UK Health Security Agency

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

Technical briefing 27

29 October 2021

This briefing provides an update on previous briefings up to 22 October 2021

Contents

Summary

This report has been published to continue to share the detailed variant surveillance analyses which contribute to the variant risk assessments and designation of new VOCs and VUIs. The specialist technical briefings contain 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 variants of concern (VOCs) and 11 variants under investigation (VUIs) (Table 1). There are no new VOCs or VUIs in the UK classification since the last briefing.
2. Delta remains the predominant variant accounting for approximately 99.8% of sequenced cases in England as of 25 October 2021.
3. The Delta sublineage AY.4.2 (VUI-21OCT-01) accounts for a slowly increasing proportion of cases in the UK. It accounts for 8.5% of Delta cases in the most recent complete week of sequencing (4 October 2021 to 10 October 2021). In more recent weeks, sequencing data are incomplete, however AY.4.2 accounts for 10.3% of Delta cases in the week 11 October 2021 to 17 October 2021 and 11.3% in the week 18 October 2021 to 24 October 2021.
4. The growth rate and secondary attack rates have been refreshed with new data and the findings remain the same as last week. Estimated growth rates remain slightly higher for AY.4.2 than for Delta, and the household secondary attack rate is higher for AY.4.2 cases than for other Delta cases.
5. A preliminary rapid vaccine effectiveness analysis does not suggest a significant reduction in vaccine effectiveness for AY.4.2 compared to Delta. However, a further analysis more comprehensive analysis using the standard test negative case control study design is being undertaken.
6. The UKHSA variant definition for VUI-21OCT-01 currently has 95.2% sensitivity and 97.5% specificity for sequencing data outside of the UK (GISAID).
7. AY.4.2 live virus isolates have been obtained from residual biological materials and assays are in process. Pseudovirus work has been initiated.

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.

Public Health England (PHE) (now UKHSA) curated a repository on 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 Pango 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 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 25 October 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	VOC-21APR-02	VOC
Delta	AY.4.2*	VUI-21OCT-01	VUI
Eta	B.1.525	VUI-21FEB-03	VUI
	B.1.1.318	VUI-21FEB-04	VUI
Kappa	B.1.617.1	VUI-21APR-01	VUI
Mu	B.1.621	VUI-21JUL-01	VUI
	C.36.3**		Monitoring
Epsilon	B.1.427/B.1.429		Monitoring
	B.1.620		Monitoring
	R.1		Monitoring
	C.1.2		Monitoring

* AY.4.2 is a sub-lineage within Delta that has been assigned as a distinct VUI.
** Previously VUI-21MAY-02, de-escalated on 20 October 2021.

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
	AV.1	VUI-21MAY-01	VUI
	P.2	VUI-21JAN-01	VUI
Lambda	C.37*		Monitoring

WHO nomenclature	Lineage	Designation	Status
	A.27		Monitoring
Iota	B.1.526		Monitoring
	B.1.1.7 with Q677H		Monitoring
	B.1 with 214insQAS		Monitoring
	AT.1		Monitoring
	B.1.629		Monitoring
	B.1.619		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 recombinant		Monitoring

* Previously VUI-21JUN-01, 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 data sets 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 to WHO variants under monitoring.

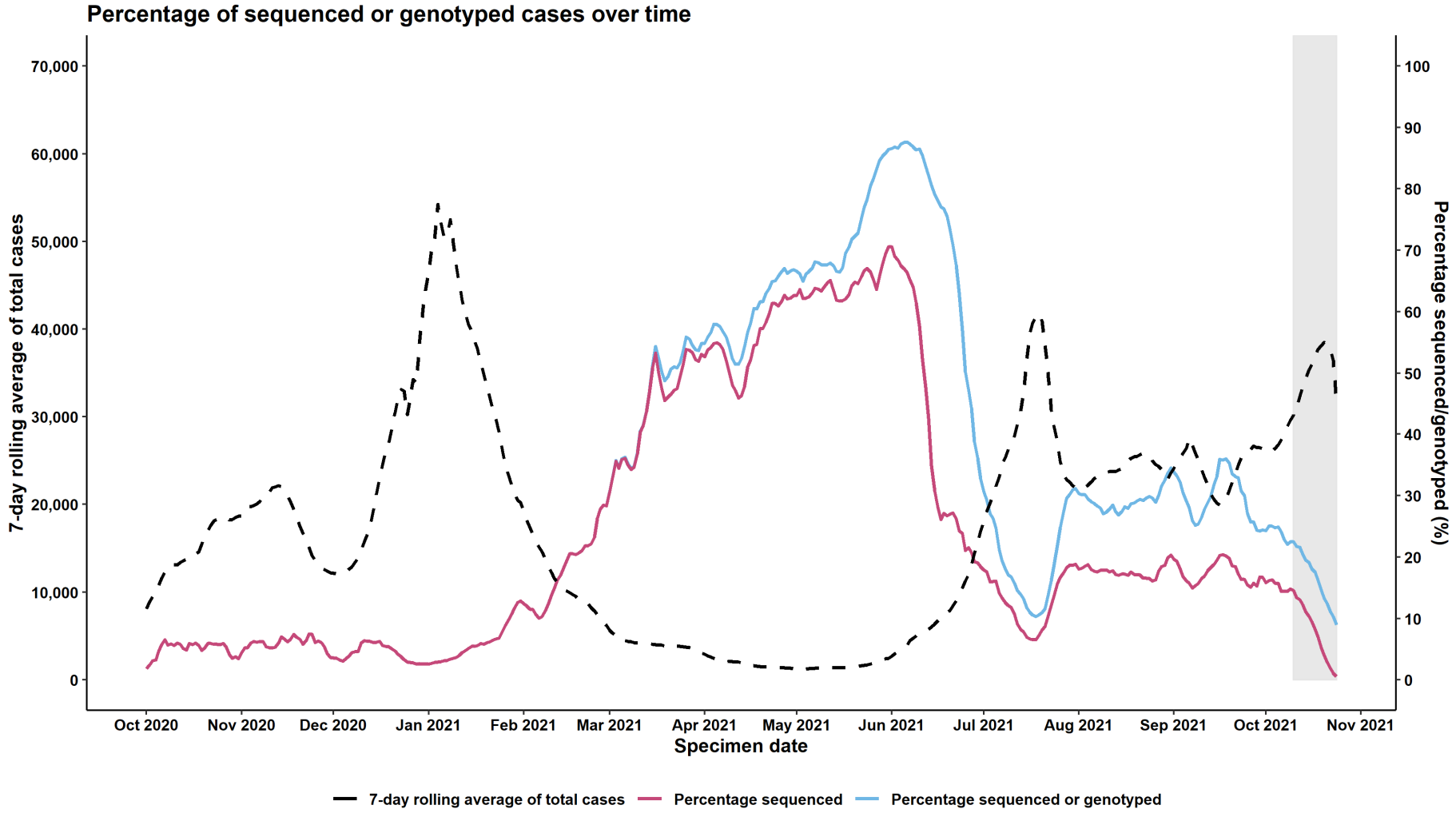
1.2 Sequencing coverage

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. Figure 4 shows coverage of sequencing and genotyping for cases by age group.

Sequencing coverage is stable (Figure 1) and similar proportions are sequenced and genotyped across each region. During the current surge period, 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 24 October 2021)



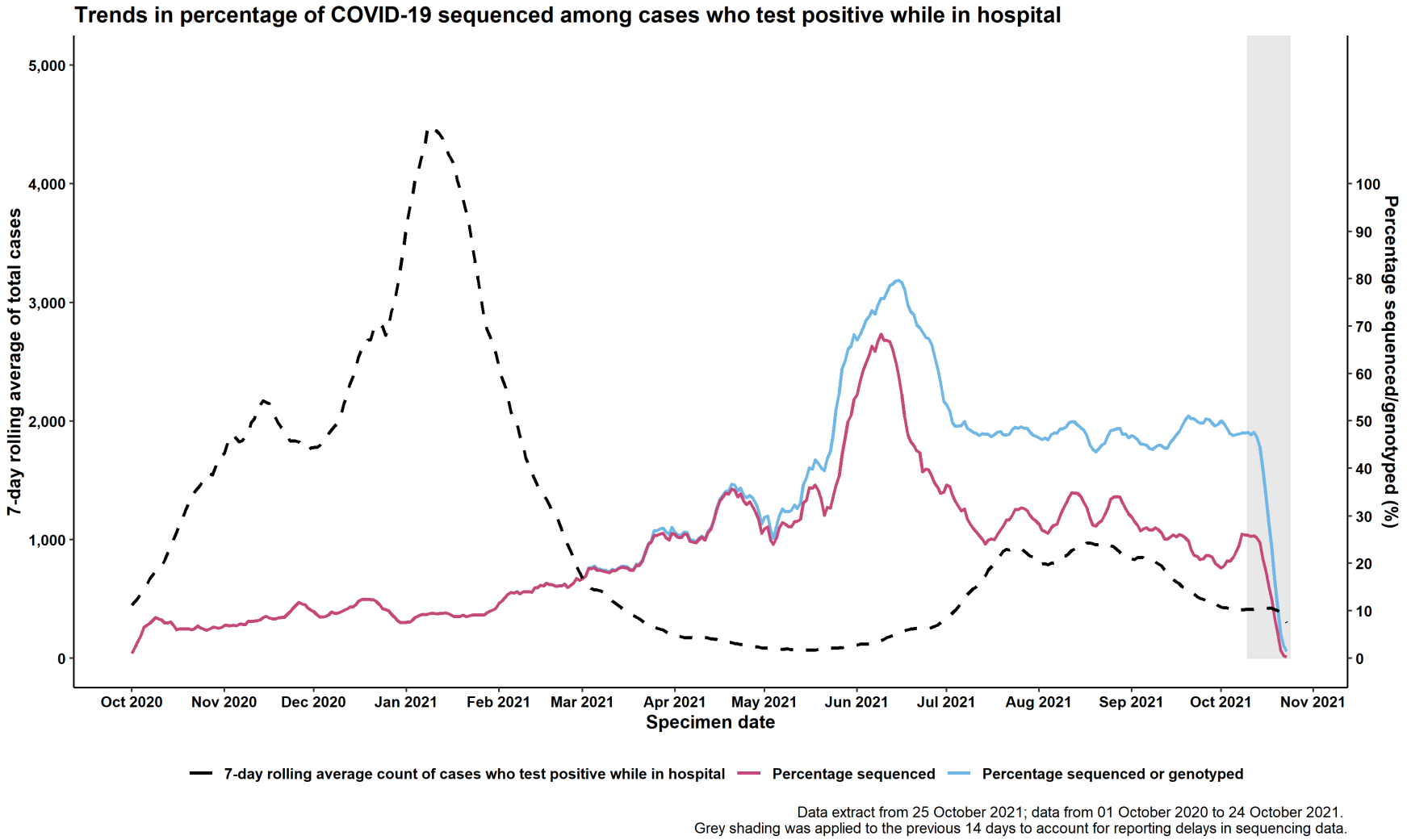
(Find accessible data used in this graph in underlying data.)
Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

Figure 2. Coverage of sequencing with a valid result and genotyping over time by region (1 October 2020 to 24 October 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.

