Public Health England

Protecting and improving the nation's health

Investigation of SARS-CoV-2 variants of concern in England

Technical briefing 6

13 February 2021

This briefing provides an update on previous briefings up to 1 February 2021

Contents

Summary

There are 4 variants of concern, designated:

- **VOC 202012/01** (B.1.1.7), first detected in Kent England is predominant in all regions and is circulating in multiple countries
- **VOC 202102/02** (B.1.1.7 cluster with E484K mutation), first detected in South West England has been detected in 23 cases
- **VOC 202012/02** (B.1.351), first detected in South Africa, 126 case have been detected in England with evidence of in country transmission. Local testing is underway and links between cases are being investigated
- **VOC 202101/02** (P.1), first detected in Brazil has not been detected in the UK

Nomenclature of variants in the UK

SARS-CoV-2 variants if considered to have concerning epidemiological, immunological or pathogenic properties are raised for formal investigation. At this point they are designated Variant Under Investigation (VUI) with a year, month, and number. Following risk assessment with the relevant expert committee, they may be designated Variant of Concern (VOC).

Variant surveillance overview UK

Data on variants of concern is updated twice weekly online. Total case numbers per VOC as of 10 February 2021 are shown in Table 1.

Table 1. Total case numbers England per VOC as of 10 February 2021

		England genomic cases 10 February 2021		
Variant	**Pangolin lineage**	**confirmed**	**probable**	**total confirmed and probable**
VOC 202012/01	B1.1.7	50,148	5,774	55,922
VOC 202102/02	B.1.1.7 with E484K cluster	23	0	23
VOC 202012/02	B.1.351	126	56	182
VOC 202101/02	P1	0	0	0

VOC 202012/01 (B.1.1.7)

This variant was designated VUI 202012/01 (B.1.1.7) on detection and on review re-designated as VOC 202012/01 (B.1.1.7) on 18 December 2020.

Genomic profile

Lineage defining mutations are shown in Table 2a/b. In addition, VOC 202012/01 has acquired other mutations in some cases. Mutation counts in the UK dataset are shown in Table 2c.

Table 2a. VOC 202012/01 (B.1.1.7) Variant defining mutations. Insertions and deletions (shaded in orange) are not currently included in variant definitions

Gene	amino_acid	actual_nucleotide
S Gene	H69_V70del	21765_21770del
	Y144del	21991_21993del
	N501Y	23063A>T
	A570D	23271C>A
	P681H	23604C>A
	T716I	23709C>T
	S982A	24506T>G
	D1118H	24914G>C
ORF1ab	T1001I	3267C>T
	A1708D	5388C>A
	I2230T	6954T>C
	3675-3677del	11288_96del
ORF8	Q27*	27972C>T
	R52I	28048G>T
	Y73C	28111A>G
N Gene	D3L	28280_2delinsCTA

Table 2b. VOC 202012/01 (B.1.1.7) Genomic case definition

CONFIRMED	All lineage defining non-synonymous changes called as alternate base
PROBABLE	At least 5 lineage defining non-synonymous changes called as alternate base and all other positions either N or mixed base
LOW_QC	Fewer than 5 lineage defining non-synonymous changes called as alternate base and all other positions either N or mixed base

Table 2c. VOC 202012/01 (B.1.1.7) Spike mutations acquired in addition to the variant defining mutations 9 November 2020 to 8 February 2021

VOC 202012/01 (B.1.1.7) Spike variants				
Amino acid change	**Total number of instances in VOC 202012/01 (B.1.1.7) (UK data)**	**12 November 2020 to 11 December 2020**	**12 December 2020 to 11 January 2021**	**12 January 2021 to 11 February 2021**
L18F	1,844 (2.7%)	8	353	867
Q677H	299 (<1%)	0	84	195
S494P	514 (<1%)	38	210	190
Y144F	207 (<1%)	8	120	65
A475A	47 (<1%)	0	13	27
T678I	56 (<1%)	0	23	25
S680F	36 (<1%)	0	12	20
E484K	33 (<1%)	1	11	19
F490S	25 (<1%)	0	9	16
Q677H (alt)	17 (<1%)	1	3	13
L455F	18 (<1%)	1	1	13
G142V	21 (<1%)	0	8	13
G446V	18 (<1%)	0	1	12
G142S	19 (<1%)	1	6	12
H146Y	22 (<1%)	0	8	12
A684V	27 (<1%)	0	9	11
R246K	16 (<1%)	1	5	10
K150E	10 (<1%)	0	0	10
Total VOC 202012/01 (B.1.1.7): 69,568				

Biological profile

VOC 202012/01 (B.1.1.7) can spread faster than some other SARS-CoV-2 virus variants currently circulating in the UK. At this time, available evidence suggests that VOC 202012/01 (B.1.1.7) is not strongly associated with antigenic escape from naturally-acquired immunity. Additionally, VOC 202012/01 (B.1.1.7) is not associated with significant antigenic escape from

vaccine-acquired immunity. VOC 202012/01 (B.1.1.7) mutations do confer escape from a subset of monoclonal antibodies that target the RBD and NTD.

Transmissibility

The VOC 202012/01 (B.1.1.7) appears to have increased transmissibility compared to previously circulating variants and has spread rapidly to become the dominant variant in the UK. Previous transmissibility assessments are available in NERVTAG papers and PHE technical briefings (secondary attack rate).

Escape from natural immunity

Changes in the genome of B.1.1.7 include changes in the spike glycoprotein. Mutation N501Y can result in decreased recognition by monoclonal antibodies that bind this epitope. Deletions in the N terminal domain at residues 69/70, and particularly 144 can results in decreased monoclonal antibody binding. Since convalescent sera and vaccine-derived antisera are polyclonal, these mutations usually do not result in consequential loss of serum neutralization. These mutations could though have large effects on efficacy of monocloncal antibodies used therapeutically if they specifically target these epitopes.

Severity of disease

Summary data and analyses on severity of disease associated with B.1.1.7 are available: NERVTAG including 11 February 2021 update on severity.

Epidemiological profile

Lineage B.1.1.7 is dispersed across the UK. Confirmed cases are those identified by whole genome sequencing. As of 10 February 2021, there were 55,922 confirmed and probable cases of VOC 202012/01 (B.1.1.7) in England.

