

Summary of SARS-CoV-2 Novel Variants

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COVID-19 Literature Report Team:

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At just over one year into the COVID-19 pandemic, evolution of SARS-CoV-2 has generated viral variants that differ in their genetic sequence from the strain first detected in December 2019. Evidence is emerging about how these variants differ in their transmission characteristics, associated clinical symptoms, and vaccine efficacy. **This document is a brief summary of published evidence about characteristics of SARS-CoV-2 variants that may impact the public health response, including transmission and response to vaccination. Included are manuscripts published in peer-reviewed journals or on pre-print servers through February 5, 2021.** References summarized in this report were drawn from the COVID-19 Literature Report (Lit Rep) team database. **References that appeared in the daily Lit Rep are marked with an asterisk***, and the summary is shown in the annotated bibliography below. This list was cross-referenced with resource pages hosted by the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO), genomics initiatives Nextstrain and GISAID, and supplemented with studies mentioned in media articles.¹⁻⁴ We encourage readers to consult these sites and the daily Lit Rep for evidence that emerges following publication of this report.

Executive Summary of SARS-CoV-2 novel variants

- **Continued evolution of SARS-CoV-2 has led to several variants with evidence or suspicion of increased transmissibility, including the B.1.1.7 variant emerging from the UK, the B.1.351 variant emerging from South Africa, and the P.1 variant emerging from Brazil.**
- **Early evidence indicates that the B.1.1.7 variant is still neutralized by sera from people who received the Pfizer or Moderna vaccine series. Novavax reported similar efficacy of its vaccine (85% vs 89%) against the B.1.1.7 variant and non-variant strains and the AstraZeneca-Oxford vaccine was reported to have similar efficacy against the B.1.1.7 variant and non-variant strains (74% vs 84%).**
- **In contrast, press releases containing preliminary findings from vaccine trial sites in South Africa during the emergence of B.1.351 suggest lower efficacy of the Novavax and Johnson & Johnson vaccines in this setting compared to sites in the US and the UK where B.1.351 was not the dominant strain, but full manuscripts have not been published.**
- **Additionally, laboratory evidence indicates reduced neutralization of B.1.351 and B.1.1.7 strains by convalescent plasma and monoclonal antibodies.**

Overview of naming conventions for SARS-CoV-2 variants

Multiple categorizations of the genetic diversity of SARS-CoV-2 have developed across research and public health organizations, resulting in several names for each variant. Researchers emphasize the importance of referring to variants by their scientific names instead of using geographic terms to avoid stigmatizing people and places and to reduce confusion as variants are detected globally.⁵ This report refers to variants with multiple leading naming conventions (Table). One leading convention described by Rambaut and

utilized by Pangolin software assigns names based on the evolutionary relationships of viruses (e.g., B.1.1.7).⁶ Another, the Nextstrain genomics project, categorizes the genetic diversity of SARS-CoV-2 into different clades, which are groups of similar viruses based on their phylogenetic relatedness, with 11 clades named thus far: 19A, 19B, 20B, 20C, 20D, 20E (EU1), 20F, 20G, 20H/501Y.V2, 20I/501Y.V1, and 20J/501Y.V3. The Global Initiative on Sharing All Influenza Data (GISAID) also uses a clade system that differs from Nextstrain (e.g., clade 20B for Nextstrain; clade GR for GISAID). Public Health England uses the 'VOC 202012/01' nomenclature in which VOC stands for 'variant of concern,' the numbers include a reference to the year and month of discovery, and variant number (01).⁷ The '501Y.V2' nomenclature refers to a substitution in the 501st amino acid site of the SARS-CoV-2 spike protein used by the team that identified the variant.

Transmission characteristics of key SARS-CoV-2 variants

Early in the pandemic, SARS-CoV-2 genomic tracking efforts identified that a variant with an amino acid change in the spike protein (D614G) had become the dominant pandemic strain by March 2020.⁸ Attention turned to other variants during the northern hemisphere autumn 2020, as COVID-19 surged in Europe and a large-scale genomic sequencing effort in the UK identified a variant known as B.1.1.7 (a.k.a. variant 20I/501Y.V1 or VOC 202012/01) associated with increased risk of transmission.⁷ Recent publications focus on B.1.1.7, B.1.351 (a.k.a. 20H/501Y.V2) emerging from South Africa, P.1 (a.k.a. 20J/501Y.V3 or descendent from B.1.1.28) emerging from Brazil, and CAL.20C, whose emergence in southern California in autumn 2020 coincided with a substantial increase in COVID-19 cases.⁹ All of these variants have been identified in samples in the US.¹

Early emergence of spike protein mutation D614G, with evidence of increased transmissibility, becomes the dominant pandemic strain by March 2020.