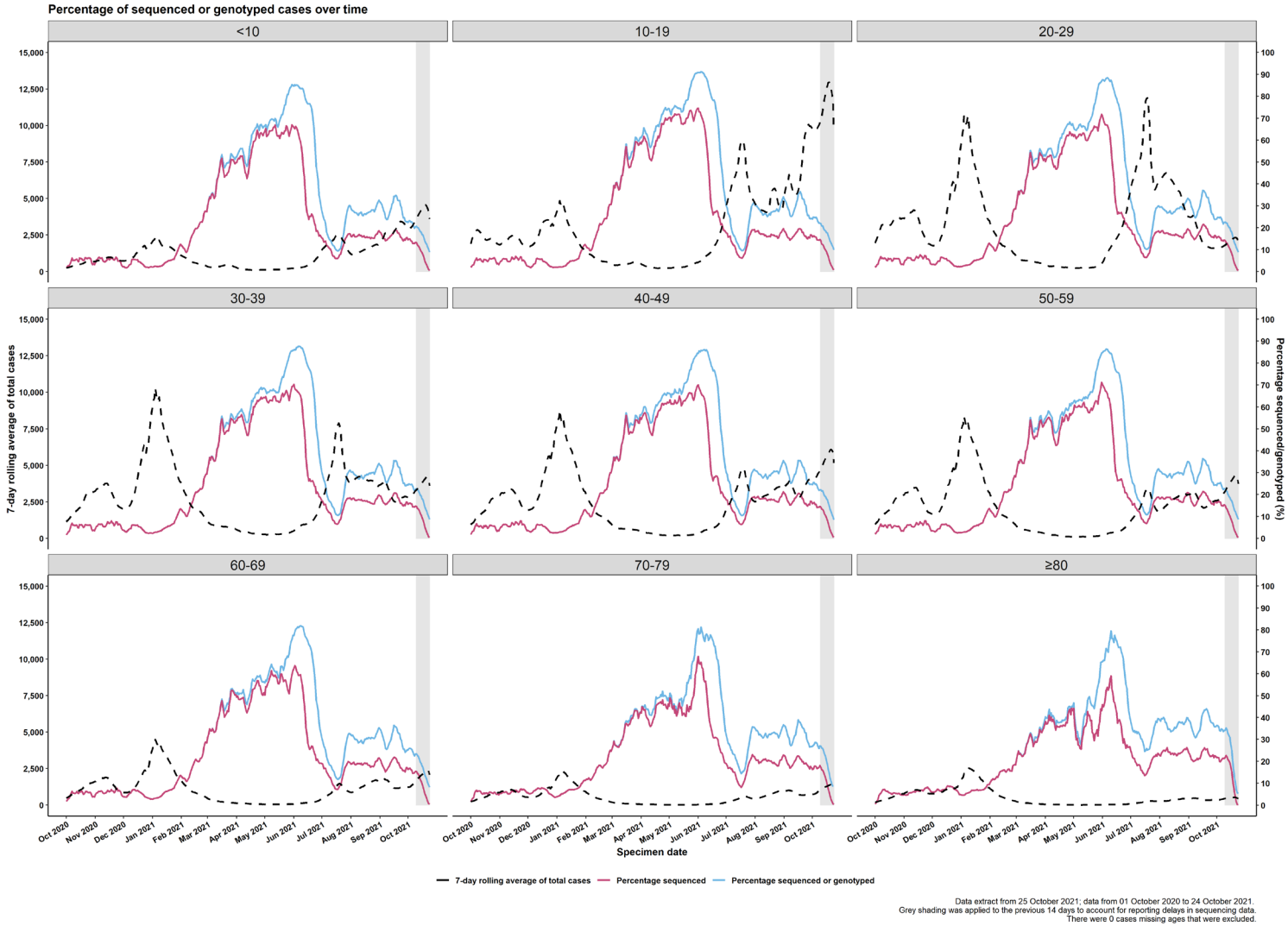
Figure 3. Coverage of sequencing with valid result and genotyping for cases who test positive in hospital (1 October 2020 to 24 October 2021)

(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 4. Coverage of sequencing with valid result and genotyping for cases by age group (1 October 2020 to 24 October 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 is shown in Table 3, case numbers are also updated online. Table 3 shows the number of sequenced, genotyped, and total cases and deaths for each variant. However, case fatality rates are not comparable across variants (see Table 3 footnote). Figure 5 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, therefore this data will not be produced in future editions of the variant technical briefing. These tables will be reinstated in the technical briefing if new variants of concern arise.

Table 3. Number of confirmed and probable cases by variant as of 25 October 2021

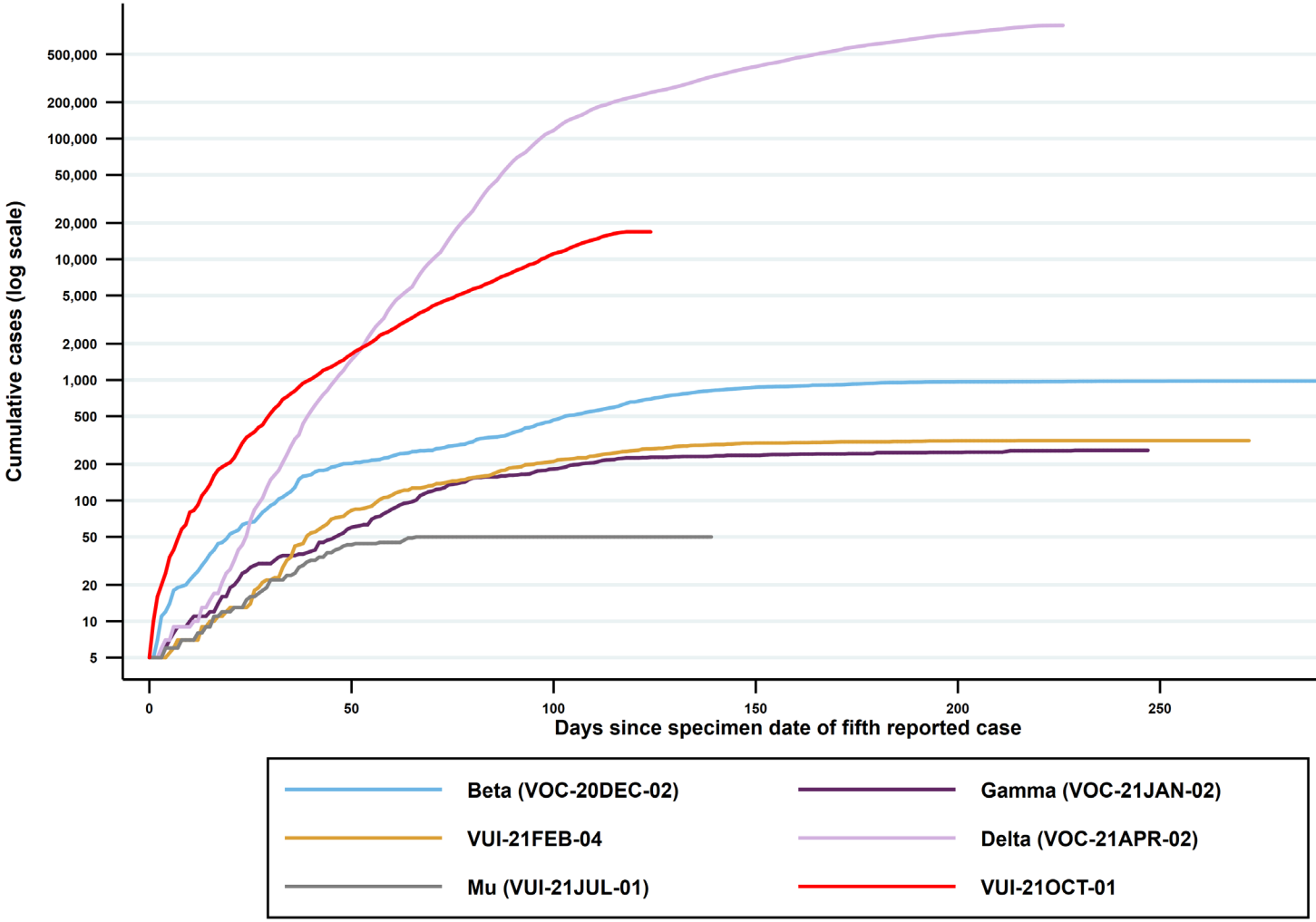
Variant	Confirmed (sequencing) case number	Probable (genotyping) case number[1]	Total case number	Case Proportion	Deaths
Alpha	221,139	5,680	226,819	20.4%	4,321
Beta	929	61*	990	0.1%	12
Delta	513,757	353,907	867,664	77.9%	4,525
Eta	461	0	461	0.0%	12
Gamma	211	55	266	0.0%	0
Kappa	474	0	474	0.0%	2
Lambda	8	0	8	0.0%	0
Mu	50	0*	50	0.0%	0
NA-20DEC-02 or 21JUL-01	0	12	12	0.0%	0
Theta	7	0	7	0.0%	0
VOC-21FEB-02	44	0	44	0.0%	1
VUI-21APR-03	15	0	15	0.0%	0
VUI-21FEB-01	78	0	78	0.0%	1

Variant	Confirmed (sequencing) case number	Probable (genotyping) case number[1]	Total case number	Case Proportion	Deaths
VUI-21FEB-04	315	0	315	0.0%	1
VUI-21MAR-01	2	0	2	0.0%	0
VUI-21MAY-01	184	0	184	0.0%	1
VUI-21MAY-02	148	0	148	0.0%	0
VUI-21OCT-01	16,876	0	16,876	1.5%	78
Zeta	51	0	51	0.0%	1

[1] Genotyping is used to identify variants Alpha, Beta, Delta and Gamma; targets were updated in mid-May 2021 to prioritise accurate identification of Delta over Alpha.

* excludes 12 genotyped cases that cannot be definitely identified as either Beta or Mu.

Figure 5. Cumulative cases in England of variants indexed by days since the fifth reported case as of 24 October 2021
(Find accessible data used in this graph in underlying data.)



1.4 Variant prevalence

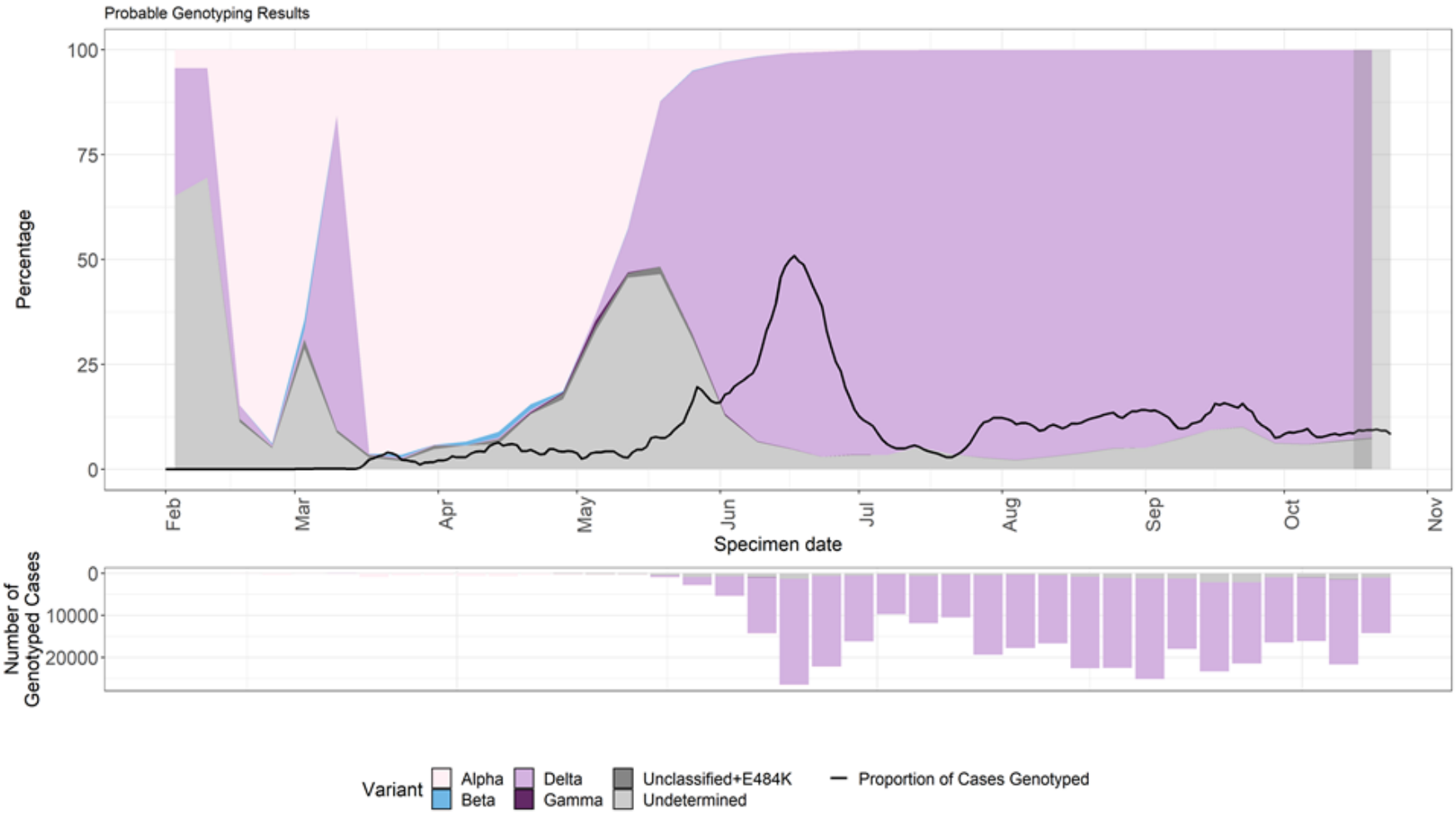
The prevalence of different variants amongst genotyped and sequenced cases is presented in Figure 6 and Figure 7 and split by region in Figure 8 and Figure 9 and by travel in Figure 10.