Figure 1. Epidemic curve for confirmed VOC 202012/01 (B.1.1.7) cases by specimen date, 1 October 2020 to 10 February 2021

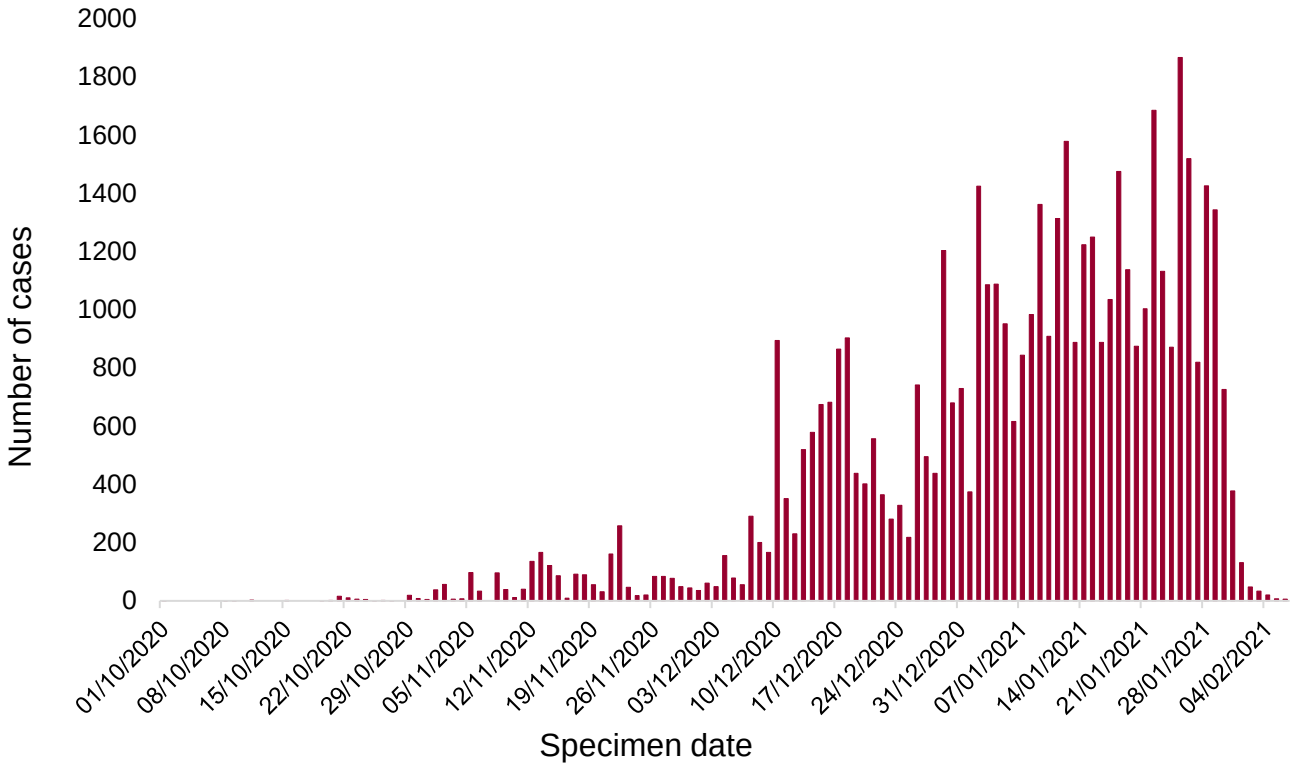


Figure 2. Age sex pyramid of VOC 202012/01 (B.1.1.7) cases, 1 October 2020 to 10 February 2021

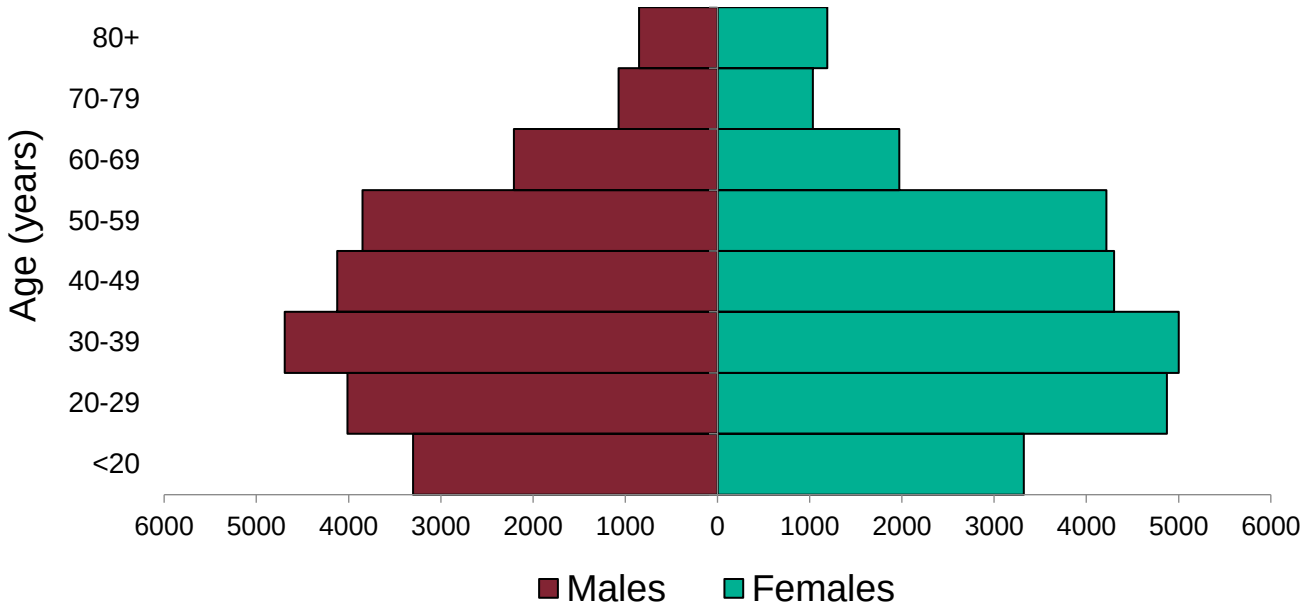


Table 3. Confirmed VOC 202012/01 (B.1.1.7) cases per region, 1 October 2020 to 10 February 2021

PHE Centre	VOC 202012/01 (B.1.1.7)		All sequenced	
	N	%	N	%
East Midlands	1,545	3.1	6,808	5.2
East of England	5,934	11.8	13,445	10.3
London	14,672	29.3	29,350	22.5
North East	2,202	4.4	8,194	6.3
North West	10,191	20.3	28,099	21.5
South East	7,720	15.4	14,630	11.2
South West	1,468	2.9	5,126	3.9
West Midlands	3,587	7.2	11,300	8.6
Yorkshire and Humber	2,471	4.9	13,657	10.5
TBC	358	0.7	77	0.1
Total	**50,148**		**130,686**	

S gene target failure/lineage correlation

The use of S gene target failure in the Taqpath assay as a good proxy for VOC 202012/01 (B.1.1.7) cases has been described in prior technical briefings. This continues to be supported by current data (Appendix 1). In samples tested with this assay in the Lighthouse Laboratories, samples with SGTF have predominated since mid December 2020, reaching 95.0% of cases in the week starting 7 February 2021. Proportions continue to rise by region (Appendix 1).

