UK Health Security Agency

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

Technical briefing 29

26 November 2021

This briefing provides an update on previous briefings up to 12 November 2021

Contents

Summary

This report has been published to share the detailed variant surveillance analyses which contribute to the variant risk assessments and designation of new variants of concern (VOC) and variants under investigation (VUI). This specialist technical briefing contains early data and analysis on emerging variants and findings have a high level of uncertainty.

A separate report is published covering surveillance data on all other VOCs and VUIs.

In summary:

1. There are 4 current VOCs and 9 VUIs (Table 1). The new Variant Under Investigation is VUI-21NOV-01, B.1.1.529.

2. Delta remains the predominant variant accounting for approximately 99.8% of sequenced cases in England from 10 October to the 22 of November 2021.

3. The Delta sublineage (VUI-21OCT-01) AY.4.2 continues to increase as a proportion of cases in the UK. It accounts for 15.2% of Delta cases in the most recent complete week of sequencing (11 November 2021 to 7 November 2021). In more recent weeks, sequencing data is incomplete, however AY.4.2 accounts for 17.8% of Delta cases in the week 8 November 2021 to 14 November 2021 and 20.3% in the week 15 November 2021 to 21 November 2021.

4. The logistic growth rate for (VUI-21OCT-01) AY.4.2 is estimated to be 15% per week compared to other circulating variants. Growth rate is context dependent and cannot be interpreted as a change in biological transmissibility.

5. Secondary attack rates amongst contacts of cases with (VUI-21OCT-01) AY.4.2 remain higher than those observed for other Delta cases for all categories (Table 6).

6. An updated analysis using more recent data confirms that there is no evidence that VUI-21OCT-01 (AY.4.2) causes more severe disease than other Delta variants.

7. Genomes from a new variant B.1.1.529 have been uploaded to GISAID by South Africa, Botswana and Hong Kong. It has a large number of mutations which are likely to be biologically significant, and which may change the behaviour of the virus with regards to immune escape, transmissibility, and susceptibility to some treatments. There are currently no detected cases in the UK. This variant was designated VUI-21NOV-01 on 25 November 2021 and is currently undergoing further rapid assessment.

All risk assessments are published separately online, except for Gamma, which was published within Technical Briefing 7 and Alpha within Technical Briefing 9. As Delta is the dominant variant in the UK, epidemiological data in the weekly surveillance report is also relevant.

Published information on variants

The collection page gives content on variants, including prior technical briefings. Definitions for variants of concern, variants under investigation, and signals in monitoring are detailed in Technical Briefing 8. Data on variants not detailed here is published in the Variant Data Update. Variant risk assessments are available in prior technical briefings.

The UK Health Security Agency (UKHSA), formerly Public Health England (PHE), has curated a repository from the 5 March 2021 containing the up-to-date genomic definitions for all VOCs and VUIs. The repository is accessible on GitHub.

World Health Organization (WHO) nomenclature from 31 May 2021 is incorporated. A table incorporating WHO and UK designations with Phylogenetic Assignment of Named Global Outbreak Lineages (Pangolin lineages) is provided below (Table 1). Following the table, variants are referred to using their WHO designation where this exists and the UK designation where it does not.

Technical briefings are published periodically. From technical briefing 15, briefings include variant diagnoses identified by whole-genome sequencing and a genotyping polymerase chain reaction (PCR) test, including the categorisation of sequenced and genotyped variant results and a rules-based decision algorithm (RBDA) to identify variant and mutation (VAM) profiles from genotype assay mutation profiles. Genotyping is used to identify variants Alpha, Beta, Delta, Gamma and Mu. Targets were updated in mid-May 2021 to prioritise accurate identification of Delta over Alpha.

Part 1. Surveillance overview

1.1 Variants under surveillance

Table 1 and Table 2 show the current VOC, VUI, and variants in monitoring detected and not detected in the UK as of 22 November 2021.

Table 1. SARS-CoV-2 variants of public health interest: variants detected in the UK

WHO nomenclature	Lineage	Designation	Status
Alpha	B.1.1.7	VOC-20DEC-01	VOC
Beta	B.1.351	VOC-20DEC-02	VOC
Gamma	P.1	VOC-21JAN-02	VOC
Delta	B.1.617.2, AY.1, AY.2, AY.3, AY.33, AY.34, AY.43	VOC-21APR-02	VOC
Delta	AY.4.2†	VUI-21OCT-01	VUI
	B.1.525	VUI-21FEB-03	VUI
	B.1.617.1	VUI-21APR-01	VUI
Mu	B.1.621	VUI-21JUL-01	VUI
	B.1.640		Monitoring
	Delta + E484K		Monitoring

† AY.4.2 is a sub-lineage within Delta that has been assigned as a distinct VUI

Table 2. SARS-CoV-2 variants of public health interest: variants present in GISAID but not detected in the UK

WHO nomenclature	Lineage	Designation	Status
	P.3	VUI-21MAR-02	VUI
	B.1.617.3	VUI-21APR-03	VUI
	P.2	VUI-21JAN-01	VUI
	B.1.1.318	VUI-21FEB-04	VUI
	B.1.1.529	VUI-21-NOV-01	VUI
Lambda	C.37*		Monitoring
	B.1.526		Monitoring
	B.1.1.7 with Q677H		Monitoring
	B.1.1.7 with S494P		Monitoring
	B.1 with 214insQAS		Monitoring
	B.1.629		Monitoring
	B.1.630, B.1.631/B.1.628		Monitoring
	P.1.8		Monitoring
	P.5		Monitoring
	B.1.1.7 + B.1.617.2 possible recombinant		Monitoring
	C.37 (S:L5F, G75V, D614G, L452Q, E484K, P499R, N501T, H655Y, P681R, T859N)		Monitoring
	C.36.3††		Monitoring
	B.1.427/B.1.429		Monitoring
	B.1.620		Monitoring
	R.1		Monitoring
	C.1.2		Monitoring
	B1.214.2		Monitoring

* Previously VUI-21JUN-01, de-escalated on 20 October 2021.

†† Previously VUI-21MAY-02, de-escalated on 20 October 2021.

Provisionally extinct variants are excluded from this table.

VOCs and VUIs are monitored weekly for observations within the last 12 weeks. If variants have not been detected in the UK within this period, they are moved to international status with continued monitoring. If a VOC or VUI has not been observed in the UK or international datasets within the preceding 12 weeks, it is designated as provisionally extinct, but monitoring remains in place.

^ Zeta and Theta were de-escalated by WHO and are no longer WHO variants under monitoring. Kappa, Iota, Eta and Epsilon were de-escalated by WHO and are now WHO variants under monitoring.

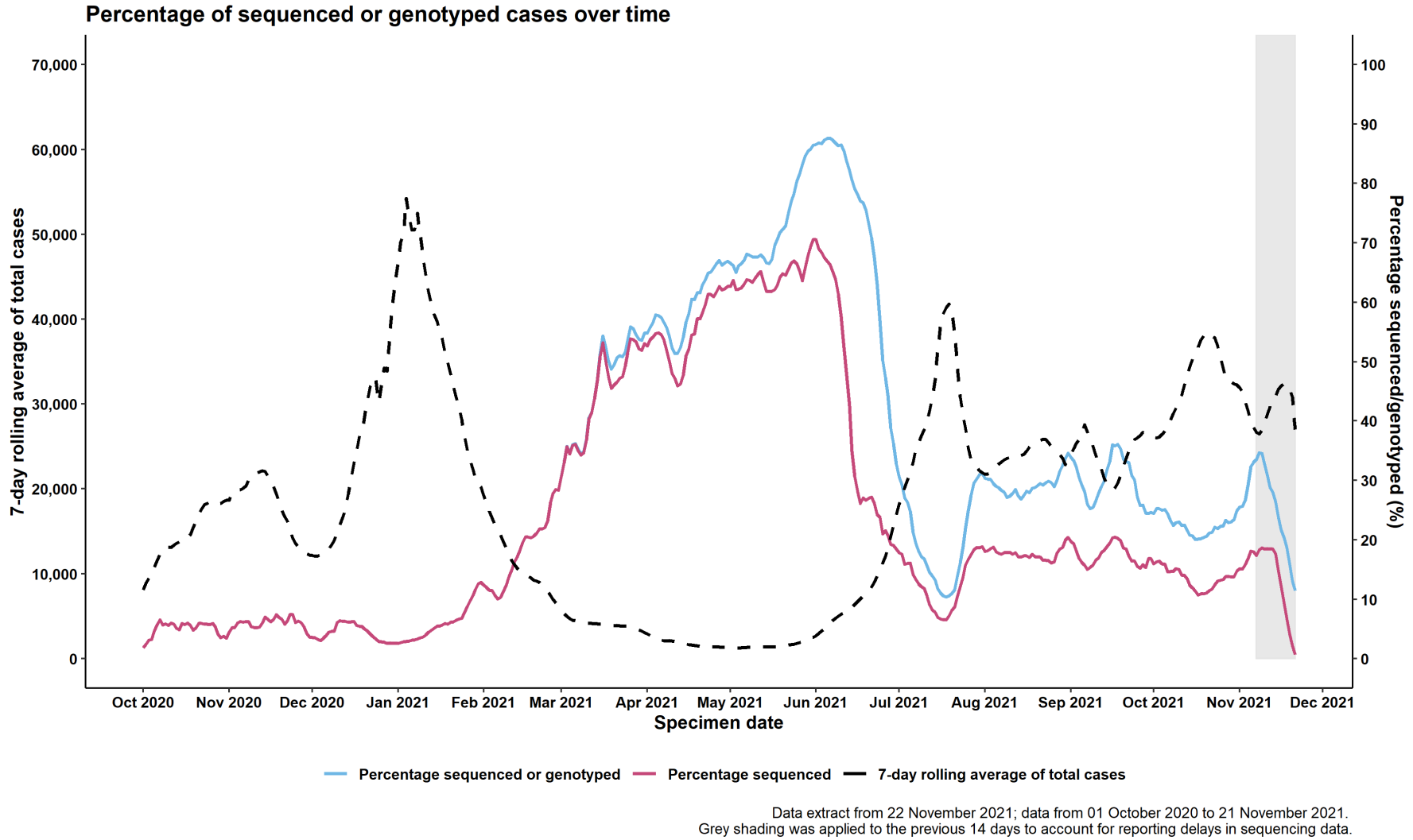
1.2 Sequencing coverage

Figure 1 shows the proportion of cases that have linked to a valid sequencing result (sequences included have 50% of the genome with sufficient read coverage) or genotyping PCR result over time. Figure 2 shows the proportion of cases sequenced and genotyped over time by regions. Figure 3 shows the proportion of cases sequenced and genotyped amongst cases who tested positive while in hospital.

Sequencing coverage is stable (Figure 1) and similar proportions are sequenced and genotyped across each region. Currently, the sequencing strategy for both Pillar 1 and 2 is:

- hospitalised cases and hospital staff
- cases among international travellers
- national core priority studies
- as near random a sample as possible from each region to the maximum coverage allowed by laboratory capacity