- A sequence analysis of 175 SARS-CoV-2 samples early in the pandemic from a southwestern US medical center from March to May 2020 indicated that 57% of samples carried the D614G substitution.^{10*}
- In an early study published in July 2020, Korber et al. found that patients infected with the SARS-CoV-2 strain carrying the D614G variant shed more viral nucleic acid compared to those without this mutation.^{8*}
- A study published as a pre-print in September 2020 using epidemiological data and phylogenetic data (35,377 sequences) estimated that the G614 mutant of SARS-CoV-2 is 31% more transmissible than the D614 wildtype.^{11*}

Mink culling in Denmark in response to 'Cluster-5' variant¹²

- A variant with 3 amino-acid changes and two deletions in the spike protein resulted in both human-to-mink and mink-to-human transmission in Denmark.^{13*}
- Danish health authorities found that some of the mutations were associated with reduced response to antibodies, as described in a letter from the Danish Chief Veterinary Officer to the World Organization for Animal Health.^{12,14}
- Whole genome sequencing showed evidence of ongoing SARS-CoV-2 transmission in mink farms and spillover events to human in the Netherlands.¹⁵
- Denmark decided to cull all farmed mink in early November 2020 due to concern that mink were acting as a viral reservoir and contributing to ongoing SARS-CoV-2 transmission, with the potential for additional mutations as viruses were transmitted between mink and humans.¹⁶

Lineage B.1.1.7 (a.k.a. variant 20I/501Y.V1 or VOC 202012/01) identified in the UK with evidence of increased transmissibility, becomes the dominant strain in the UK by December, 2020.⁷

- 90% of samples tested across England between January 18 and 24, 2021 carried S gene target failure (SGTF), with higher proportions in London, the South East, and East of England. SGTF is used as a proxy for monitoring B.1.1.7 in the UK based on the predominant assay in UK lighthouse laboratories.⁷
- An analysis of contact tracing data by Public Health England found that the secondary attack rate was higher for SGTF, increasing from 10% to 13% of named contacts, yielding an estimate of 25% - 40% higher attack rate for the variant strain.⁷
- The receptor binding domain (RBD) of the 501Y.V1 SARS-CoV-2 variant was reported to have around a 10-times higher binding affinity for human ACE2 than the RBD of the parent N501 strain, suggesting a potential mechanism for the higher rate of contagiousness observed with this strain.^{17*}
- An earlier mathematical modeling study for 3 regions in England estimated that VOC 202012/01 is 56% (range 50-74%) more transmissible than earlier strains using testing data and cell phone data.^{18*}
- CDC identified 76 reported cases of B.1.1.7 variant in US through January 13, 2021. Models predicted that B.1.1.7 may become the dominant strain in the US by March, 2021.^{19*}

Lineage B.1.351 (a.k.a. variant 20H/501Y.V2) identified in South Africa

- This variant with multiple spike protein mutations became the dominant strain by early November 2020 in the Eastern Cape and Western Cape Provinces of South Africa.⁹²⁰
- It is estimated to be more transmissible than non-variant strains, though less quantified than B.1.1.7 variant.
- It exhibits evidence of escape from neutralization by convalescent plasma and vaccinated donor sera, as described in detail below.

P.1 variant (a.k.a. 20J/501Y.V3, branch from B.1.1.28 lineage) in Brazil

- This variant has 12 mutations to the spike protein, including three mutations of concern in common with 20H/501Y.V2 (K417N/T, E484K and N501Y) which may affect transmissibility and host immune response.¹
- Using phylogenetic analysis, Voloch et al estimate that it emerged in Rio de Janeiro in July 2020 and increased in frequency among sampled genomes.²¹
- A new SARS-CoV-2 variant was one hypothesis raised to potentially explain the resurgence of COVID-19 cases in Manaus, Brazil despite high estimated seroprevalence of antibodies against SARS-CoV-2 of 76%.^{22*}

CAL.20C variant in California

- A novel SARS-CoV-2 strain, CAL.20C, emerging from Southern California, was detected through genome sequence analysis. The strain's increasing dominance coincided with an increased positivity rate in that region. While first observed in July, CAL.20C accounted for 24% of cases by December 2020. CAL.20C is characterized by multiple mutations in the spike protein, similar to variants emerging from the UK and South Africa. Though predominant in Southern California, CAL.20C has been isolated in samples from New York and Washington DC.^{23*} (Zhang summarized Jan 21)

Implications of variants for SARS-CoV-2 re-infection and vaccine efficacy

Greaney et al. identified the E484 site in the spike protein receptor binding domain (characteristic of variants B.1.351 and P.1) as a place where mutations reduce neutralization by convalescent serum by more than 10-fold.²⁴ Convalescent plasma from people recovering from COVID-19 had attenuated neutralization to the B.1.351 variant.^{25,26*} The SARS-CoV-2 variant B.1.1.7 was resistant to neutralization by several monoclonal antibodies (mAbs) targeting either the N-terminal domain (NTD) of the virus's spike protein or its receptor-binding domain (RBD). The B.1.351 variant resisted neutralization by most NTD mAbs, multiple individual mAbs directed against the RBD, convalescent plasma (about 11-33 fold), and sera from vaccinated people (about 6.5-8.6 fold).^{27*} The SARS-CoV-2 B.1.1.7 variant was shown to reduce neutralizing activity of monoclonal antibodies (mAbs) targeting subdominant epitopes in the SARS-CoV-2 spike protein.^{28*} Cases of SARS-CoV-2 re-infection have been reported for the D614G mutation, B.1.1.7 variant, B.1.351 variant, and P.1 variant.²⁹⁻³¹ For B.1.1.7, the two infection episodes were separated by eight months and the second infection episode was with a B.1.1.7 variant.³⁰

