Public Health England

Protecting and improving the nation's health

SARS-CoV-2 variants of concern and variants under investigation in England

Technical briefing 7

11 March 2021

This briefing provides an update on previous briefings up to 13 February 2021

Contents

Summary

- There are 4 variants of concern and 5 variants under investigation (Table 1).
- A slightly increased risk of hospitalisation has been now been detected for VOC 202012/01 (B.1.1.7), supporting previous findings on fatality.
- The first VOC 202101/02 (P.1) cases have been detected in England. The VOC 202101/02 (P.1) risk assessment indicates that it is plausible that there is some degree of either immune escape or increased transmissibility, or both. This is based on laboratory data and modelling; the magnitude and clinical significance of these effects have yet to be determined.
- VOCs (excluding VOC 202012/01 B.1.1.7) and VUIs remain low at less than 1% of samples with a sequence result available.

Table 1. Total case numbers England per VOC/VUI as of 10 March 2021

		England genomic cases 10 March 2021, of 329734 total sequences with unique identifier		
Variant	**Pangolin lineage**	**Confirmed**	**Probable**	**Total confirmed and probable**
VOC 202012/01	B1.1.7	98,422	10,671	109,093
VOC 202102/02	B.1.1.7 with E484K cluster	34	0	34
VOC 202012/02	B.1.351	190	76	266
VOC 202101/02	P1	5	2	7
VUI 202101/01	P2	46	0	46
VUI 202102/01	A.23.1 with E484K	59	19	78
VUI 202102/03	B.1.525	79	28	107
VUI 202102/04	B.1.1.318	18	0	18
VUI 202103/01	B.1.324.1 with E484K	2	0	2

Case numbers on variants of concern (VOC) and variants under investigation (VUI) are updated online. Note table excludes variant cases not linked to a known COVID-19 case, which may represent duplicate results or non-England residents.

Variants in Monitoring

Variants in monitoring are those which have been identified through horizon scanning, do not have sufficient clear signals of concern to escalate further, but for which case numbers and available data are being monitored regularly. These variants are in the monitoring category:

- B.1.429 first detected in California (10/329,734 UK sequences as of 10 March 2021)
- B.1.1.7 with S494P first detected in the UK (761/329,734 UK sequences as of 10 March 2021)
- A.27 first detected in Mayotte (4/329,734 UK sequences as of 10 March 2021)
- B.1.526 first detected in New York (2/329,734 UK sequences as of 10 March 2021)

Variant assessment tools

Repository of human and machine readable genomic case definitions

A repository containing the up-to-date genomic definitions for all VOC and VUI as curated by Public Health England was created 5 March 2021. The repository can be accessed on GitHub. They are provided in order to facilitate standardised VOC and VUI calling across sequencing sites and bioinformatics pipelines and are the same definitions used internally at Public Health England. Definition files are provided in YAML format so are compatible with a range of computational platforms. The repository will be regularly updated.

Variant risk assessment.

Variant risk assessment includes the following confidence grading categorisations and utilises the framework in Table 2.

- Low: Little or poor-quality evidence, uncertainty or conflicting views amongst experts, no experience with previous similar incidents.
- Moderate: Adequate quality evidence, including consistent results published only in grey literature, reliable source(s), assumptions made on analogy and agreement between experts or opinion of at least 2 trusted experts.
- High: Good quality evidence, multiple reliable sources, verified, expert opinion concurs, experience of previous similar incidents.

Table 2. Variant risk assessment framework.

Indicator	Risk assessment framework			
Zoonotic emergence and transmission to humans	Animal reservoir identified but no evidence of transmission from animals to humans	Sporadic transmission from animals to humans	Frequent transmission from animals to humans	
Transmissibility between humans	No demonstrated person to person transmission	Limited human case clusters	Established human to human transmission, which appears similar to wild type virus	Transmissibility appears greater than the wild type virus
Infection severity	Evidence of less severe clinical picture or lower infection fatality than from wild type SARS-CoV-2 infections	Similar clinical picture and infection fatality to wild type SARS-CoV-2 infections OR ex perimental animal data suggesting potential for increased disease severity in humans	More severe clinical picture or higher infection fatality than from wild type SARS-CoV-2 infections (limited to specific risk groups)	More severe clinical picture or higher infection fatality than from wild type SARS-CoV-2 infections
Susceptibility and immunity – natural infection	Evidence of no antigenic difference from other circulating wild type virus	Structural data suggesting antigenic difference from other circulating wild type virus	Experimental evidence of functional evasion of naturally acquired immunity	Evidence of frequent infection in humans with known prior infection with earlier virus variant.
Vaccines	Evidence of no structural or antigenic difference in vaccine targets	Structural data suggesting difference in vaccine target epitopes	Experimental evidence of functional evasion of vaccine derived immunity	Evidence of frequent vaccine failure or decreased effectiveness in humans
Drugs and therapeutics	Evidence of no structural or antigenic difference in therapeutic targets	Structural data suggesting difference in therapeutic target epitopes	Experimental evidence of reduced drug susceptibility	Evidence of frequent drug or therapeutic failure or decreased effectiveness in humans

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 technical briefing 6. In addition, VOC 202012/01 has acquired other mutations in some cases. Mutation counts in the UK dataset are shown in Table 3.

Table 3. VOC 202012/01 (B.1.1.7) Spike mutations acquired in addition to the variant defining mutations 11 December 2020 to 10 March 2021

(Percentage indicates all sequences of VOC 202012/01 (B.1.1.7) per period in header).

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) to 10 March 2021**	**11 December 2020 to 10 January 2021**	**11 January 2021 to 10 February 2021**	**11 February 2021 to 10 March 2021**
L18F	3720 (2.7%)	314 (0.7%)	1431 (2.1%)	549 (1.7%)
Q677H	851 (0.6%)	92 (0.2%)	366 (0.5%)	348 (1.1%)
S494P	761 (0.6%)	208 (0.4%)	339 (0.5%)	88 (0.3%)
G142V	131 (0.1%)	8 (0%)	25 (0%)	84 (0.3%)
S680F	103 (0.1%)	13 (0%)	36 (0.1%)	42 (0.1%)
Y144F	354 (0.3%)	120 (0.3%)	164 (0.2%)	37 (0.1%)
T678I	144 (0.1%)	25 (0.1%)	54 (0.1%)	30 (0.1%)
H146Y	70 (0.1%)	7 (0%)	23 (0%)	27 (0.1%)
F490S	109 (0.1%)	10 (0%)	64 (0.1%)	24 (0.1%)
A475A	121 (0.1%)	11 (0%)	64 (0.1%)	23 (0.1%)
E484K	65 (0%)	10 (0%)	37 (0.1%)	13 (0%)
Q493K	14 (0%)	0 (0%)	1 (0%)	11 (0%)
A684V	51 (0%)	8 (0%)	23 (0%)	10 (0%)
Total VOC 202012/01 (B.1.1.7) 135,310				

Epidemiological profile

Lineage B.1.1.7 is dispersed across the UK. Confirmed cases are those identified by whole genome sequencing. As of 10 March 2021, there were 109,093 confirmed and probable cases of VOC 202012/01 (B.1.1.7) in England (98,422 confirmed and 10,671 probable). 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 99% of cases in the week starting 3 March 2021. Proportions in all regions are >97% (Appendix 1). Confirmed and probable cases by specimen date are shown in Figure 1 and age-sex pyramid in Figure 2.

Figure 1. Confirmed and probable VOC 202012/01 (B.1.1.7) cases by specimen date, 1 October 2020 to 10 March 2021