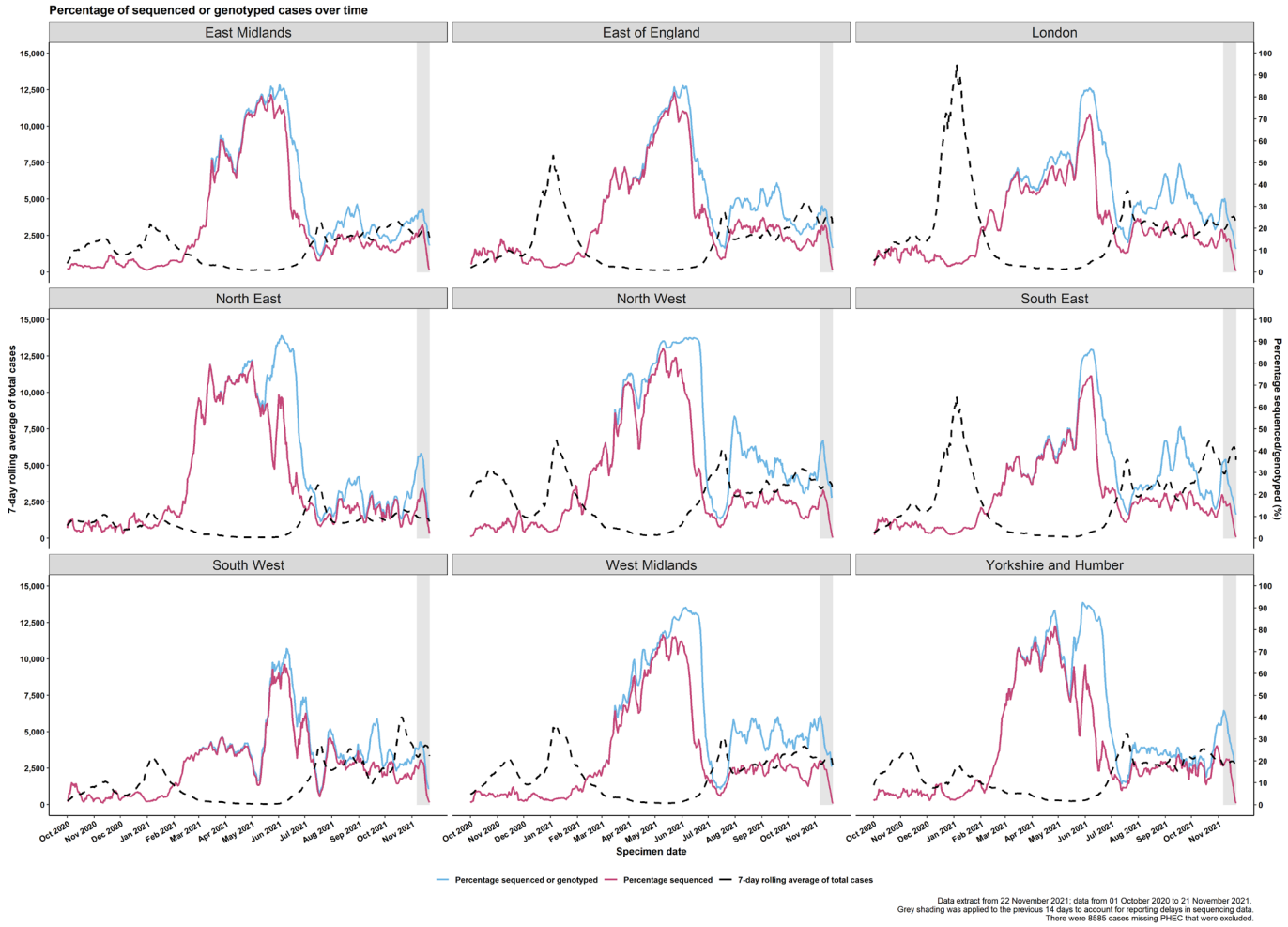
Figure 1. Coverage of sequencing with a valid result and genotyping over time (1 October 2020 to 21 November 2021)



(Find accessible data used in this graph in underlying data.)

Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

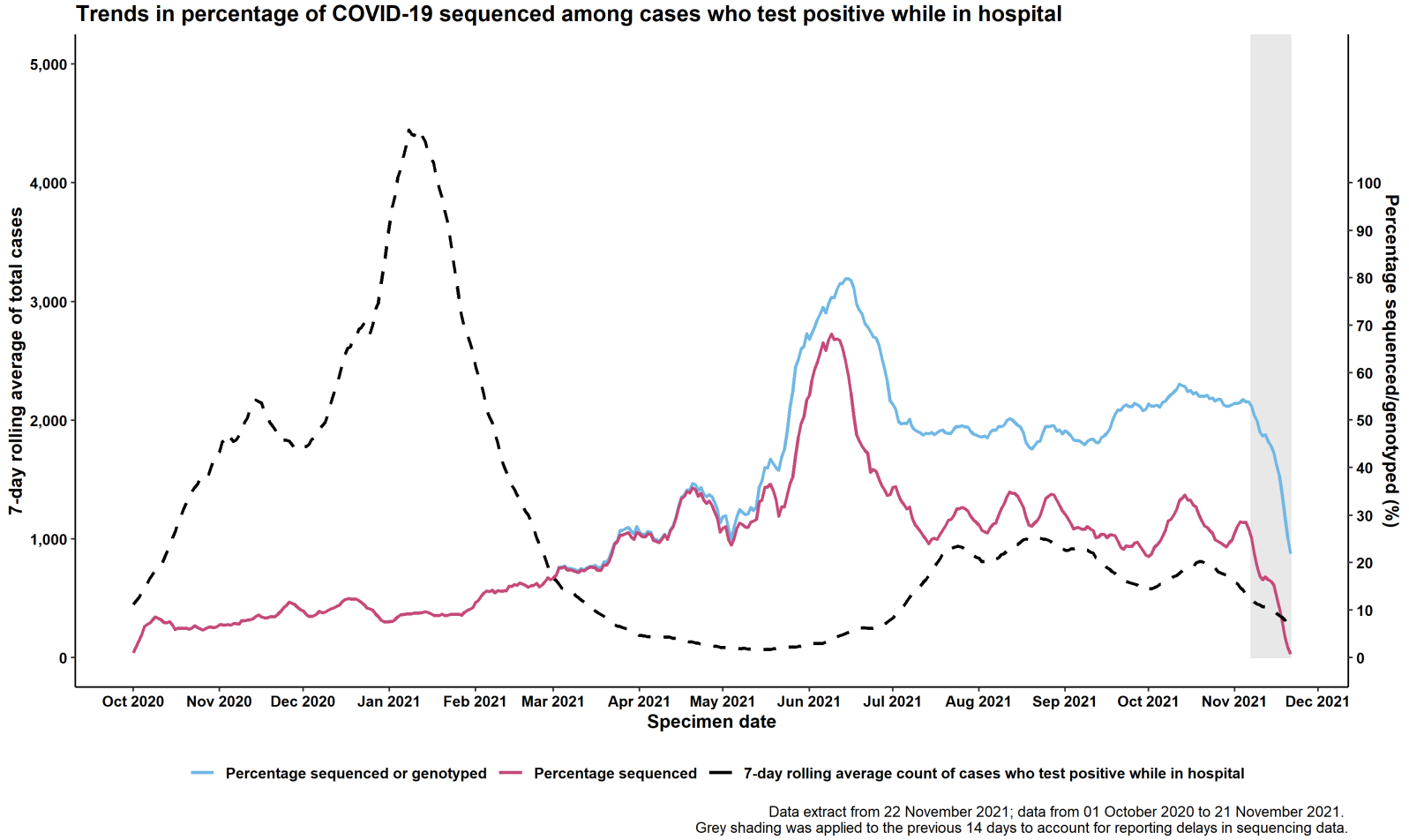
Figure 2. Coverage of sequencing with a valid result and genotyping over time by region (1 October 2020 to 21 November 2021)



(Find accessible data used in this graph in underlying data.)

Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

Figure 3. Coverage of sequencing with valid result and genotyping for cases who test positive in hospital (1 October 2020 to 21 November 2021)



(Find accessible data used in this graph in underlying data.)

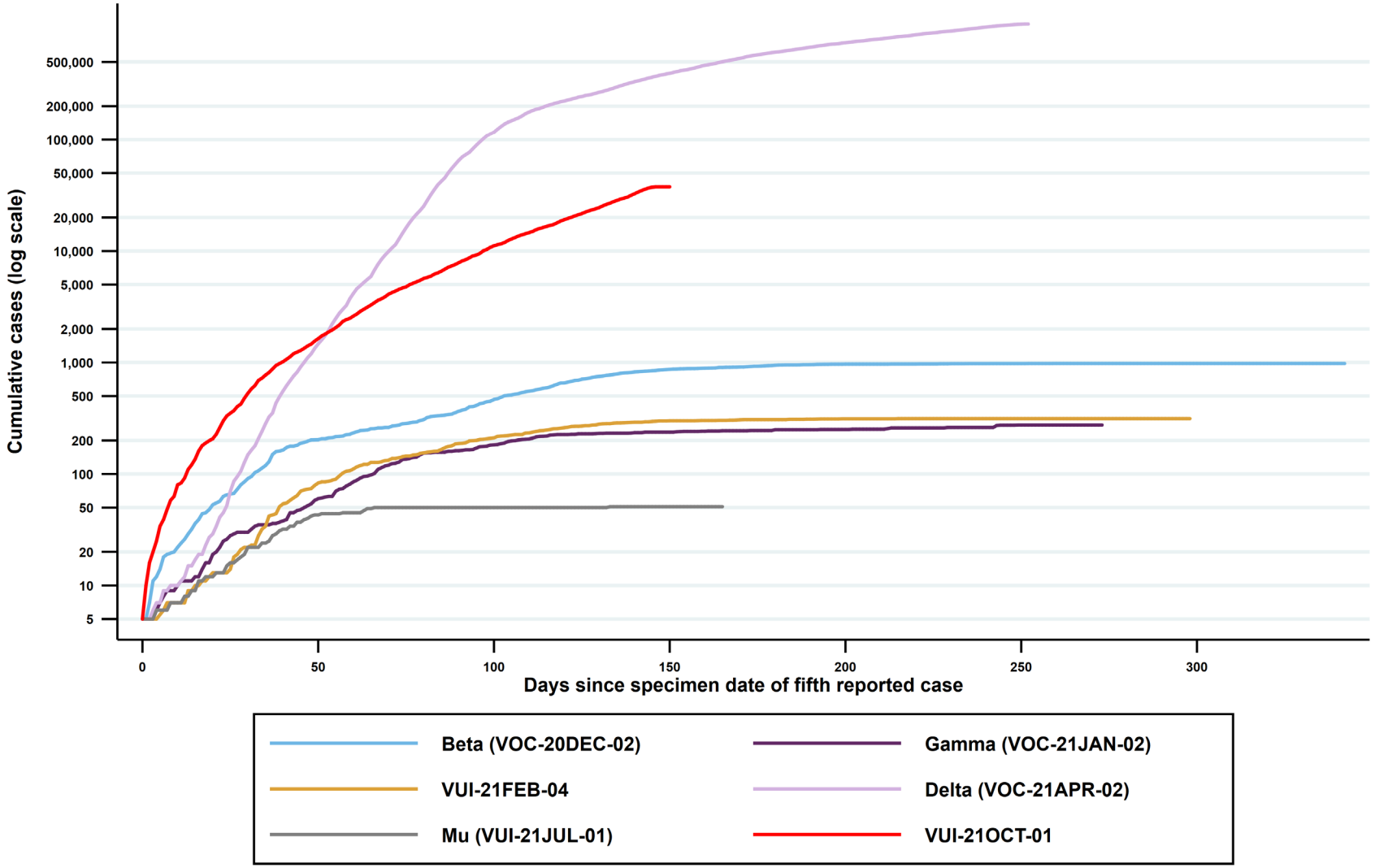
Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

1.3 VOC and VUI case numbers, proportion and deaths

Summary epidemiology for each variant and case numbers are updated online.
Figure 4 shows the cumulative number of cases per variant indexed by days since the first report.

Cases, hospitalisation, attendance and deaths by vaccination status are now presented in the COVID-19-vaccine-surveillance-report. These tables will be reinstated in the technical briefing for new VOC when they are identified.

Figure 4. Cumulative cases in England of variants indexed by days since the fifth reported case as of 21 November 2021



(Find accessible data used in this graph in underlying data.)

1.4 Variant prevalence

The prevalence of different variants amongst sequenced cases is presented in Figure 5 and split by region in Figure 6 and by travel in Figure 7.

Genotyping provides probable variant results with a shorter turnaround time of 12 to 24 hours after initial confirmation of coronavirus (COVID-19) by PCR. The initial panel of targets began trials in March 2021, using single nucleotide polymorphisms that included N501Y, E484K, K417N, and K417T. Results have been reported and used for public health action since 29 March 2021. On 11 May 2021, after rapid validation of targets to allow identification of Delta variant, P681R was introduced in the panel to replace N501Y. Genotyping results have now been fully integrated into the variant data reports and analyses. Changes in the use of genotyping over time should be considered when interpreting prevalence from genotyped data.

The ‘Other’ category in Figure 5 to 7 includes genomes where the quality is insufficient to determine variant status and genomes that do not meet the current definition for a VUI or VOC. The supplementary data for figures are available.

Figure 5. Variant prevalence for all England available sequenced cases from 1 February 2021 as of 22 November 2021 (excluding 264 cases where the specimen date was unknown).

(Find accessible data used in this graph in underlying data.) Dashed lines indicate period incorporating issue at a sequencing site. Black line indicates proportion of cases sequenced.

