COV2-2050, 1B07, COVOX-384, and S2H58. Ablates Class 3 N-terminal domain targeting antibody COV2-2489, diminishes COV2-2676.   | B.1.351  | Chen et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Of 50 mAbs tested, major loss of neutralization observed for S2N28, S2X615, S2N12, S2X192, S2H7, S2X16, S2X58, S2H70, S2X613, S2D19, S2N22, S2D32, S2H58, S2M11, S2D106, S2X30.  | B.1.351  | Collier et al. (2021)    | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Ablates binding by class 2 mAbs such as C144 that directly interfere with ACE2 binding, but clonal somatic mutations of memory B cells at 6.2 months (evolving humoral immune response) show pronounced increase in binding to the variant.  | B.1.351  | Gaebler et al. (2021)    | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Abolished neutralization by mAbs CQ026 and CQ038, greatly diminished neutralization by CQ012 and CQ046.  | B.1.351  | Hu et al. (2021)         | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Monoclonal antibodies 13G9 and 58G6 maintain fairly high neutralization potency, compared to others interfacing with E484K.  | B.1.351  | Li et al. (2021)         | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Mutant screen in neutralization assay with a broad range of monoclonal antibodies shows high resistance to 4 antibodies, and broad low level resistance against much of the rest of the panel.   | B.1.351  | Liu et al. (2020)        | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Massive reduction in binding efficiency vs wild type for mAb LY-CoV555.  | B.1.351  | Rappazzo et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Anti-NTD CV1 mAb isolated from an early pandemic case was unable to neutralize either partial B.1.351 variant pseudovirus used (A701V or L242del). The neutralization potency of mAb CV30, which contacts K417 and N501 but not E484, was extasciitilde10-fold weaker toward both B.1.351 variants. The neutralization potency of anti-RBD mAb CV3-1 was 3-4-fold less potent against the B.1.351 variants, while anti-RBD mAb CV2-75 was modestly less effective. | B.1.351  | Stamatatos et al. (2021) | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category             | Function   | Lineages | Citation             | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|--------------------------|--|----------|----------------------|----------------|------------------|------------------|---------------------|
| E484K     | antibody epitope effects | Complete loss of binding in ELISA by the variant against monoclonal antibody VH-Fc ab8   | B.1.351  | Sun et al. (2021)    | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Complete loss of binding in ELISA by the variant against monoclonal antibodies ab8 and IgG1 ab1. Complete loss for the same antibodies was also observed against S1 pseudotyped and full Spike protein trimers with both B.1.351 and P.1 lineage variants, with slight binding signal for P.1 against IgG1 at the highest concentration tested (1uM). Complete loss of neutralization by these two antibodies was also observed.   | B.1.351  | Sun et al. (2021)    | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Pseudotyped virus model ablates neutralization by RBD-directed mAbs 4-20, 2-4, 2-43, 2-30, 2-15, LY-Cov555, C121. Pseudotyped virus model impairs neutralization by RBD-directed mAb COV2-2196 (somewhat more than fully pseudotyped B.1.351 or live virus)  | B.1.351  | Wang et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Resistant to all seven class 2 (Spike 'up' or 'down' conformation, RBD targeting) antibodies tested, with 10-fold or greater reduction in neutralization (plus notable reduction in two unclassified mAbs).  | B.1.351  | Wang et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | antibody epitope effects | Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody CA1 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody LyCoV016 (also known as CB6 or JS016) on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 1 (Spike 'up' conformation only, RBD targeting) monoclonal antibody CC12.1 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody BD23 on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody C119 (also known as CB6 or JS016) on 501Y.V2 ("South African") lineage background Ablates ELISA test binding for class 2 (Spike 'up' or 'down' conformation, RBD targeting) monoclonal antibody P2B-2F6 on 501Y.V2 ("South African") lineage background | B.1.351  | Wibmer et al. (2021) | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category                | Function   | Lineages | Citation               | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|-----------------------------|--|----------|------------------------|----------------|------------------|------------------|---------------------|