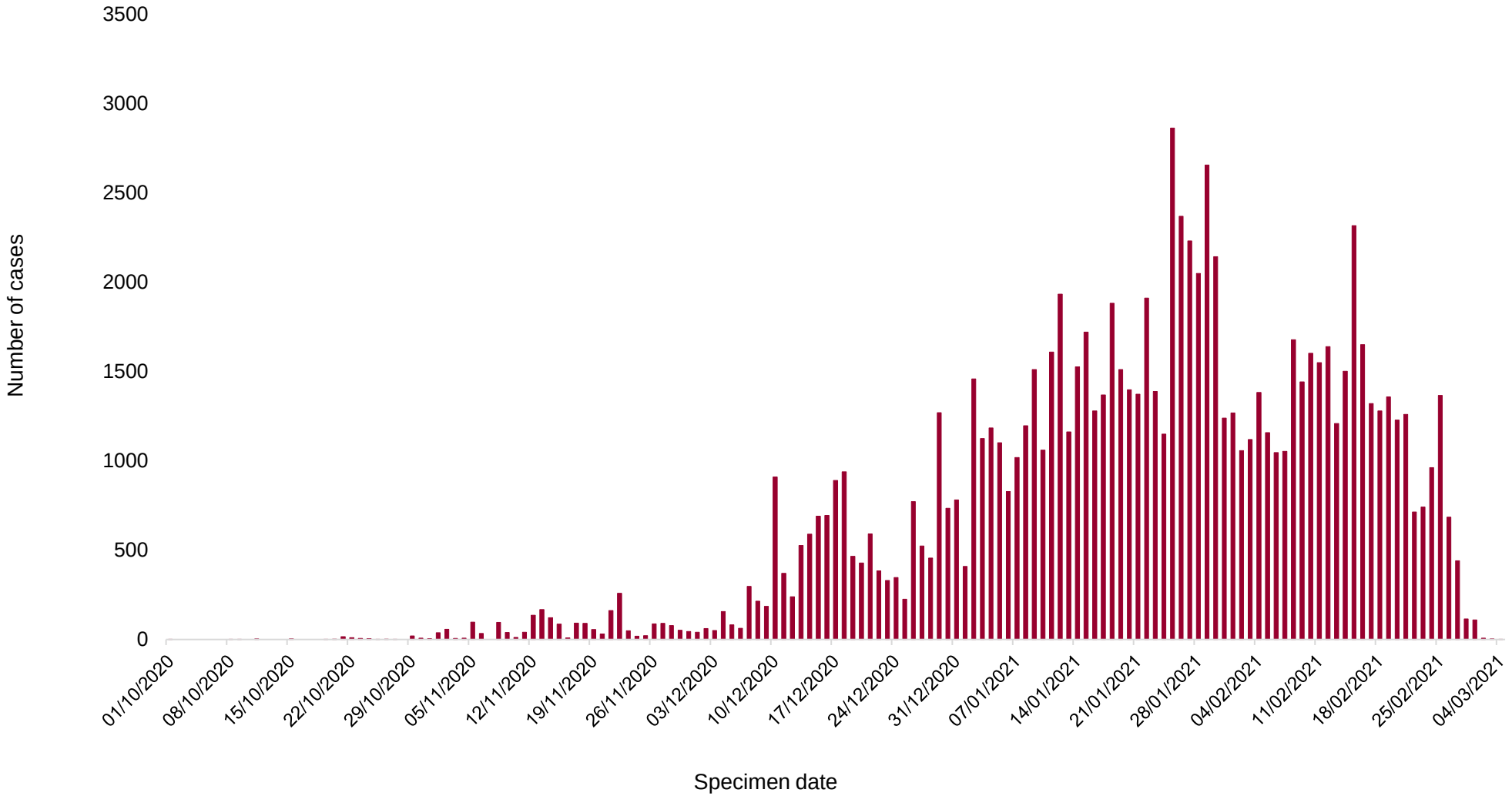
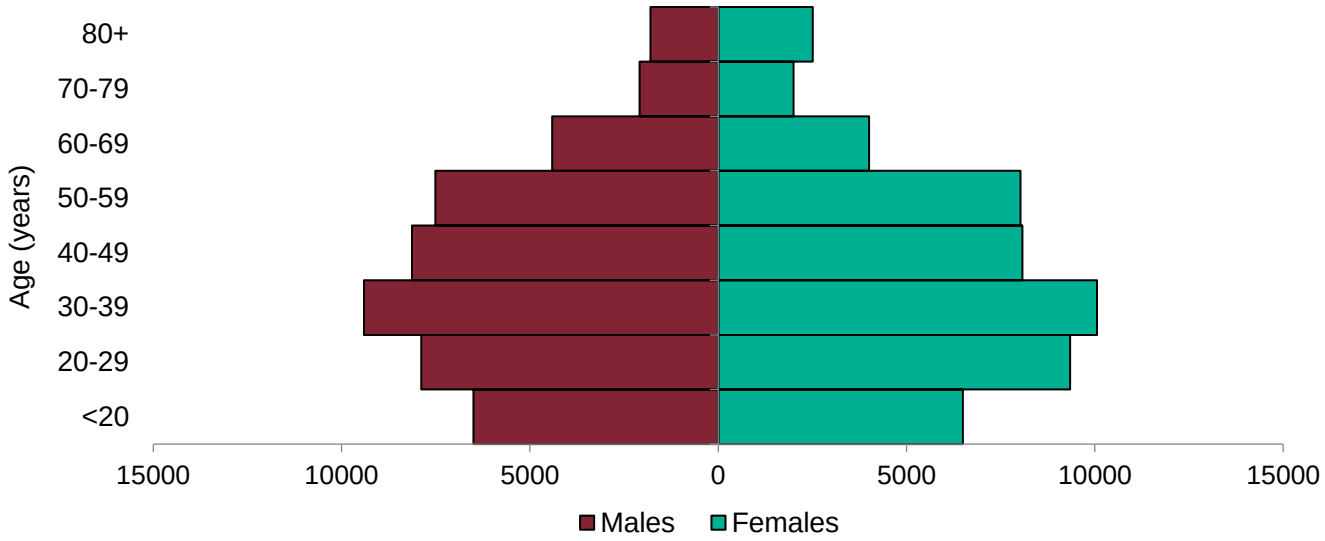


Figure 2. Age-sex pyramid of VOC 202012/01 (B.1.1.7) cases, 1 October 2020 to 10 March 2021



Hospitalisations

PHE undertook a record linkage to analyse sequenced confirmed VOC 202012/01 (B.1.1.7) cases between October and December 2020. A Cox proportional hazard analysis of 63,609 sequenced cases identified a significantly increased risk of hospitalisation within 14 days of specimen date among VOC 202012/01 (B.1.1.7) cases compared to non-variant cases (HR 1.34, 95% CI:1.07-1.66, p=0.01), after adjusting for confounders (sex, age, ethnicity, residence type and week of diagnosis). This analysis used NHS hospital admission data from the NHS Digital Secondary Uses Service (SUS) which is subject to reporting delays, therefore these results represent a minimum estimate of hospital admission risk.

Deaths

As of 10 March 2021, there were 2,858 deaths (within 28 days) in the 109,093 cases with confirmed or probable VOC 202012/01 (B.1.1.7) (case fatality 2.6%).

Immunisation

Two interim assessments have been published covering B.1.1.7 and the UK vaccine programme[1],[2].

[1] Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in the UK: a test negative case control study Jamie Lopez Bernal *et al.,* 2021 Link

[2] Effectiveness of BNT162b2 mRNA Vaccine Against Infection and COVID-19 Vaccine Coverage in Healthcare Workers in England, Multicentre Prospective Cohort Study (the SIREN Study) Hall *et al.,* 2021 Link

International Epidemiology

As of the 08 March 2021, there are 113 countries or territories (including the UK) reporting cases of the UK variants globally. Of countries/territories outside of the UK, 19 report, or there is evidence of, community transmission. However for many countries the information available on the extent of transmission within the country is not clear.

GISAID (gisaid.org) includes data on sequences available internationally; as of the 10 March 2021 27,003 VOC 202012/01 (B.1.1.7) sequences (excluding UK) are available from 94 countries/territories.

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 (65 of 135,310 sequences as of 10 March 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 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. The genomic and biological profile is as previously described.