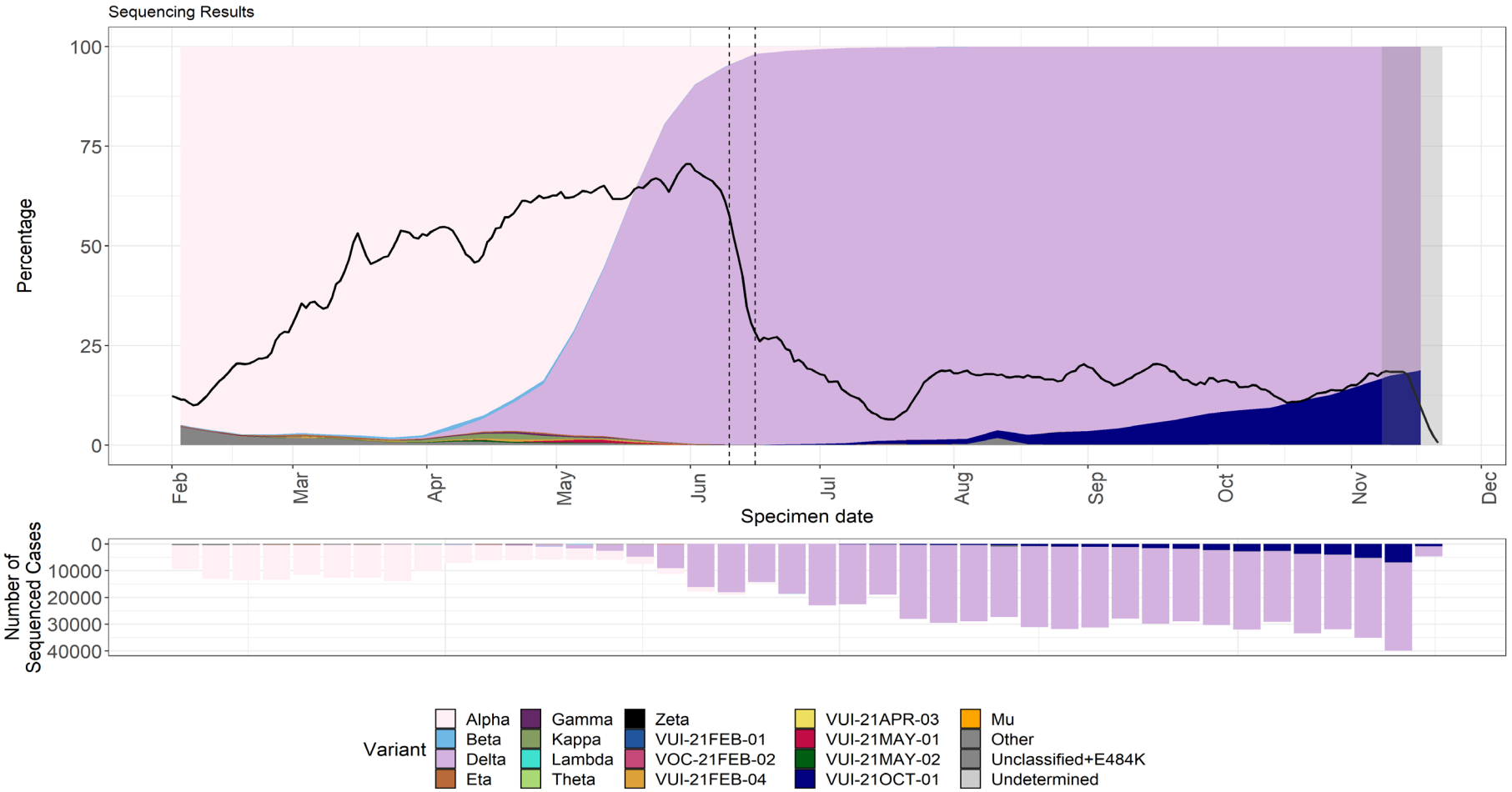


Figure 6. Variant prevalence from 1 February 2021 as of 22 November 2021 by region for all sequenced cases in England (excluding 5,396 cases where the region or specimen date were unknown).

(Find accessible data used in this graph in underlying data.)

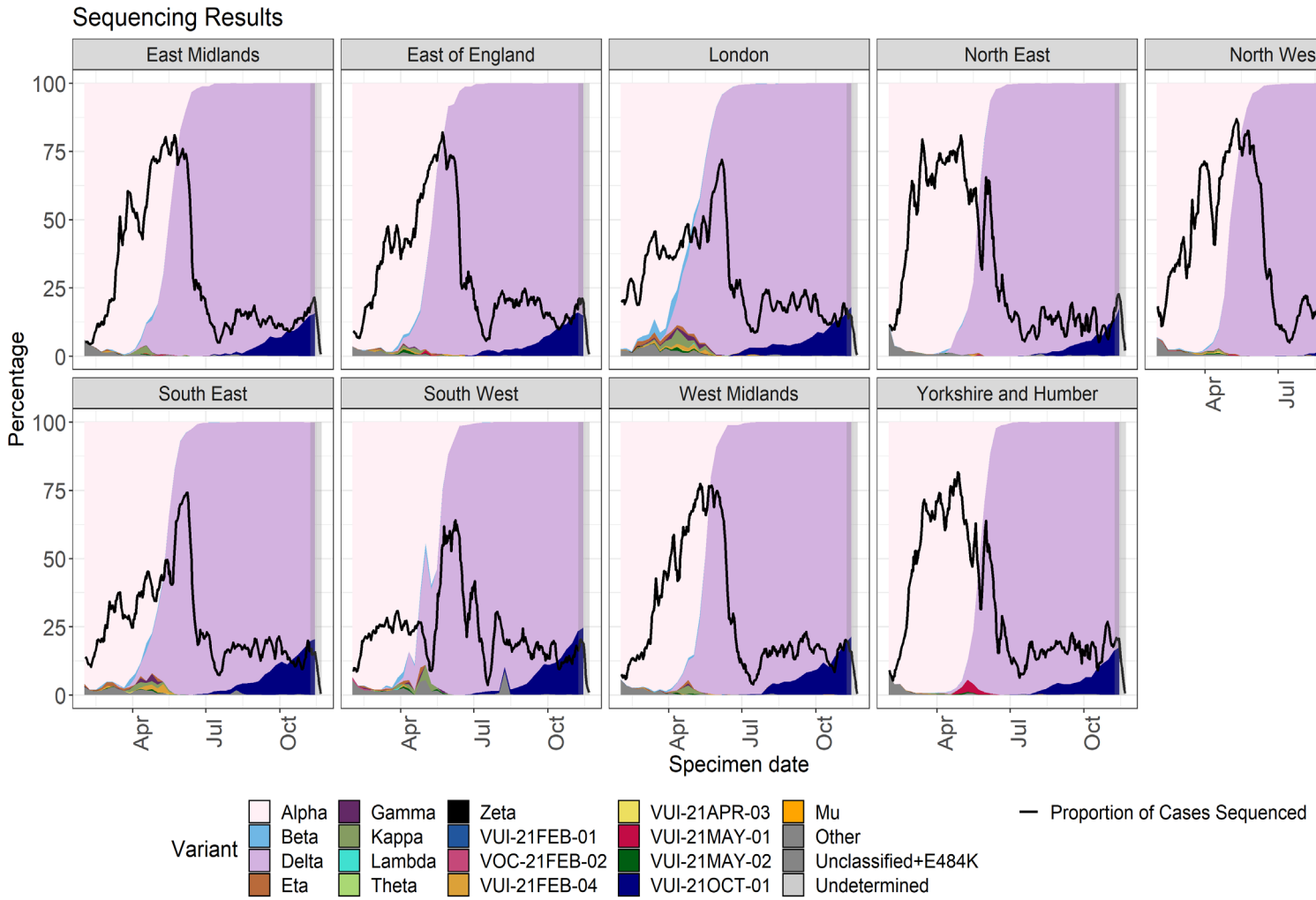
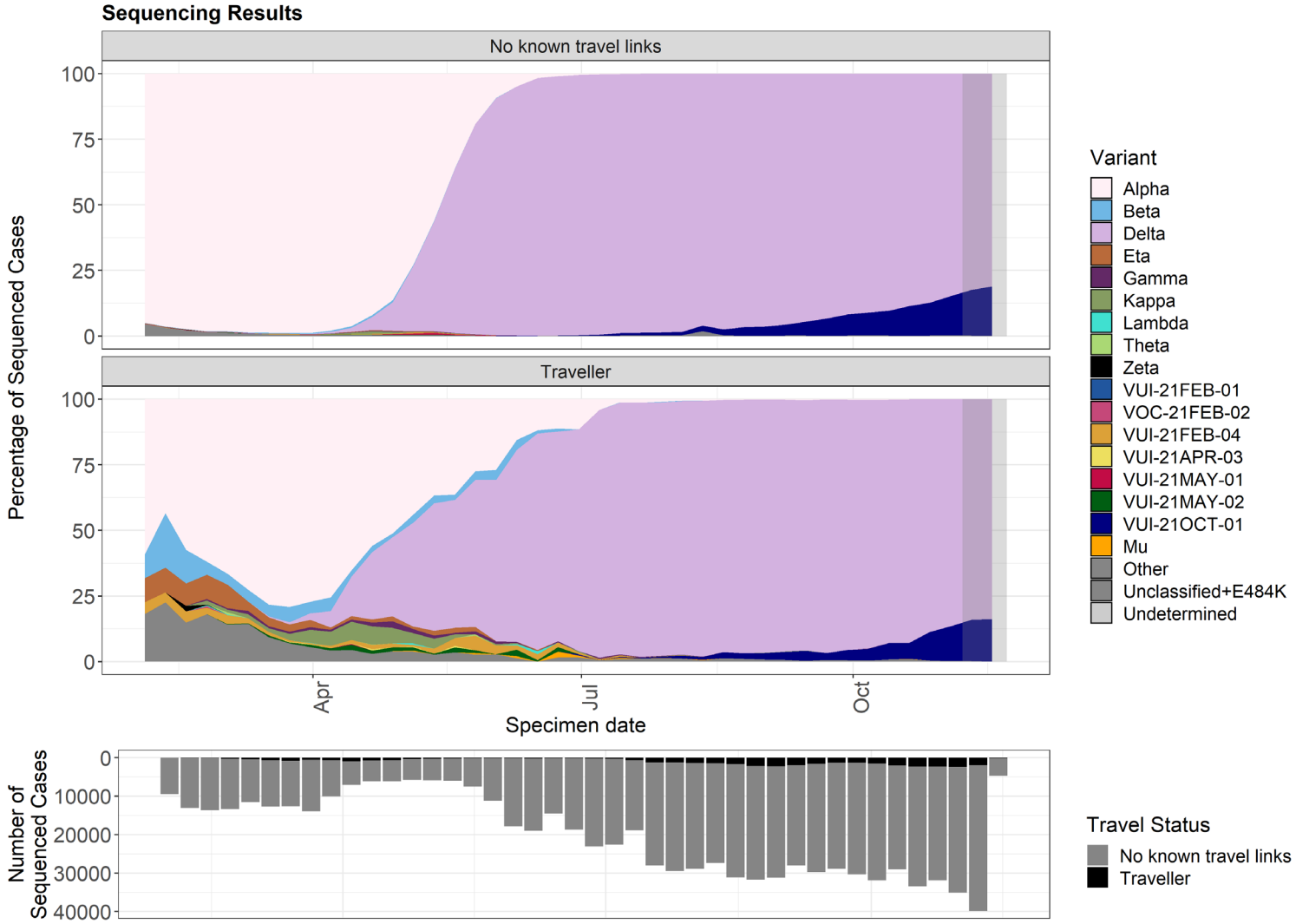


Figure 7. Prevalence of variants over time: all sequenced cases in England, split by travel status as of 22 November 2021.

(Find accessible data used in this graph in underlying data.)



1.5 Novel variant – VUI-21NOV-01 (B.1.1.529)

A new variant with 32 spike mutations was detected on GISAID on 23 November and designated B.1.1.529 on 24 November. This variant was designated VUI-21NOV-01 on 25 November 2021 and is currently undergoing further rapid assessment. The mutation profile is shown below. The mutation profile includes multiple spike mutations, including in the receptor binding domain and furin cleavage site, and additional mutations outside spike of uncertain significance. Based on location in the genome, structural modelling and experience from other variants, these may change the behaviour of the virus with regards to immune escape, transmissibility, and susceptibility to some treatments, particularly therapeutic monoclonal antibodies. There is no confirmatory laboratory data.

The genome also contains the spike deletion at position 69-70 which is associated with S gene target failure in some widely used PCR tests. PCR results pattern from affected test(s) can be used to assess spread.

Genomes from this variant have been uploaded from Botswana, Hong Kong and South Africa. South Africa has also shared data on the increase in S gene target failure in multiple regions of the country.

There are currently no detected cases in the United Kingdom. A rapid assessment of this variant is currently in process.

From the genomes available so far, the shared mutation profile is:

S: A67V, Δ69-70, T95I, G142D/Δ143-145, Δ211/L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F.

NSP3: K38R, V1069I, Δ1265/L1266I, A1892T

NSP4: T492I; NSP5 – P132H

NSP6: Δ105-107, A189V

NSP12: P323L

NSP14: I42V

E: T9I

M: D3G, Q19E, A63T

N: P13L, Δ31-33, R203K, G204R

This may be refined when more genomes are available. A UKHSA case definition will be published shortly.

Part 2. Enhanced analysis on specific variants. Delta-VOC-21APR-02 (B.1.617.2)

The lineage B.1.617.2 was escalated to a VOC in the UK on 6 May 2021 (VOC-21APR-02). This variant was named Delta by WHO on 31 May 2021.