Summary of vaccine efficacy by manufacturer

Pfizer-BioNTech

- Neutralizing activity of participants three weeks after receiving the first dose of the Pfizer vaccine was similar against the three key spike protein mutations in the B.1.1.7 variant, compared to the wild-type SARS-CoV-2 strain. However, neutralization titers were reduced up to 6-fold (median 3.85-fold) against a pseudovirus with the full set of 8 spike protein mutations present in the B.1.1.7 variant.^{32*}
- A subsequent analysis found sera from recipients who completed the 2-dose regimen of the Pfizer vaccine BNT162b2 (n=20) had similar neutralizing geometric mean titers (GMTs) against SARS-CoV-2 viruses engineered to contain key spike protein mutations from variants emerging from the UK (B.1.1.7) and South Africa (B.1.351) compared to GMTs against the wild-type virus. The authors note a limitation that the engineered viruses do not contain the full set of mutations present in variants B.1.1.7 and B.1.351.^{33*}

Moderna

- Sera from human subjects or non-human primates that received the mRNA-1273 (Moderna) vaccine showed no significant reduction in neutralization activity against the SARS-CoV-2 B.1.1.7 variant emerging from the UK, but reduced activity against the B.1.351 variant emerging from South Africa.^{34*}
- Using a lentivirus-based pseudovirus assay, the SARS-CoV-2 B.1.1.7 (UK) variant was shown to exhibit only modestly reduced susceptibility to neutralization from convalescent sera (1.5-fold average reduction) and sera from recipients of both the Moderna and Novavax vaccine phase 1 studies (2-fold average reduction after two inoculations).^{35*}

Novavax

- Preliminary results reported on January 28 for phase 2/3 trials for the recombinant protein-based COVID-19 vaccine NVX-CoV2373 made by Novavax showed up to 89% efficacy in the UK cohort (n >15,000), with an estimated 86% efficacy against the B.1.1.7 variant.^{36*}

- Preliminary Novavax results from the South Africa cohort (n >4,400) showed efficacy of 60% in the HIV-negative study population vs. 49% in the overall study population, with 29 COVID-19 cases observed in the placebo group vs. 15 in the vaccine group. Among 27 of the 44 cases with sequence data, mutations consistent with the B.1.351 variant were detected in 25 (93%).^{36*}

Johnson & Johnson

- Preliminary analysis of the ENSEMBLE trial reported the efficacy of single-dose vaccination with the Johnson & Johnson vaccine was lower among trial participants in South Africa (57%) than at sites in Latin America (66%) and the US (72%) in the setting of B.1.351 emergence in South Africa.^{37*}

Oxford – AstraZeneca

- The efficacy the ChAdOx1 nCoV-19 vaccine against the B.1.1.7 variant of SARS-CoV-2 was similar to the efficacy against parent lineages, with 74% efficacy (95% CI, 42-89%) against B.1.1.7 compared to 84% efficacy (95% CI, 71-91%) against non- B.1.1.7 lineages.^{38*}

Implications of variants for diagnostic testing

- A potential consequence of emerging variants is the ability to evade detection by specific viral diagnostic tests. CDC reports that most commercial RT-PCR-based tests have multiple targets to detect the virus, so that even if a mutation impacts one of the targets, the other RT-PCR targets will still work.¹
- There is minimal impact on the performance of antigen-based tests (including rapid lateral flow devices) and there has been no impact on the performance of serological antibody tests reported on these variants.³⁹
- The World Health Organization advises laboratories using S-gene based assays to monitor for dropout and consider implementing assays specific for other genomic targets (e.g., E or RdRP genes) if not already included as part of the existing panel.⁴⁰
- Lineage B.1.1.7 (a.k.a. variant 20I/501Y.V1 or VOC 202012/01):
 - Minimal impact on performance of molecular diagnostics (69–70 deletion causes S gene dropout).⁴¹
 - A UK government assessment found that all five SARS-CoV-2 rapid antigen tests evaluated (Abbott Panbio, Fortress, Innova, Roche/SD Biosensor nasal swab, and Surescreen) were able to successfully detect the variant.⁴²
 - Abdel-Sater et al. reported the development of a rapid molecular test to identify the SARS-CoV-2 B.1.1.7 variant using a set of RT-PCR primers that were designed to confirm the deletion mutations $\Delta 69/\Delta 70$ in the spike and the $\Delta 106/\Delta 107/\Delta 108$ in the NSP6 gene. The large-scale screening method may help bypass the need for widespread sequencing to confirm the presence of both the B.1.1.7 variant and variants with similar deletions.^{43*} (Summarized Jan 29)
- Lineage B.1.351 (a.k.a. variant 20H/501Y.V2):
 - We did not find data on assay performance impact yet, but there is potential of impacting assays that target S gene sequences.