Hospitalisations

Assessment of hospitalisation is in process.

Deaths

1,072 deaths (within 28 days) of 50,148 confirmed cases have been reported in patients with VOC 202012/01 (B.1.1.7) as of 10 February 2021.

Cases in individuals who have been vaccinated

Assessment of vaccination data is in process.

International Epidemiology

As of the 10 February 2021 there are 90 countries/territories reporting cases of the UK variants globally. Of these, 7 report, or there is evidence of community transmission (Canada, Denmark, Ireland, Netherlands, Slovakia and USA), however for many countries the information available on the extent of transmission within the country is not always clear.

GISAID (gisaid.org) includes data on sequences available internationally; as of the 12 February 2021 6,982 cases of VOC202012/01 (B.1.1.7) other than those in the UK are listed (Argentina 1, Australia 84, Austria 233, Bangladesh 2, Belgium 579, Bosnia and Herzegovina 1, Brazil 19, Canada 61, Caribbean 3, Czech Republic 17, Democratic Republic of the Congo 2, Denmark 1,577, Ecuador 7, Finland 41, France 598, Gambia 3, Germany 92, Gibraltar 1, Greece 3, Hong Kong 4, Hungary 5, Iceland 20, India 32, Iran 1, Ireland 398, Israel 230, Italy 432, Jamaica 4, Japan 37, Jordan 42, Kuwait 1, Latvia 2, Luxembourg 32, Macedonia 2, Malaysia 2, Mayotte 18, Mexico 5, Netherlands 486, New Zealand 26, Nigeria 28, North Macedonia 3, Norway 51, Oman 1, Pakistan 2, Peru 1, Poland 10, Portugal 203, Romania 11, Singapore 45, Slovakia 69, Slovenia 1, South Africa 1, South Korea 13, Spain 468, Sri Lanka 2, St.Lucia 9, Sweden 64, Switzerland 245, Taiwan 1, Thailand 5, Trinidad and Tobago 1, Turkey 103, UAE 19, USA 522, Vietnam 1).

VOC 202102/02 (B.1.1.7 cluster with E484K)

Through routine scanning of variation in VOC 202012/01 (B.1.1.7) a small number of B.1.1.7 sequences (33 of 258504 sequences as of 11 February 2021), had acquired the spike protein mutation E484K. Information suggested more than one independent acquisition event and on investigation, this forms one predominant cluster and several separate cases or small clusters. The predominant cluster consists of 17 cases primarily in South West England, 6 elsewhere in England. This cluster was designated VUI on detection and on review re-designated as VOC 202102/02 (B.1.1.7 cluster with E484K) on 5 February 2021.

Genomic and biological profile

The cluster (VOC 202102/02 (B.1.1.7 cluster with E484K)) has the mutations previously described for VOC 202012/01 (B.1.1.7) with the addition of E484K in spike gene, L730F in orf1ab, and A173V, A398T in N gene in all cases. E484K is a mutation of concern with regards to antigenic change and receptor binding avidity, and is potentially more concerning when combined with N501Y. E484K is currently the mutation with most evidence of causing antigenic change. It arises in the presence of convalescent and vaccine-derived antisera. Several independent studies showing the impact of different antigenic variants have concluded E484K is among the single mutations with the greatest impact. Secondly, E484K is associated with increased binding to human ACE2, though it is unclear what impact this has on virus phenotype. Finally, E484K is associated with multiple variants of concern including the B.1.351 and P.1 lineages, as well as being identified as a long-term adaptation in several different immunocompromised patient studies. The other mutations specific to this cluster are not associated with any known phenotypic changes and are not present in other VOCs.

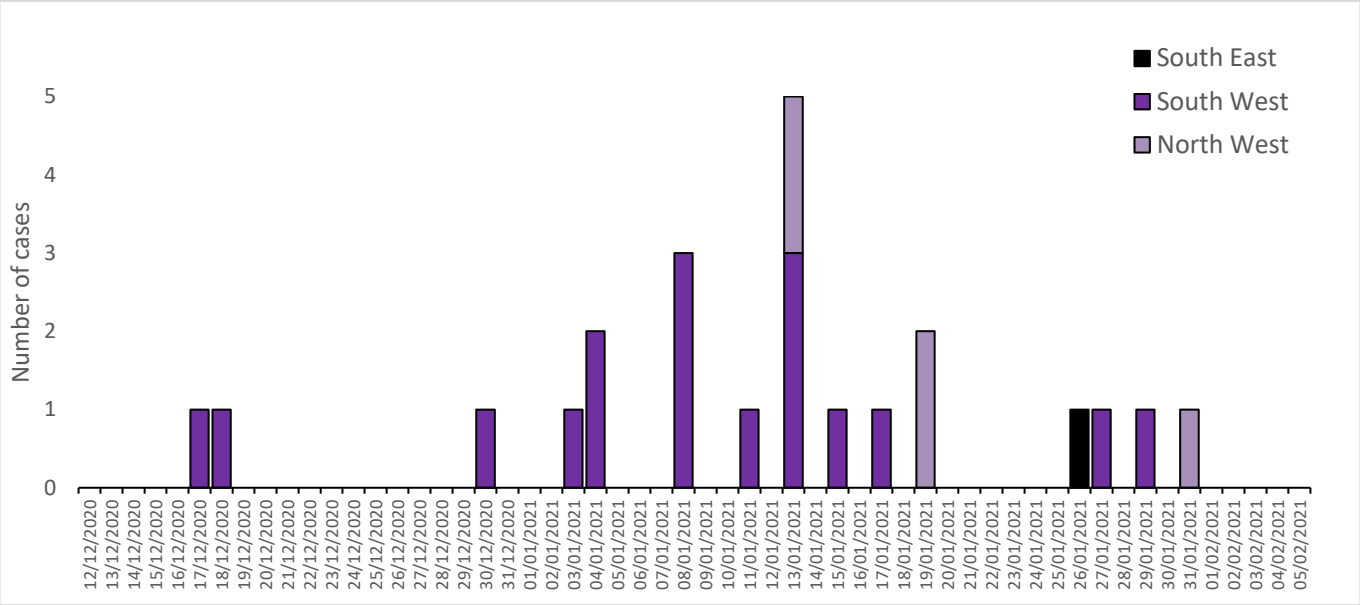
Epidemiological profile

As of 11 February 2021, there were 23 genomically confirmed cases, 17 with an epidemiological link to Bristol and an additional 6 cases elsewhere in England, with a specimen date range of 17 December 2020 to 31 January 2021. The epidemiological curve for confirmed cases is shown in Figure 3. Links between cases are being investigated.