Genotyping provides probable variant results with a shorter turnaround time of 12 to 24 hours after initial confirmation of coronavirus (COVID-19). 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 7 and Figure 9 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 is available.

Delta variant accounted for approximately 99.8% of sequenced and 91.4% genotyped cases from 12 September 2021 as of 11 October 2021.

Figure 6. Variant prevalence for all England available genotyped cases from 1 February 2021 as of 25 October 2021
(Find accessible data used in this graph in underlying data.)



A small number of cases identified as Beta (B.1.351) on genotyping since May 2021 without confirmatory sequencing may be Mu with an additional K417N mutation.

Figure 7. Variant prevalence for all England available sequenced cases from 1 February 2021 as of 25 October 2021 (excluding 245 case 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.

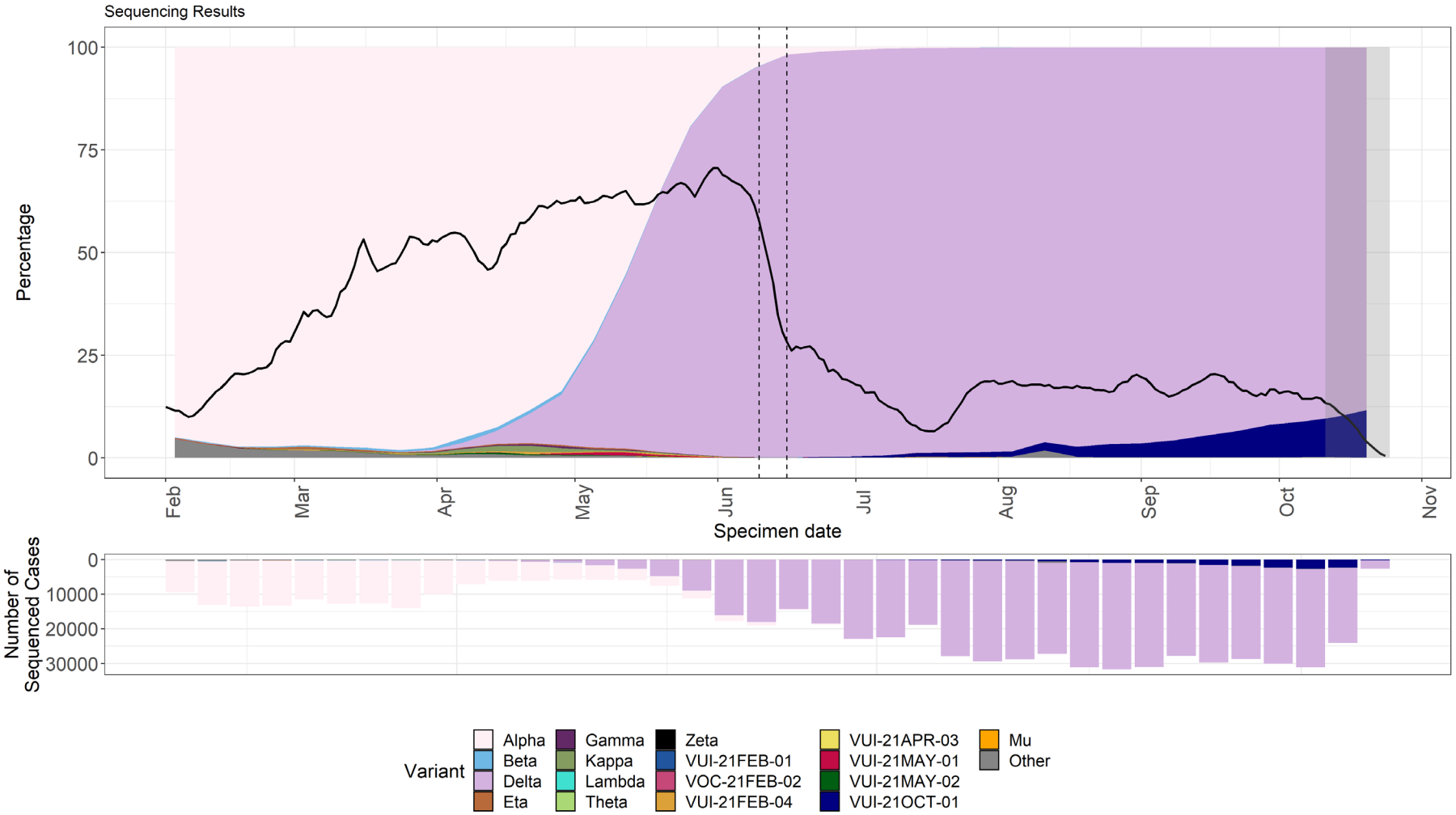


Figure 8. Variant prevalence from 1 February 2021 as of 25 October 2021 by region for all genotyped cases in England (excluding 2,570 cases where the region or specimen date were unknown)

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

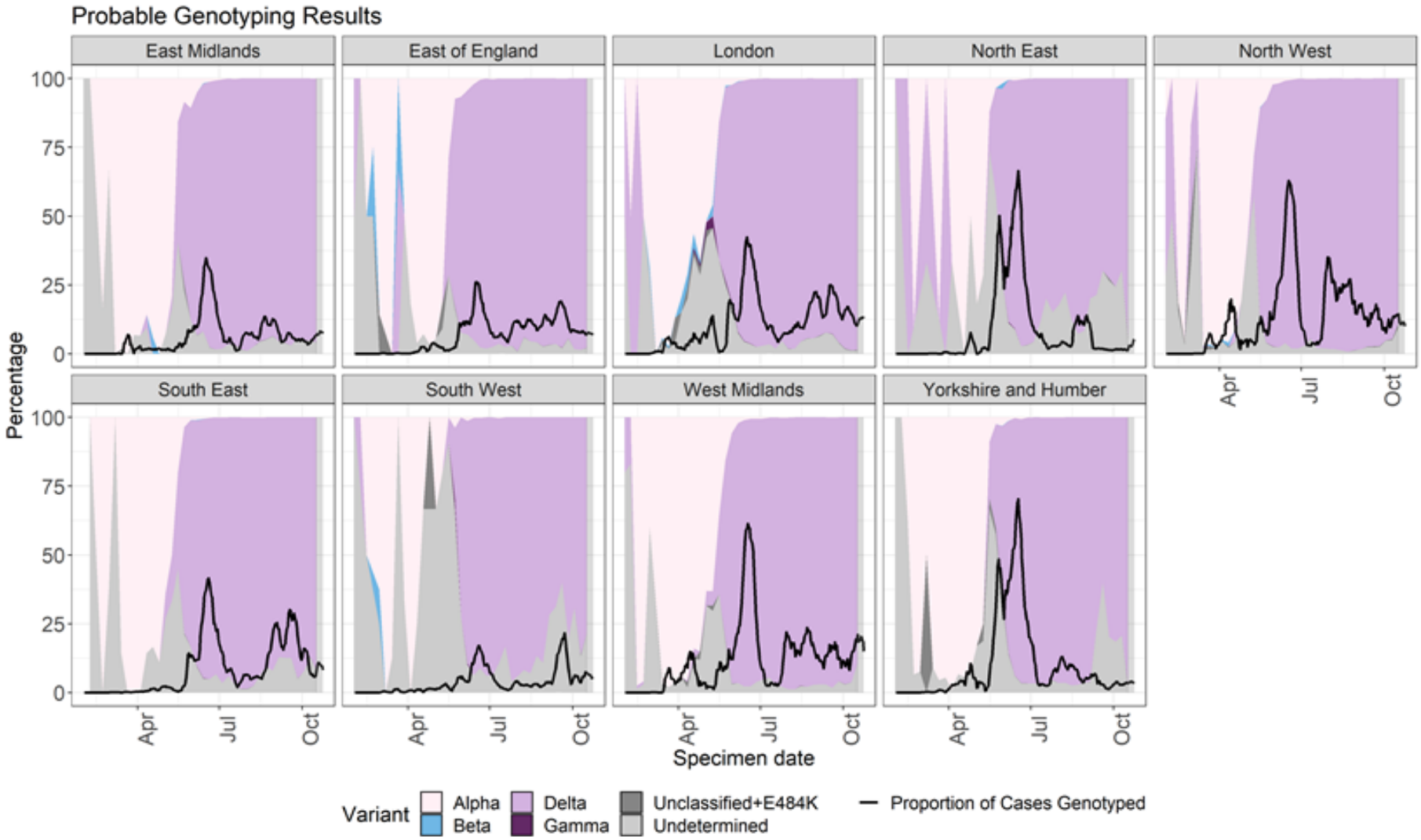


Figure 9. Variant prevalence from 1 February 2021 as of 25 October 2021 by region for all sequenced cases in England (excluding 4,148 cases where the region or specimen date were unknown)