Current variants and clinical severity

- The UK New and Emerging Respiratory Virus Threats Advisory Group reported on January 21, 2021 that the B.1.1.7 SARS-CoV-2 variant quickly became dominant in the UK, and it is

possible that infection with this variant is associated with increased risk of death. The statement cites evidence of increased case fatality from several independent UK studies of samples with s-gene target failure, a proxy for the B.1.1.7 variant.^{44*}

- Further evidence was published on February 3 in a pre-print by Davies et al. reporting that the B.1.1.7 variant may increase the risk of death by 30%, based on an analysis of SARS-CoV-2 community test results in the UK that identified B.1.1.7-associated infections using S gene target PCR failure.^{45*}
- An earlier analysis found that patients with the B.1.1.7 were equally likely to be asymptomatic.^{46*}
- An analysis found no association between the proportion of the SARS-CoV-2 variant B.1.1.7 in circulation in the UK and reported disease severity, according to data obtained from reporting of symptoms and test results via the COVID Symptom Study application.^{47*}

Resources for tracking

- The World Health Organization (WHO) publishes weekly COVID-19 [situation reports](#) with global epidemiological and operational updates, including special coverage on novel variants. Additionally, WHO has a [summary](#) of SARS-CoV-2 variants through 12/31/2020.
- In addition to providing updated COVID-19 guideline, the US Centers for Disease Control and Prevention (CDC) has a periodically updated [page](#) on emerging SARS-CoV-2 variants.
- [GISAID](#) a global science initiative that provides open-access genomic data of influenza viruses and SARS-CoV-2. [CoVsurver](#) is a tool that allows users to perform mutation analyses based on input sequences compared to a reference strain.
- [Nextstrain](#) is an open-source project to harness the scientific and public health potential of pathogen genome data. Nextstrain provides a continually updated view of publicly available SARS-CoV-2 data and includes SARS-CoV-2 [resources](#) as well as [FAQs](#) on COVID-19.

Table: Key characteristics of novel SARS-CoV-2 variants

Variant Name	Identification Date	Locations of Emergence	Key Mutations	Relative Transmissibility	Vaccine Efficacy
D614G spike protein substitution	February 2020	China; Germany	The spike protein D614G amino acid change is caused by an A-to-G nucleotide substitution at position 23,403 in the Wuhan reference strain	G614 mutant of SARS-CoV-2 is 31% more transmissible than the D614 wildtype ¹¹	D164G SARS-CoV-2 was the dominant pandemic strain during the Moderna and Pfizer/BioNTech trials.
'Cluster 5' variant	November 2020	Denmark	Causes 3 amino-acid changes and two deletions in the spike	Not quantified. A WHO post from December 3, 2020 suggests that there is an increased risk of COVID-19 among people involved in mink farming. ¹⁶	Preliminary findings: Antibodies from some people who had recovered from COVID-19 found it more difficult to recognize the Cluster-5 variant than to spot coronaviruses that did not carry these mutations. ¹² The potential for mink to act as a reservoir for ongoing SARS-CoV-2 transmission led to a decision in early November, 2020 to cull all farmed mink in Denmark. ¹⁶
Lineage B.1.1.7 (a.k.a. variant 20I/501Y.V1 or VOC 202012/01)	October 2020	United Kingdom	N501Y: A mutation in the receptor binding domain (RBD) of the spike protein at position 501, where the amino acid asparagine (N) has been replaced with tyrosine (Y). 69/70 deletion: Occurred spontaneously many times and likely leads to a conformational change in the spike protein. P681H: Near the S1/S2 furin cleavage site, a site with high variability in coronaviruses. This mutation has also emerged spontaneously multiple times.	56% (range 50-74%) more transmissible than earlier strains. ¹⁸	The mRNA-1273 (Moderna) vaccine showed no significant reduction in neutralization activity against the SARS-CoV-2 B.1.1.7 variant. ³⁴ Novavax reported that its NVX-CoV2373 vaccine has an estimated 85.6% efficacy against the B.1.1.7 variant. ³⁶ The Oxford-AstraZeneca vaccine was reported to have 74% efficacy against B.1.1.7 compared to 84% efficacy against non- B.1.1.7 lineages. ³⁸
Lineage B.1.351 (a.k.a. variant 20H/501Y.V2)	December 2020 ⁹	South Africa	This variant has multiple mutations in the spike protein, including K417T, E484K, N501Y. Unlike the B.1.1.7 lineage detected in the UK, this variant does not contain the deletion at 69/70.	Not quantified. Tegally et al. 2020 report that this variant became the dominant strain in by early November 2020 in the Eastern Cape and Western Cape Provinces of South Africa. "Whilst the full significance of the	The mRNA-1273 (Moderna) vaccine showed reduced activity against the B.1.351 variant emerging from South Africa. ³⁴ Preliminary Novavax results from the South Africa cohort showed efficacy of 60% in the HIV-negative study population vs. 49.4% in the overall study

				mutations is not yet clear, the genomic and epidemiological data suggest increased transmissibility associated with the virus.” ⁹	population. Among 27 of the 44 cases with sequence data, mutations consistent with the B.1.351 variant were detected in 25 (93%). ³⁶
Variant P.1 (a.k.a. 20J/501Y.V3 or descendent from B.1.1.28)	December 2020 ²¹	Brazil	This variant contains three mutations in the spike protein receptor binding domain: K417T, E484K, and N501. ¹	Not quantified. CDC reports, “There is evidence to suggest that some of the mutations in the P.1 variant may affect its transmissibility and antigenic profile, which may affect the ability of antibodies generated through a previous natural infection or through vaccination to recognize and neutralize the virus.” ¹	Vaccine efficacy has not been reported for this strain as of the date of this report, but there is potential for this strain also to show reduced vaccine efficacy because it contains the same three spike protein mutations as lineage B.1.351.
CAL.20C	July 2020	California	Defined by five mutations: ORF1a: I4205V, ORF1b: D1183Y, S: S13I, S: W152C, S: L452R (Zhang et al., 2021)	Not quantified.	Not reported.