2.1 Monitoring diversity within Delta – overview

Diversity within Delta is monitored through lineages and through individual mutations.

Figure 8 shows the prevalence of Delta lineages over time in sequences in England, as defined using Pangolin. VUI-21OCT-01 AY.4.2 remains dominant but other lineages introduced to the UK early have persisted over time. New sublineages of Delta are regularly identified and designated. This means that some sequences may be reclassified as the lineages are declared.

Mutations arising on Delta are shown in Figure 9 (heatmap of mutation proportion in S gene for any mutation seen in at least 5,000 genomes), and Table 3 (limited to S gene mutations with evidence for impact on antigenicity, avidity or furin cleavage site). Figure 10 shows the mutations arising on VUI-21OCT-01 (AY.4.2) as a proportion of total VUI-21OCT-01 (AY.4.2) sequences where that amino acid position can be called, and the mutation is seen in more than 100 sequences.

Figure 8. Prevalence of Pangolin lineages within Delta from 5 April 2021 to 22 November 2021

The plot excludes 370 that were not assigned Pangolin lineage due to sequence quality. The total number of sequences per week is shown by the black line. Only lineages with more than 1000 sequences are shown. Smaller lineages are either merged with parent lineages (for example, AY.3.1 is included in AY.3) or are included in 'Other'. (Find accessible data used in this graph in underlying data.)

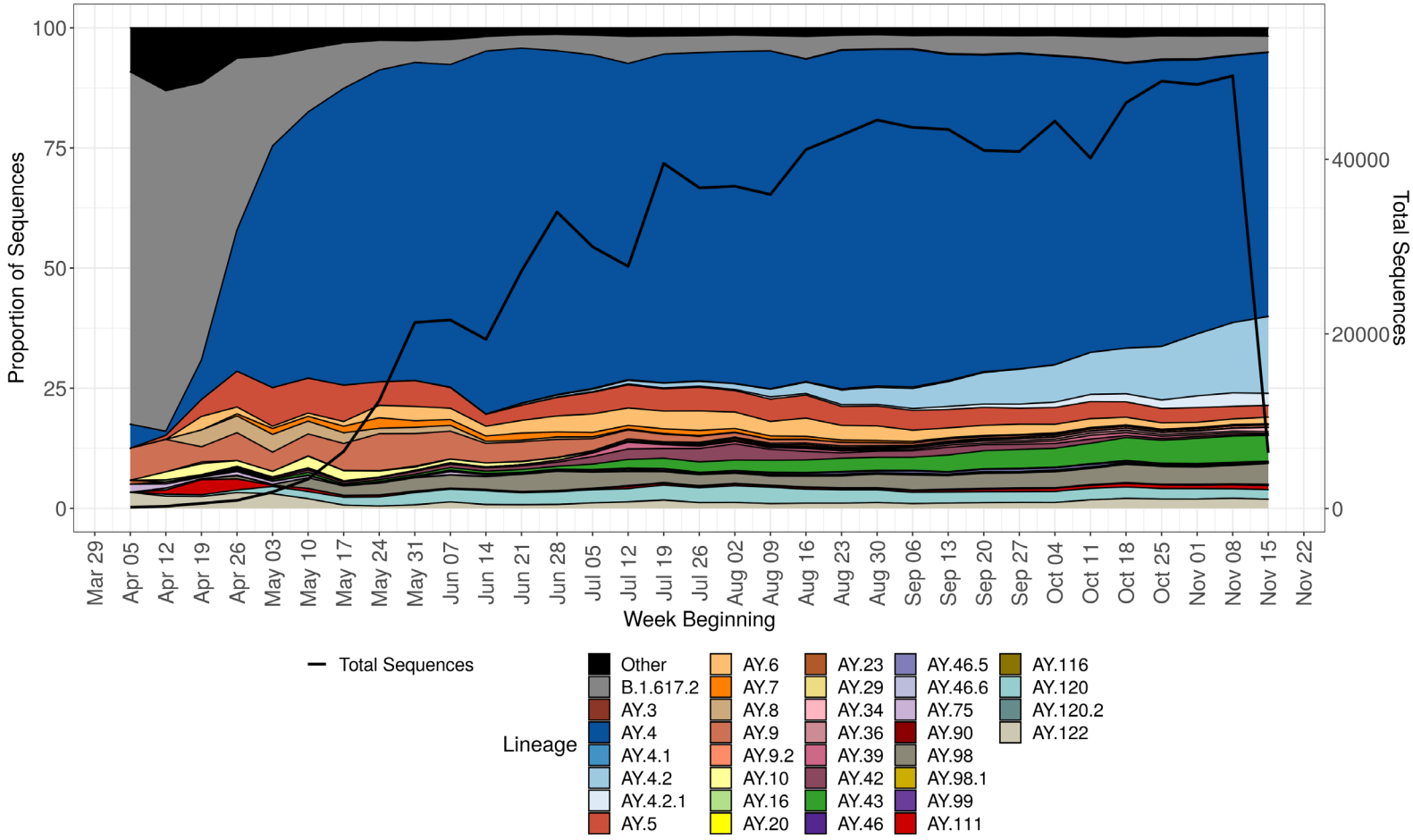


Figure 9. Proportion of Delta sequences (excluding VUI-21OCT-01 sequences) from UK containing mutations in spike, restricted to those mutations which are observed in at least 5,000 sequences

The proportion is calculated based on sequences where the amino acid is present in the sequencing data rather than the total number of genomes. The total number of Delta sequences per week are shown in the bottom panel. The number of sequences with each mutation is shown in each cell. VUI-21OCT-01 sequences are excluded from this data set. Mutations are split into those that are expected in all Delta sequences and those acquired subsequently (right hand axis label). (Find accessible data used in this graph in underlying data.

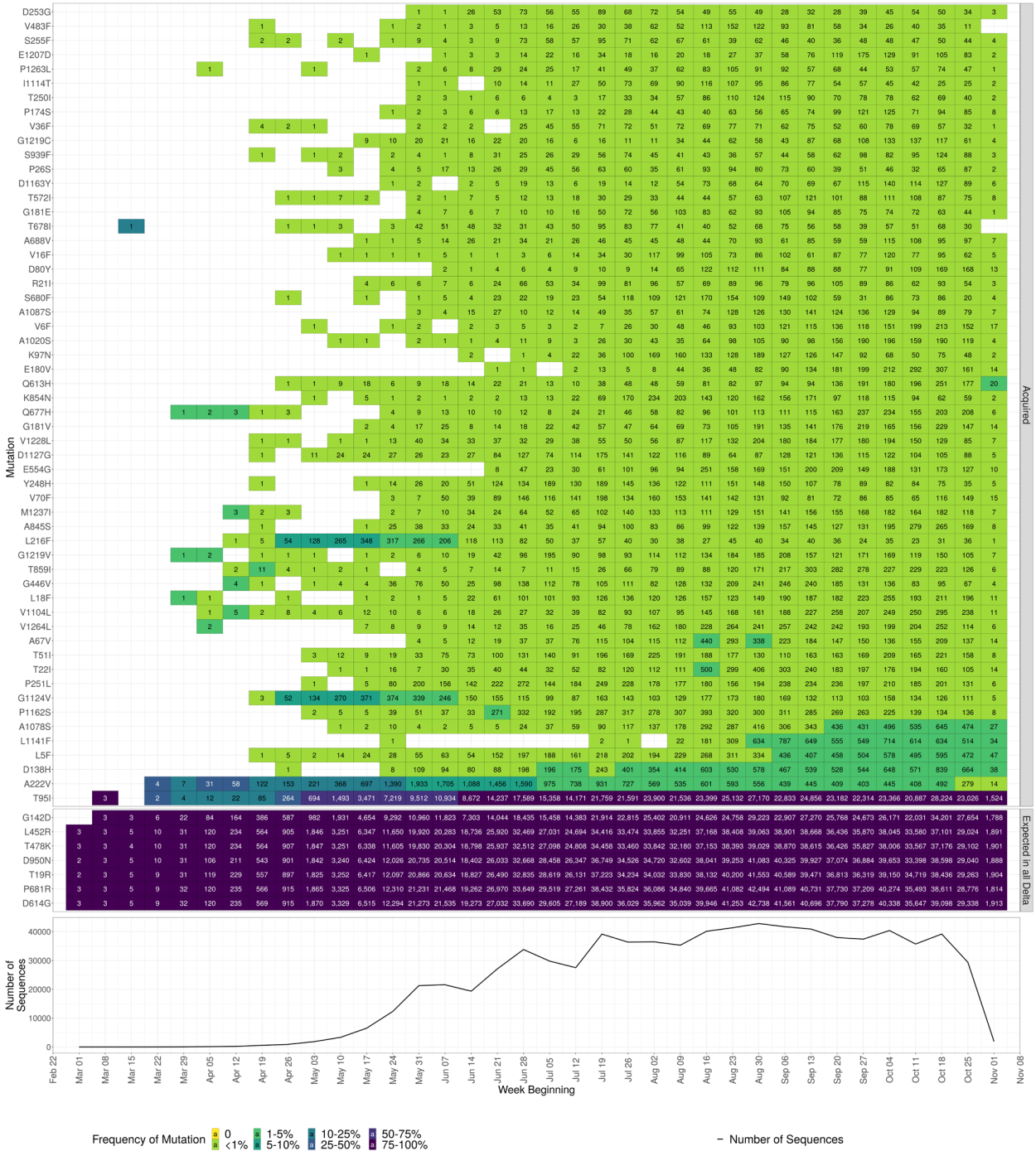


Figure 10. Proportion of VUI-21OCT-01 sequences from UK containing mutations in spike, restricted to those mutations which are observed in at least 100 sequences

The proportion is calculated based on sequences where the amino acid is present in the sequencing data rather than the total number of genomes. The total number of VUI-21OCT-01 sequences per week are shown in the bottom panel. The number of sequences with each mutation is shown in each cell. Mutations are split into those that are expected in all VUI-21OCT-01 sequences (including Delta mutations) and those acquired subsequently (right hand axis label). (Find accessible data used in this graph in underlying data.)

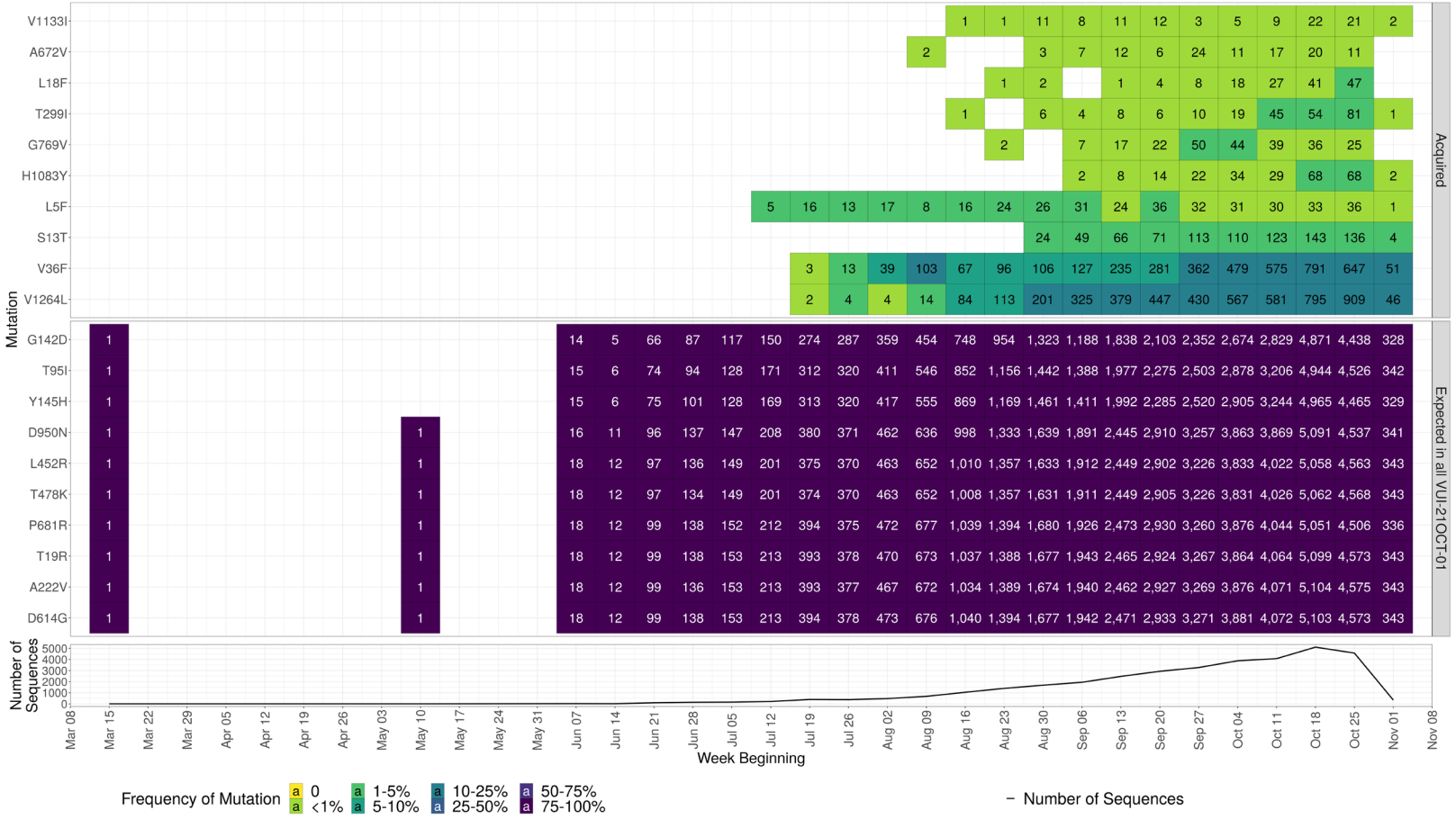


Table 3. Additional spike mutations of possible functional significance detected in Delta genomes in the UK as of 22 November 2021