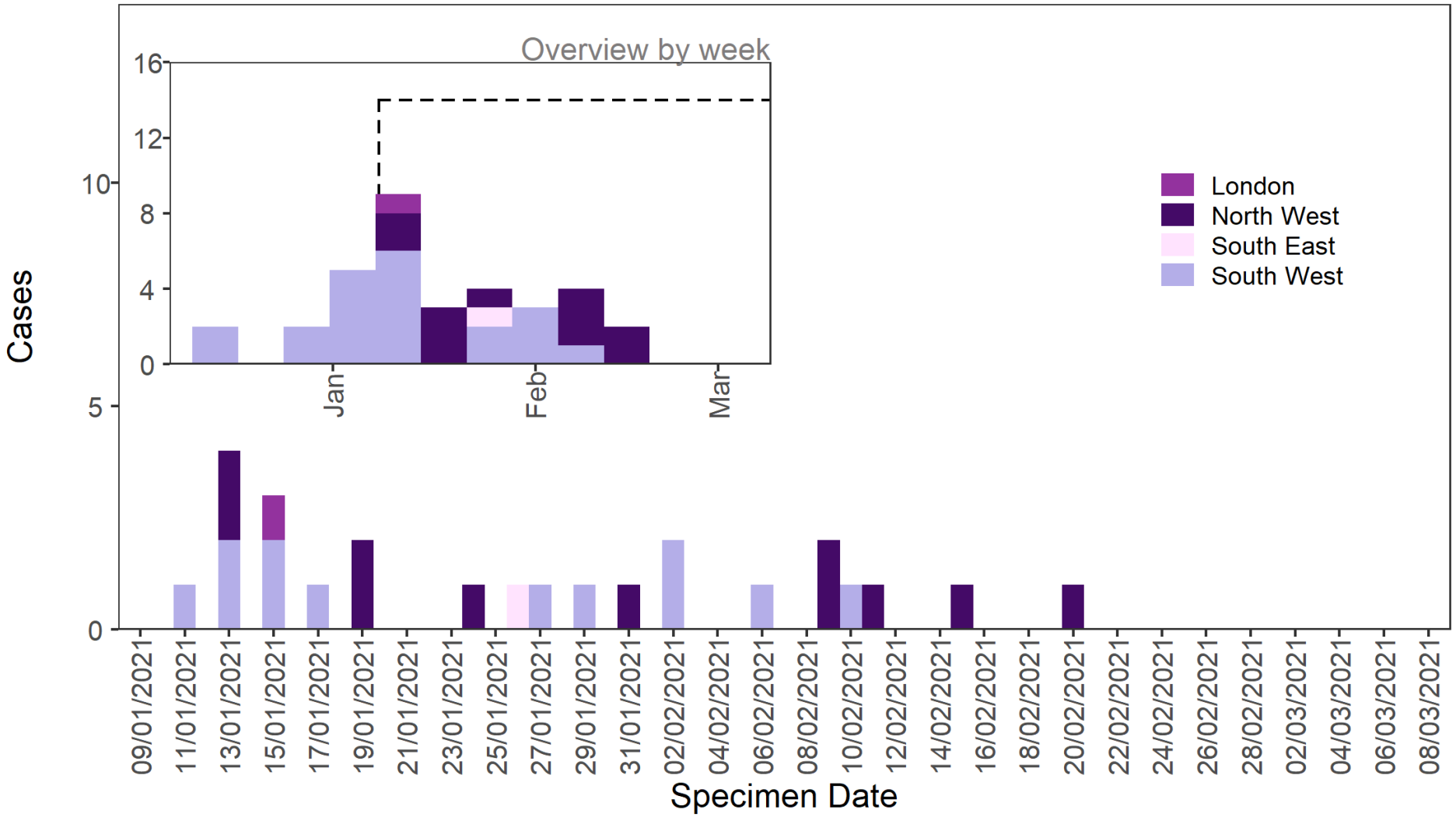
Epidemiological profile

As of 10 March 2021, 34 genomically confirmed cases of VOC 202012/01 (B.1.1.7) have been identified; 21 with an epidemiological link to the South West and an additional 13 cases resident elsewhere in England (Table 4). Specimen dates range from 17 December 2020 to 20 February 2021, confirmed and probable cases by specimen date are shown in Figure 3.

Table 4. Number of confirmed and probable VOC 202102/02 (B.1.1.7 cluster with E484K) cases, by region of residence (as of 10 March 2021)

Region	Confirmed	Probable	Total	Percent of England total
London	1	0	1	2.9
North West	11	0	11	32.4
South East	1	0	1	2.9
South West	21	0	21	61.8
Total	34	0	34	100.0

Figure 3. Confirmed and probable VOC 202102/02 (B.1.1.7 cluster with E484K) cases by specimen date, from 17 December 2020 as of 10 March 2021. Larger plot includes last 60 days only.



Deaths

As of 10 March 2021, one death (within 28 days) among 34 cases with confirmed VOC 202102/02 (B.1.1.7 cluster with E484K) has been reported.

International Epidemiology

As of the 8 March 2021, international cases have been reported in 2 countries and 2 sequences from the Netherlands have been identified on GISAID.

Variant in monitoring B.1.1.7 with S494P Clade

On 17 February 2021 the acquisition of Spike mutation S494P in VOC 202012/01 (B.1.1.7) samples was identified as a signal as part of the horizon scanning process for routine scanning of variation. Due to the large number of sequences identified, further analysis was undertaken. This mutation appears to have been acquired multiple times by VOC 202012/01 (B.1.1.7). However, the majority of these sequences position within one clade, for which further information is presented here.

Genomic and biological profile

The cluster VOC 202102/02 (B.1.1.7) cluster with S494P has the mutations previously described for VOC 202012/01 (B.1.1.7) in technical briefing 6 with the addition of S494P in spike gene and 2 mutations in orf1ab (NSP8 Q24Rand NSP5 SNP G10870T). S494P allows evasion of binding or neutralization by several monoclonal antibodies but has not been shown to impact on neutralization by convalescent or vaccine-induced polyclonal antisera. S494P confers increased binding to hACE2.[3,4]

Epidemiological profile

As of 10 March 2021, there were 761 genomically confirmed cases. Cases of VOC 202012/01 (B.1.1.7) with S494P have been increasing in recent weeks.

The distribution of cases over time shows that the clade began in the South East in November 2020 and spread throughout this area in December 2020. It was also seen in the North West during December 2020, expanding in January 2021.

[3]Broad and potent activity against SARS-like viruses by an engineered human monoclonal antibody Rappazzo *et al.,* 2021 Science DOI: 10.1126/science.abf4830 link
[4]Whelan Landscape analysis of escape variants identifies SARS-CoV-2 spike mutations that attenuate monoclonal and serum antibody neutralization Liu *et al.,* 2020. bioRxiv 2020.11.06.372037 link

VOC 202012/02 (B.1.351)

B.1.351 was initially detected in South Africa. This variant was designated VUI on detection and on review re-designated as VOC 202012/02 (B.1.351) on 24 December 2020.

Epidemiological profile

VOC 202012/02 (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 March 2021, 266 cases of VOC 202012/02 (B.1.351) were identified (190 confirmed cases and 76 probable cases). An international travel link was identified for 181 cases, and 68 cases had no travel link (17 awaiting further information). Confirmed and probable cases by specimen date are shown in Figure 4, age-sex pyramid in Figure 5, and regional breakdown in Table 5.

Figure 4. Confirmed and probable VOC 202012/02 (B.1.351) cases by specimen date, from 10 December 2020 as of 10 March 2021 (3 cases are omitted without specimen date)

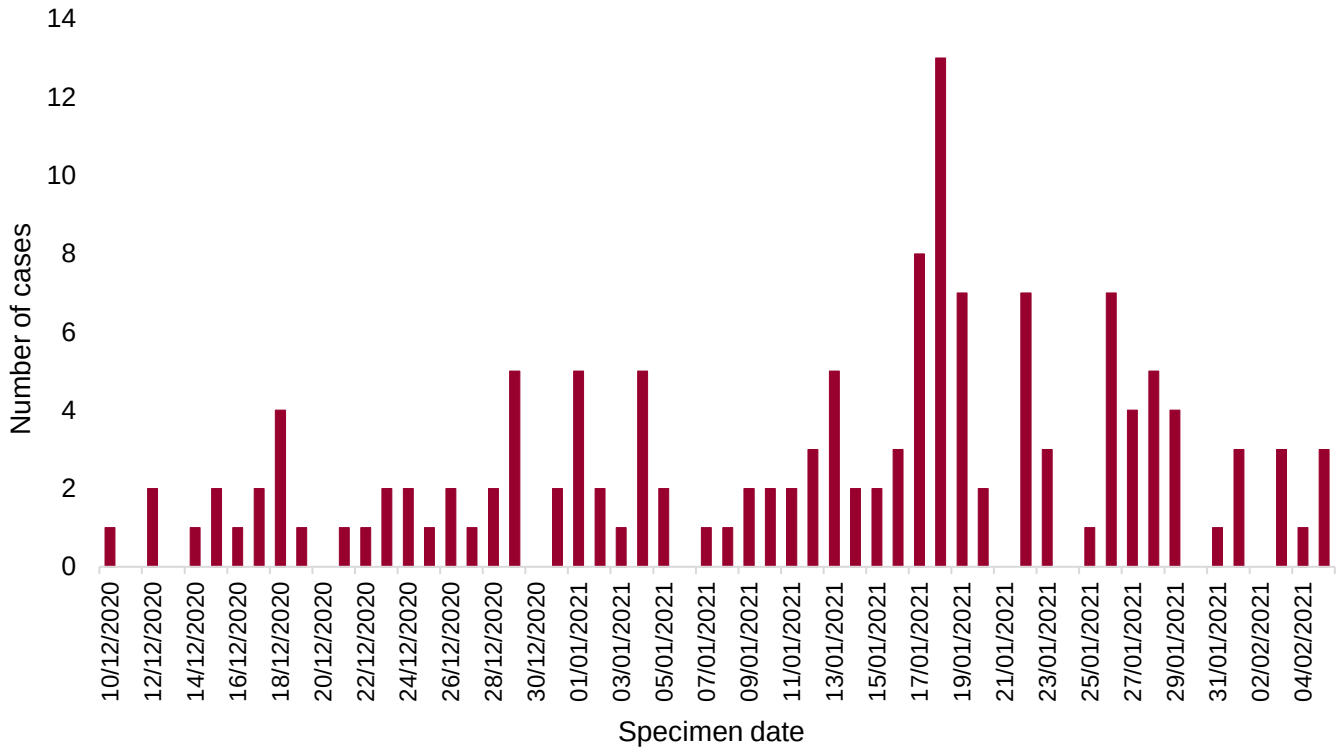


Figure 5. Age-sex pyramid of VOC 202012/02 (B.1.351) cases, from 10 December 2020 as of 10 March 2021