Annotated Bibliography

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Korber *et al.* present evidence that SARS-CoV-2 viruses with the G614 mutation in the Spike protein are more prevalent than the original D614 form identified in the first human cases in Wuhan, China. In a follow-up study of 999 COVID-19 patients at the Sheffield Teaching Hospitals, patients infected with G614 shed more viral nucleic acid compared with those with D614 ($p=0.037$), and G614-viruses show significantly higher infectious titers *in vitro* than their D614 counterparts (2.6- to 9.3-fold increase, $p<0.0001$).

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[*pre-print, not peer reviewed*] McNamara *et al.* demonstrated SARS-CoV-2 evolution in a suburban Southern US region using high-density amplicon sequencing of 175 symptomatic cases. The presence of spike D614G variant, a mutation implicated in higher pathogenicity of the virus, was observed among 57% of strains and was associated with a higher genome copy number ($p<0.002$). The single nucleotide variant pattern is consistent with the idea that SARS-CoV-2 was introduced into North Carolina by travelers from the continental US. No strain had mutations in the target sites used in common diagnostic assays.

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[Pre-print, not peer-reviewed] The SARS-CoV-2 lineage carrying the amino acid change D614G has become the dominant variant in the global COVID-19 pandemic. A study using epidemiological data and phylogenetic data (35,377 sequences) estimated that the G614 mutant of SARS-CoV-2 is 31% more transmissible than the D614 wildtype.
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Serologic and phylogenetic investigation of three mink farms in Denmark indicate rapid SARS-CoV-2 transmission among mink, as well as human-to-mink and mink-to-human transmission. Samples from 30 mink on 3 farms indicate that seroprevalence ranged from 66% to >95%, with one mink farm jumping from 3% to >95% within 8 days. Sequencing of SARS-CoV-2 samples from each mink farm suggests a human index case in one mink farm, followed by mink-to-human transmission, which spread to mink in other farms via human-to-human transmission.
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[Pre-print, not peer-reviewed] The receptor binding domain (RBD) of the 501Y.V1 SARS-CoV-2 variant (first identified in the UK) has around a 10-times higher binding affinity for human ACE2 than the RBD of the parent N501 strain, suggesting a potential mechanism for the higher rate of contagiousness observed with this strain. Sera collected from individuals immunized with the Pfizer-BioNTech vaccine could block the binding of Y501-RBD to ACE2, albeit to a slightly lesser degree than wild type. The therapeutic antibody bamlanivimab, however, bound the Y501-RBD as efficiently as the N501-RBD.
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[pre-print; not peer-reviewed] A mathematical modeling study for 3 regions in England estimated that the novel SARS-CoV-2 variant, VOC 202012/01, is 56% (range 50-74%) more transmissible than earlier strains. The analysis incorporated testing data and cell phone data to estimate population movements in order to assess for the contribution of behavioral change as an alternate explanation for increased spread of SARS-CoV-2 in these regions. The analysis did not find evidence for differences in mobility and contact patterns to explain differences in prevalence of the variant, but found that a modeling scenario incorporating higher transmissibility of the variant strain was the best fit to data observed in these regions. <https://doi.org/10.1101/2020.12.24.20248822>

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A more highly transmissible variant of SARS-CoV-2, lineage B.1.1.7, has been confirmed to have caused 76 cases in at least 10 states in the US as of January 13, 2021. Models suggest that this variant has potential to drive a new phase of exponential growth in cases in the US, and that even if vaccination protects against infection, substantial transmission of the variant will continue until it becomes the dominant strain. Although there is no known difference in clinical outcomes associated with the B.1.1.7 variant, a higher rate of transmission will lead to more cases, strain on healthcare systems, and deaths. The authors recommend urgent mitigation efforts, including physical distancing and masking, to limit the spread of the variant and allow more time for ongoing vaccination to achieve higher population-level immunity.

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Despite a high SARS-CoV-2 seroprevalence of 76% among blood donors in Manaus, Brazil by October 2020, the area experienced a sudden rise in COVID-19 hospitalizations from 552 in December 2020 to 3,431 in January 2021. The authors suggest possible explanations for the resurgence in this setting where seroprevalence was higher than common estimates of the herd immunity threshold, including overestimating seroprevalence, waning immunity, introduction of new variants capable of escaping prior infection, and circulation of variants with higher inherent transmissibility.

Sabino *et al.* (Jan 27, 2021). Resurgence of COVID-19 in Manaus, Brazil, despite High Seroprevalence. *The Lancet*. [https://doi.org/10.1016/S0140-6736\(21\)00183-5](https://doi.org/10.1016/S0140-6736(21)00183-5)

23. Zhang, W. *et al.* Emergence of a novel SARS-CoV-2 strain in Southern California USA. *medRxiv* (2021) doi:10.1101/2021.01.18.21249786.

[pre-print, not peer reviewed] A novel SARS-CoV-2 strain, CAL.20C, emerging from Southern California, was detected through genome sequence analysis. The strain's increasing dominance has coincided with an increased positivity rate in that region. While first observed in July, CAL.20C accounted for 24% of cases by December 2020. CAL.20C is characterized by multiple mutations in the spike protein, similar to variants emerging from the UK and South Africa. Though predominant in Southern California, CAL.20C has been isolated in samples from New York and Washington DC.