Amino acid change	Delta sequences in UK dataset	Delta sequences outside UK (GISAID)	Delta sequences 23 August to 22 September		Delta sequences 23 September to 22 October		Delta sequences 23 October to 22 November	
			England	Outside UK	England	Outside UK	England	Outside UK
P251L	5077	19245	563	5252	565	3498	549	1110
G446V	3126	3840	494	1171	359	1029	255	296
Q613H	2567	26289	368	11171	743	4559	701	1599
V483F	1068	895	137	280	53	252	28	55
Q493E	409	247	95	44	31	26	1	0
S494L	497	789	125	264	84	166	90	53
E484Q	650	3456	93	787	168	810	201	480
K417N	344	5784	46	862	37	300	94	74
L455F	249	713	37	240	53	180	19	50
V445I	108	60	14	35	3	3	1	2
F490L	208	447	25	160	23	114	76	45
K444N	139	394	20	124	20	82	22	24
S494P	173	537	8	188	29	136	30	35
N501Y	108	647	9	54	18	56	21	17

F490S	174	350	33	89	52	139	56	51
A475V	81	122	16	35	8	37	19	14
K458N	58	103	7	22	0	28	11	7
R246I	67	162	9	65	14	29	1	2
P681H	102	455	3	126	10	78	35	28
E484K	232	527	25	171	61	94	86	39
K444R	117	188	16	66	19	59	2	18
L452Q	55	197	9	85	15	31	11	10
E484A	54	627	20	143	11	281	5	140
P499L	47	89	6	30	5	22	11	9
V445F	37	77	11	22	12	15	5	7
N439K	20	8	7	3	1	2	0	0
S494A	22	38	16	12	3	5	0	0
N501T	20	87	0	41	3	25	0	7
E484G	26	100	2	36	2	38	9	4
E484V	20	108	5	36	1	37	4	10
Q493L	22	71	1	18	3	5	5	1
D80N	15	79	1	34	0	18	6	2
V483A	11	97	3	35	1	25	3	6
F486L	7	7	1	4	0	0	0	1

V445A	41	75	1	22	17	25	15	1
E484D	24	105	0	20	9	28	5	10
G446D	7	36	1	12	0	12	1	4
G485D	6	4	2	2	0	1	1	0
T478I	3	23	0	10	0	4	0	2
Y453F	7	41	3	9	0	18	3	8
Q498R	6	64	0	20	0	14	0	12
Q493H	5	26	0	7	0	8	0	0
D80A	5	225	1	19	2	6	0	2
K444E	3	7	0	1	0	1	0	1
I472V	11	17	0	5	0	6	2	2
R246G	30	42	3	6	7	16	10	0
Q493R	3	13	1	6	0	5	2	0
Q493K	2	3	2	0	0	0	0	0
N450K	1	21	1	6	0	11	0	0
K458Q	1	8	0	1	0	5	0	0
K417T	4	25	1	9	1	8	1	0
K417E	6	16	0	6	0	0	3	0
V483G	1	17	0	5	0	1	0	0
V503L	1	4	0	1	0	2	0	0

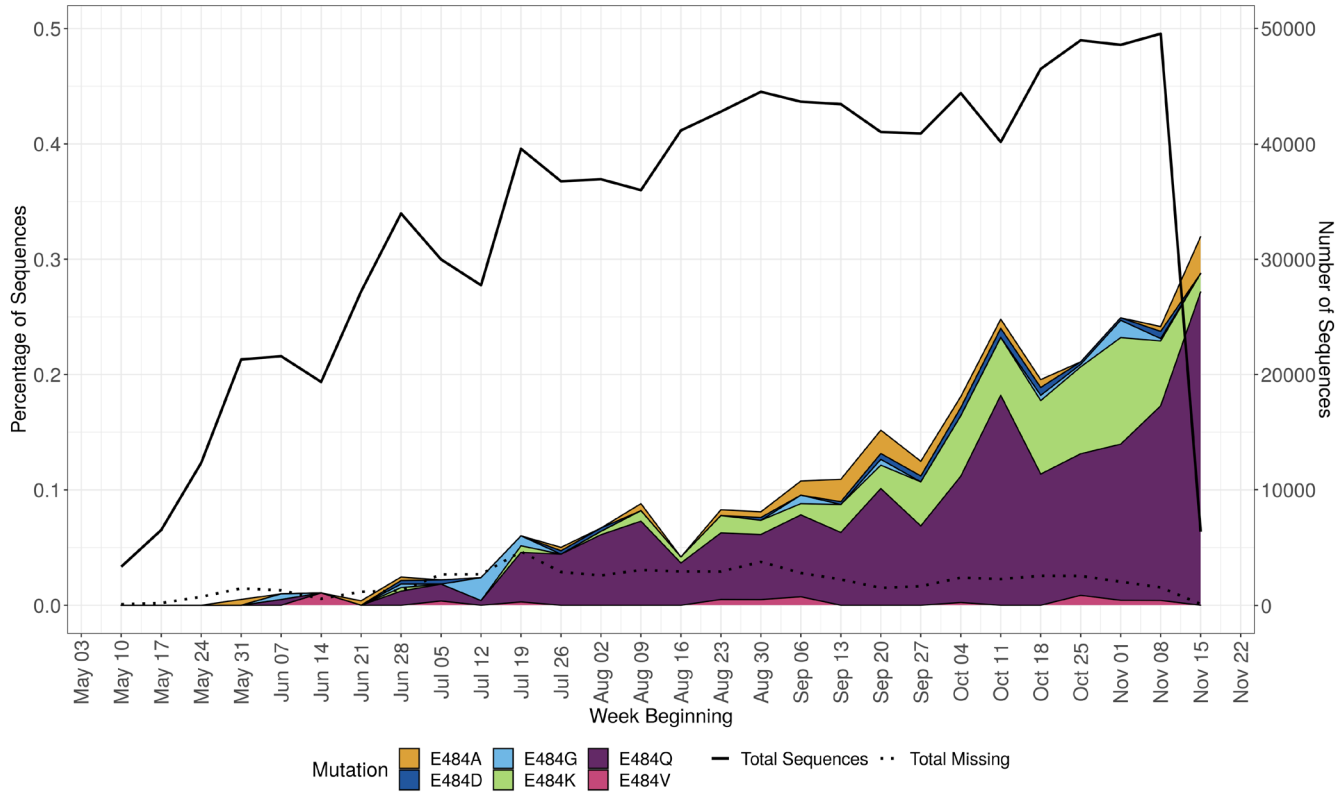
Y144N	1	3	0	0	0	0	0	0
N501H	1	9	0	4	0	2	0	0
Total	929360	1758889	134892	516360	131215	322048	121582	93838

*This data uses the numbers of genomes in the national genomic data set rather than case numbers. The unlinked sequences represent the number of sequences not present within the English surveillance system. These sequences include those samples from the Devolved Administrations and cannot be associated with a date by UKHSA.

2.2 Monitoring diversity within Delta-VOC-21APR-02 – Delta with mutations at Spike:484

Changes at position 484 in spike are potentially antigenically significant. Figure 11 shows the proportion of Delta sequences with a mutation at position 484 in spike. The proportions of Delta sequences with mutations at 484 remains extremely low.

Figure 11: Proportion of Delta sequences with non-synonymous mutations at position 484 in spike (where this position could be called)



Total number of sequences is indicated by the black line, the number of sequences where the amino acid at position 484 could not be determined is indicated by the dotted line.

Delta with E484Q was first identified through horizon scanning on the 3 August 2021 after being detected in 6 Scottish samples between 22 and 28 July 2021. As of the 22 November 2021, 653 sequences have been identified with 613 from England, 28 from Scotland, 8 from Wales and 4 from Northern Ireland. This is an increase of 176 sequences since the last report. The prevalence of Delta with E484Q in the most recent complete week of sequencing data (week beginning 08 November 2021) is 0.17% (where the mutation can be called). Internationally, as of 22 November 2021 the prevalence of Delta with E484Q mutations is 0.16% of Delta genomes on GISAID (including the UK).

Epidemiology in England

As of 22 November 2021, there are 653 Delta with E484Q sequences in the UK, 515 of which were linked to epidemiological data in England. This is an increase of 133 since the briefing of 12 November 2021. Cases have been detected across all 9 English regions, with most cases in the London (173, 33.6%) as shown by region in Table 4 and age in Figure 12. Of the 515 cases 156 have history of travel.

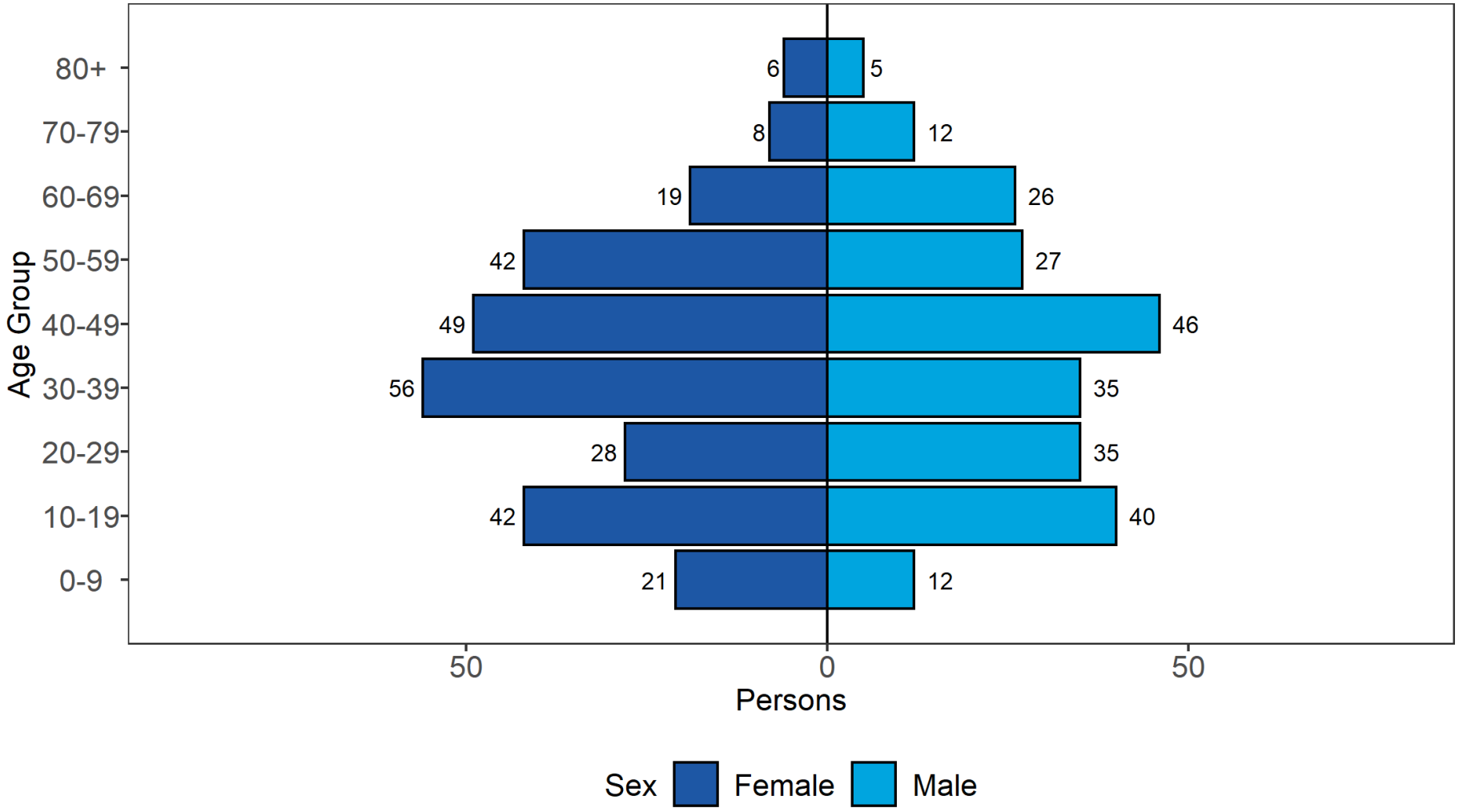
Table 4. Number of confirmed (sequencing) Delta cases with E484Q mutation, by region of residence as of 22 November 2021

Region	Confirmed (sequencing) case number	Case proportion
East Midlands	27	5.2%
East of England	44	8.5%
London	173	33.6%
North East	67	13.0%
North West	41	8.0%
South East	60	11.7%
South West	17	3.3%
West Midlands	26	5.0%
Yorkshire and Humber	41	8.0%
Unknown region	19	3.7%
Total	515	-

515 of the 653 Delta + E484Q sequences linked to a case.