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

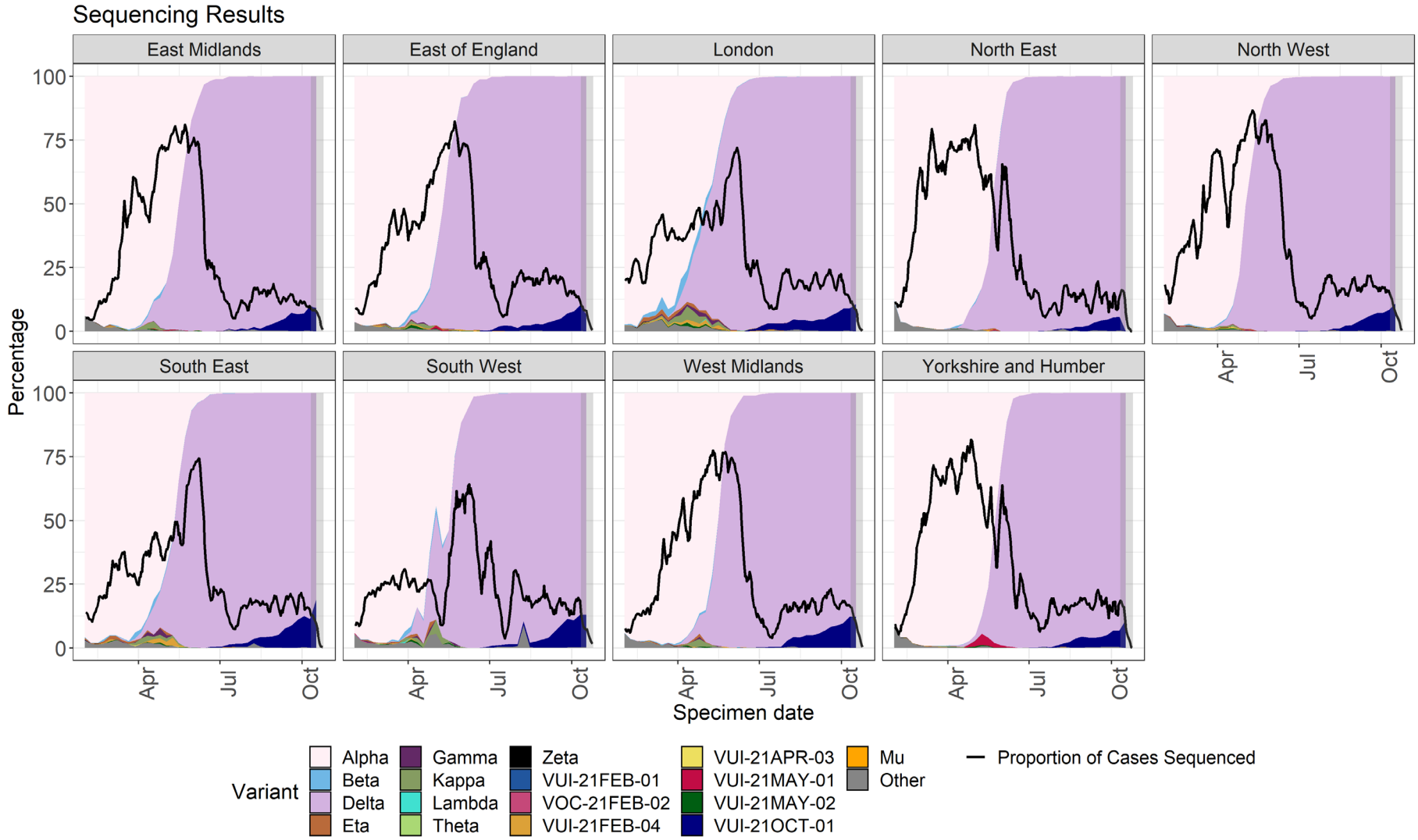
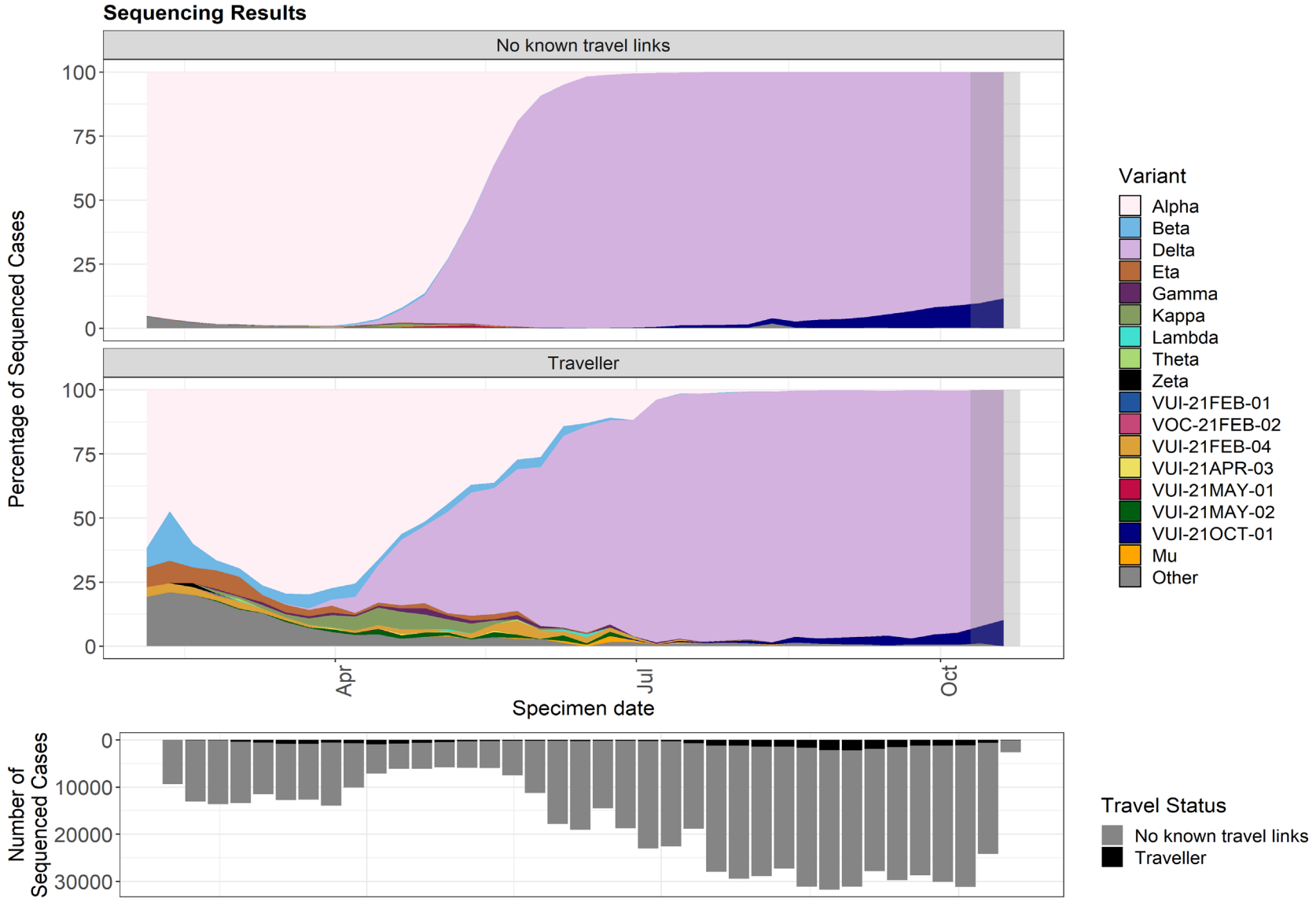


Figure 10. Variant prevalence plot (all cases in England, genomic surveillance case definitions) by travel status as of 25 October 2021

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



Part 2. Enhanced analysis on specific variants. Delta (B.1.617.2)

The lineage B.1.617.2 was escalated to a variant of concern 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 11 shows the prevalence of Delta lineages over time in sequences in England, as defined using Pangolin. AY.4 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 12 (heatmap of mutation proportion in S gene for any mutation seen in at least 1,000 genomes), and Table 4 (limited to S gene mutations with evidence for impact on antigenicity, avidity or furin cleavage site). Figure 13 shows the mutations arising on VUI-21OCT-01 as a proportion of total VUI-21OCT-01 sequences where that amino acid position can be called.

Figure 11. Prevalence of Pangolin lineages within Delta from 1 March 2021 to 23 October 2021

The plot excludes 28,672 sequences that were not linked to date information and a further 83 that were not assigned a lineage by Pangolin due to sequence quality. The total number of sequences per week is shown by the black line. Only lineages with more than 100 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.)

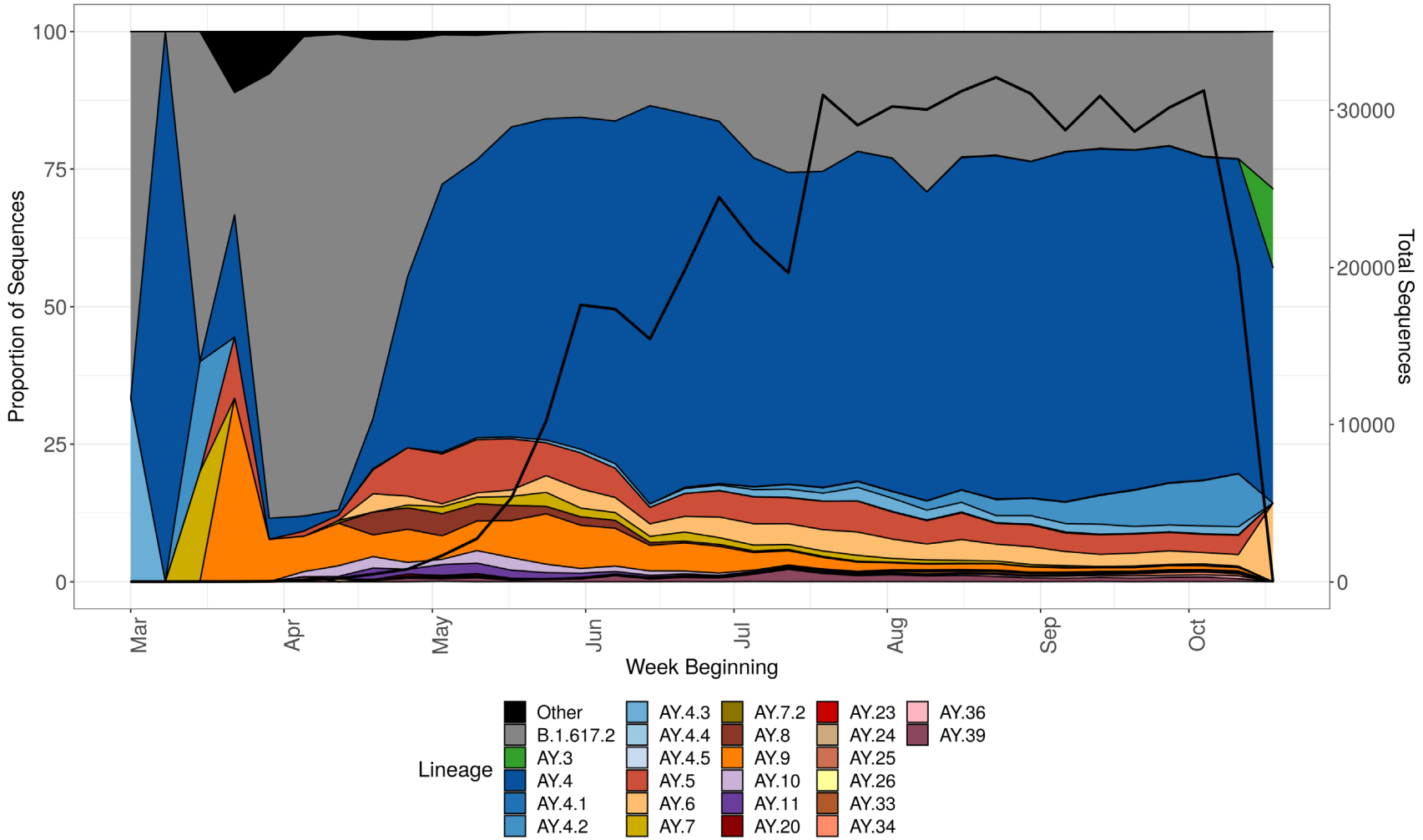


Figure 12. Proportion of Delta sequences (excluding VUI-21OCT-01 sequences) from England containing mutations in spike, restricted to those mutations which are observed in at least 1,000 sequences

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. Sequences with no date information (n=28,672) and those that are not of sufficient quality (n=83) are excluded. 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). Those present in all Delta are not limited to those used in the UKHSA variant definition for this VOC as the definition excludes some due to sequencing issues (for example, G142D) or because they are shared with other lineages (for example, D950N). (Find accessible data used in this graph in underlying data.)

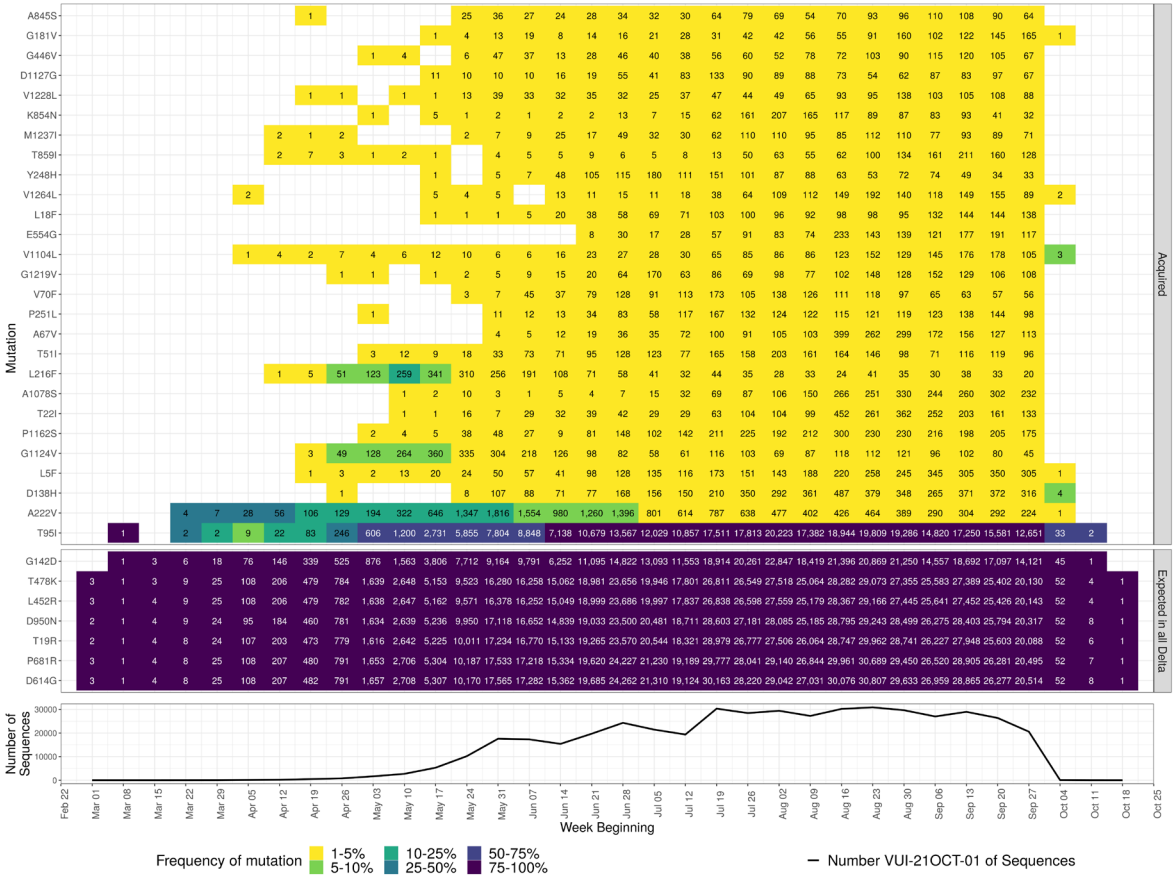


Figure 13. Proportion of VUI-21OCT-01 sequences from England containing mutations in spike, restricted to those mutations which are observed in at least 100 sequences

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. Sequences with no date information (n=28,672) and those that are not of sufficient quality (n=83) are excluded. 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.)