<https://doi.org/10.1101/2021.01.18.21249786>

24. Greaney, A. J. *et al.* Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies. *bioRxiv* (2021) doi:10.1101/2020.12.31.425021.

[Pre-print, not peer reviewed] Mutations in three main epitopes of the SARS-CoV-2 spike receptor-binding domain (RBD) affect neutralizing activity of convalescent polyclonal serum. Mutations that affect neutralizing activity usually occur at only a few sites and mutations occurring at the E484 site had the largest average effect with a >10-fold reduction in the neutralization activity from some donors. This mutation has been described in recent lineages from South Africa. Of note, the authors found substantial variation in the impact of mutations on the neutralization potential of polyclonal serum both between individuals and within the same individual over time. No mutations eliminated neutralization.

<https://doi.org/10.1101/2020.12.31.425021>

25. Wibmer, C. K. *et al.* SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma. *bioRxiv* (2021) doi:10.1101/2021.01.18.427166.
26. Cele, S. *et al.* Escape of SARS-CoV-2 501Y.V2 variants from neutralization by convalescent plasma. *medRxiv* 2021.01.26.21250224 (2021) doi:10.1101/2021.01.26.21250224.
27. Wang, P. *et al.* Increased Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 to Antibody Neutralization. *bioRxiv* (2021) doi:10.1101/2021.01.25.428137.

[Pre-print, not per-reviewed] The SARS-CoV-2 variant B.1.1.7 (UK) was resistant to neutralization by several monoclonal antibodies (mAbs) targeting either the N-terminal domain (NTD) of the virus's spike protein or its receptor-binding domain (RBD). This variant was also modestly more resistant to neutralization with convalescent plasma (about 3 fold) and sera from people who had received the Pfizer or Moderna vaccines (about 2 fold). The B.1.351 (South Africa) variant resisted neutralization by most NTD mAbs, multiple individual mAbs directed against the RBD, convalescent plasma (about 11-33 fold), and sera from vaccinated people (about 6.5-8.6 fold). The authors note that loss of neutralizing activity against the B.1.1.7 variant is unlikely to have an adverse impact, while the reduction in activity levels against the B.1.351 variant were potentially concerning.

<https://doi.org/10.1101/2021.01.25.428137>

28. Muir, L. *et al.* Impact of the B.1.1.7 variant on neutralizing monoclonal antibodies recognizing diverse epitopes on SARS-CoV-2 Spike. *bioRxiv* (2021) doi:10.1101/2021.02.03.429355.

[Pre-print, not peer reviewed] The SARS-CoV-2 B.1.1.7 variant (first identified in the UK) was shown to reduce neutralizing activity of monoclonal antibodies (mAbs) targeting subdominant epitopes in the SARS-CoV-2 spike protein. In particular, the B.1.1.7 (UK) variant reduced neutralizing activity of mAbs specific to the N-terminal domain (NTD) by up to 16-fold. NTD-specific mAbs consisted of roughly a third of mAbs isolated from three convalescent donors and only 29% of NTD-specific mAbs showed neutralizing activity. In contrast, only small reductions in neutralization by mAbs specific to the dominant epitope receptor-binding domain (RBD) were observed.

<https://doi.org/10.1101/2021.02.03.429355>

29. Goldman, J. D. *et al.* Reinfection with SARS-CoV-2 and Failure of Humoral Immunity a case report. *medRxiv* (2020) doi:10.1101/2020.09.22.20192443.
30. Harrington, D. *et al.* Confirmed Reinfection with SARS-CoV-2 Variant VOC-202012/01. *Clin. Infect. Dis.* (2021) doi:10.1093/cid/ciab014.
31. Vasques Nonaka, C.K.; Miranda Franco, M.; Gräf, T.; Almeida Mendes, A.V.; Santana de Aguiar, R.; Giovanetti, M.; Solano de Freitas Souza, B. Genomic Evidence of a Sars-Cov-2 Reinfection Case With E484K Spike Mutation in Brazil. *Preprints* (2021) doi:doi: 10.20944/preprints202101.0132.v1.
32. Collier, D. *et al.* Impact of SARS-CoV-2 B.1.1.7 Spike variant on neutralisation potency of sera from individuals vaccinated with Pfizer vaccine BNT162b2. *medRxiv* (2021) doi:10.1101/2021.01.19.21249840.

[pre-print, not peer reviewed] Sera from participants who received the first dose of the Pfizer vaccine BNT162b2 three weeks prior had no reduction in neutralizing activity against a pseudovirus with the three key spike protein mutations (N501Y, A570D, and 69/70 deletion) in the SARS-CoV-2 B.1.1.7 variant with higher transmission potential, compared to the wild-type SARS-CoV-2 strain. However, among 15 participants with neutralization activity three weeks after the Pfizer vaccine, 10 showed evidence of reduction in efficacy of antibodies against the B.1.1.7 mutant and neutralization titers were reduced up to 6-fold (median 3.85-fold) against the full set of 8 spike protein mutations present in the B.1.1.7 variant.

<https://doi.org/10.1101/2021.01.19.21249840>

33. Xie, X. *et al.* Neutralization of spike 6970 deletion E484K and N501Y SARS-CoV-2 by BNT162b2 vaccine-elicited sera. *bioRxiv* (2021) doi:10.1101/2021.01.27.427998.