Figure 12. Age-sex pyramid of confirmed (sequencing) Delta with E484Q mutation cases as of 22 November 2021

(Find accessible data used in this graph in underlying data.)



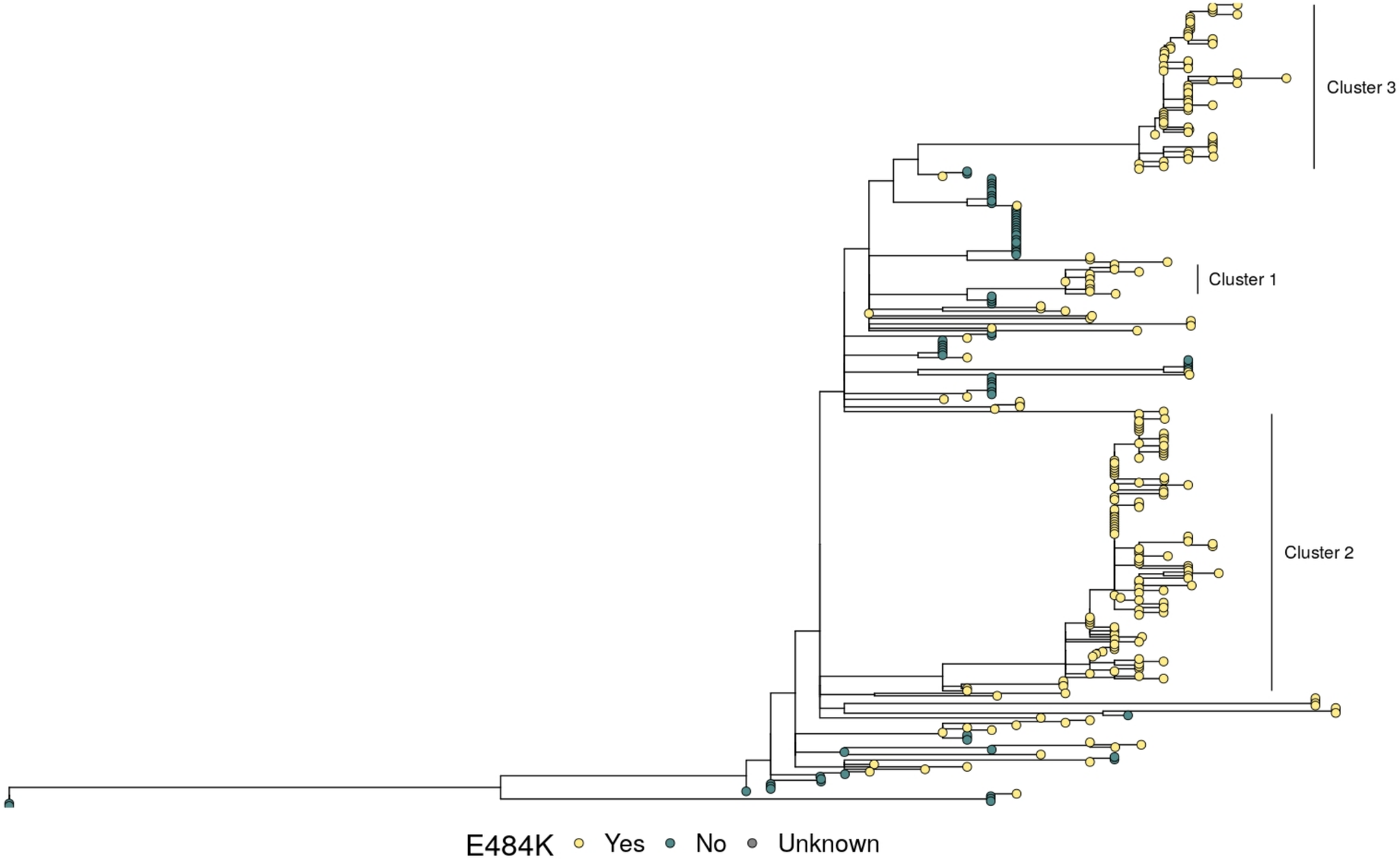
6 cases excluded where sex or age not reported

Delta with E484K was first detected on 8 July 2021 in a UK sequence with a collection date of 28 June 2021. As of 22 November 2021, 232 sequences have been identified with 211 from England, 17 from Scotland and 4 from Wales, an increase of 80 since the briefing of 8 November 2021. The prevalence of this mutation is 0.06% of Delta sequences (where the mutation could be called) for the week beginning 22 November 2021, which is the last complete week of sequencing data. Internationally, as of 22 November 2021 the prevalence of Delta with E484K mutations is 0.03% of Delta genomes on GISAID (including the UK).

The phylogenetic tree of UK Delta with E484K cases is shown in Figure 13, which includes 3 small clusters and multiple independent occurrences of the mutation (Delta with E484K is shown in yellow on Figure 13).

Figure 13. Maximum likelihood tree of UK Delta (B.1.617.2) with E484K cases as of 22 November 2021

Maximum likelihood tree was built using CIVET3 with default settings of 2 SNP distance to the query sequences (Delta with E484K) and sub-sampling of the tree to 239 sequences. Presence of the E484K mutation is indicated by the tip colour (Yellow indicates E484K cases). Three clusters of Delta with E484K have been identified with 4 or more sequences, which are highlighted on the tree. Cluster 1 has grown by one sequence, cluster 2 by 29 sequences and cluster 3 by 41 sequences since the last report. Four sequences of Delta with E484K were placed on separate catchment trees by the CIVET3 algorithm and so are not part of this tree. Supplementary data is not available for this figure.



Epidemiology in England

As of 22 November 2021, there are 231 Delta with E484K sequences in the UK, of which 175 could be linked to epidemiological data in England. Cases have been detected across 9 English regions, with most cases in the North West (87, 49.7%) as shown by region in Table 5, Figure 14 and by age in Figure 15. Of the 175 cases, 18 have history of travel.

Table 5. Number of confirmed (sequencing) Delta cases with E484K mutation, by region of residence as of 22 November 2021

Region	Confirmed (sequencing) case number	Case proportion
East Midlands	11	6.3%
East of England	7	4.0%
London	4	2.3%
North East	39	22.3%
North West	87	49.7%
South East	7	4.0%
South West	8	4.6%
West Midlands	1	0.6%
Yorkshire and Humber	8	4.6%
Unknown region	3	1.7%
Total	175	-

175 of the 184 Delta + E484K sequences linked to a case

Figure 14. Confirmed (sequencing) Delta with E484K mutation cases by specimen date and region of residence as of 22 November 2021

(Find accessible data used in this graph in underlying data.)

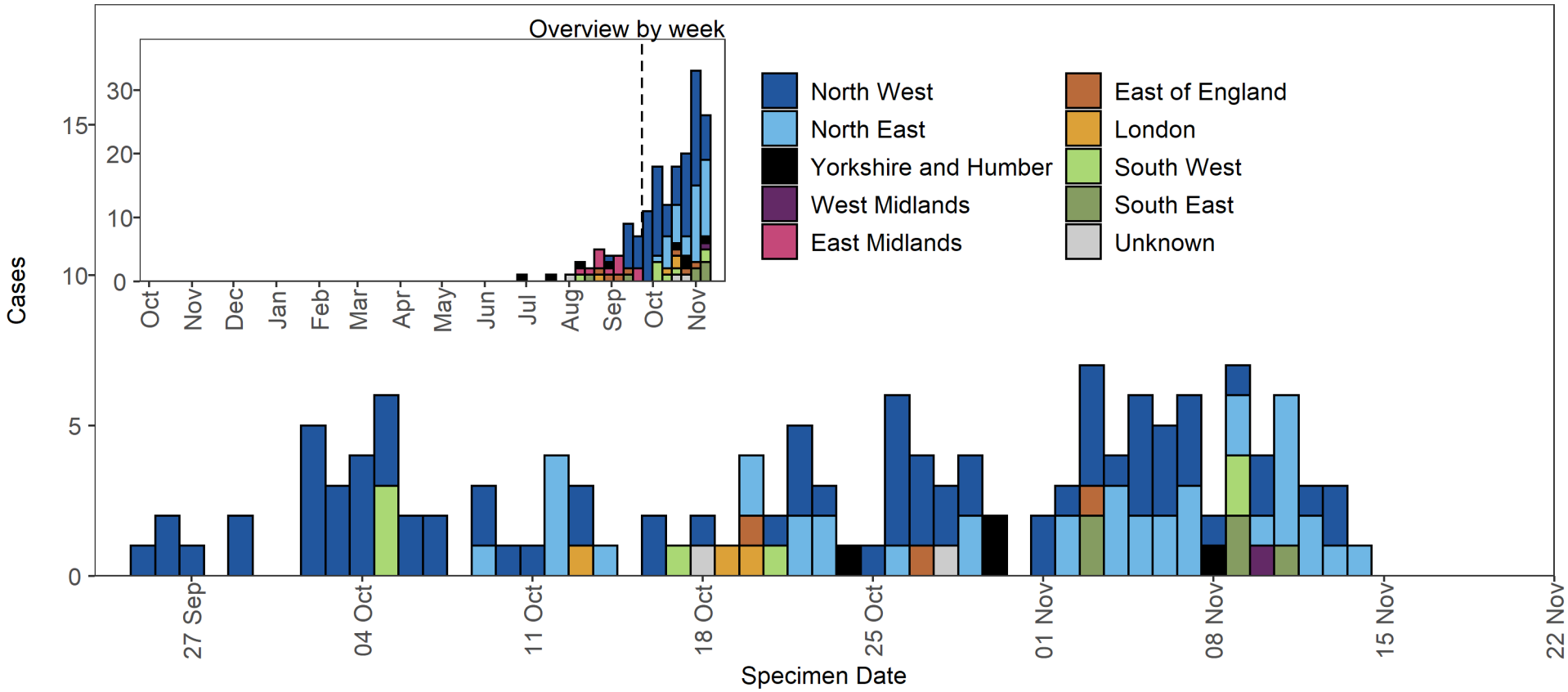
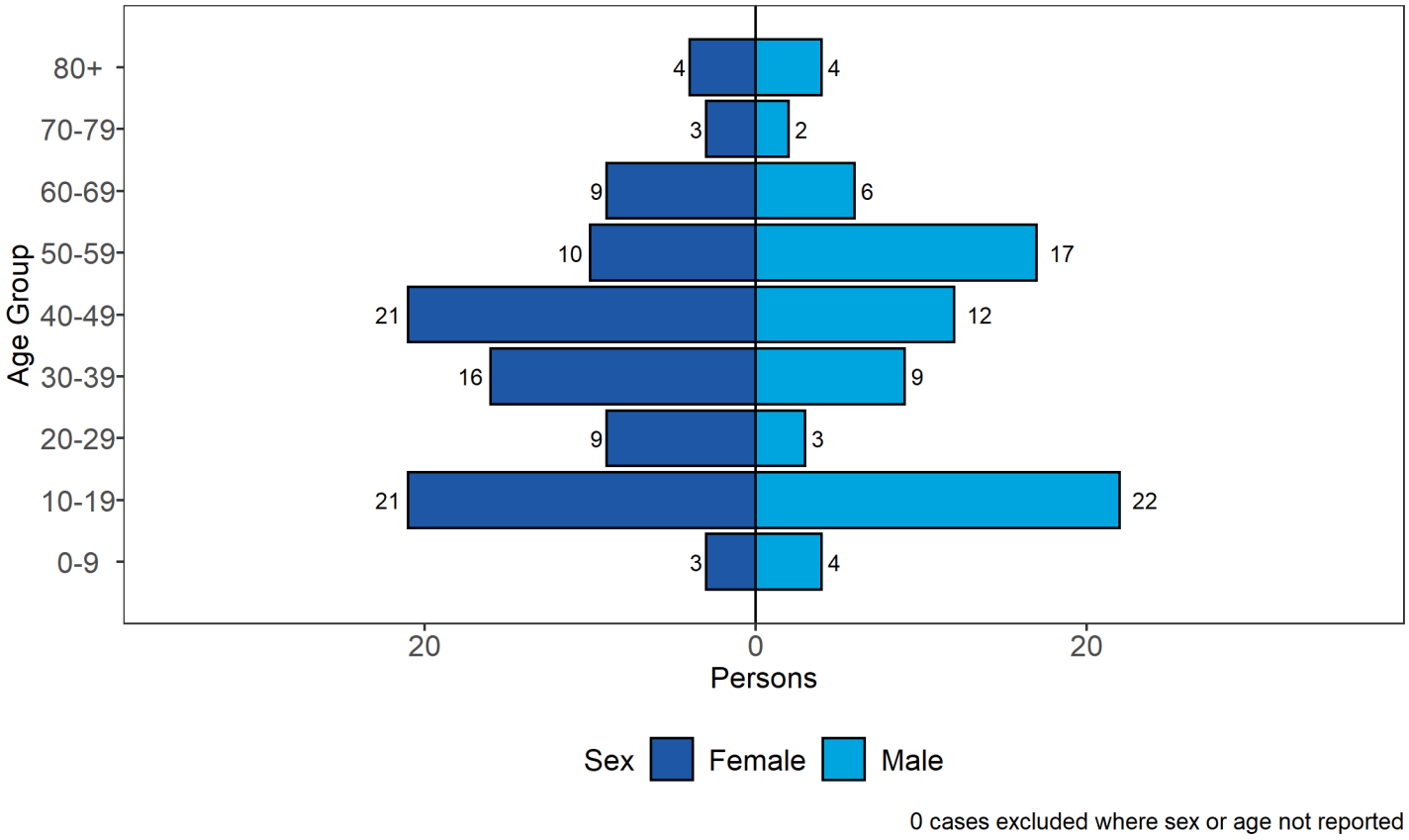