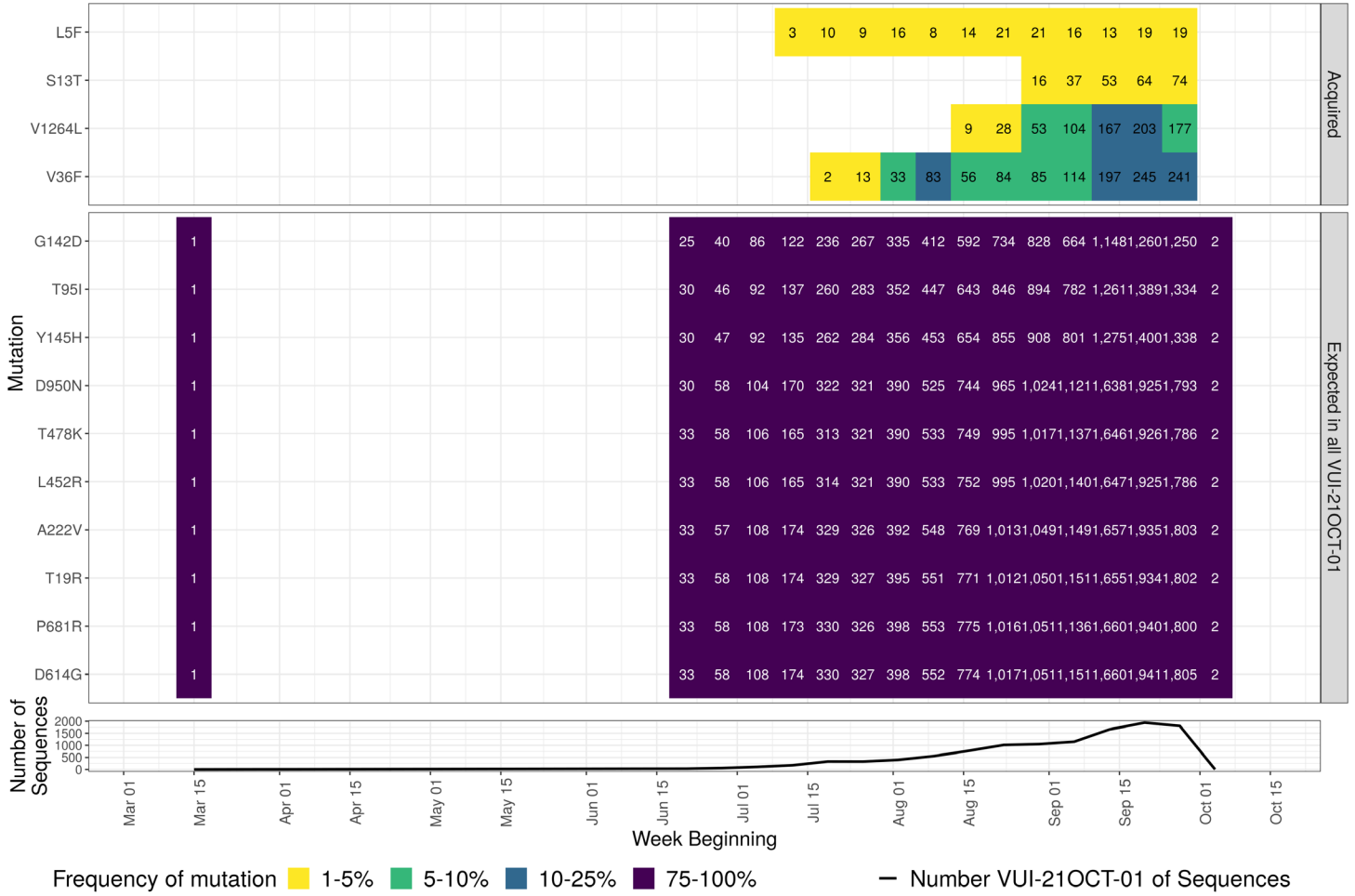


Table 4. Additional spike mutations of possible functional significance detected in Delta genomes in the UK as of 26 October 2021

Amino acid change	Delta sequences in UK data set	Delta sequences outside UK (GISAID)	Delta sequences 27 July to 26 August 2021		Delta sequences 27 August to 26 September 2021		Delta sequences 27 September to 26 October 2021	
			England	Outside UK	England	Outside UK	England	Outside UK
P251L	3,901	15,236	542	5,807	584	3,993	337	993
G446V	2,620	2,536	306	845	491	881	227	217
Q613H	1,425	19,696	227	8,961	400	7,997	452	1,073
V483F	940	617	114	205	131	214	27	69
Q493E	405	216	173	73	88	35	16	3
S494L	350	558	105	276	123	164	55	25
E484Q	357	2,091	70	750	102	542	96	129
K417N	213	4,791	59	1,703	44	501	14	43
L455F	217	478	71	169	37	172	43	39
V445I	107	48	42	11	13	28	2	2
F490L	119	261	49	104	21	109	14	27
K444N	107	285	32	94	19	98	15	19
S494P	100	361	12	124	10	151	19	23
N501Y	79	561	22	299	10	32	10	6
F490S	90	164	12	53	35	59	29	25
A475V	56	79	19	26	20	33	3	7
K458N	44	71	14	34	6	14	0	7

Amino acid change	Delta sequences in UK data set	Delta sequences outside UK (GISAID)	Delta sequences 27 July to 26 August 2021		Delta sequences 27 August to 26 September 2021		Delta sequences 27 September to 26 October 2021	
R246I	65	134	16	61	11	46	11	9
P681H	51	327	12	163	5	84	5	11
E484K	93	372	11	150	25	138	39	10
K444R	63	126	5	35	19	57	15	18
L452Q	39	139	11	58	7	59	12	1
E484A	47	280	4	37	20	127	8	83
P499L	28	57	3	19	6	24	5	1
V445F	30	56	6	26	12	20	9	0
N439K	19	6	9	2	5	3	1	0
S494A	21	21	5	18	12	2	1	0
N501T	20	54	4	7	0	32	3	6
E484G	15	59	0	18	3	28	0	6
E484V	12	56	1	8	4	28	1	6
Q493L	12	63	4	22	1	12	1	0
D80N	9	56	2	23	1	19	0	5
V483A	8	67	2	17	3	29	1	10
F486L	6	5	0	1	1	3	0	0
V445A	19	52	3	22	2	16	10	5
E484D	15	64	2	39	0	13	5	3

Amino acid change	Delta sequences in UK data set	Delta sequences outside UK (GISAID)	Delta sequences 27 July to 26 August 2021		Delta sequences 27 August to 26 September 2021		Delta sequences 27 September to 26 October 2021	
G446D	5	21	1	6	1	7	0	4
G485D	4	2	0	0	2	1	0	0
T478I	3	16	0	8	0	7	0	0
Y453F	3	17	0	4	3	11	0	1
Q498R	5	43	0	10	0	20	0	4
Q493H	3	22	0	6	0	9	0	2
D80A	4	168	0	29	1	14	1	1
K444E	3	3	0	3	0	0	0	0
I472V	2	8	0	1	0	4	0	1
R246G	13	27	1	18	3	5	4	0
Q493R	1	10	0	3	1	4	0	2
Q493K	2	2	0	1	2	0	0	0
N450K	1	15	0	3	1	8	0	3
K458Q	1	3	1	2	0	1	0	0
K417T	2	17	0	5	1	9	1	0
K417E	2	16	0	12	0	3	0	0
V483G	1	13	1	7	0	2	0	1
V503L	1	1	0	0	0	1	0	0
Y144N	1	3	0	1	0	0	0	0

Amino acid change	Delta sequences in UK data set	Delta sequences outside UK (GISAID)	Delta sequences 27 July to 26 August 2021		Delta sequences 27 August to 26 September 2021		Delta sequences 27 September to 26 October 2021	
N501H	1	8	0	3	0	3	0	2
Total	710,598	1,327,492	130,366	539,520	132,012	376,019	80,910	73,858

*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 – Delta with E484Q

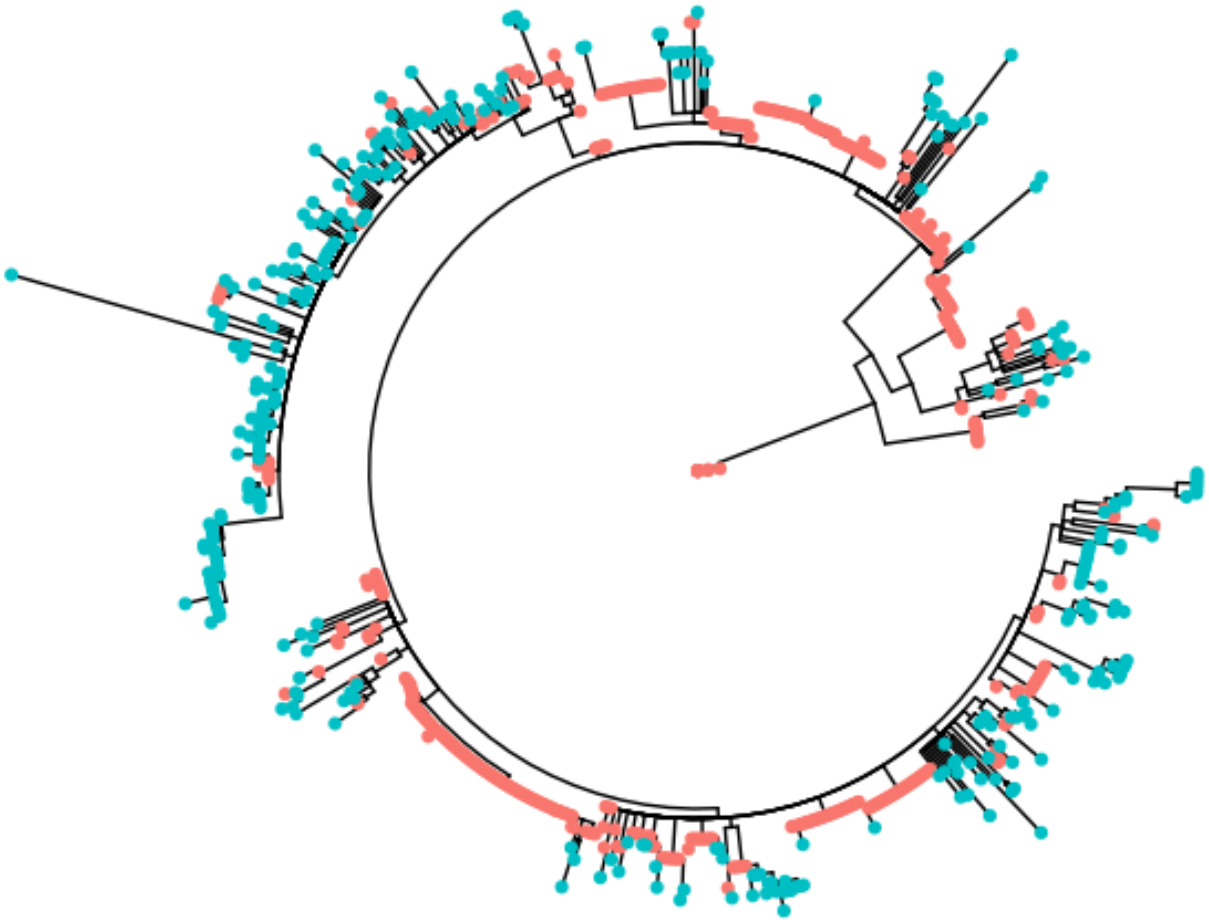
Changes at position 484 in spike are potentially antigenically significant. Delta with E484Q was first identified through horizon scanning on the 3 August 2021 after being detected in 6 Scottish samples between 22 and 28 July 2021. Three hundred and sixty five sequences have been identified as of the 25 October 2021, with 231 from England, 19 from Scotland, 8 from Wales and 1 from Northern Ireland.

The phylogenetic tree of UK Delta with E484Q cases is shown in Figure 14, which includes a cluster of 11 genetically indistinguishable samples from Yorkshire and Humber (10) and the West Midlands (1) (no change), a cluster of 5 samples from the North East (no change), a node of 4 samples (3 genetically indistinguishable) from the East Midlands (no change), a node of 6 genetically indistinguishable samples including an additional 4 London samples annotated with E484Q (the 2 pre-existing samples have ambiguous bases in at amino acid position 484).