| E484K     | convalescent plasma binding | 1.42x increase in Spike binding (relative to D614G alone) by 5 plasma collected 8 months post-symptom-onset.   | B.1.351  | Gong et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | Average extasciitilde5-fold reduction in neutralization efficacy in convalescent sera of 16 health workers infected in Spring 2020.  | B.1.351  | Alenquer et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | Average extasciitilde10-fold reduction in neutralization efficacy in convalescent sera of 16 health workers infected in Spring 2020.   | B.1.351  | Alenquer et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | This mutation occurred in 100% of sequenced virions after 12 passages and led to a 4-fold decrease in convalescent plasma neutralization activity  | B.1.351  | Andreano et al. (2020) | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | The 501Y.V2 to first wave IC50 ratio ranged from 6 to 200-fold. Averaging across all 7 participant convalescent sera highlighted the dramatic decrease in sensitivity to neutralization of authentic 501Y.V2 variants. PG: I'm purposefully ignoring D614G and A701V as contributors                 | B.1.351  | Cele et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | In 19 convalescent human sera extasciitilde1mo post infection had mild to moderate resistance against most samples   | B.1.351  | Chen et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | In 19 convalescent human sera extasciitilde1mo post infection had mild to moderate resistance against all samples.   | B.1.351  | Chen et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | Neutralizing antibody titers of 18 samples (90%) decreased against this B.1.351 pseudotyped virus below an ID50 threshold of 40 (sera collected extasciitilde8mo post Jan 2020 first wave in China).   | B.1.351  | Hu et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | extasciitilde7x reduction in neutralization by key B.1.351 lineage RBD variant combination in sera collected from cohort of 10 with severe disease 21 to 63 days post-onset. Two of the cohort showed no neutralization against this variant.  | B.1.351  | Kuzmina et al. (2021)  | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | Remarkably, several of the E484 escape mutants were resistant to neutralization at the highest concentration (1:80 initial dilution) of all 4 convalescent sera tested (triplicate experiments). Against a wider panel of 16 convalescent plasma (no replicates), all but one show major resistance. | B.1.351  | Liu et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape  | Escape mutant found after in passage in plasma pool of 26 convalescents mean 1.5 post symptom onset.   | B.1.351  | Schmidt et al. (2021)  | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category               | Function   | Lineages | Citation                 | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|----------------------------|--|----------|--------------------------|----------------|------------------|------------------|---------------------|
| E484K     | convalescent plasma escape | Using convalescent sera from 15 early pandemic patients (Seattle Flu Study), mean 220 days post symptom onset (IQR 125-269, and three asymptomatic cases) with 27% WHO disease severity scale 3, one third (5/15) of sera neutralized this B.1.351 pseudotype and only three had ID50 titers above 100. Only two of the 15 sera achieved 80% neutralization.   | B.1.351  | Stamatatos et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape | The only mutation in the B.1.351 lineage that appears to contribute to neutralization reduction (extasciitilde1.7x across 10 convalescent sera from April 2020 infectees)  | B.1.351  | Tada et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape | Pseudotyped viruses for B.1.618 was 2.5-fold resistant to neutralization by convalescent sera compared to wild type - a finding that was similar to that of the 3-fold resistance of the South Africa B.1.351 variant using the same assay. The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618. [details on the convalescent patient sera collection are not abundantly clear in the preprint] | B.1.351  | Tada et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape | As measured by surface plasmon resonance, RBD with the E484K mutation alone showed a mean 19.1x decrease in binding affinity for six batches of hyper-immune immunoglobulin (hCoV-2IG) preparations generated from SARS-CoV-2 convalescent plasma.   | B.1.351  | Tang et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape | Demonstrate (via competitive assays in human and mouse) immune escape from polyclonal antibodies induced by vaccination or infection, comparable to what was previously shown with monoclonal antibodies for N501Y and more importantly for E484K. Even though viral mutations may more strongly affect monoclonal antibodies than sera activity, the latter may also be reduced as confirmed here.  | B.1.351  | Vogel et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape | The neutralizing activity of 15/20 convalescent sera was significantly lower against this pseudotyped virus model  | B.1.351  | Wang et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape | 27% of 44 early pandemic exposure convalescent plasma/sera lose all activity against a RBD triple mutant pseudovirus (RBD mutants of the 501Y.V2 "South African" lineage), while only 23% retained high titres   | B.1.351  | Wibmer et al. (2021)     | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category                              | Function   | Lineages | Citation                | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---|--|----------|-------------------------|----------------|------------------|------------------|---------------------|