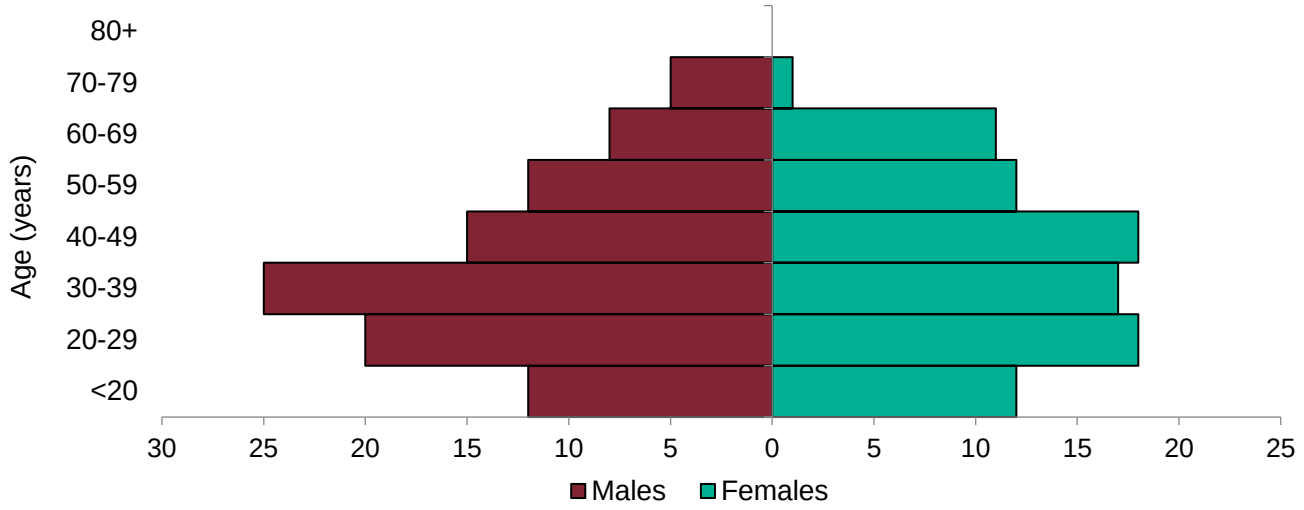


Table 5. Confirmed and probable cases by region, 10 December 2020 to 10 March 2021

Region	VOC 202012/02 (B.1.351)	
	n	%
East Midlands	6	2.3
East of England	40	15.0
London	83	31.2
North East	6	2.3
North West	32	12.0
South East	54	20.3
South West	13	4.9
West Midlands	22	8.3
Yorkshire and Humber	10	3.8
TBC	0	0.0
Total	**266**	

Deaths

As of 10 March 2021, there were 6 deaths (within 28 days) in the 266 cases with confirmed or probable VOC 202012/02 (B.1.351) (case fatality 2.3%).

International Epidemiology

As of 8 March 2021 there are 62 countries (including the UK) that have reported cases of this variant globally. As of 08 March 2021 the epidemiological profile in South Africa is as follows:

- The case incidence is continuing to decrease. Currently, the reported weekly incidence is 12.9 per 100,000 population. Weekly test positivity has also been decreasing with current test positivity of 4.3%. Testing rates have been declining since mid-January although remained relatively stable over the previous 2 weeks (current weekly testing rate is 3.0 per 1,000 population).
- The fatality rate is decreasing (the weekly fatality rate is 1.2 per 100,000 population).
- The number of patients in hospital and ICU has also reduced slightly. As of 08 March 2021, 914 COVID-19 patients are in ICU and 6,105 are in hospital.

GISAID (gisaid.org) includes data on sequences available internationally. As of the 10 March 2021 2,643 sequences of VOC 202012/02 (B.1.351), excluding UK, are available from 46 countries/territories.

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. The clinical risk assessment for P1 is shown in Table 6.

Table 6. Risk assessment for VOC 202101/02 (P.1)

Indicator	RAG	Confidence	Assessment and rationale
Zoonotic emergence		NA	Not applicable
Transmissibility between humans		MOD	Transmissibility appears greater than wild type virus in the context of Manaus, and there is MODERATE confidence that this represents a true change in phenotype.

Indicator	RAG	Confidence	Assessment and rationale
Infection severity		NA	Insufficient information. Reports from Manaus are confounded by healthcare system stresses. Clinical cohort studies currently underway in Brazil may provide data in the medium term.
Naturally acquired immunity		HIGH	There is experimental evidence of evasion of naturally acquired immunity (HIGH confidence). There was a severe second wave in Manaus, despite apparently high seroprevalence. Better quality evidence, for example comparing the rate of confirmed reinfections in P1 and non P1 cohorts is required to raise the risk to red.
Vaccine derived immunity		MOD	There is experimental evidence of evasion of vaccine derived immunity in laboratory studies (MODERATE confidence). The magnitude of the effect may be less than that of B.1.351 (South Africa), based on limited laboratory data . Clinical trial and surveillance data are required.
Drugs and Therapeutics		MOD	There is experimental evidence that variants containing E484K may have reduced susceptibility to some monoclonal antibody based therapies in laboratory conditions (MODERATE confidence).
Overall assessment of level and nature of risk, and level of confidence			There are limited data available on P.1. It is a successful lineage in Brazil and is showing some evidence of international spread. The spread of P1 in the UK, where the prevalent virus is B.1.1.7, cannot be extrapolated from the trajectory observed in Manaus. There is laboratory evidence supporting antigenic change, and this is consistent with the epidemiology reported from Brazil. In the context of the situation in Manaus, it is difficult to differentiate immune escape and increased transmissibility, and some degree of both is plausible. . However, there are no robust, comparative clinical re-infection or vaccine efficacy data. There is an urgent need to assess severity.

Epidemiological profile

As of 10 March 2021, 7 genomically confirmed and probable cases of VOC 202101/02 (P.1) have been identified in England. All cases have been linked to international travel.

Deaths

As of 10 March 2021, there were no reported deaths in cases of VOC 202101/02 (P.1) in England.

International Epidemiology

As of 8 March 2021, cases of VOC 202101/02 (P.1) have been reported in 20 countries or territories. 8 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 10 March 2021 562 sequences of VOC 202101/02 (P.1) are listed (Brazil 304, Italy 102, Belgium 29, Peru 24, USA 18, Colombia 17, Switzerland 16, Portugal 11, France 9, Japan 8, Ireland 6, Netherlands 4, French Guiana 3, Romania 2, South Korea 1, Canada 1, Mexico 1, Spain 1, Sint Maarten 1, Germany 1, Turkey 1, Australia 1, Faroe Islands 1).

VUI 202101/01 (P2)

First identified in Brazil, the P.2 lineage is a descendant of B.1.1.28. This variant was designated VUI on detection and on review re-designated as VUI 202101/01 (P.2) on 13 January 2021.

Genomic profile

VUI 202101/01 is lineage P.2 (first sequence detected in Brazil and was first sequenced in the UK in November 2020). The complete mutation profile of VUI 202101/01 (P.2) is shown in Table 7 and genomic case definition in Table 8.

Table 7. VUI 202101/01 (P.2) Variant defining mutations

Gene	Amino Acid	Actual Nucleotide	Note
	-	100>T	not included in definition due to masking
orf1ab	L3468V	10667T>G	nsp5:L205V
	-	11824C>T	nsp6:I248I
	-	12964A>G	nsp9:G93G; not lineage defining
S Gene	E484K	23012G>A	
orf8	F120F	28253C>T	
N Gene	A119S	28628G>T	
	M234I	28975G>T	
	-	29754>T	not included in definition due to masking

Table 8. VUI 202101/01 (P.2) Genomic case definition

CONFIRMED	All variant defining changes called as alternate base or 6 of 7 changes called as alternate base and remaining position either N or mixed base
PROBABLE	NA
LOW_QC	Fewer than 6 positions are called but at least one is called as alternate (variant) base and all other defining positions reported as N (unknown) or mixed bases.

Epidemiological profile

As of 10 March 2021, 46 cases of VUI 202101/01 (P.2) have been identified in England. 9 cases have been linked to international travel, and 32 cases had no travel link (5 awaiting further information). Confirmed and probable cases by specimen date are shown in Figure 6 and age-sex pyramid in Figure 7.