Figure 15. Age-sex pyramid of confirmed (sequencing) Delta with E484K mutation cases as of 22 November 2021

(Find accessible data used in this graph in underlying data.)



Part 3. Enhanced analysis on specific variants. Delta-VUI-21OCT-01 (AY.4.2)

The lineage B.1.617.2 was escalated to a VOC in the UK on 6 May 2021 (VOC-21APR-02). This variant was named Delta by WHO on 31 May 2021. New sub-lineages of Delta are regularly identified and designated. The Delta sublineage AY.4.2 was designated VUI-21OCT-01 on 20 October 2021.

3.1 Secondary attack rates

This section includes secondary attack rates for contacts of traveller cases and separate rates for household and non-household contacts of non-traveller cases with Delta and VUI-21OCT-01 (AY.4.2) from the period 1 September 2021 to 1 November 2021. Secondary attack rates are based on positive tests amongst contacts named to NHS Test and Trace by an original case identified with a sequenced or genotyped VOC or VUI.

Delta cases are identified using sequencing results supplemented with genotyping results and exclude low-quality results, VUI-21OCT-01 (AY.4.2) are identified by sequencing only. Secondary attack rates are shown for cases with and without travel history. In non-travel settings, only close contacts named by the original case are included, that is, household members, face-to-face contact, people within one metre of the case for one minute or longer, or people within 2 metres for 15 minutes. In travel settings, the contacts reported are not restricted to only close contacts named by the case. For example, they may include contacts on a plane linked by additional contact tracing efforts. This likely deflates secondary attack rates amongst travellers compared to non-travellers. In addition, people recently returning from overseas are subject to stricter quarantine measures and may moderate their behaviour towards contacts. Travel history suggests where infection of the original case may have occurred.

Table 6 shows the secondary attack rates split by type of contact. Secondary attack rates amongst contacts of cases with VUI-21OCT-01 (AY.4.2) continue to be higher than those observed for other Delta cases for all categories.

Table 6. Secondary attack rates for contacts of cases with VUI-21OCT-01 and other Delta

(1 September 2021 to 1 November 2021, variant data as of 15 November 2021 and contact tracing data as of 22 November 2021).

Variant	Travel-related cases (with contacts)	Non-travel cases (with contacts)	Travel-related case proportions	Secondary attack rate in contacts of travel-related cases (95% CI) [secondary cases/contacts]	Secondary attack rate in household contacts of non-travel or unknown cases (95% CI) [secondary cases/contacts]	Secondary attack rate in non-household contacts of non-travel or unknown cases (95% CI) [secondary cases/contacts]
VUI-21OCT-01 (AY.4.2)	930 (75.3% with contacts)	20,834 (74.4% with household, 19.1% with non-household contacts)	4.3%	2.1% (1.9% - 2.3%) [304/14,522]	12.3% (12.0% - 12.7%) [4,897/39,688]	4.2% (3.9% - 4.6%) [490/11,539]
Other Delta	16,828 (70.9% with contacts)	376,624 (73.4% with household, 18.2% with non-household contacts)	4.3%	1.5% (1.5% - 1.6%) [4,740/308,261]	11.3% (11.3% - 11.4%) [79,633/701,812]	3.5% (3.5% - 3.6%) [6,987/197,601]

Other Delta includes all Delta cases identified by sequencing and provisional genotyping, except those identified as Delta with E484K or VUI-21OCT-01 by sequencing. Secondary attack rates are marked as ‘Unavailable’ when count of contacts is fewer than 50 or count of cases is fewer than 20. Travel-linked cases for secondary attack rates are identified positively in NHS Test and Trace data using multiple UKHSA sources. Some travel-linked cases may be missed by these methods and would be marked as non-travel-linked or unknown.

Secondary attack rates from NHS Test and Trace should generally be considered lower bounds due to the nature of contact tracing and testing. Data provided is for period until 1 November 2021 in order to allow time for contacts to become cases, hence case counts are lower than other sources. Cases are included in case counts if their onset or (if asymptomatic) test is during the period of study, contacts are included in secondary attack rates if their exposure date or onset or test of exposing case if the contact is a household contact is during the period of study. Secondary attack rates are suppressed when count of contacts is less than 50 or count of cases is less than 20. Probable (genotyping) results are included, low quality genomic results are not.

3.3 Epidemiology of Delta-VUI-21OCT-01 (AY.4.2) in England

As of 22 November 2021, VUI-21OCT-01 (AY.4.2) accounts for 15.2%, 17.8%, 20.3% of sequenced Delta cases in England in the weeks beginning 1 November, 8 November, 15 November 2021 respectively (last two week incomplete).

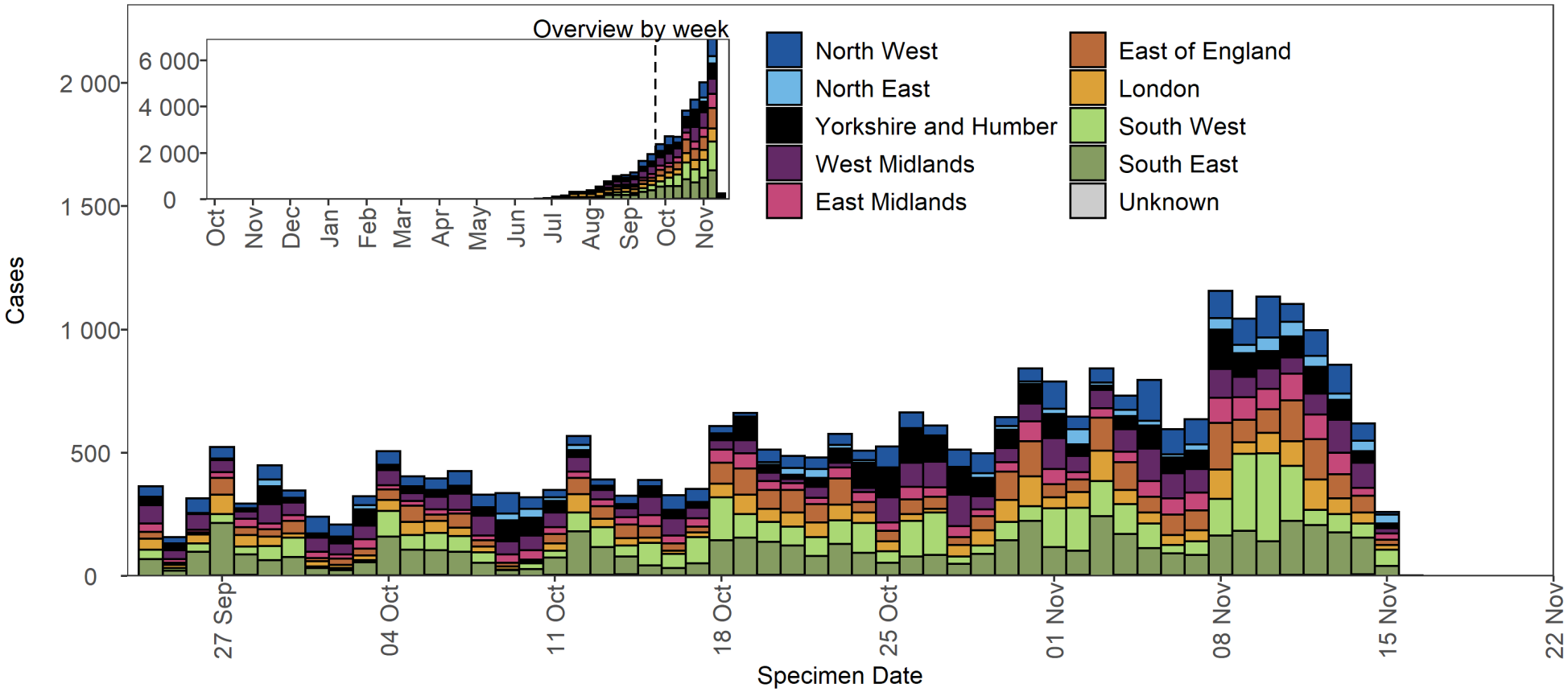
Variant prevalence for all cases in England as of 21 October 2021 is shown by region in Figure 16.

Figure 8 shows VUI-21OCT-01 (AY.4.2) as a proportion of all Delta cases (Pangolin lineage call).

Cases have been detected across all regions in England (Figure 16). Of the 37,657 cases in England, 1,649 had a recent travel history. At least 82 countries of travel have been reported.

Figure 16. Confirmed and provisional Delta-VUI-21OCT-01 (AY.4.2) cases by specimen date and region of residence as of 22 November 2021

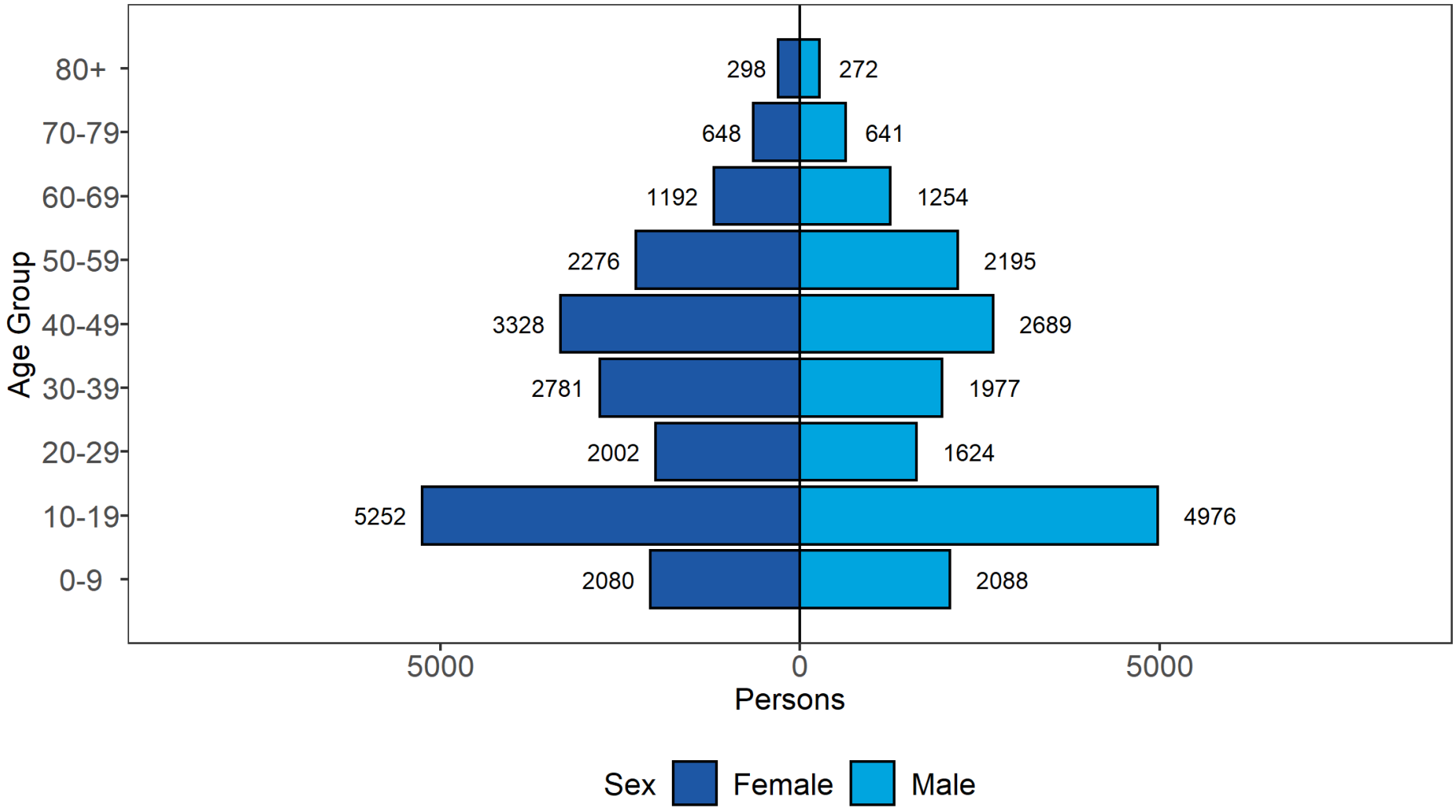
(Find accessible data used in this graph in underlying data.)