The tree also contains a large node of diverse (genetically and geographically) samples that are predominantly annotated with the E484Q mutation; 44 samples were added to this node this week. This large node contains a cluster of 6 genetically indistinguishable samples from East of England (2 new sequences), and an additional cluster of 5 genetically indistinguishable samples from London (3) and Yorkshire and Humber (2) (no change).

Figure 14. Phylogenetic tree of UK Delta (B.1.617.2) with E484Q cases with a down-sampled international background data set as of 25 October 2021

The tree is generated using Civet which down-samples UK and international samples for background context. Presence of the E484Q mutation is indicated by the tip colour (blue indicates E484Q annotated, red indicates E484Q not annotated), note 11 samples excluded from the tree by Civet due to a technical issue. Supplementary data is not available for this figure.



Epidemiology in England

As of 25 October 2021, there are 365 Delta with E484Q sequences in the UK, 280 of which were linked to epidemiological data in England. This is an increase of 108 since the briefing of 11 October 2021. Cases have been detected across all 9 English regions, with most cases in the London (77, 27.5%) as shown by region in Table 5 and Figure 15 and age in Figure 16. Of the 280 cases 99 have history of travel.

Table 5. Number of confirmed (sequencing) Delta cases with E484Q mutation, by region of residence as of 25 October 2021

Region	Confirmed (sequencing) case number	Case proportion
East Midlands	15	5.4%
East of England	27	9.6%
London	77	27.5%
North East	32	11.4%
North West	20	7.1%
South East	31	11.1%
South West	11	3.9%
West Midlands	21	7.5%
Yorkshire and Humber	29	10.4%
Unknown region	17	6.1%
Total	280	-

Figure 15. Confirmed (sequencing) Delta cases with E484Q mutation cases by region of residence as of 25 October 2021
(Find accessible data used in this graph in underlying data.)

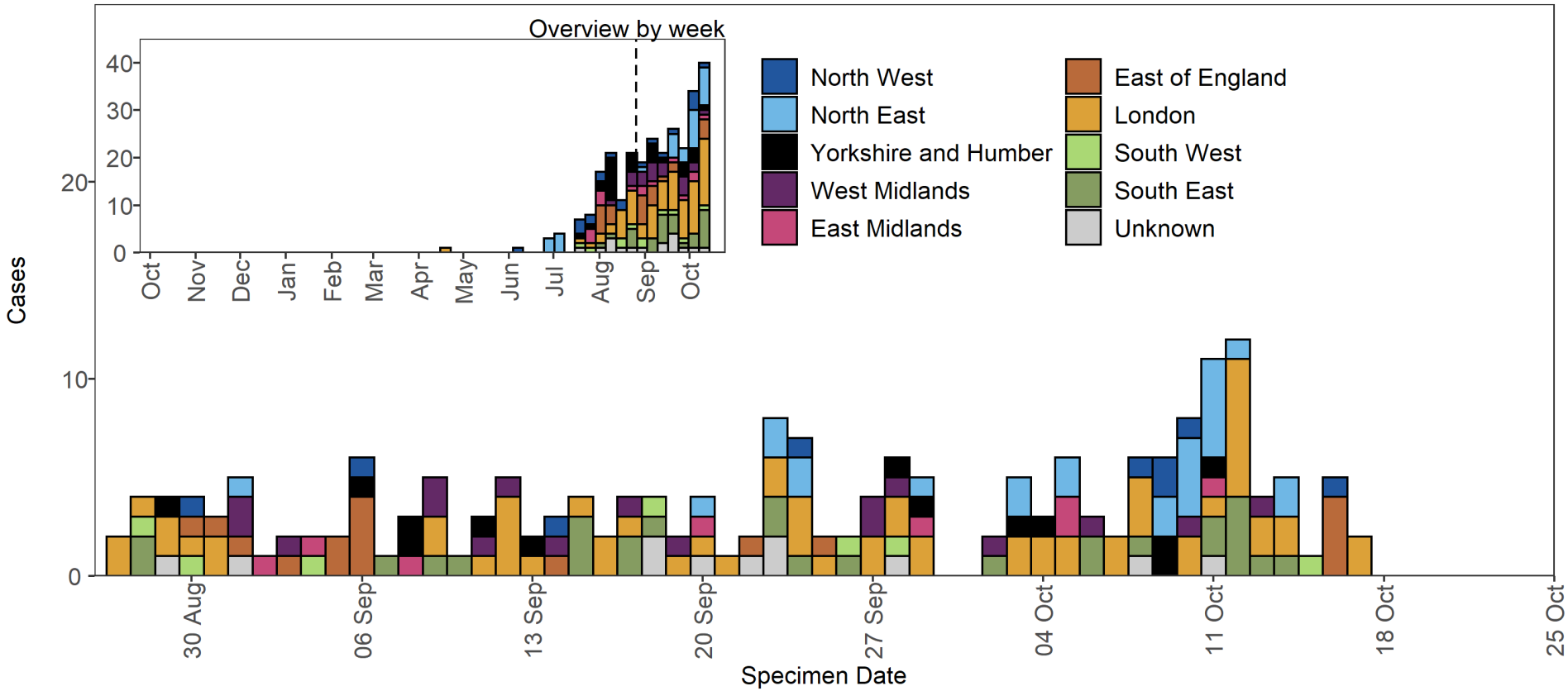
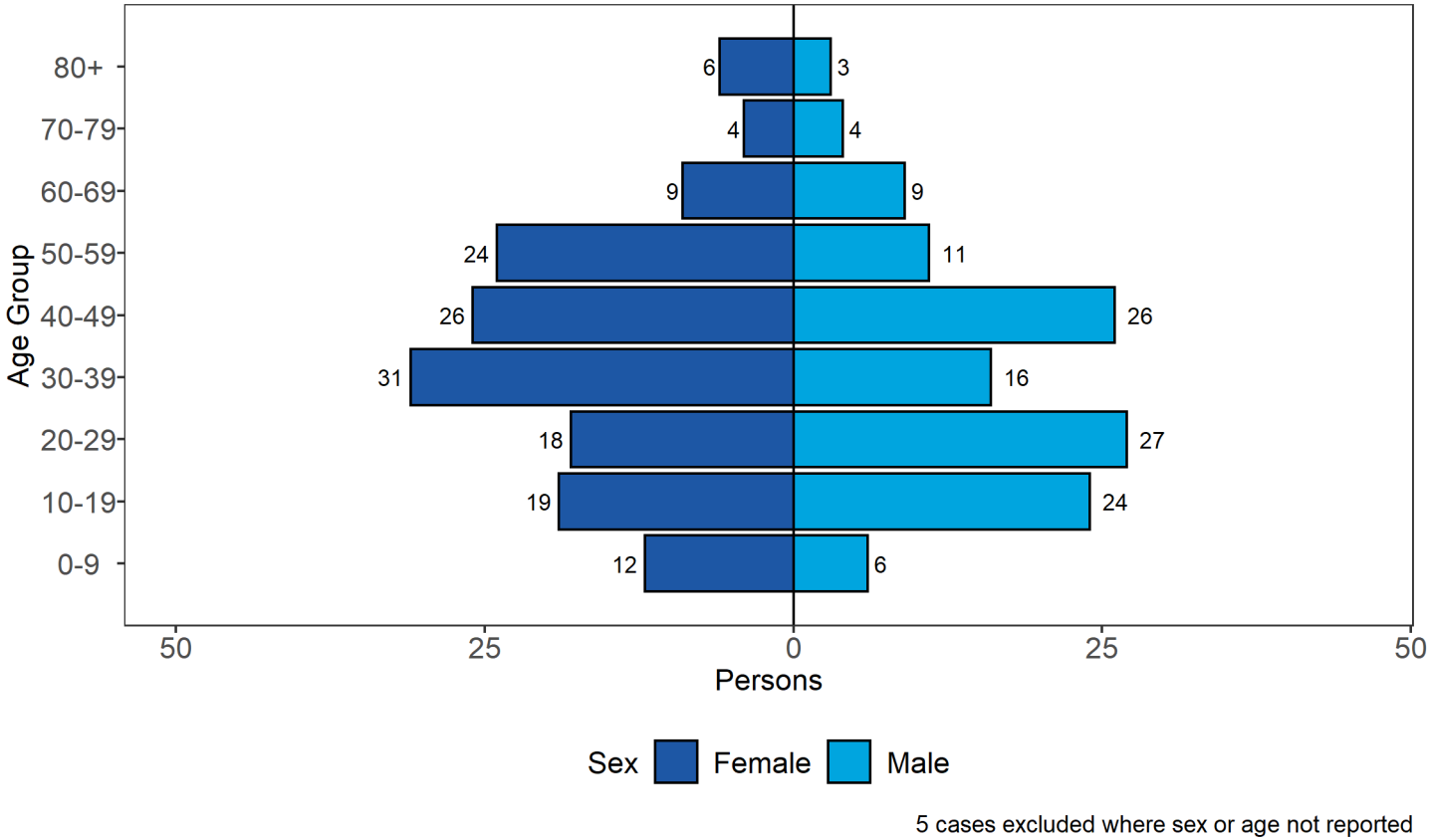


Figure 16. Age-sex pyramid of confirmed (sequencing) Delta cases with E484Q mutation cases as of 25 October 2021
(Find accessible data used in this graph in underlying data.)



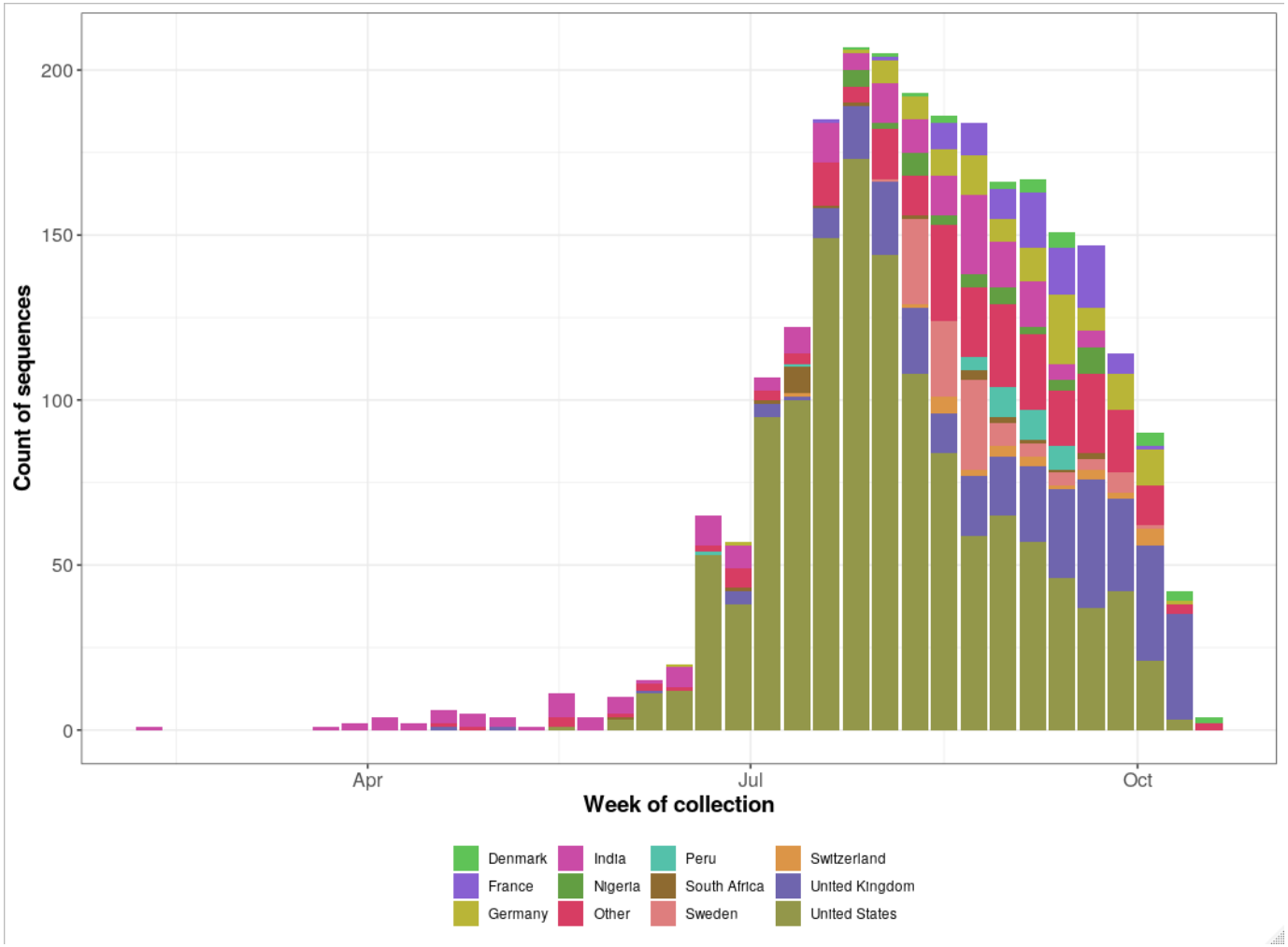
5 cases excluded where sex or age not reported

International epidemiology

As of 25 October 2021, 2,478 GISAID sequences have been assigned to the B.1.617.2 and AY sub-lineages with the additional E484Q mutation, of those 2,477 sequences had appropriate date information. Sequences have been uploaded from USA (1301), India (185), Germany (105), Sweden (102), France (86), Nigeria (39), Peru (31), Switzerland (26), Denmark (25), South Africa (23) and 48 other countries with 10 or fewer samples. Figure 17 shows the distribution of cases per country over time, based on GISAID data, indicating an increase in observations of Delta with E484Q from July through to October 2021.