Figure 6. Confirmed and probable VUI 202101/01 (P.2) cases by specimen date, from 14 November 2020 as of 10 March 2021

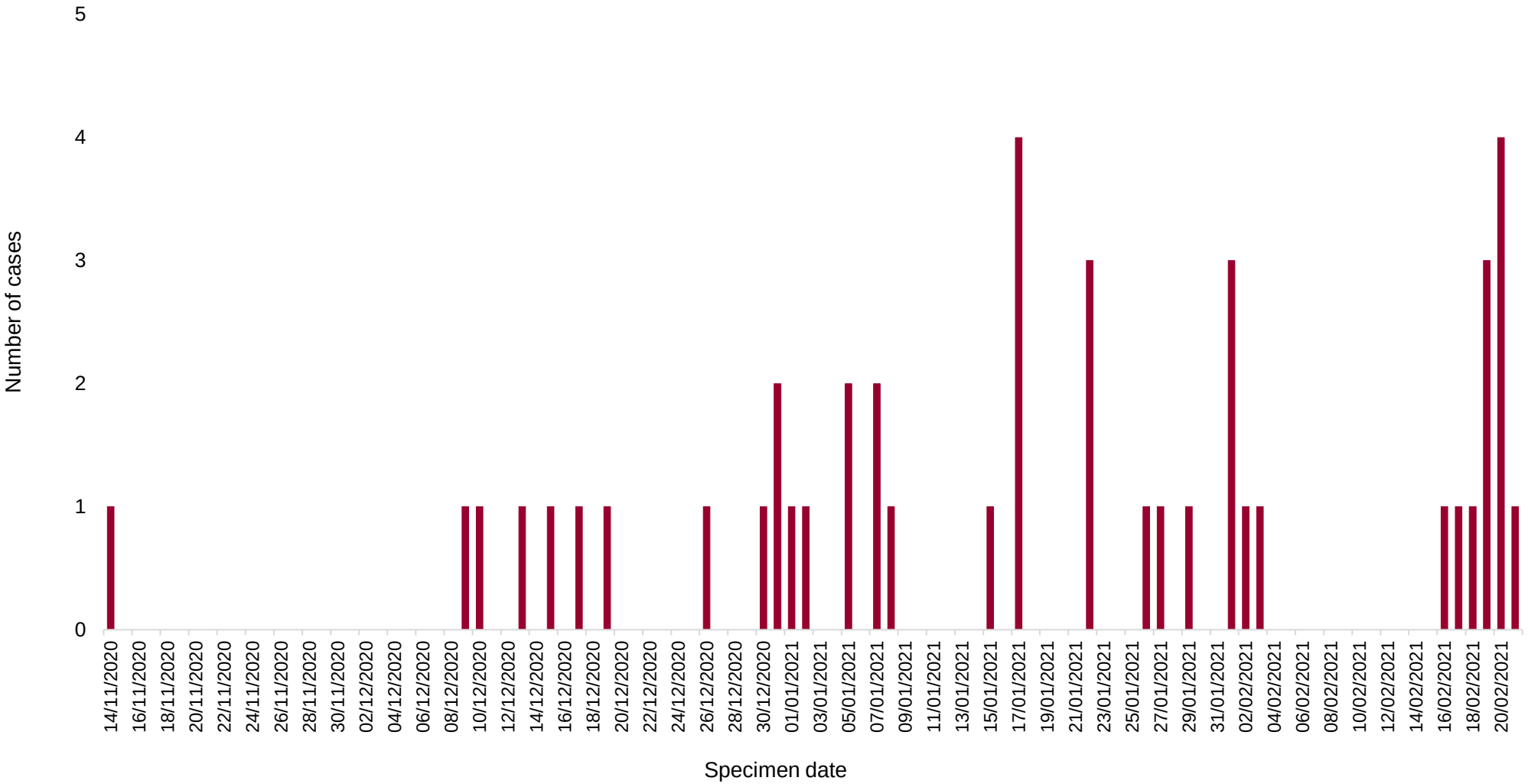
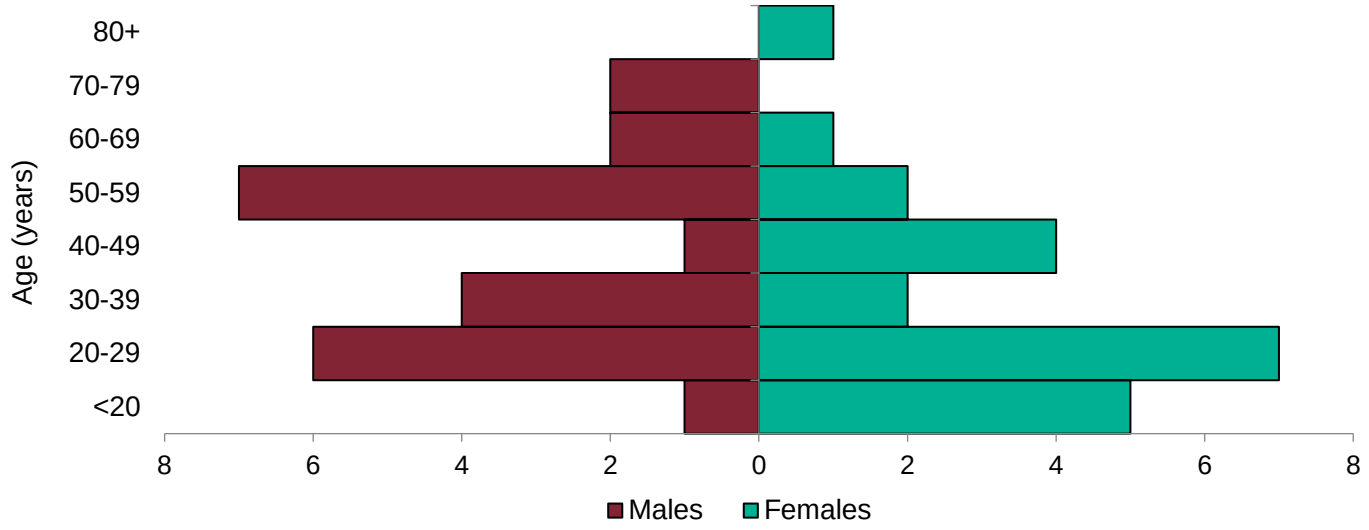


Figure 7. Age-sex pyramid of VUI 202101/01 (P.2) cases, 10 December 2020 to 10 March 2021



International Epidemiology

As of 8 March 2021, cases of VUI 202101/01 (P.2) have been reported in 11 countries or territories.

GISAID (gisaid.org) includes data on sequences available internationally. As of the 10 March 2021 862 sequences (excluding UK) of VUI 202101/01 (P.2) are listed (Brazil 382, USA 267, French Guiana 42, Canada 23, Switzerland 22, Netherlands 21, Denmark 18, Portugal 16, Spain 11, Ireland 11, France 10, Norway 6, Chile 6, Argentina 5, Germany 4, Australia 3, Japan 3, Sweden 3, Mexico 3, Singapore 1, Austria 1, Italy 1, Sint Maarten 1, Belgium 1, Malaysia 1).

VUI 202102/01 (A.23.1 with E484K)

This variant was first identified in Liverpool, UK, derived from a lineage first identified in Uganda without E484K. The variant was designated VUI on detection and on review re-designated as VUI 202102/01 (A.23.1 with E484K) 5 February 2021.

Genomic profile

VUI 202102/01 (A.23.1 with E484K) is lineage A.23.1 (first sequence detected in the UK in December 2020). The complete mutation profile of VUI 202102/01 (A.23.1 with E484K) is shown in Table 9 and genomic case definition in Table 10.

Table 9. VUI 202102/01 (A.23.1 with E484K) Variant defining mutations

Gene	Amino Acid	Actual Nucleotide	Note
orf1ab	L1559F	4940C>T	nsp3:L741F
	M3655I	11230G>T	nsp6:M86I
	L3667F	11266G>T	nsp6:L98F
	M3752I	11521G>T	nsp6:M183I
S Gene	R102I	21867G>T	
	F157L	22033C>A	
	V367F	22661G>T	
	E484K	23012G>A	
	Q613H	23401G>T	
	P681R	23604C>G	
orf8	L84S	28144T>C	
N Gene	E92K	28167G>A	
	S202N	28878G>A	