Contact tracing and control measures

Contact tracing is ongoing. Large scale testing in impacted geographies has been implemented commencing on 7 February 2021. Identification of unlinked cases through Pillar 2 is limited by sequencing coverage and time lag of at least 2 weeks between isolation and genomic confirmation. The current number of confirmed cases with this mutation may be underestimated.

Figure 3. Epidemic curve for confirmed VOC 202102/02 (B.1.1.7 cluster with E484K) cases by specimen date, 12 December 2020 to 5 February 2021



Hospitalisations

Of 23 cases, data are available for 18, of which are none were hospitalised following their infection.

Deaths

Of 23 cases, data are available for 18, of which none have died.

Cases in individuals who have been vaccinated

Of 23 cases, data are available for 18, of which 1 was known to be vaccinated before the onset of infection (5 days prior).

International Epidemiology

International cases have not been reported.

VOC 202012/02 (B.1.351)

As of 10 February 2021, 126 confirmed and 56 probable cases of VOC 202012/02 (B.1.351, initially detected in South Africa) have been identified in England. This variant was designated VUI on detection and on review re-designated as VOC 202012/02 (B.1.351) on 24 December 2020.

Genomic profile

The VOC is lineage B1.351 (first sequence detected in South Africa in October 2020; and in the UK in December 2020). The complete mutation profile is shown in Table 4.

Table 4a. VOC 202012/02 (B.1.351) Variant defining mutations. Red text indicates acquisition in subset of isolates within the lineage

Gene	amino_acid	actual_nucleotide
S Gene	L18F	21614C>T
	D80A*	21801A>C
	D215G*	22206A>G
	R246I	22299G>T
	K417N*	22813G>T
	E484K*	23012G>A
	N501Y*	23063A>T
	A701V*	23664C>T
	242-244del	
ORF1ab	T265I	1059C>T
	K1655N*	5230G>T
	K3353R	10323A>G
	3675-3677del	11288_96del
ORF3a	Q57H	25563G>T
	S171L	25904C>T
E Gene	P71L*	26456C>T
N Gene	T205I*	28887C>T

Table 4b. VOC 202012/02 (B.1.351) Genomic case definitions

CONFIRMED	All lineage defining non-synonymous changes called as alternate base excluding those in red text in Table 4a
PROBABLE	At least 4 lineage defining non-synonymous changes called as alternate base and all other positions either N or mixed base OR at least 5 of the 9 non-synonymous changes indicated by * in the Table 4a
LOW_QC	Fewer than 4 lineage defining non-synonymous changes called as alternate base and all other positions either N or mixed base

Biological profile

This variant has 9 mutations associated with transmissibility and antigenic change, of which E484K and N501Y are most significant. The significance of E484K has been described previously in this briefing. Variants with the combined N501Y and E484K substitutions have been shown to have enhanced ACE2 receptor binding.

Escape from natural immunity

Multiple studies with pseudovirus and live virus neutralization assays indicate a significant loss of antibody binding and neutralization to B.1.351, both with convalescent, as well vaccine-derived polyclonal antisera.

Epidemiological profile

B1.351 is dispersed across the UK in low numbers. Confirmed cases are those identified by whole genome sequencing; probable cases are COVID-19 cases without sequencing, but who are contacts of confirmed cases. As of 10 February 2021, there are 126 confirmed cases of B.351.1 and 56 probable cases. For 18 cases, no travel link has been established indicating within country transmission. Identification of unlinked cases through Pillar 2 is limited by sequencing coverage and lag and cases are likely to be an underestimate.

Figure 4. Epidemic curve for confirmed VOC 202012/02 (B.1.351) cases by specimen date, 10 December 2020 to 10 February 2021 (7 cases are omitted without specimen date)

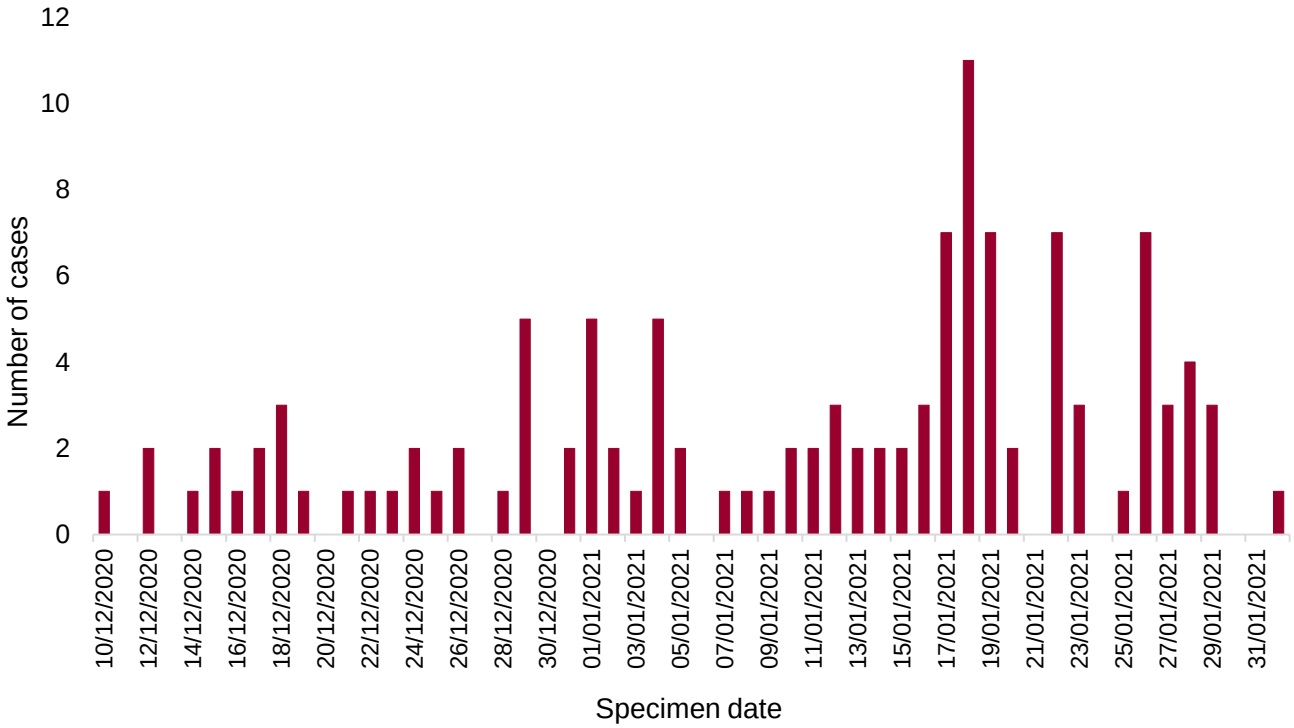


Figure 5. Age sex pyramid of VOC 202012/02 (B.1.351) confirmed cases, 10 December 2020 to 10 February 2021 (3 cases are omitted without age sex data)