Figure 17. Count of Delta with E484Q classified sequences by week of collection uploaded to GISAID by week as of 25 October 2021

Countries with 20 or fewer sequences have been grouped together as Other. (Find accessible data used in this graph in underlying data.) Note time to upload data into GISAID varies by country and therefore recent weeks are likely to be incomplete.



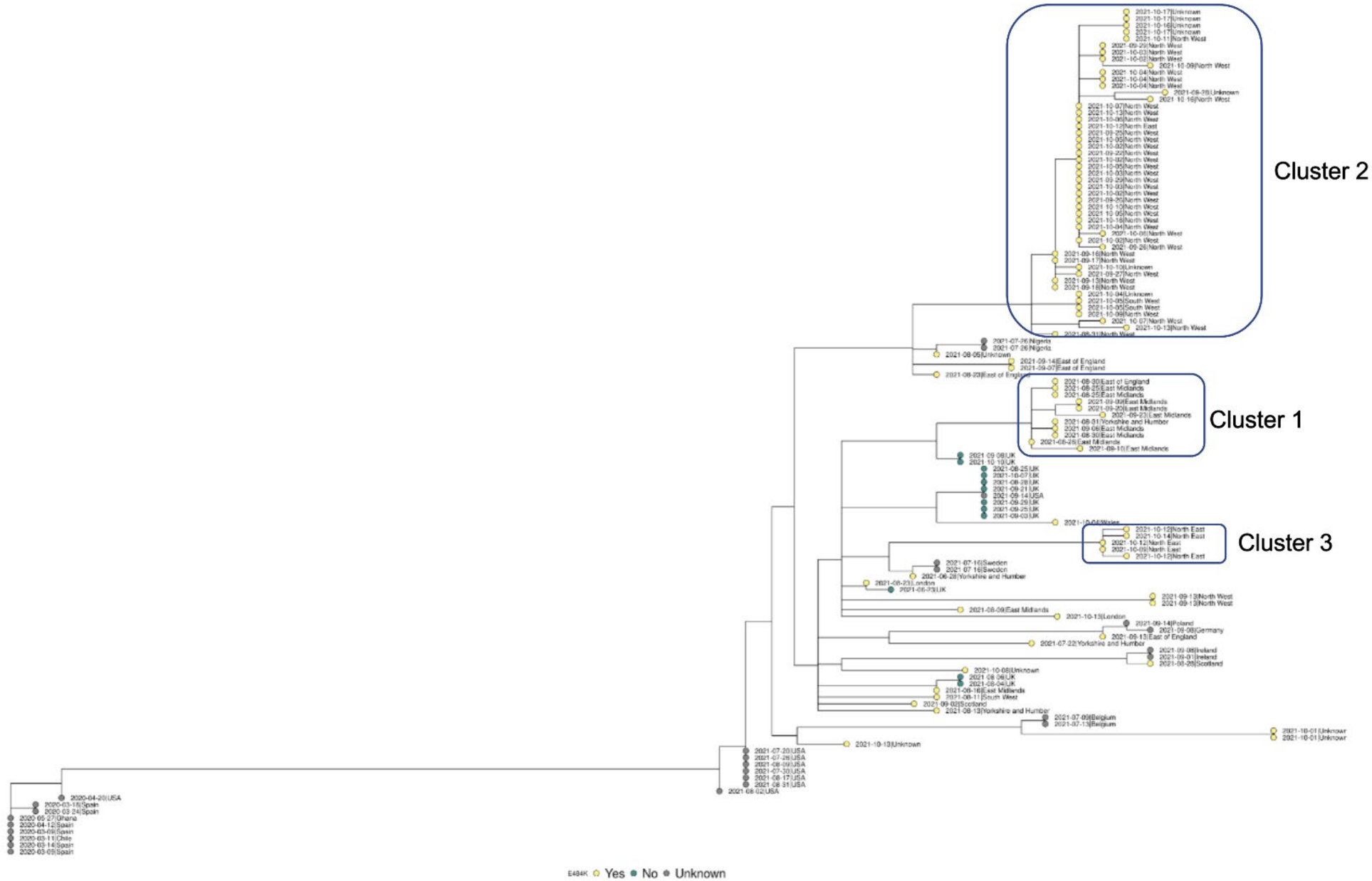
2.3 Monitoring diversity within Delta – Delta with E484K

Changes at position 484 in spike are potentially antigenically significant. Delta with E484K was was first detected on 22 July 2021 in UK sequences. 93 sequences have been identified as of the 25 October 2021, with 90 from England, 2 from Scotland and 1 from Wales, an increase of 37 since the briefing of 15 October 2021.

The phylogenetic tree of UK Delta with E484K cases is shown in Figure 18, which includes 3 small clusters and multiple independent occurrences of the mutation (Delta with E484K is shown in yellow on Figure 18).

Figure 18. Maximum likelihood tree of UK Delta (B.1.617.2) with E484K cases as of 25 October 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 126 sequences. Presence of the E484K mutation is indicated by the tip colour (Yellow indicates E484K cases). Sample date and location of case is shown in the label for each tip. Three clusters of Delta with E484K have been identified with 4 or more sequences, cluster 1 and 2 which are highlighted on the tree. Cluster 1 has grown by 0 sequences and cluster 2 by 27 sequences since the last report, cluster 3 contains 5 sequences. Four additional sequences with E484K have been added to the tree outside these clusters. Six sequences were excluded from the tree due to a technical issue with CIVET. Supplementary data is not available for this figure.



Epidemiology in England

As of 25 October 2021, there are 93 Delta with E484K sequences in the UK, of which 76 could be linked to epidemiological data in England. Cases have been detected across 8 English regions, with most cases in the North West (43, 56.6%) as shown by region in Table 6, Figure 19 and by cluster in Figure 20 and by age in Figure 21. Of the 76 cases, 6 have history of travel.

Table 6. Number of confirmed (sequencing) Delta cases with E484K mutation, by region of residence as of 25 October 2021

Region	Confirmed (sequencing) case number	Case proportion
East Midlands	11	14.5%
East of England	4	5.3%
London	2	2.6%
North East	6	7.9%
North West	43	56.6%
South East	2	2.6%
South West	3	3.9%
West Midlands	0	0.0%
Yorkshire and Humber	4	5.3%
Unknown region	1	1.3%
Total	76	-

Figure 19. Confirmed (sequencing) Delta cases with E484K mutation cases by specimen date and region of residence as of 25 October 2021

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

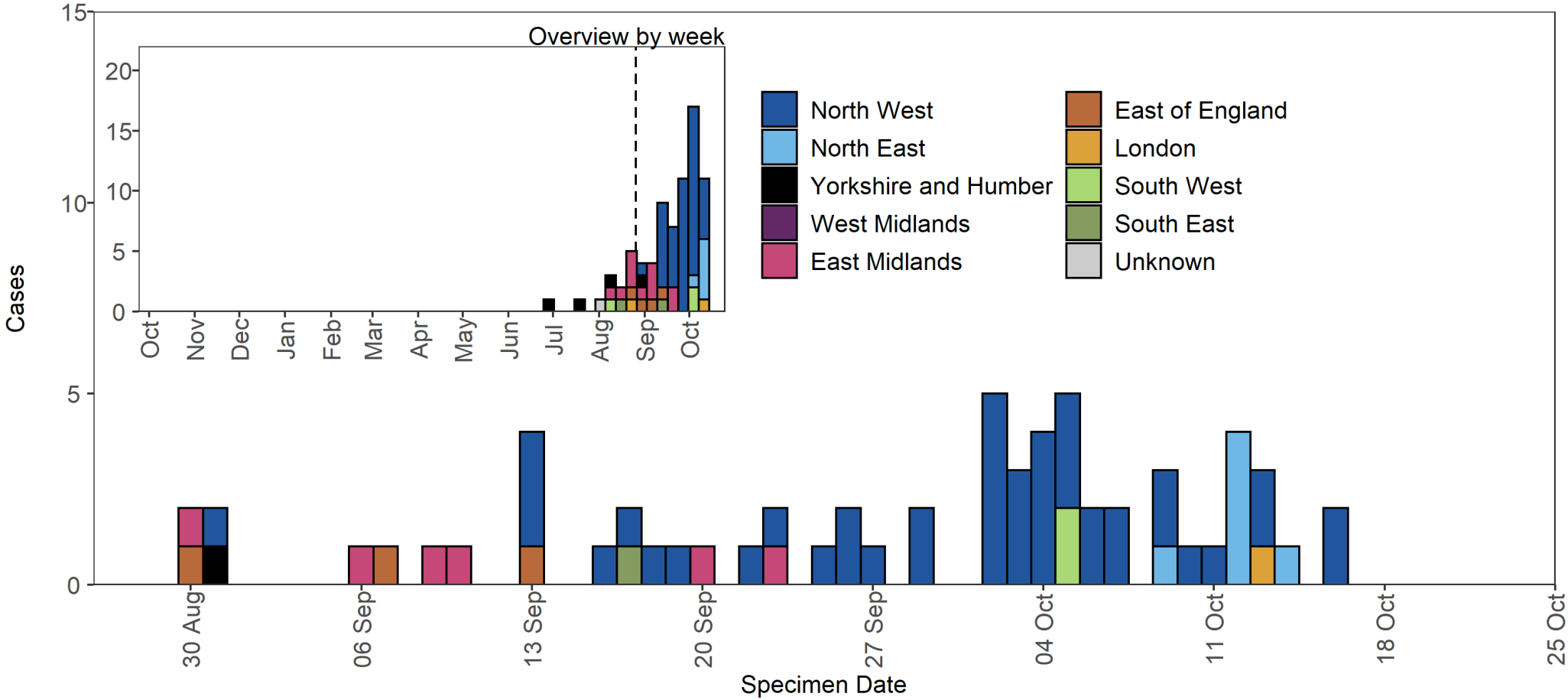


Figure 20. Confirmed (sequencing) Delta cases with E484K mutation cases by specimen date and detected cluster as of 25 October 2021