Table 10. VUI 202102/01 (A.23.1 with E484K) Genomic case definition

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

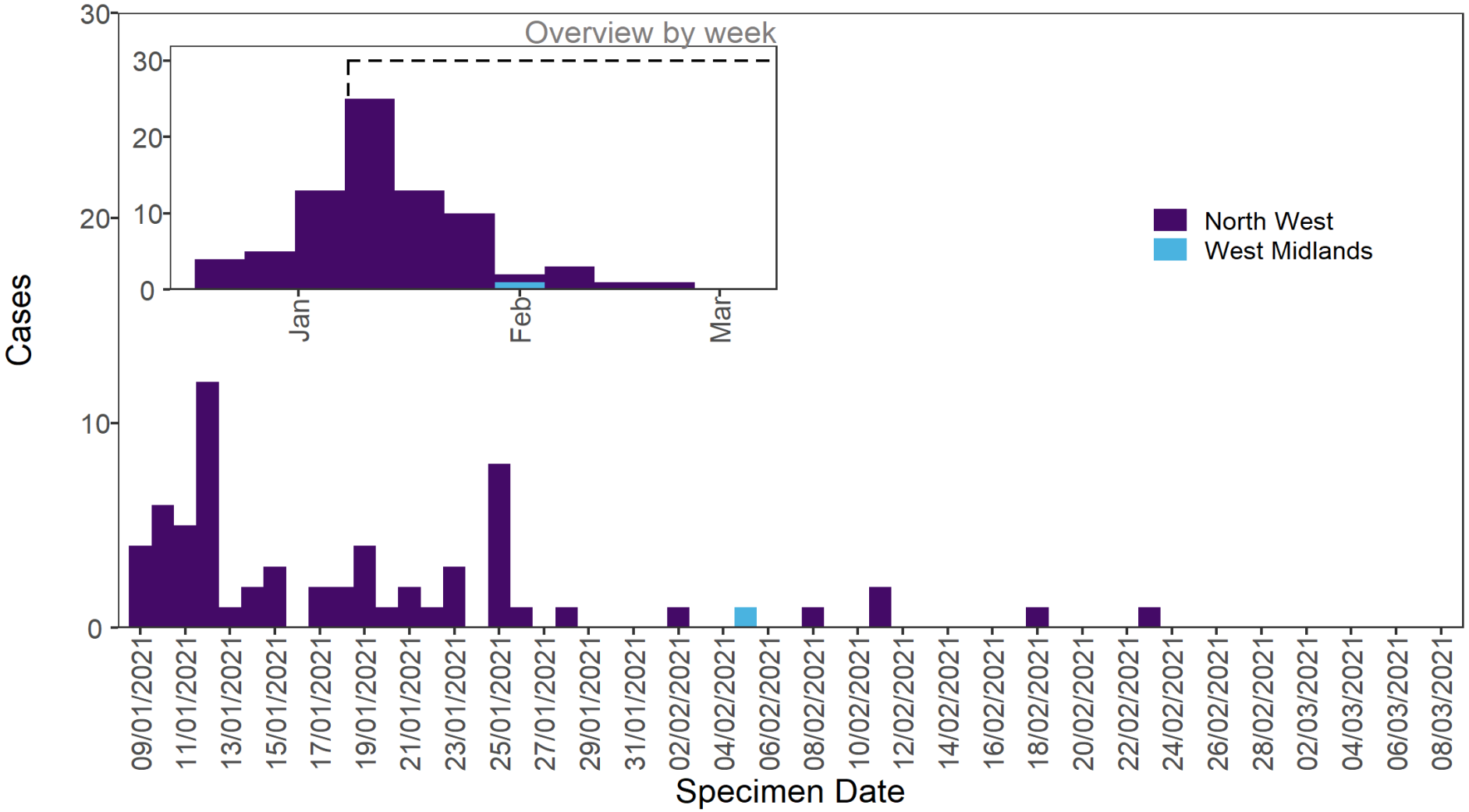
Epidemiological profile

As of 10 March 2021, 59 genomically confirmed and 19 genomically probable cases of VUI 202102/01 (A.23.1 with E484K) have been identified; 78 in total. The majority of these are residents of the North West of England (Table 11). Specimen dates range from 26 December 2020 to 23 February 2021 (Figure 8).

Table 11. Number of confirmed and probable VUI 202102/01 (A.23.1 with E484K) cases, by region of residence (as of 10 March 2021)

Region	Confirmed	Probable	Total	Percent of England total
North West	58	19	77	98.7
West Midlands	1	0	1	1.3
Total	59	19	78	100.0

Figure 8. Confirmed and probable VUI 202102/01 (A.23.1 with E484K) cases by specimen date, from 26 December 2020 as of 10 March 2021. Larger plot includes last 60 days only. Excludes 1 case with unknown specimen date.



Deaths

As of 10 March 2021, 1 death (within 28 days) in 78 cases with VUI 202102/01 (A.23.1 with E484K) has been reported (case fatality 1.3%).

International Epidemiology

The are no cases reported internationally as of the 8 March 2021.
GISAID (gisaid.org) includes data on sequences available internationally. As of the 10 March 2021 1 sequence is listed of VUI 202102/01 (A.23.1 with E484K) (excluding UK) from Netherlands.

VUI 202102/03 (B.1.525)

First identified as a geographically dispersed cluster in UK on the 2 February 2021. This variant was designated VUI on detection and on review re-designated as VUI 202102/03 (B.1.525) on 12 February 2021.

Genomic profile

VUI 202102/03 (B.1.525) is lineage B.1.525 (first sequence detected in the UK in February 2021). The complete mutation profile of VUI 202102/01 (A.23.1 with E484K) is shown in Table 12 and genomic case definitions in Table 13.

Table 12. VUI 202102/03 (B.1.525) Variant defining mutations

Gene	Amino Acid	Actual Nucleotide	Note
orf1ab	-	1498C>T	nsp2:F231F
	-	1807A>G	nsp2:G334G
	-	2659G>A	
	T2007I	6285C>T	nsp3:T1189I
	-	8593T>C	nsp4:V13V
	-	9565C>T	nsp4:F337F
	3675_7del	11288_96del	nsp6:106_8del
	P4715S	14407C>T	nsp12:P323S
	-	18171C>T	nsp14:G44G
	-	20724A>G	nsp16:L22L
S Gene	Q52R	21717A>G	
	A67V	21762C>T	

Gene	Amino Acid	Actual Nucleotide	Note
	69_70del	21765_70del	
	144del	21991_3del	
	E484K	23012G>A	
	Q677H	23593G>C	
	F888L	24224T>C	
	-	24748C>T	F1062F
E Gene	L21F	26305C>T	
M Gene	I82T	26767T>C	
orf6	2del	27205_7del	
N Gene	2_3del	28278_80del	
	A12G	28308C>G	
	-	28699A>G	P142P
	-	29543G>T	

Red text indicates acquisition in subset of isolates within the lineage, non-variant defining mutations. Indels (shaded in orange) are not currently included in variant definitions.

Table 13. VUI 202102/03 (B.1.525) Genomic case definition

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

Biological profile

The significance of E484K has been described previously in this briefing. Q677H is proximal to the furin cleavage site, it is unclear what the impact of this mutation might be, however mutations around the furin cleavage site are known to modulate transmissibility. The deletions in the NTD (Δ69-70 and Δ144) are also found in the VOC 202012/01 (B.1.1.7) variant, Δ144 is an antigenic escape mutant and is highly associated with virus replication in immunocompromised patients. The deletion in NSP6 (Δ106-108) is found in multiple variants of concern (VOC 202012/01 (B.1.1.7) variant, VOC 202012/02 (B.1.351) and VOC 202101/02 (P.1) variants). NSP6 is involved in immune evasion but the impact of this deletion is currently unclear.

Epidemiological profile

As of 10 March 2021, there were 107 cases of VUI 202102/03 (B.1.525) in England (79 confirmed cases and 28 probable cases). In this geographically dispersed genomic cluster, 27 were linked to international travel, and 51 cases had no travel link. Travel history for 27 cases is pending and 2 cases were not contactable.

Deaths

As of 10 March 2021, 4 deaths in 107 cases with VUI 202102/03 (B.1.525) has been reported (case fatality 3.7%).

International Epidemiology

As of 8 March 2021, cases of VUI 202102/03 (B.1.525) have been reported in 11 countries or territories.

GISAID (gisaid.org) includes data on sequences available internationally. As of the 10 March 2021 328 sequences of VUI 202102/03 (B.1.525) are listed, excluding UK. (Denmark 120, Nigeria 76, USA 42, Italy 15, Slovenia 41, Canada 8, Japan 7, Netherlands 7, Germany 7, Ireland 6, France 6, Norway 4, Belgium 3, Australia 2, Jordan 2, Cameroon 2, Malaysia 2, Switzerland 2, Austria 2, Singapore 1, Finland 1, Thailand 1, Mayotte 1, Spain 1).

VUI 202102/04 (B.1.1.318)

The VUI 202102/04 (B.1.1.318) was identified in England in mid February 2021 through routine horizon scanning for the development of new clusters within the E484K genomes. This analysis identified an initial cluster of 6 cases containing E484K and other spike mutations, designated VUI 202102/04 (B.1.1.318) 23 February 2021.

Genomic profile

VUI 202102/04 (B.1.1.318) is lineage B.1.1.318. The complete mutation profile of VUI 202102/04 (B.1.1.318) is shown in Table 14 and genomic case definitions in Table 15.

Table 14. VUI 202102/04 (B.1.1.318) Variant defining mutations

Indels (shaded in orange) are not currently included in variant definitions.