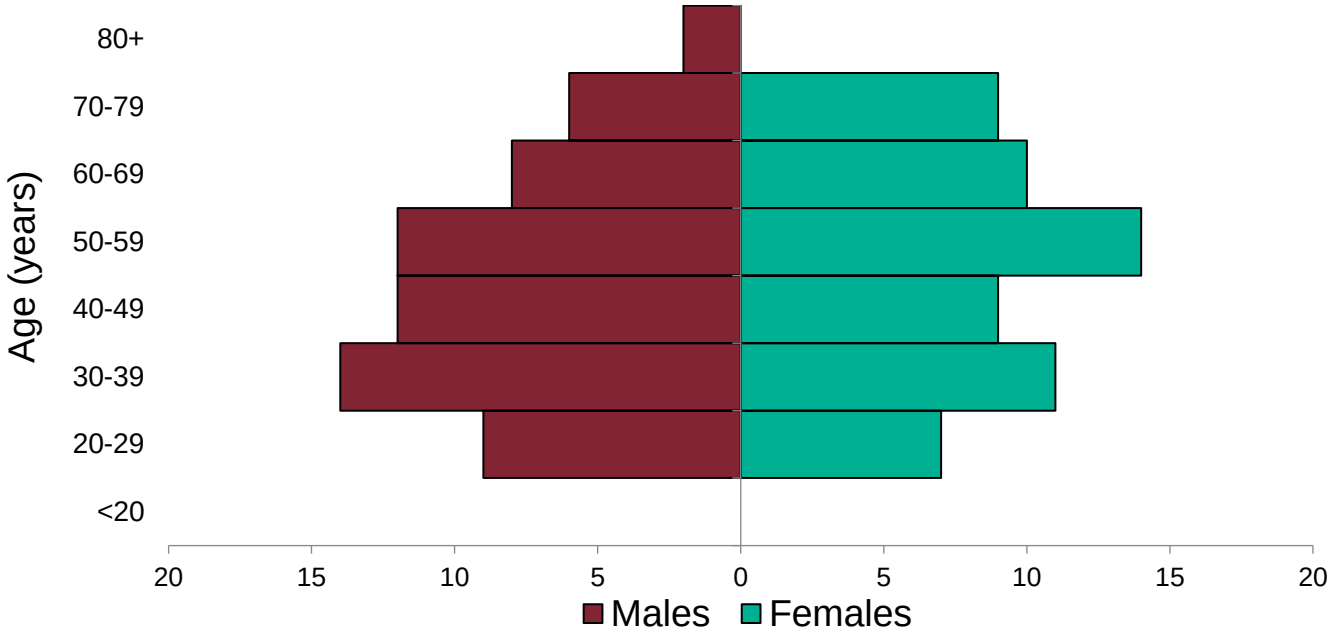


Table 5. Confirmed cases by region, 10 December 2020 to 10 February 2021

PHE Centre	VOC 202012/02 (B.1.351)		All sequenced	
	n	%	n	%
East Midlands	3	2.4	6,808	5.2
East of England	26	20.6	13,445	10.3
London	31	24.6	29,350	22.5
North East	2	1.6	8,194	6.3
North West	14	11.1	28,099	21.5
South East	30	23.8	14,630	11.2
South West	4	3.2	5,126	3.9
West Midlands	11	8.7	11,300	8.6
Yorkshire and Humber	5	4.0	13,657	10.5
TBC	0	0.0	77	0.1
Total	**126**		**130,686**	

Community prevalence studies

REACT study: Altogether 4 VOC 202012/02 (B.1.351) genomes were identified. SARS-COV-2 was detected in 2,282 of 167,642 samples during 6 to 22 January 2021. Of these, samples with CT values of 34 or less had sequencing attempted; 659 have available sequences, of which 4/659 are VOC 202012/02 (B.1.351) from East of England (2), London (1) and South East (1). All have sample dates between 7 to 11 January 2021. (Link to Study protocol.)

Office for National Statistics Survey

The ONS survey identified 2 cases of VOC 202012/02 (B.1.351) in samples from December 2020. A total of 1,816 sequences were available for 1 December 2020 to 20 January 2021.

Deaths

1 death (within 28 days) of 126 confirmed cases with data has been reported in patients with VOC 202012/02 (B.1.351) as of 10 February 2021.

Cases in individuals who have been vaccinated

Vaccination data is being assessed.

International Epidemiology

As of 10 February 2021 there are 40 countries (including the UK) that have reported cases of this variant globally.

As of 10 February 2021 the epidemiological profile in South Africa is as follows:

- The case incidence is continuing to decrease. Currently, the reported weekly incidence is 34.2 per 100,000 population. Weekly test positivity has also been decreasing with current test positivity of 9.7% (testing rates had increased over the period from around 2 per 1,000 population to over 6 per 1,000 population, although have declined slightly over the last 2 weeks to 3.5 per 1,000 population).
- The fatality rate is decreasing (the weekly fatality rate is 3.2 per 100,000 population).
- The number of patients in hospital and ICU has also reduced slightly. Currently, 1,839 COVID-19 patients are in ICU and 11,618 are in hospital.

GISAID (gisaid.org) includes data on sequences available internationally. As of the 12 February 2021 1,130 cases of VOC 202012/02 (B.1.351) are listed (Australia 17, Austria 3, Bangladesh 1, Belgium 59, Botswana 35, Canada 1, Denmark 7, Dominican Republic of the Congo 1, Finland 2, France 39, Germany 8, Ireland 10, Israel 7, Japan 5, Kenya 6, Luxembourg 2, Mayotte 23, Mozambique 42, Netherlands 31, New Zealand 7, Norway 1, Panama 1, Portugal 1, South Africa 749, South Korea 1, Spain 2, Sweden 1, Switzerland 23, Turkey 2, UAE 5, USA 7, Zambia 31).

VOC 202101/02 (P.1)

First identified in Japan amongst travellers from Brazil, the P.1 lineage is a descendant of B.1.1.28. This variant was designated VUI on detection and on review re-designated as VOC 202101/02 (P.1) on 13 January 2021.