Sera from recipients who completed the 2-dose regimen of the Pfizer vaccine BNT162b2 (n=20) had similar neutralizing geometric mean titers (GMTs) against SARS-CoV-2 viruses engineered to contain key spike protein mutations from variants emerging from the UK (B.1.1.7) and South Africa (B.1.351) compared to GMTs against the wild-type virus. Compared to the GMTs against the wild-type virus, GMTs against viruses with the N501Y mutation (present in both variants) and the key B.1.1.7 mutations (Δ 69/70+N501Y+D614G) were 1.46- and 1.41-fold higher, respectively. In contrast, GMTs against the key B.1.351 mutations (E484K+N501Y+D614G) were 19% lower than wild-type. The authors note that the engineered viruses do not contain the full set of mutations present in variants B.1.1.7 and B.1.351.

<https://doi.org/10.1101/2021.01.27.427998>

34. Wu, K. *et al.* mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. *bioRxiv* 2021.01.25.427948 (2021) doi:10.1101/2021.01.25.427948.
[Pre-print, not peer-reviewed] Sera from human subjects or non-human primates (NHPs) that received the mRNA-1273 (Moderna) vaccine showed no significant reduction in neutralization activity against the SARS-CoV-2 B.1.1.7 variant emerging from the UK, but reduced activity against the B.1.351 variant emerging from South Africa. The study used two pseudovirus neutralization assays expressing spike proteins of different SARS-CoV-2 variants, and found that pseudoviruses with spike containing K417N-E484K-N501Y-D614G and full B.1.351 mutations resulted in 2.7 and 6.4-fold geometric mean titer (GMT) reduction, respectively, when compared to the D614G pseudovirus. The GMT of these human sera to the full B.1.351 spike variant was 1/290; all evaluated sera were able to fully neutralize.
<https://doi.org/10.1101/2021.01.25.427948>
35. Cheng, K. *et al.* SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral Spike vaccines. *bioRxiv* (2021) doi:10.1101/2021.01.27.428516.
[Pre-print, not peer-reviewed] Using a lentivirus-based pseudovirus assay, the SARS-CoV-2 B.1.1.7 (UK) variant was shown to exhibit only modestly reduced susceptibility to neutralization from convalescent sera (1.5-fold average reduction) and sera from recipients of both the Moderna and Novavax vaccine phase 1 studies (2-fold average reduction after two inoculations. The authors used the prototypic D614G variant as a comparator.
<https://doi.org/10.1101/2021.01.27.428516>
36. Novavax. *Novavax COVID-19 Vaccine Demonstrates 89.3% Efficacy in UK Phase 3 Trial.* <https://ir.novavax.com/node/15506/pdf> (2021).
[Press release, not peer-reviewed] Preliminary results for phase 2/3 trials for the recombinant protein-based COVID-19 vaccine NVX-CoV2373 made by Novavax showed up to 89.3% efficacy in the UK cohort (n= >15,000), where 56 participants in the placebo group developed COVID-19 vs 6 in the vaccine group. Of note, the B.1.1.7 variant was observed in 32 of the COVID-19 cases, yielding an estimate of 85.6% efficacy against the variant. Preliminary results from the South Africa cohort (n= >4,400) showed efficacy of 60% in the HIV-negative study population vs. 49.4% in the overall study population, with 29 COVID-19 cases observed in the placebo group vs. 15 in the vaccine group. Among 27 of the 44 cases with sequence data, mutations consistent with the B.1.351 variant were detected in 25 (93%). Approximately 1/3 of patients in the South Africa cohort (but not included in the preliminary results) were seropositive at baseline, indicating prior COVID-19 infection.
<https://ir.novavax.com/node/15506/pdf>
37. Johnson & Johnson. Johnson & Johnson Announces Single-Shot Janssen COVID-19 Vaccine Candidate Met Primary Endpoints in Interim Analysis of its Phase 3 ENSEMBLE Trial. *Johnson & Johnson* (2021).
[Press release, not peer-reviewed] The Johnson and Johnson single-dose COVID-19 candidate vaccine had 66% efficacy against moderate to severe COVID-19, based on a press release describing the phase 3 clinical trial results from the ENSEMBLE trial. Among all participants including those infected with an emerging viral variant the vaccine prevented moderate to

severe COVID-19 28 days after vaccination with the first evidence of protection observed as early as day 14. The level of protection against moderate to severe COVID-19 infection was 72% in the United States, 66% in Latin America, and 57% in South Africa 28 days post-vaccination. <https://www.nj.com/johnson-johnson-announces-single-shot-janssen-covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-ensemble-trial>

38. Emary, K. R. W. *et al.* Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 VOC. *SSRN* **19**, 1–40.

The efficacy the ChAdOx1 nCoV-19 vaccine (Oxford-AstraZeneca; AZD1222) against the B.1.1.7 variant of SARS-CoV-2 was similar to the efficacy against parent lineages, with 74% efficacy (95% CI, 42-89%) against B.1.1.7 compared to 84% efficacy (95% CI, 71-91%) against non- B.1.1.7 lineages. Vaccine-induced antibodies had an approximately nine-fold reduction in neutralization activity against the B.1.1.7 variant compared to a canonical non-B.1.1.7 lineage in a live-virus neutralization assay.