Gene	Amino Acid	Nucleotide	Note
orf1ab	E378V	3852A>T	nsp3:E378V
	-	3961C>T	
	K2511N	7798G>T	nsp3K1693N
	T2936I	9072C>T	nsp4:T173I

Gene	Amino Acid	Nucleotide	Note
	A3209V	9891C>T	nsp4:A446V
	T3284I	10116C>T	nsp5:T21I
	3675_7del	11288_96del	nsp6:106_8del
	V6672M	20578G>A	nsp15:V320M
S	T95I	21846C>T	
	144del	21991_3del	
	E484K	23012G>A	
	-	23287T>C	
	P681H	23604C>A	
	D796H	23948G>C	
	-	24382C>T	
	-	25276C>A	
M	I82T	26767T>C	
orf8	1_3del	27894_901del	
	E106	28209G>T	
	-	28271A>G	
N	A208_A209delinsG	28896_8del	

Table 15. VUI 202102/04 (B.1.1.318) Genomic case definition

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

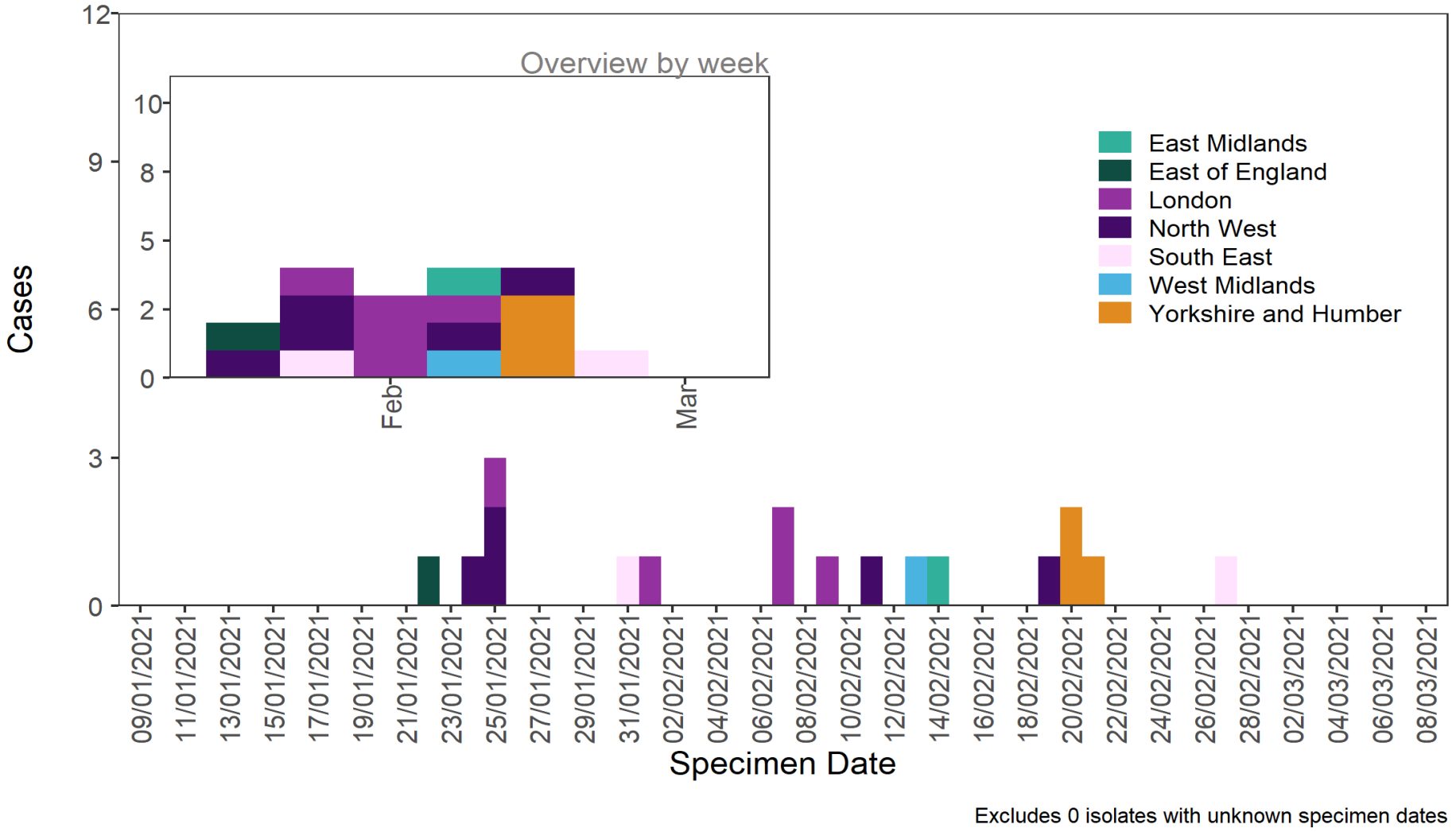
Epidemiological profile

As of 10 March 2021, there were 18 genomically confirmed cases of VUI 202102/04 (B.1.1.318). Cases are based across England (Table 16), with specimen dates ranging from 22 January 2021 to 27 February 2021 (Figure 9). Three of the initial 6-person cluster are related to cases that travelled to Nigeria, however the wide geographic spread suggests this VUI may be a result of multiple importations or could be an undersampled within the UK.

Table 16. Number of confirmed and probable VUI 202102/04 (B.1.1.318) cases, by region of residence (as of 10 March 2021)

Region	Confirmed	Probable	Total	Percent of England total
East Midlands	1	0	1	5.6
East of England	1	0	1	5.6
London	5	0	5	27.8
North West	5	0	5	27.8
South East	2	0	2	11.1
West Midlands	1	0	1	5.6
Yorkshire and Humber	3	0	3	16.7
Total	18	0	18	100.2

Figure 9. Confirmed and probable VUI 202102/04 (B.1.1.318) cases by specimen date, from 22 January 2021 as of 10 March 2021.
Larger plot includes last 60 days only



Deaths

No deaths (within 28 days of specimen date) among confirmed or probable VUI 202102/04 (B.1.1.318) have been reported as of 10 March 2021.

International Epidemiology

As of 8 March 2021 there are no cases reported internationally.
GISAID (gisaid.org) includes data on sequences available internationally. As of the 10 March 2021, there are no international VUI 202102/04 (B.1.1.318) sequences.

VUI 202103/01 (B.1.324.1 with E484K)

First identified via horizon scanning of genomes with spike mutations characteristic of VOCs (including both N501Y and E484K) on 3 March 2021, the variant VUI 202103/01 (B.1.324.1 with E484K) was designated VUI on detection as VUI 202103/01 (B.1.324.1 with E484K) on 4 March 2021.

Genomic profile

The complete mutation profile of VUI 202103/01 (B.1.324.1 with E484K) is shown in Table 17 and genomic case definitions in Table 18.

Table 17. VUI 202103/01 (B.1.324.1) Variant defining mutations

Indels (shaded in orange) are not currently included in variant definitions.

Gene	Amino Acid	Nucleotide	Note
orf1ab	T265I	1059C>T	nsp2: T85I
	G894S	2945G>A	nsp3: G76S
	-	3037C>T	
	-	6730C>T	
	T2196P	6851A>C	nsp3: T1378P
	-	8704T>C	from wider lineage
	-	8986C>T	
	T2952I	9120C>T	nsp4: T189I
	T3202M	9870C>T	nsp4: T439M
	H3580Q	11005C>A	nsp6: H11Q
	P4197S	12854C>T	nsp9: P57S
	S4398L	13458C>T	nsp12: S6L
	-	13617G>A	from wider lineage
	P4715L	14408C>T	nsp12: P323L
	-	14559G>A	
	G5530C	16852G>T	nsp13: G206C

S Gene	-	22388C>T	
	E484K	23012G>A	
	S494P	23042T>C	
	N501Y	23063A>T	
	D614G	23403A>G	
	P681H	23604C>A	
	E1111K	24893G>A	
orf3a	Q57H	25563G>T	
orf8	10_21del	27922_56del	
	-	28272A>T	from wider lineage
N Gene	M234I	28975G>A	

Table 18. VUI 202103/01 (B.1.324.1) Genomic case definition

CONFIRMED	All 8 variant defining changes called as alternate base
PROBABLE	N/A
LOW_QC	Fewer than 8 variant defining changes called as alternate base and all other positions either N or mixed base

Epidemiological profile

As of 10 March 2021, there are 2 confirmed cases in the UK in a single group of returning travellers. Two additional households note contact of which one has tested positive, sequence data not available. There is no current evidence of spread in the UK based on sequencing data. No deaths were reported.

International Epidemiology

As of 8 March 2021 there are no cases reported internationally.

GISAID (gisaid.org) includes data on sequences available internationally. As of the 10 March 2021, 0 sequences are listed internationally of VUI 202103/01 (B.1.324.1 with E484K).

Appendices

Appendix 1. SGTF Surveillance

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.'

Considering pillar 2 samples where we know both the sequence and the SGTF status, 99.6% of Δ69-70 sequences are SGTF, compared to 0.05% of sequences without the deletion. Since 1 January 2021, > 99.7% of Δ69-70 sequences are VOC 202012/01 (B.1.1.7) in all regions of England.