Age data is shown in Figure 17. The risk assessment for VUI-21OCT-01 AY.4.2 can be found at Risk assessment for SARS-CoV-2 variant: VUI-21OCT-01 AY.4.2.

Figure 17. Age-sex pyramid of Delta-VUI-21OCT-01 (AY.4.2) cases as of 22 November 2021

(Find accessible data used in this graph in underlying data.)



84 cases excluded where sex or age not reported

Severity outcomes

This is an update to the analysis of severity of VUI-21OCT-01 (AY.4.2) previously presented in Variant Technical Briefing 27, the risk of hospitalisation within 14 days and risk of death within 28 days after positive test were compared between cases of VUI-21OCT-01 (AY.4.2) and cases of other Delta lineages. Between 21 June 2021 and 29 October 2021, a total of 431,819 Delta cases and 19,584 VUI-21OCT-01 (A. 4.2) Cases were reported. These were followed up until 5 November 2021.

Stratified Cox regression was used to calculate hazard ratios for hospitalisation or death between the 2 variants. After adjusting for age, sex, ethnicity, vaccination status, relative deprivation and international travel and stratifying on week of specimen and area of residence, the hazard ratio for hospitalisation or attendance to emergency care was 0.92 (95% confidence interval 0.84-1.01). Using the same adjustments, the hazard ratio for death was 0.87 (95% confidence interval 0.68-1.10).

From these preliminary results, there is no statistical evidence that the outcomes of VUI-21OCT-01 (AY.4.2) are more severe than those of Delta cases.

Growth rates

Logistic growth rates for VUI-21OCT-01(AY.4.2) for the country as a whole and for each UK region are shown in Figure 18 and Figure 19. Growth rates are computed relative to non-AY.4.2 variants circulating in the same region (geo-matched sample). Sample inclusion criteria are:

- a non-traveller as determined by matching each case against passenger locator forms and managed quarantine service test codes
- collected from Pillar 2 testing
- if multiple sequences are collected from the same patient which show the same variant, the first sample is retained – additionally, samples with missing or unknown date of sample collection or upper tier local authority (UTLA) of residence are excluded

The growth rate is estimated by conditional logistic regression of the variant on time of sample collection relative to a geographically matched sample of non-VUI-21OCT-01 (AY.4.2). A growth rate of 0 would indicate parity with other circulating variants. Based on a logistic growth model, the country-wide analysis yields a logistic growth rate of 15% per week for VUI-21OCT-01 (AY.4.2). Growth rate is context dependent and cannot be interpreted as a change in biological transmissibility.

Figure 18. Sample frequency of VUI-21OCT-01 (AY.4.2) as compared to a sample of non-AY.4.2 Supplementary data is not available for this figure

The sample frequency of VUI-21OCT-01 (AY.4.2) across the UK has increased since the beginning of August 2021.

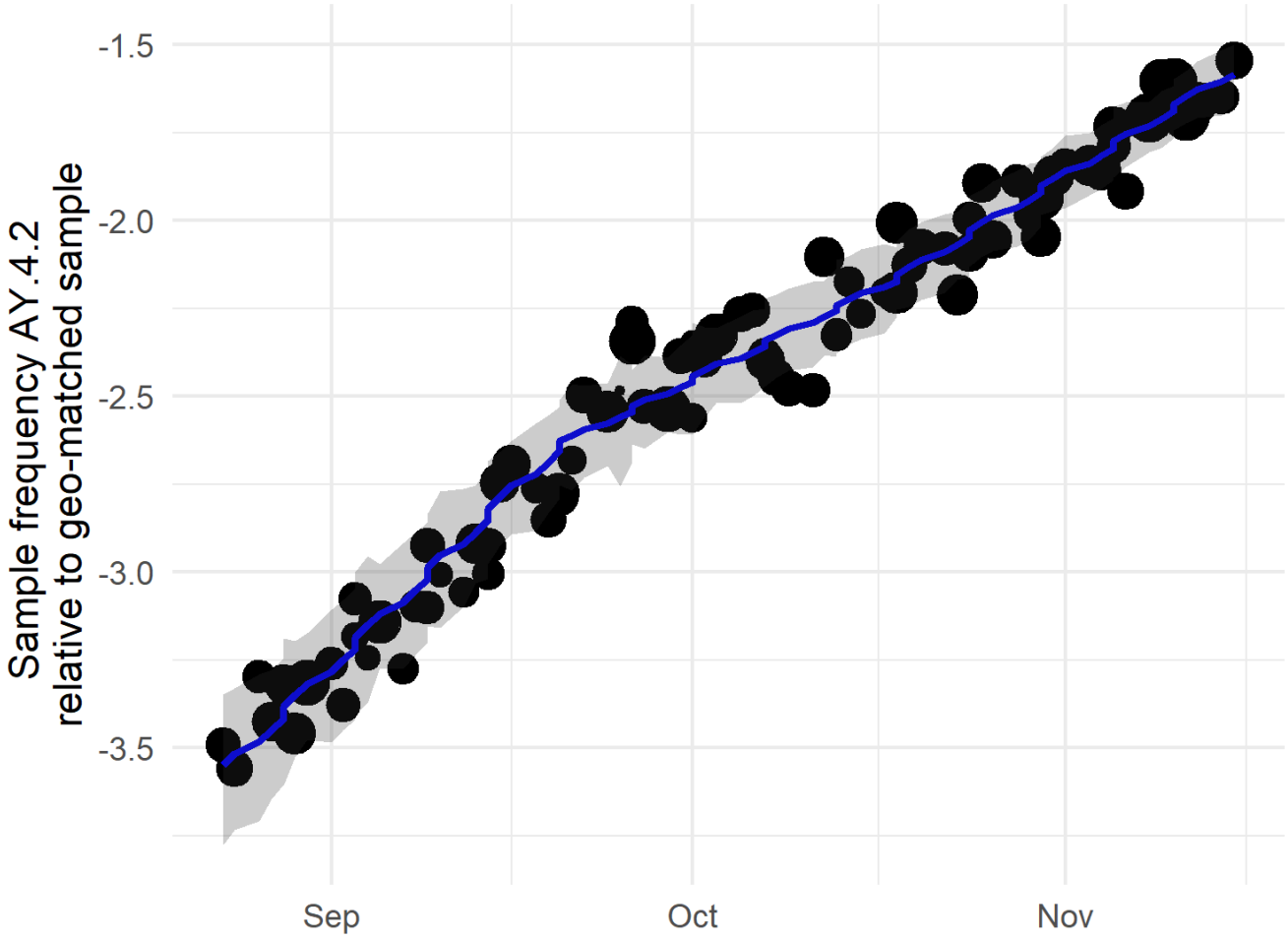
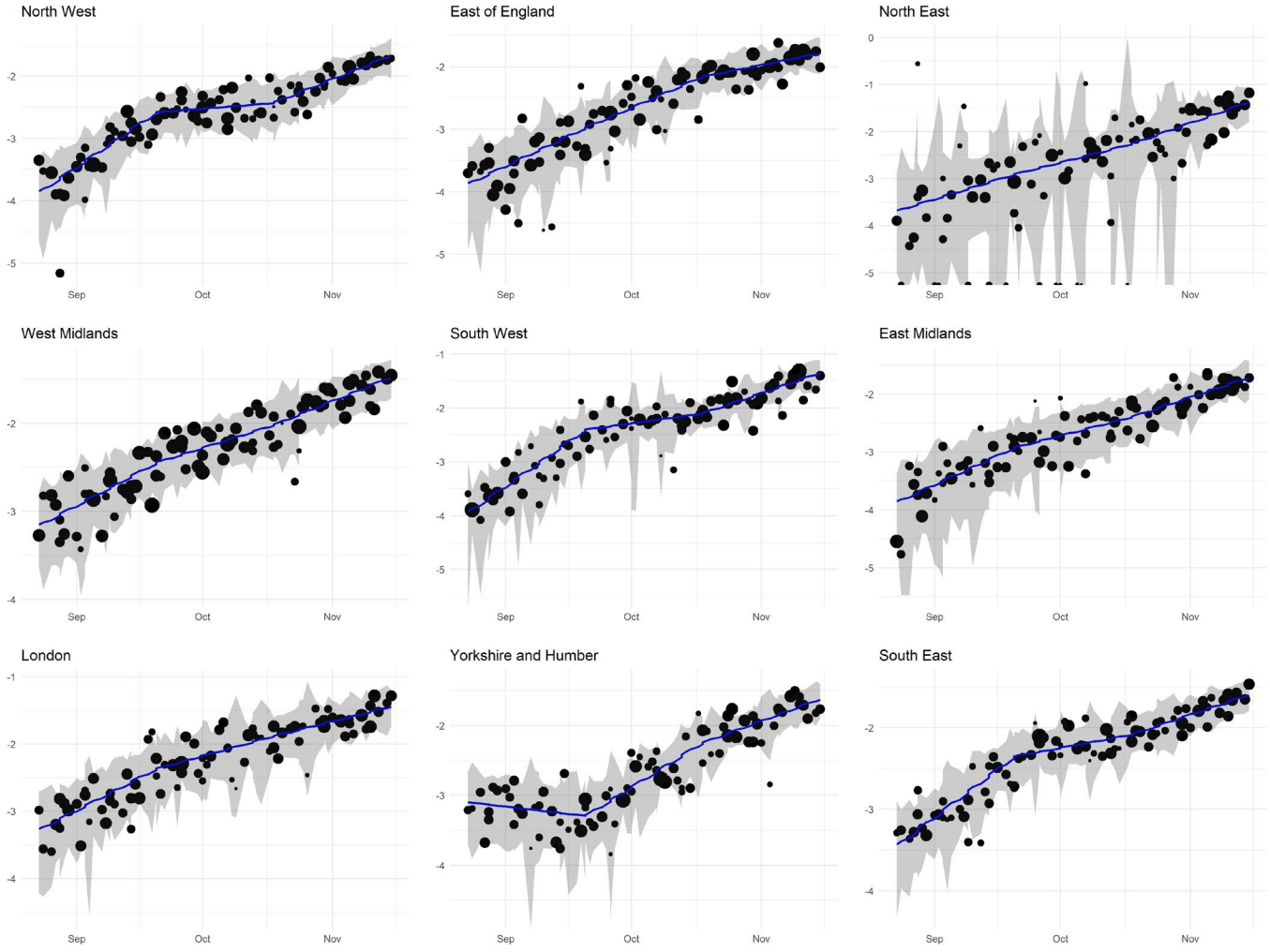


Figure 19. Sample frequency of VUI-21OCT-01 (AY.4.2) as compared to geography-matched sample of non-AY.4.2 for each UK region

Supplementary data is not available for this figure. The change in VUI-21OCT-01 (AY 4.2) frequency has not been constant across time or regions.



Sources and acknowledgments

Data sources

Data used in this investigation is derived from the COG-UK and UKHSA genomic programme data set, the UKHSA Second Generation Surveillance System (SGSS), the Secondary Uses Service (SUS) data set, Emergency Care Data Set (ECDS), and the UKHSA Case and Incident Management System (CIMS). Data on international cases are derived from reports in GISAID.

Repository of human and machine-readable genomic case definitions

Genomic definitions for all VOC and VUI 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 UKHSA. Definition files are provided in YAML format so are compatible with a range of computational platforms. The repository will be regularly updated. The genomic and biological profiles of VOC and VUI are also detailed on first description in prior technical briefings.

Variant Technical Group

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Variant Technical Group members and contributors

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