| E484K     | convalescent plasma escape                | Nearly half (21 of 44, 48%) of early pandemic exposure convalescent plasma/sera failed to neutralize the 501Y.V2 ("South African") lineage pseudovirus construct. Only 3 of 44 convalescent sera (those with the highest titer, which correlated directly with initial infection severity) had high neutralization against this 501Y.V2 PG: note that lineage variant R246I was excluded from the text in reference to these sera assays, not sure if that was an oversight. | B.1.351  | Wibmer et al. (2021)    | 1033           | G                | A                | 1.0                 |
| E484K     | convalescent plasma escape                | Subtype of the B.1.526 "New York" lineage, lentivirus pseudotyped with this mutation combination in showed 3.3x reduction in IC50 serum dilution concentration for 6 convalescent sera.  | B.1.351  | Zhou et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | monoclonal antibody serial passage escape | The engineered mutation cause 10-fold or more increase in the disassociation constant with many monoclonal antibodies (C144/C002/C121/C104/C110).  | B.1.351  | Barnes et al. (2020)    | 1033           | G                | A                | 1.0                 |
| E484K     | monoclonal antibody serial passage escape | Escape variant 100% appearance in 2 passages against Regeneron monoclonal antibody REGN10989 @ 50ug/mL (99% after one passage)   | B.1.351  | Baum et al. (2020)      | 1033           | G                | A                | 1.0                 |
| E484K     | monoclonal antibody serial passage escape | Mildly effective mutant against this position in the RBD for highly neutralizing COV2-2479 monoclonal antibody. Effective mutant against this position in the RBD for highly neutralizing COV2-2050 monoclonal antibody  | B.1.351  | Greaney et al. (2020)   | 1033           | G                | A                | 1.0                 |
| E484K     | monoclonal antibody serial passage escape | Escape mutation against monoclonal antibody LY-CoV555 (antibody that forms the basis for Eli Lilly's bamlanivimab)   | B.1.351  | Starr et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | monoclonal antibody serial passage escape | Class 2 antibodies C627, C602, C671, C643, and class 2/3 antibody C603 selected for the emergence of the E484K mutation in vitro.  | B.1.351  | Wang et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | monoclonal antibody serial passage escape | Strong positive selection (up to 50% of supernatant sequences) after C121 monoclonal antibody assay, decreasing in subsequent passages. Strong positive selection (up to 44% of supernatant sequences) after after one round of C144 monoclonal antibody passage, then waning on subsequent passages   | B.1.351  | Weisblum et al. (2020)  | 1033           | G                | A                | 1.0                 |
| E484K     | pharmaceutical effectiveness              | Bamlanivimab (LY-CoV555) lost extasci-tilde16x binding against this isolated mutation. Casirivimab lost extasci-tilde16x binding against this isolated mutation.   | B.1.351  | Engelhart et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | pharmaceutical effectiveness              | Tixagevimab, Regdanvimab and COR-101 display reduced binding affinity to virus pseudotyped as RBD from B.1.351.  | B.1.351  | Engelhart et al. (2021) | 1033           | G                | A                | 1.0                 |

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|-----------|------------------------------|---|----------|-------------------------|----------------|------------------|------------------|---------------------|
| E484K     | pharmaceutical effectiveness | Bamlanivimab (LY-CoV555) lost extasci-tilde32x binding against this double mutation. COR-101 lost extasci-tilde160x binding against this double mutation. Casirivimab lost extasci-tilde16x binding against this double mutation. Estesevimab lost extasci-tilde32x binding against this double mutation. Regdanvimab lost extasci-tilde4x binding against this double mutation. Tixagevimab lost extasci-tilde12x binding against this double mutation.  | B.1.351  | Engelhart et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | pharmaceutical effectiveness | Bamlanivimab (LY-CoV555) lost extasci-tilde64x binding against this double mutation. COR-101 lost extasci-tilde50x binding against this double mutation. Casirivimab lost extasci-tilde250x binding against this double mutation. Estesevimab lost extasci-tilde16x binding against this double mutation. Regdanvimab lost extasci-tilde32x binding against this double mutation. Tixagevimab lost extasci-tilde10x binding against this double mutation. | B.1.351  | Engelhart et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | pharmaceutical effectiveness | This mutated version of RBD completely abolishes the binding to a therapeutic antibody, Bamlanivimab, in vitro.   | B.1.351  | Liu et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | reinfection                  | 4 health care workers in the 20's and 30's with no underlying conditions and seropositivity or confirmed 2020 SARS-CoV-2 infections were confirmed to have B.1.351 infection during a February 2021 hospital outbreak in Luxembourg. Symptoms were mostly mild on first infection, and milder on second infection.  | B.1.351  | Staub et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | reinfection                  | Hamsters re-infected with B.1.351 virus after seroconversion from previous infection with a lineage A virus did not transmit virus to naive sentinels via direct contact transmission, in contrast to the non-seroconverted animals. They had little infectious virus and no pathology in the lungs. Initial infection with SARS-CoV-2 lineage A does not prevent heterologous reinfection with B.1.351, but prevents disease and onward transmission.    | B.1.351  | Yinda et al. (2021)     | 1033           | G                | A                | 1.0                 |