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, and has remained above 95% since the beginning of February 2021 (Figure 10). All regions in England are >98% SGTF in the most recent week (3 March to 9 March 2021; Figure 11). 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 10. 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 (1 September 2020 to 9 March 2021)

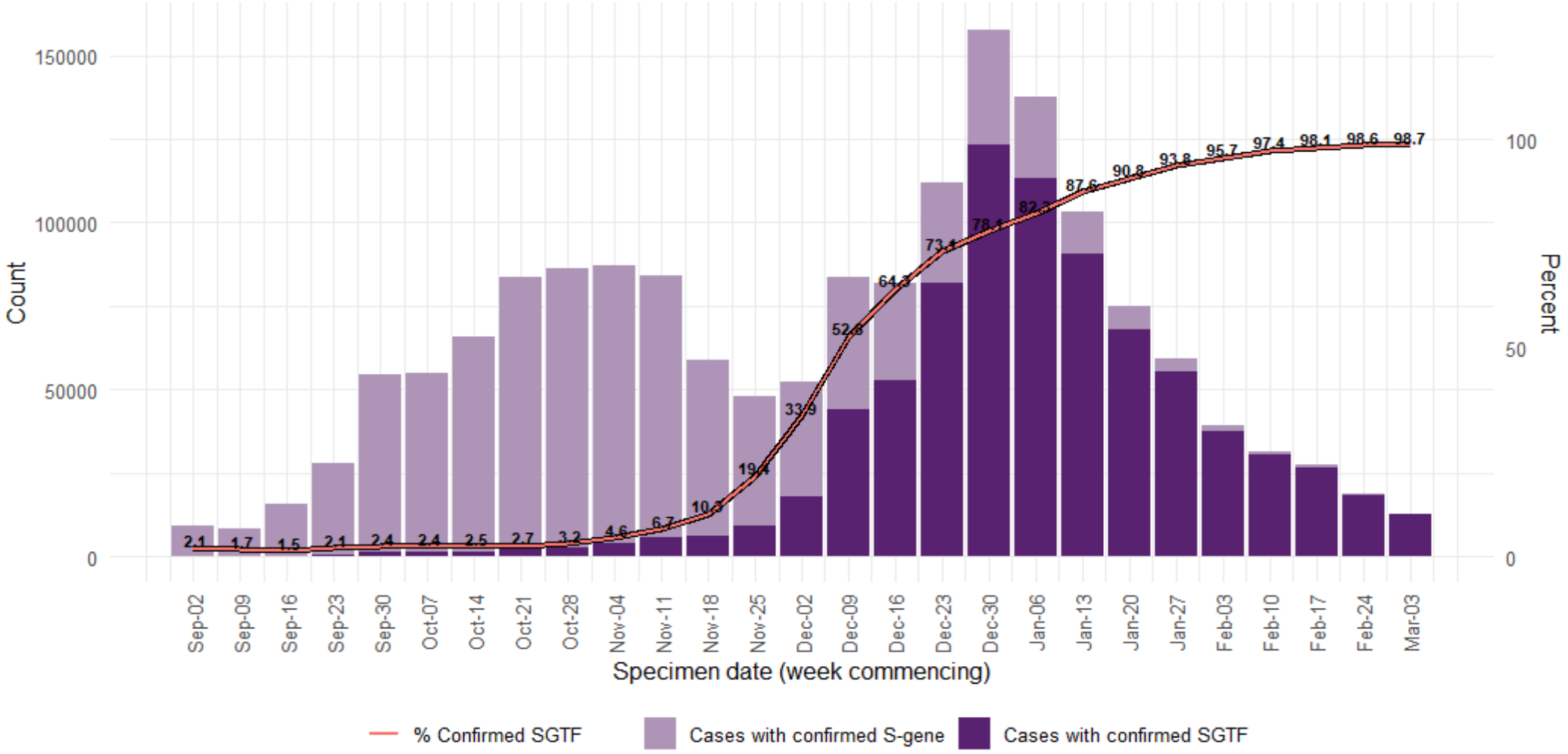
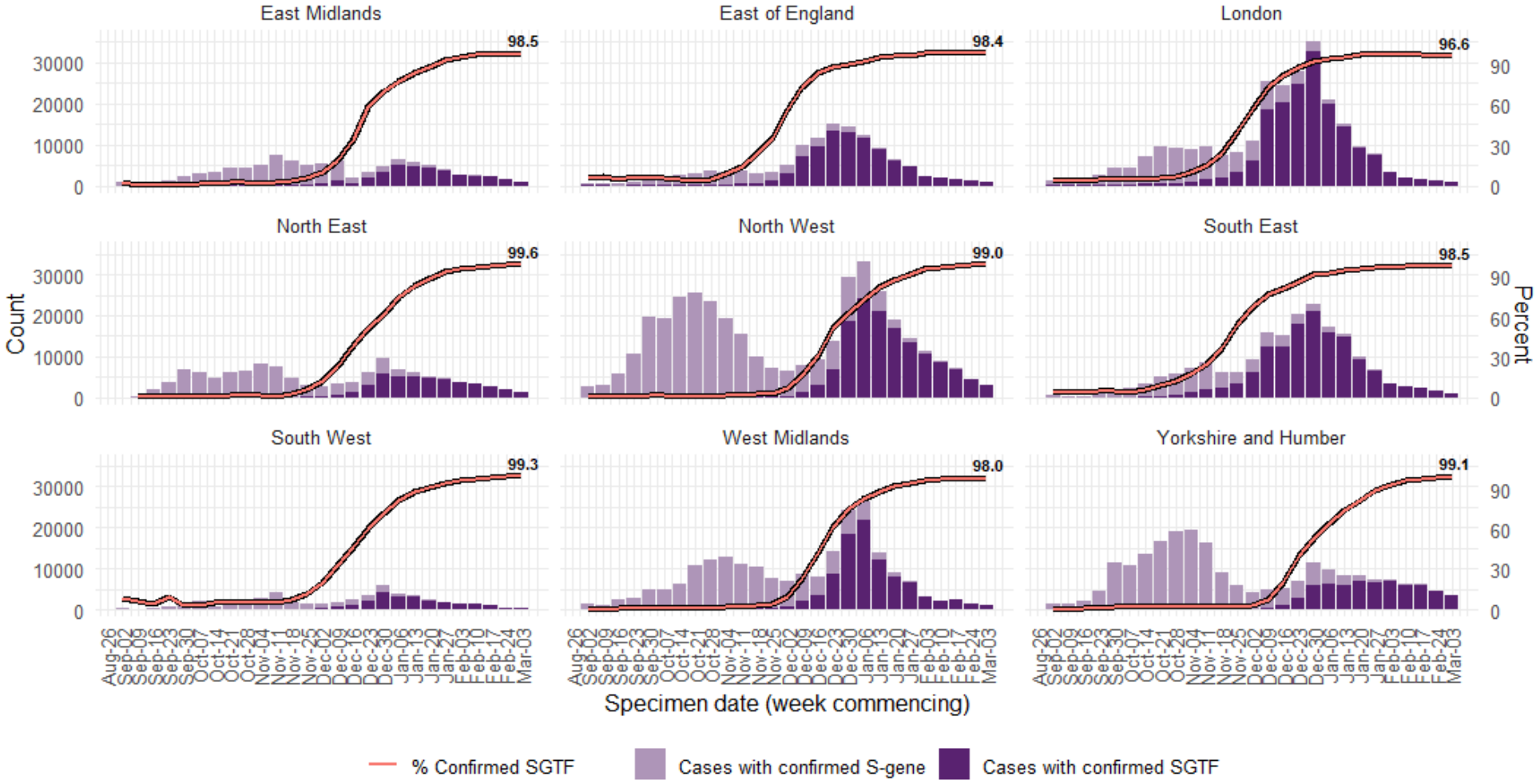


Figure 11. Weekly number and proportion of England Pillar 2 COVID-19 cases with SGTF among those tested with the TaqPath assay and with S gene detection results, by region of residence (1 September 2020 to 9 March 2021)



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).

Sources and acknowledgments

Data sources

Data used in this investigation is derived from the COG-UK dataset, the PHE Second Generation Surveillance System (SGSS), 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.

Acknowledgements

The authors are grateful to those teams and groups provid
ing data for this analysis, including: the Lighthouse Laboratories, COG-UK, the Wellcome Sanger Institute, the PHE Epidemiology Cell, Contact Tracing, Genomics and Outbreak Surveillance Teams.

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, research, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

Public Health England
Wellington House
133-155 Waterloo Road
London SE1 8UG
Tel: 020 7654 8000

Website: www.gov.uk/phe
Twitter: @PHE_uk
Facebook: www.facebook.com/PublicHealthEngland

Contact: All enquiries should be addressed to phe.enquiries@phe.gov.uk

Published: March 2021
PHE gateway number: GW-1991

PHE supports the UN Sustainable Development Goals

SUSTAINABLE DEVELOPMENT GOALS