Genomic profile

VOC 202101/02 (P.1) is part of a larger international cluster, designated Lineage P.1 (first sequence noted in GISAID from Brazil in December 2020) and contains 17 unique amino acid changes, 3 deletions, 4 synonymous mutations, and one 4 nucleotide insertion. The complete mutation profile is shown in Table 6a.

Table 6a. VOC 202101/02 (P.1) Variant defining mutations

gene	amino_acid	actual_nucleotide
S Gene	L18F	21614C>T
	T20N	21621C>A
	P26S	21638C>T
	D138Y	21974G>T
	R190S	22132G>T
	K417T	22812A>C
	E484K	23012G>A
	N501Y	23063A>T
	H655Y	23525C>T
	T1027I	24642C>T
orf1ab	-	733T>C
	-	2749C>T
	S1188L	3828C>T
	K1795Q	5648A>C
	-	11288_96del
	-	12778C>T
	-`	13860C>T
	E5665D	17259G>T
orf8	E92K	28167G>A
	-	28263insAACA
N Gene	P80R	28512C>G
	-	28877A>T
	-	28878G>C

Red text indicates acquisition in subset of isolates within the lineage, non-variant defining mutations. Blue text indicates mutations present in the lineage but also observed in other isolates in lineage B.1.1.28, these are not included in the variant definition. Indels (shaded in orange) are not currently included in variant definitions.

Table 6b. VOC 202101/02 (P.1) Genomic case definition

CONFIRMED	All lineage defining non-synonymous changes called as alternate base
PROBABLE	At least 5 lineage defining non-synonymous changes called as alternate base and all other positions either N or mixed base
LOW_QC	Fewer than 5 lineage defining non-synonymous changes called as alternate base and all other positions either N or mixed base

Biological profile

This variant has mutations associated with both transmissibility and antigenic change including several in common with the B.1.351 lineage (N501Y, E484K and K417N/T). The significance of E484K has been described previously in this briefing.

Transmissibility

P.1 has been a been identified in Manaus, Brazil which experienced a rapid growth in numbers of COVID hospitalisations. Variants with the combined N501Y and E484K substitutions have been shown to have enhanced ACE2 receptor binding. Increased transmissibility is biologically and epidemiologically plausible, but at this time there is insufficient evidence to confirm or refute this. The frequency of such variants within the Brazilian population is difficult to assess.

Re-infections in healthcare workers have been reported in Brazil.

Epidemiological profile

There are no cases in the UK as of 10 February 2021

International Epidemiology

As of 10 February 2021, cases of VOC 202101/02 (P.1) have been reported in 11 countries/territories. 3 countries have reported cases of a Brazilian variant additional information is awaited to clarify if this is with VOC 202101/02 (P.1).

GISAID (gisaid.org) includes data on sequences available internationally. As of the 12 February 2021 91 cases of VOC 202101/02 (P.1) are listed (Brazil 62, Colombia 9, Faroe Islands 1, France 3, Italy 3, Japan 6, Netherlands 2, Peru 1, South Korea 1, USA 3).

Diagnostics

Lateral flow devices

Tested lateral flow devices detect VOC 202012/01 (B.1.1.7) and VOC 202012/02 (B.1.351) when assessed in a laboratory setting using variant virus materials.

Testing of VOC 202102/02 (B.1.1.7 with E484K) and VOC 202101/02 (P.1) are pending availability of virus material.

qPCR/Molecular amplification testing

A pathway is being established by MHRA to provide continued assurance of performance for diagnostic devices in use in the UK. This includes a process of analytical evaluation by PHE and NHSE, where appropriate, to formally test the impact on detection, of variants of concern, by specific products used for clinical diagnostics.

Appendices

Appendix 1. SGTF Correlation

One S gene mutation in VOC 202012/01 (B.1.1.7) causes deletion of amino acids 69 and 70 (Δ69-70), with a reproducible S gene target failure (SGTF). This is detected by the ThermoFisher TaqPath assay used in UK lighthouse laboratories (see Technical Briefing 1), 'TaqPath laboratories.'

This coincidental occurrence provides a good proxy for monitoring trends in VOC 202012/01 (B.1.1.7). SGTF correlates almost perfectly with presence of Δ69-70. Considering 49,945 tested pillar 2 samples where we know both the sequence and the SGTF status, 99.6% of Δ69-70 sequences (27,001 of 27,099) are SGTF, compared to 0.04% of sequences without the deletion (10 of 22,846).

Because Δ69-70 has arisen multiple times, and SGTF is a proxy for any lineage with that mutation, the utility of SGTF as a proxy for VOC 202012/01 varies over time and region. Table 7 shows, for all pillar 2 sequences, the weekly proportion of Δ69-70 sequences that were confirmed to be VOC 202012/01 (B.1.1.7). Table 8 shows the proportion of Δ69-70 that is the VOC 202012/01 (B.1.1.7) in England since 21 December 2020, broken down by region. It is now over 99% in all regions of England. The numbers in these tables are based on sequenced samples, some of which may have come from the same individual (this effect is likely to be small).

Table 7. Percentage of Pillar 2 Δ69-70 sequences that are VOC 202012/01 (B.1.1.7), 12 October 2020 to 31 January 2021

Week beginning	Percentage VOC of all Δ69-70	Number of pillar 2 Δ69-70 sequences
2020-10-12	3%	116
2020-10-19	15%	220
2020-10-26	29%	156
2020-11-02	64%	399
2020-11-09	81%	711
2020-11-16	88%	805
2020-11-23	93%	390
2020-11-30	95%	433
2020-12-07	98%	2,712
2020-12-14	99%	4,300
2020-12-21	99%	2,407
2020-12-28	99.7%	5,070
2021-01-04	99.7%	5,621
2021-01-11	99.9%	7,473
2021-01-18	99.8%	6,088
2021-01-25	100%	1,222

Table 8. Percentage Pillar 2 Δ69-70 sequences from that are VOC 202012/01 (B.1.1.7), by region of England, 1 to 31 January 2021

Region	Percentage VOC 202012/01 (B.1.1.7) of all Δ69-70	Number of Pillar 2 Δ69-70 1 to 31 January 2021
East Midlands	99.9%	669
East of England	99.9%	2095
London	99.8%	4819
North East	100%	871
North West	99.8%	6615
South East	99.6%	2875
South West	99.9%	671
West Midlands	99.6%	2100
Yorkshire and the Humber	99.6%	1283

Surveillance of SGTF, as a proxy for VOC 202012/01 (B.1.1.7), is based on positive tests reported by 3 lighthouse laboratories that use the Thermo Fisher TaqPath RT-PCR, and for which CT values are low enough to classify if the S gene is detectable. Specifically, positive tests with CT values >30 for any gene target are excluded. SGTF is defined as a positive test with CT values <=30 for the N and ORF1ab genes and an undetectable S gene. S gene positive is a positive test for which all 3 gene targets (N, ORF1ab, S) have CT values <=30.