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|-----------|---------------------|--|----------|-----------------------|----------------|------------------|------------------|---------------------|
| E484K     | symptom prevalence  | Inoculation with the B.1.351 isolate resulted in lower clinical scores in 6 rhesus macaques that correlated with lower virus titers in the lungs, less severe histologic lung lesions and less viral antigen detected in the lungs. Our comparative pathogenicity study suggests that ongoing circulation under diverse evolutionary pressure favors transmissibility and immune evasion rather than an increase in intrinsic pathogenicity. | B.1.351  | Munster et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | syncytium formation | extasciitilde50% Vero cell membrane fusion assay under infection with VSV pseudotyped virus relative to wild type, significantly higher than D614G.  | B.1.351  | Kim et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | This variant alone shows a extasciitilde5x decrease in cell entry efficiency (RLU measurement in 293T cells) compared to D614G.  | B.1.351  | Ferriera et al (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | The entry efficiencies of Spike pseudotyped viruses bearing N501Y Variant 2 (B.1.351) mutant were about 3 to 4.4 times higher than that of the WT pseudovirus when viral input was normalized, suggesting that these spike variants promote the infectivity of SARS-CoV-2.   | B.1.351  | Hu et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | More efficient infectivity (24h) compared to wild type, in Caco-2 cells extasciitilde11x, Vero extasciitilde10x, and Calu-3 extasciitilde11x. Compare to wild type at extasciitilde5x across cell types.   | B.1.351  | Kim et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | extasciitilde6x more efficient S2 domain cleavage compared to wild type, compared to 4x by D614G alone in Caco-2 cells, mid-range of three cell line tested (Vero and Calu-3). [N501Y+D614G does not show an increase in cleavage, therefore a synergistic effect of the trio is implied]  | B.1.351  | Kim et al. (2021)     | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | extasciitilde2x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction.   | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | Approximately as infective as D614G alone in HEK293T-ACE2 cells 48h post-transduction ( extasciitildeadditive effects of the individual variants).   | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | extasciitilde13x more infective as D614G alone in HEK293T-ACE2 cells 48h post-transduction.  | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | extasciitilde12x more infectivity than D614G alone in HEK293T-ACE2 cells 48h post-transduction ( extasciitildeadditive effects of 501 and 484).  | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | trafficking         | Lentiviral pseudotyped with this individual mutation from B.1.351 was tested on ACE2.293T cells. Luciferase activity was measured two days postinfection, showing no change in infection rate amongst the cells.   | B.1.351  | Tada et al. (2021)    | 1033           | G                | A                | 1.0                 |

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|-----------|---------------------------------|--|----------|------------------------------|----------------|------------------|------------------|---------------------|
| E484K     | transmissibility                | Assuming complete cross-protection, we estimate 501Y.V2/B.1.351 was 1.50 (95% CrI: 1.20-2.13) times as transmissible than previously circulating variants. Assuming instead that 501Y.V2 is identically transmissible, the new variant evades 21% (95% CrI: 11-36%) of previously acquired immunity. Reality may lie between these extremes, with an intermediate increase in transmissibility and mildly imperfect cross-protection from past exposure.   | B.1.351  | Pearson et al. (2021)        | 1033           | G                | A                | 1.0                 |