All participants received weekly nasal swabs for surveillance. Among those vaccinated with ChAdOx1 who subsequently became infected with SARS-CoV-2, both the duration of shedding and viral load was lower than among control participants. The authors suggest that this may result in a lower potential for transmission with vaccination.

<https://ssrn.com/abstract=3779160>

39. FIND. Novel variants of SARS-CoV-2 and the impact on diagnostic testing. <https://www.finddx.org/covid-19/novel-variants/> (2021).
40. World Health Organization. *Molecular assays to diagnose COVID-19: Summary table of available protocols*. <https://www.who.int/publications/m/item/molecular-assays-to-diagnose-covid-19-summary-table-of-available-protocols> (2020).
41. Public Health England. *Investigation of novel SARS-COV-2 variant: Technical briefing 1*. <https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201> (2020).
42. Public Health England. *SARS-CoV-2 lateral flow antigen tests: evaluation of VUI-202012/01*. <https://www.gov.uk/government/publications/sars-cov-2-lateral-flow-antigen-tests-evaluation-of-vui-20201201/sars-cov-2-lateral-flow-antigen-tests-evaluation-of-vui-20201201> (2020).
43. Abdel-Sater, F. *et al.* A Rapid and Low-Cost protocol for the detection of B.1.1.7 lineage of SARS-CoV-2 by using SYBR Green-Based RT-qPCR. *medRxiv* (2021) doi:10.1101/2021.01.27.21250048.

[Pre-print, not peer-reviewed] Abdel-Sater *et al.* reported the development of a rapid molecular test to identify the SARS-CoV-2 B.1.1.7 (UK) variant using a set of RT-PCR primers that were designed to confirm the deletion mutations $\Delta 69/\Delta 70$ in the spike and the $\Delta 106/\Delta 107/\Delta 108$ in the NSP6 gene. The large-scale screening method may help bypass the need for widespread sequencing to confirm the presence of both the B.1.1.7 variant and variants with similar deletions.

<https://doi.org/10.1101/2021.01.27.21250048>

44. Horby, P. *et al.* NERVTAG note on B.1.1.7 severity. 1–8 (2021).

[Report, not peer-reviewed] The UK New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) states the B.1.1.7 SARS-CoV-2 variant has quickly become dominant in the UK, and that there is a possibility that infection with this variant is associated with increased risk of death compared to previous strains. NERVTAG cites evidence of increased case fatality from several independent UK studies of samples with s-gene target failure, a proxy for the B.1.1.7 variant. The COVID Clinical Information Network has not found evidence of increased hospital case fatality with this variant.
<https://www.gov.uk/government/publications/nervtag-paper-on-covid-19-variant-of-concern-b117>

45. Davies, N. G. *et al.* Increased hazard of death in community-tested cases of SARS-CoV-2 Variant of Concern 20201201. *medRxiv* (2021) doi:10.1101/2021.02.01.21250959.

[Pre-print, not peer reviewed] The SARS-CoV-2 B.1.1.7 variant (first identified in the UK) was estimated to increase the risk of death by 30%, based on an analysis of a database of SARS-CoV-2 community test results in the UK. This dataset represents approximately 47% of all SARS-CoV-2 community tests and 7% of COVID-19 deaths in England from September 1, 2020 to January 22, 2021. The authors identified B.1.1.7-associated infections using S gene target PCR failure.
<https://doi.org/10.1101/2021.02.01.21250959>

46. Walker, A. S. *et al.* Increased infections, but not viral burden, with a new SARS-CoV-2 variant. *medRxiv* 2021.01.13.21249721 (2021) doi:10.1101/2021.01.13.21249721.

[Pre-print, not peer-reviewed] A large community surveillance study in the UK found evidence for increases in S-gene target failures (SGTF) of SARS-CoV-2, consistent with expansion of the B.1.1.7 variant, at a time in mid-November when non-SGTF strains were stable or declining. Data were analyzed from nose and throat swabs (n=1,553,687) collected from September 28, 2020 to January 2, 2021 and tested by RT-PCR. Rates of symptomatic SGTF infections were similar to asymptomatic SGTF infections, and the authors suggest that asymptomatic infections may contribute substantially to B.1.1.7 spread. SGTF positivity rates increased on average 6% more rapidly than rates of non-SGTF positives. Excess growth rates for SGTF vs non-SGTF positives were similar in those up to high school age (5%) and older individuals (6%).
<https://doi.org/10.1101/2021.01.13.21249721>

47. Graham, M. S. *et al.* The effect of SARS-CoV-2 variant B.1.1.7 on symptomatology re-infection and transmissibility. *medRxiv* (2021) doi:10.1101/2021.01.28.21250680.

[Pre-print, not peer-reviewed] No association was found between the proportion of the UK SARS-CoV-2 variant B.1.1.7 in circulation and reported disease severity, according to data obtained from reporting of symptoms and test results via the COVID Symptom Study application. The authors controlled for both demographic characteristics (age, sex) and seasonal variables (temperature, humidity). No effects were observed based on the number of different reported symptoms, hospitalizations, frequency any of the individual symptoms, or the proportion of individuals with long symptom duration (≥ 28 days). The proportion of individuals with duration of symptoms ≥ 28 days did not change in association with the presence

of the B.1.1.7 variant. The proportion of users with asymptomatic disease did not significantly change as B.1.1.7 increased in prevalence.

<https://doi.org/10.1101/2021.01.28.21250680>