Samples with SGTF have predominated since mid-December 2020, reaching 95.9% of cases in the week starting 4 February 2021 (Figure 6). All regions in England have reached >93% SGTF in the most recent week (Figure 7). Total cases detected using the TaqPath assay have also been declining since the first week of 2021, reflecting the general decline in case rates across England.

Figure 6. Weekly number and proportion of England Pillar 2 COVID-19 cases with SGTF among those tested with the TaqPath assay and with S gene detection results (3 September 2020 to 10 February 2021)

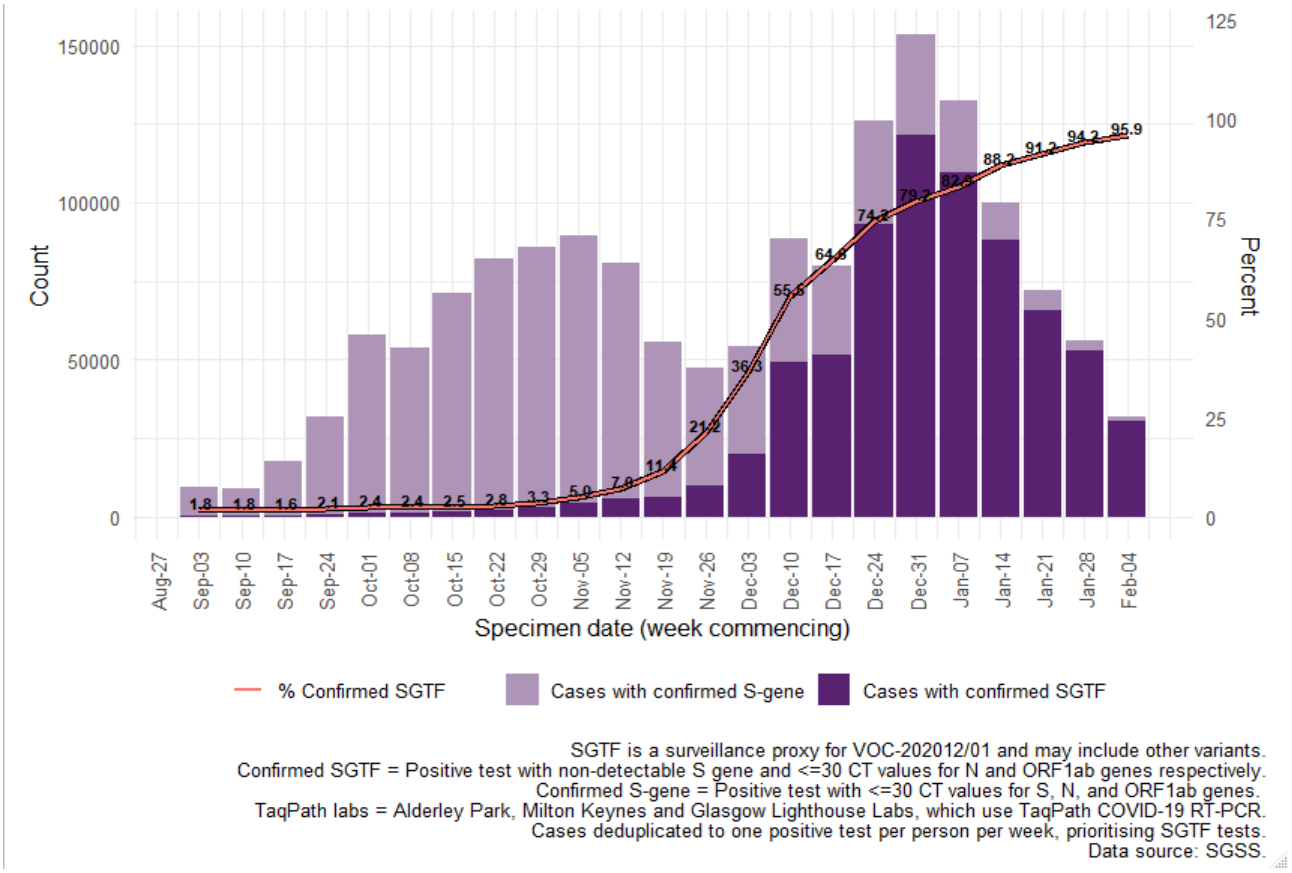
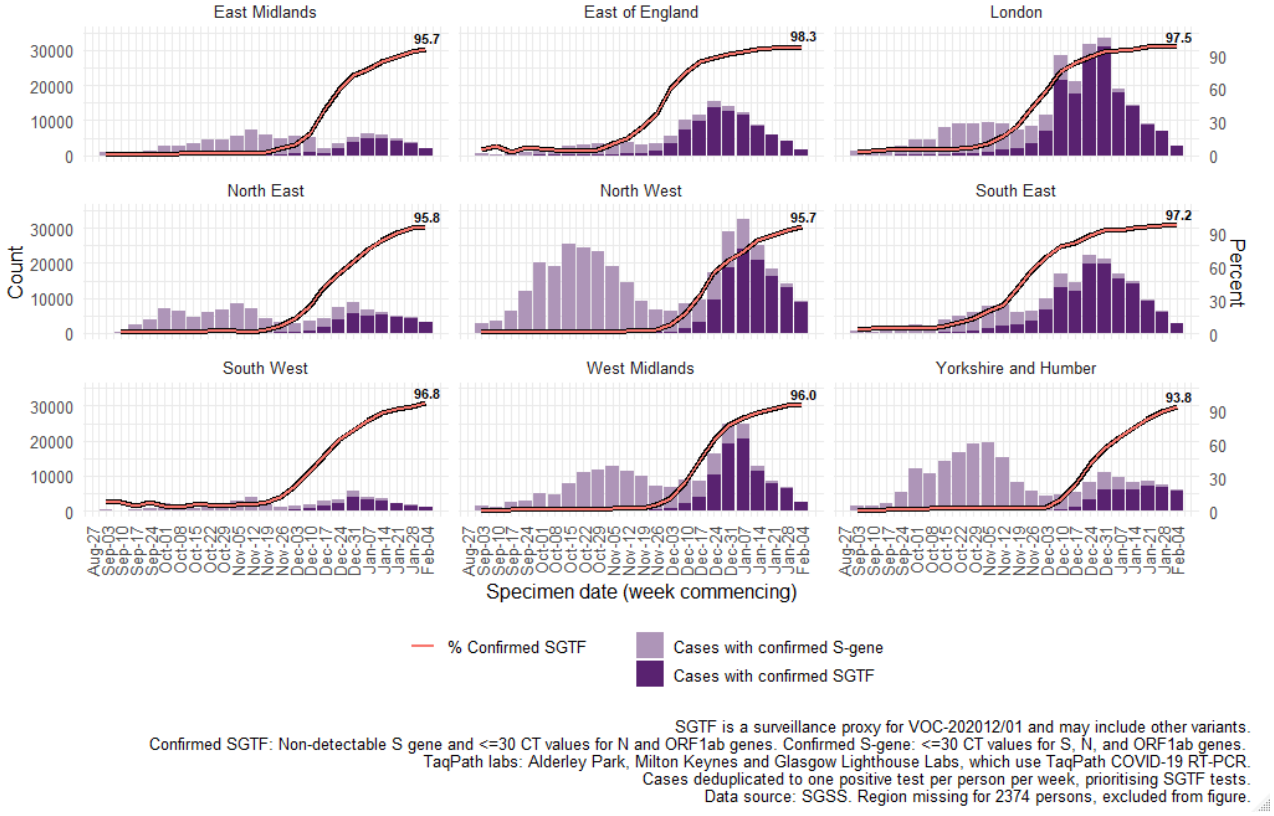