| E484K     | transmissibility                | 36,590 variant-specific RT-PCR tests were performed on samples collected between April 12 and May 7, 2021 in France to compare variant spread. Compared to January to March 2021, B.1.351 variant had a significant transmission advantage over B.1.1.7 in some regions (15.1 to 16.1% in Île-de-France and 16.1 to 18.8% in Hauts-de-France). This shift in transmission advantage is consistent with the immune evasion abilities of B.1.351 and the high levels of immunization in these regions. | B.1.351  | Roquebert et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | Using B.1.351 defining mutations for Spike, observed 4x average decrease in neutralization efficiency (but still relevant titres) for sera from 10 BNT162b2 vaccinees 12 days after second dose, but only one relevant titre 12 days after first dose. Compares unfavorably to wild type or B.1.1.7 titres.  | B.1.351  | Alenquer et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | Observed 1.4-fold reduction in neutralization efficiency of Pfizer vaccinee sera (collected 14 days after second dose) against pseudotype B.1.351 key variants lentivirus. Compare to 8.8-fold reduction against cultured B.1.351 virus.   | B.1.351  | Bates et al. (2021)          | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | The neutralizing activity of vaccine was slightly to significantly lower against this variant combination in sera from all 24 patients with the BNT162b2 mRNA vaccine. (Fig. 4) [In stark contrast to this combination plus K417N, which had no effect ( $P < 0.0001$ vs. P  | B.1.351  | Chen et al. (2021)           | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | Nine stored sera from Pfizer BNT162b2 vaccinees were tested against a range of spike mutation bearing PV. E484K conferred a ten-fold reduction in neutralisation by vaccine sera.  | B.1.351  | Ferreira et al. (2021)       | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | Pseudotyped P.2 virus has reduced neutralization activity vs wild type: 5.8x (30 sera Pfizer median 9 days post 2nd dose) and 2.9x (35 sera Moderna median 18 days post 2nd dose). This was significant by ANOVA.  | B.1.351  | Garcia-Beltran et al. (2021) | 1033           | G                | A                | 1.0                 |

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|-----------|---------------------------------|---|----------|-----------------------|----------------|------------------|------------------|---------------------|
| E484K     | vaccine neutralization efficacy | E484K pseudotyped VSV was tested for neutralization in a clonal HEK-293T ACE2 TMPRSS2 cell line optimized for highly efficient S-mediated infection. A cohort of 12 Argentinian recipients of the Gamaleya Sputnik V Ad26 / Ad5 vaccine showed a mean 2.8x decrease in neutralization efficacy.   | B.1.351  | Ikegame et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | Human sera from 5 two-dose Pfizer vaccinated individuals (47-68 days post 1st-dose) neutralized this variant 3.4x less relative to reference USA-WA1/2020 strain. 8 convalescent plasma with weak IgG ELISA titre neutralized this variant 2.4x less relative to reference USA-WA1/2020 strain. One plasma failed to neutralize at all. 11 convalescent plasma with moderate IgG ELISA titre neutralized this variant 4.2x less relative to reference USA-WA1/2020 strain. 11 convalescent plasma with high IgG ELISA titre neutralized this variant 2.6x less relative to reference USA-WA1/2020 strain. | B.1.351  | Jangra et al. (2021)  | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | This variant showed only minor in Pfizer sera (one or two dose) neutralization efficiency vs D614G (using lentivirus pseudotype).   | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | This variant showed extasciitilde10x decrease in Pfizer sera (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | This variant of key B.1.351 lineage mutations showed extasciitilde10x decrease in Pfizer sera (3 weeks post-first dose: n   | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | This variant showed >5x decrease in Pfizer sera (3 weeks post-first dose: n   | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | In post-vaccination sera from individuals who received one (3 weeks post-first dose: n  | B.1.351  | Kuzmina et al. (2021) | 1033           | G                | A                | 1.0                 |

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|-----------|---------------------------------|---|----------|--------------------------|----------------|------------------|------------------|---------------------|
| E484K     | vaccine neutralization efficacy | In a multicenter, double-blind, randomized, controlled trial to assess the safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) with enrollment June 24 and November 9, 2020 from extasciitilde2000 HIV-negative 18-64 year olds (1:1 placebo to treatment), incidence of serious adverse events 14 or more days post- 2nd dose was balanced between the vaccine and placebo groups. A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant. Serum samples obtained from 13 ChAdOx1 nCoV-19 vaccine recipients without SARS-CoV-2 infection through 41 days after vaccination showed 3.5x reduction in neutralization (ID50) for B.1.351 RBD pseudotype HIB-1 virus compared to D614G alone. This RBD variant combination's neutralization by a placebo control group of 6 naturally infected patients showed a similar 3.2x drop (though with D614G starting at a 1.7x higher titre than vaccinee sera). | B.1.351  | Madhi et al. (2021)      | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | Neutralizing antibody titers of non-human primate sera after one or two doses of Ad26.COV2.S (Janssen vaccine) against the variants containing the E484K substitution in the RBD were present but reduced (fold reduction between 3.35–7.78, 95% confidence interval all above twofold difference, one-sample t test).  | B.1.351  | Solfrosi et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | In sera collected from 15 early pandemic patients (Seattle Flu Study), mean 16 days post first dose with either Pfizer/BioNTech or Moderna vaccines, the median ID50 titers were extasciitilde3-fold lower against this B.1.351 pseudotyped virus relative to wild type. A single asymptomatic patient, who had no detectable RBD-specific IgG memory before vaccination, also did not elicit nAbs against the B.1.351 variant. [compare to extasciitilde10 fold with L242del] ID50 titres in non-infected mRNA vaccines more than two weeks post-booster were significant, but >100x weaker than in previously infected patients after first dose.   | B.1.351  | Stamatatos et al. (2021) | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category                    | Function  | Lineages | Citation           | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|---------------------------------|---|----------|--------------------|----------------|------------------|------------------|---------------------|
| E484K     | vaccine neutralization efficacy | Pseudotyped viruses for B.1.618 was 2.7-fold resistant to neutralization by 6 BNT162b2 vaccine sera 28 days post-booster compared to wild type - a finding that was similar to that of the 3.4-fold resistance of the South Africa B.1.351 variant using the same assay. Neutralization by 3 Moderna vaccine sera 28 days post-booster was 3-fold resistant (vs. 2.2-fold for B.1.351). The resistance of B.1.618 was caused by the E484K mutation, based on results from viruses pseudotyped for individual variants within B.1.618. | B.1.351  | Tada et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | In a cohort of 20 patients 8+ weeks after second vaccine dose of Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines, ELISA tests show 10x reduced efficacy of a majority of isolated antibodies, but only a modest decrease for vaccine plasma overall.   | B.1.351  | Wang et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | In a cohort of 20 patients 8+ weeks after second vaccine dose of Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines, a significant (0.5 to 20-fold, but average extasciitilde2x) decrease in neutralization by vaccine plasma was observed.   | B.1.351  | Wang et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | In Moderna vaccinee sera, 2.7x reduction in neutralization, and 6.4 for the full B.1.351 Spike mutation complement, but despite the observed decreases, titers in human vaccinee sera against the B.1.351 variant remained at clinically significant level of extasciitilde1/300.   | B.1.351  | Wu et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | vaccine neutralization efficacy | In 20 sera from BNT162b2 mRNA vaccine inoculated participants, 6 displayed mild (2x) reductions in neutralization. This variant combination showed the highest reduction, but the magnitude of the differences was small compared to the >4x differences in HA-inhibition titers that have been used to signal potential need for a strain change in influenza vaccines.  | B.1.351  | Xie et al. (2021)  | 1033           | G                | A                | 1.0                 |
| E484K     | vaccinee plasma binding         | 1.16x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in previously non-seroconverted subjects. 1.06x increase in Spike binding (relative to D614G alone) by 5 plasma collected 3 weeks after one dose of Pfizer/BioNtech BNT162b2 vaccine in post-infection vaccinees.  | B.1.351  | Gong et al. (2021) | 1033           | G                | A                | 1.0                 |

| Mutations | Sub-category     | Function   | Lineages | Citation                | Sequence Depth | Reference Allele | Alternate Allele | Alternate Frequency |
|-----------|------------------|--|----------|-------------------------|----------------|------------------|------------------|---------------------|
| E484K     | viral load       | B.1.351 and P.1 samples showed average Ct cycle threshold of 22.2 vs 23 for wildtype (i.e. extasciitilde60% higher viral load) comparing 3360 and 22535 samples respectively.  | B.1.351  | Roquebert et al. (2021) | 1033           | G                | A                | 1.0                 |
| E484K     | viral load       | The 62 B.1.351 (a.k.a. N501Y.V2) variant cases in three Paris hospital labs had a extasciitilde2-fold viral load increase ( extasciitilde1 Ct drop in both N and ORF1ab probes) compared to 332 ancestral lineage cases from the same time frame (2020-12-20 to 2021-02-26). | B.1.351  | Teyssou et al. (2021)   | 1033           | G                | A                | 1.0                 |
| E484K     | virion structure | Estimated free energy change (ddG) for this variant is -0.6 kcal/mol (i.e. destabilizing relative to wild type)  | B.1.351  | Spratt et al. (2021)    | 1033           | G                | A                | 1.0                 |

The results here are in whole or part based upon data hosted at the Canadian VirusSeq Data Portal: <https://virusseq-dataportal.ca/>. We wish to acknowledge the following organisations/laboratories for contributing data to the Portal: Canadian Public Health Laboratory Network (CPHLN), CanCOGGeN VirusSeq and the list of labs available at <https://virusseq-dataportal.ca/acknowledgements>)