Figure 7. Weekly number and proportion of England Pillar 2 COVID-19 cases with SGTF among those tested with the TaqPath assay and with S gene detection results, by region of residence (3 September 2020 to 10 February 2021)



SGTF is a surveillance proxy for VOC-202012/01 and may include other variants.
Confirmed SGTF: Non-detectable S gene and <=30 CT values for N and ORF1ab genes. Confirmed S-gene: <=30 CT values for S, N, and ORF1ab genes.
TaqPath labs: Alderley Park, Milton Keynes and Glasgow Lighthouse Labs, which use TaqPath COVID-19 RT-PCR.
Cases deduplicated to one positive test per person per week, prioritising SGTF tests.
Data source: SGSS. Region missing for 2374 persons, excluded from figure.

Data on coverage of TaqPath laboratories testing and numbers/proportions of cases with SGTF are shared daily with Local Authorities (Sunday to Friday) on the COVID-19 PHE Local Authorities Report Store (Sharepoint).

Appendix 2 – Variant case definition validation

To determine if case definitions for VOC 202012/02 (B.1.351) are sufficiently sensitive, an analysis was undertaken. The current definition includes 2 different 'probable' definitions, outlined in Table 9. The amino acid and nucleotide substitutions characterising the variant are shown in Table 10.

Table 9. Confirmed, Probable and low-quality definitions currently used to call VOC 202012/02

Category	Definition
Confirmed	All lineage defining mutations (not in red text in Table 10) called as alternate base.
Probable 1	At least 4 lineage defining mutations (not in red text in Table 10) called as alternate base and all other lineage defining positions N or mixed base.
Probable 2	At least 5 of the 5 mutations (marked with * in Table 10) called as alternate base with any combination of other bases.
Low Quality	Fewer than 4 lineage defining mutations called as alternate base, and all other lineage defining positions N or mixed base.

Table 10. Defining mutations for VOC202012/02 (B.1.351). Mutations in red are not considered lineage defining. Mutations indicated by * are included in the probable 2 definition for this variant

Gene	Amino Acid	Actual Nucleotide	Note
S Gene	L18F	21614C>T	not lineage defining
	D80A*	21801A>C	
	D215G*	22206A>G	
	R246I	22299G>T	not lineage defining
	K417N*	22813G>T	not lineage defining
	E484K*	23012G>A	
	N501Y*	23063A>T	
	A701V*	23664C>T	
ORF1ab	T265I	1059C>T	nsp2T85I
	K1655N*	5230G>T	nsp3K837N
	K3353R	10323A>G	nsp5K90R

Gene	Amino Acid	Actual Nucleotide	Note
ORF3a	Q57H	25563G>T	
	S171L	25904C>T	
E Gene	P71L*	26456C>T	
N Gene	T205I*	28887C>T	

Two data sets were included, the COG-UK genomes, and the GISAID dataset. Analysis with the COG-UK data set identified 110 confirmed UK VOC 202012/02 (B.1.351) genomes. Analysis using the GISAID data identified 463 international confirmed genomes (UK data not included). Table 11 shows the number of sequences in each category when the current probable 1 definition is used (no non-variant nucleotides NVN, sometimes referred to as wild-type, at VOC defining positions) compared to allowing one or 2 NVN calls at any of the positions.

Table 11. Number of genomes meeting the different definitions for VOC 202012/02 (B.1.351) allowing an increasing number of NVN positions in the probable 1 definition. A: COG-UK data, B: GISAID data

A Definition	Allowing 0 NVN	Allowing 1 NVN	Allowing 2 NVN
Both Probable	38	43	46
Probable 1 Only	13	13	14
Probably 2 Only	8	3	0
Total Probable	59	59	60
B Definition	**Allowing 0 NVN**	**Allowing 1 NVN**	**Allowing 2 NVN**
Both Probable	96	259	278
Probable 1 Only	5	5	5
Probably 2 Only	190	27	8
Total Probable	291	291	291

Spike drop out and mutations or bases of poor quality data impact variant assignment using both probable 1 and 2 definitions. Analysis shows probable 1 definition detects sequences that the probable 2 definition does not, because of uncalled nucleotides in the genomes. Probable 1 definition enables variant assignment of lower QC VOC 202012/02 (B.1.351) sequences. Conversly, there are genomes that are detected using the probable 2 definition only, potentially due to reversions at some of the lineage defining positions. Currently the low-quality definition does not allow for NVN calls and therefore will not detect genomes that include data omissions, and partially meet the probable 2 definition. Therefore both definitions must be used for variant assignment. Low quality genomes currently undergo a manual review to determine whether they are considered likely to be

VOC 202012/02 (B.1.351) genomes and public health action is required. Therefore, it is recommended that the low-quality definition is expanded to capture these genomes. Both probable definition 1 and definition 2 must continue to be used to enable maximum assignment of variants in addition to manual check of low-quality sequences.

Data sources

Data used in this investigation is derived from the COG-UK dataset, the PHE Second Generation Surveillance System, NHS Test and Trace, the secondary uses service (SUS) dataset and Emergency Care Data Set (ECDS).

Variant Technical Group

Organisations

This group includes representation from the following organisations: PHE, DHSC, BEIS, Wales NHS, PHScotland, NHS Scotland, Health and Social Care Northern Ireland, Imperial College London, London School of Hygiene and Tropical Medicine, University of Birmingham, University of Cambridge, University of Edinburgh, University of Liverpool, the Wellcome Sanger Institute.

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