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

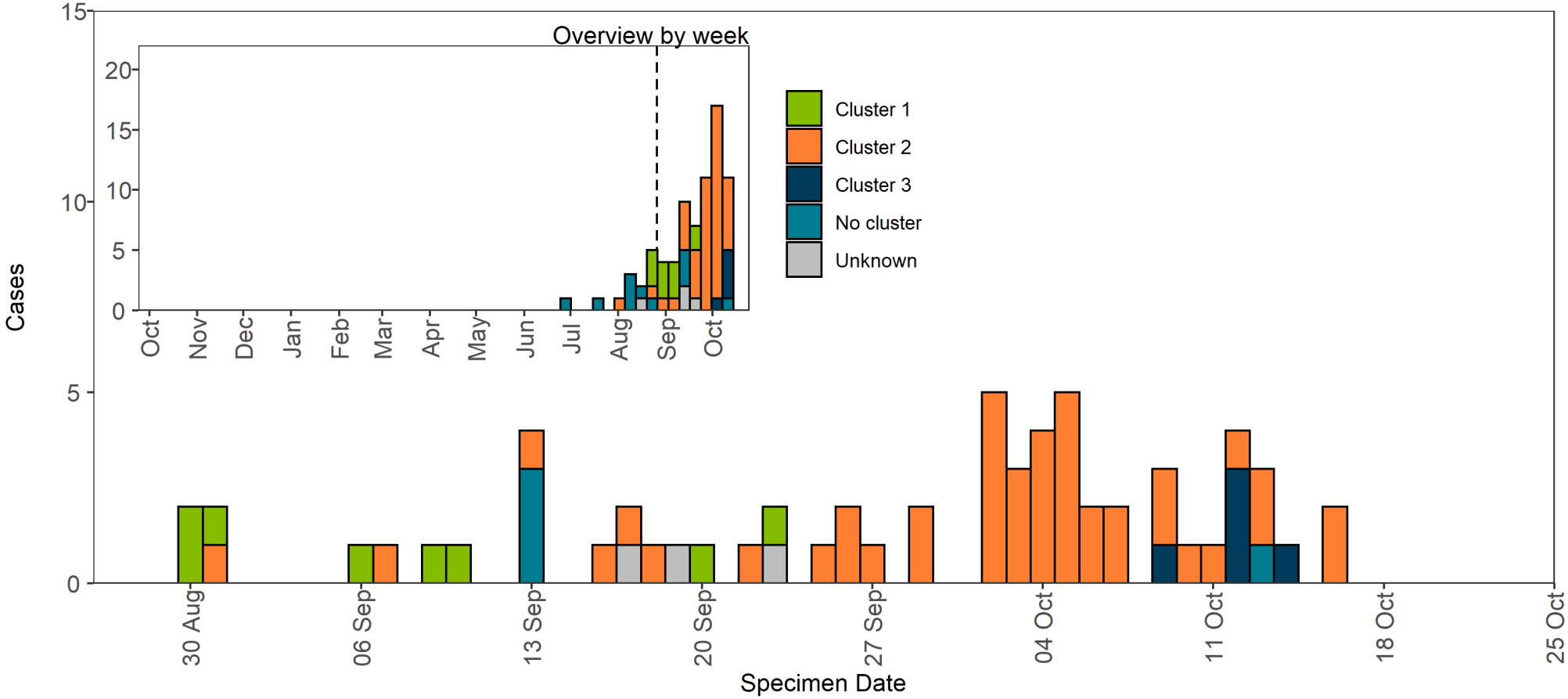
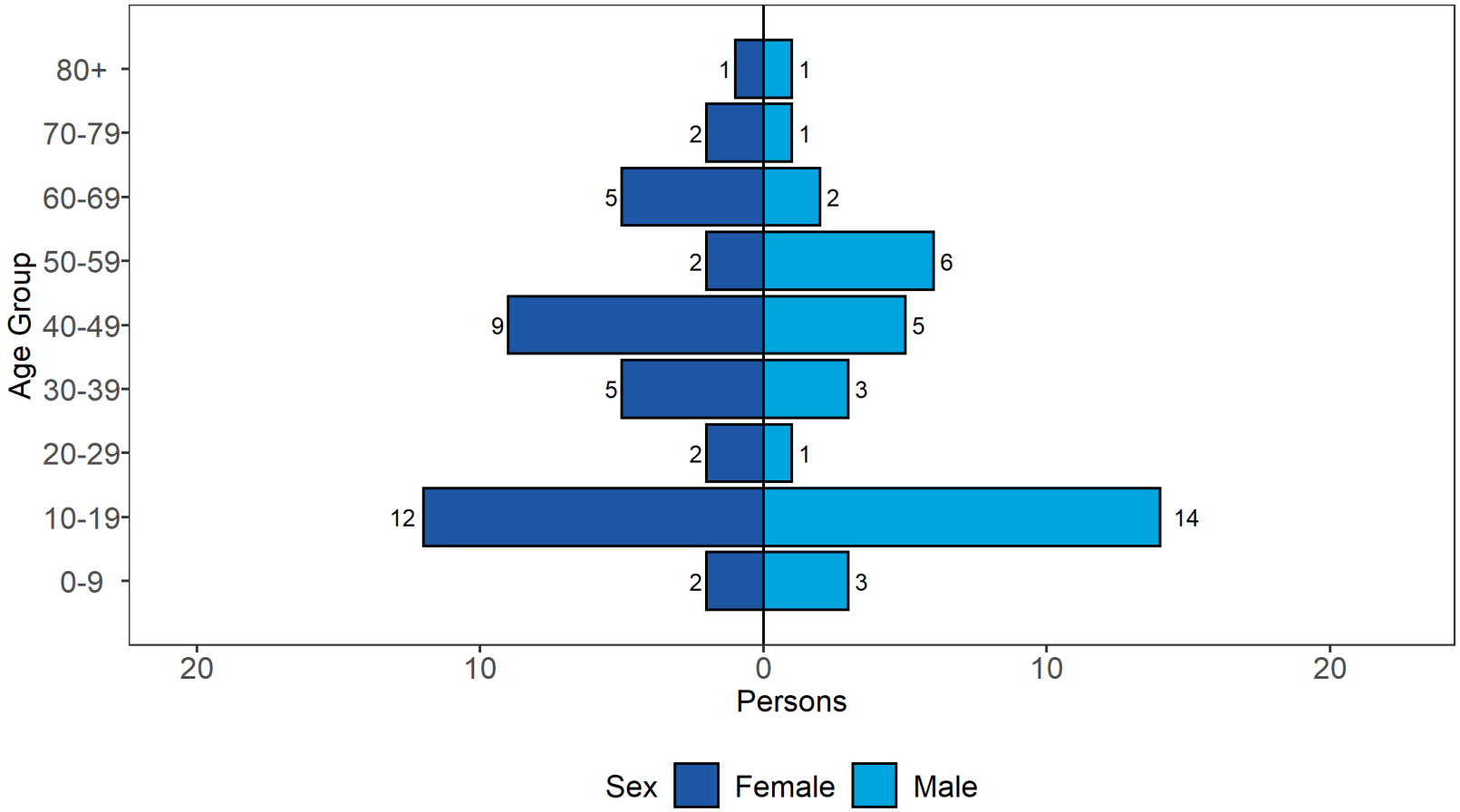


Figure 21. Age-sex pyramid of confirmed (sequencing) Delta cases with E484K mutation cases as of 25 October 2021
(Find accessible data used in this graph in underlying data.)



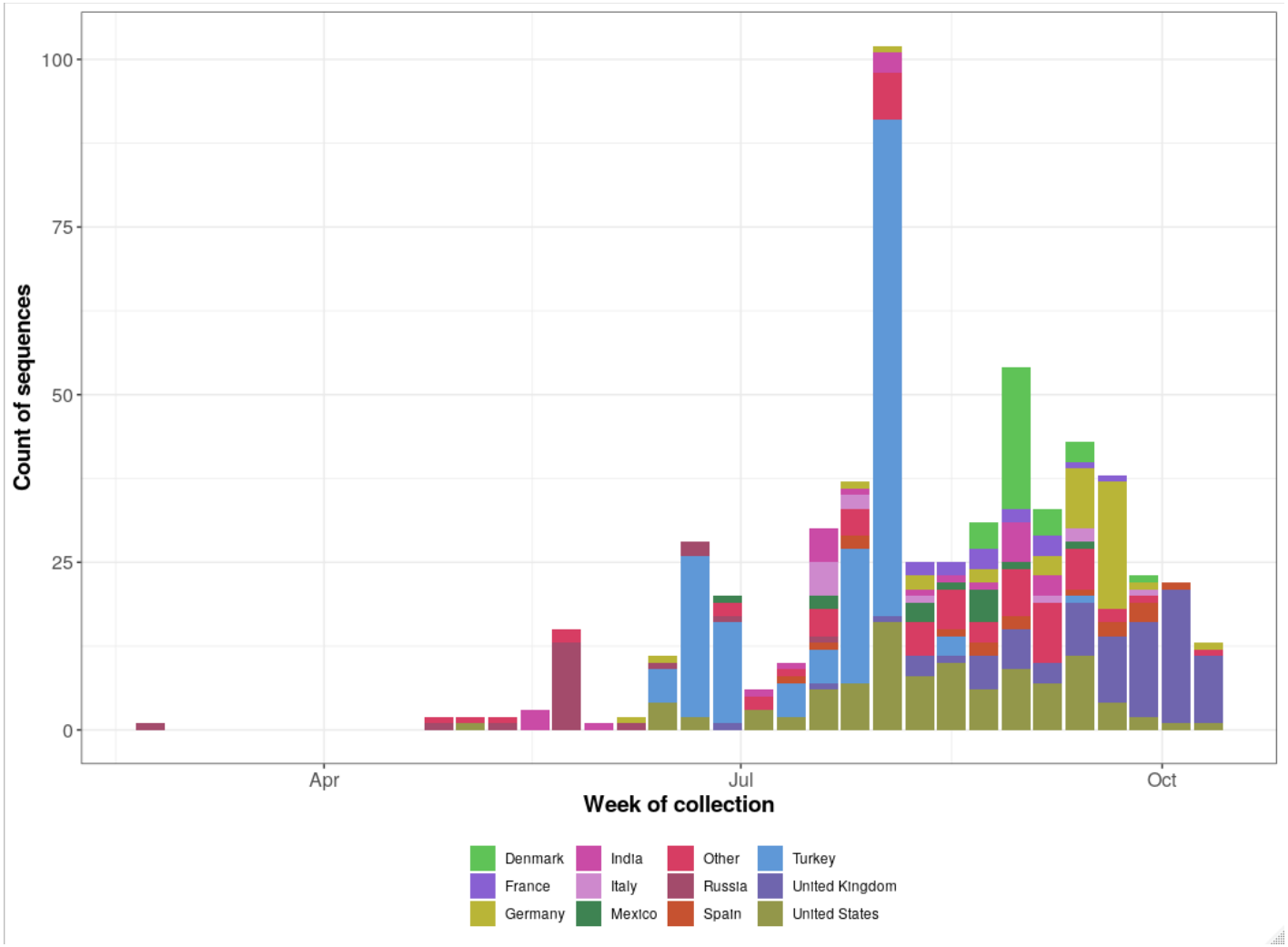
0 cases excluded where sex or age not reported

International epidemiology

As of 26 October 2021, 604 sequences on GISAID have been assigned to the B.1.617.2 and AY sub-lineages with the additional E484K mutation, of those 578 had appropriate date information. Sequences have been uploaded from 38 countries including Turkey (152), USA (100), Denmark (33), Germany (41), India (27), Russia (21), Spain (16), France (14), Mexico (14), Italy (12), Nigeria (8), Belgium (6), South Africa (6), Japan (5), Indonesia (5), Switzerland (5), Brazil (4), Kenya (2), Netherlands (2), Pakistan (2), Poland (2), Sri Lanka (2), Argentina (1), Australia (1), Botswana (1), Ecuador (1), Ethiopia (1), Lebanon (1), Lithuania (1), Luxembourg (1), Malta (1), Mozambique (1), Norway (1), Paraguay (1), Portugal (1), Ukraine (1). Figure 22 shows the distribution of cases per country over time, based on GISAID data, indicating an increase in observations of Delta with E484K in August and September 2021, which are continuing into October 2021.

Figure 22. Count of Delta with E484K classified sequences by week of collection uploaded to GISAID by week as of 26 October 2021

Countries with 10 or fewer sequences have been grouped together as Other. (Find accessible data used in this graph in underlying data.) Note: time to upload data into GISAID varies by country, and therefore recent weeks, are likely to be incomplete.



2.4 Monitoring diversity within Delta – Delta with K417N mutation

As of 25 October 2021, there are 243 Delta with K417N cases in England. Cases have been detected across 9 English regions, with most cases in the East of England (30%) as shown in Table 7 and Figure 23 with cases by age shown in Figure 24.

Table 7. Number of confirmed (sequencing) and probable (genotyping) Delta cases with K417N mutation, by region of residence as of 25 October 2021

Region	Confirmed (sequencing) case number	Probable (genotyping) case number[1]	Total case number	Case proportion
East Midlands	9	3	12	4.9%
East of England	51	22	73	30.0%
London	27	18	45	18.5%
North East	4	3	7	2.9%
North West	7	7	14	5.8%
South East	29	12	41	16.9%
South West	7	1	8	3.3%
West Midlands	17	6	23	9.5%
Yorkshire and Humber	13	3	16	6.6%
Unknown region	4	0	4	1.6%
Total	168	75	243	-

[1] Genotyping is used to identify variants Alpha, Beta, Delta and Gamma; targets were updated in mid-May 2021 to prioritise accurate identification of Delta over Alpha.

Figure 23. Confirmed (sequencing) and probable (genotyping) Delta cases with K417N mutation cases by specimen date and region of residence as of 25 October 2021

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

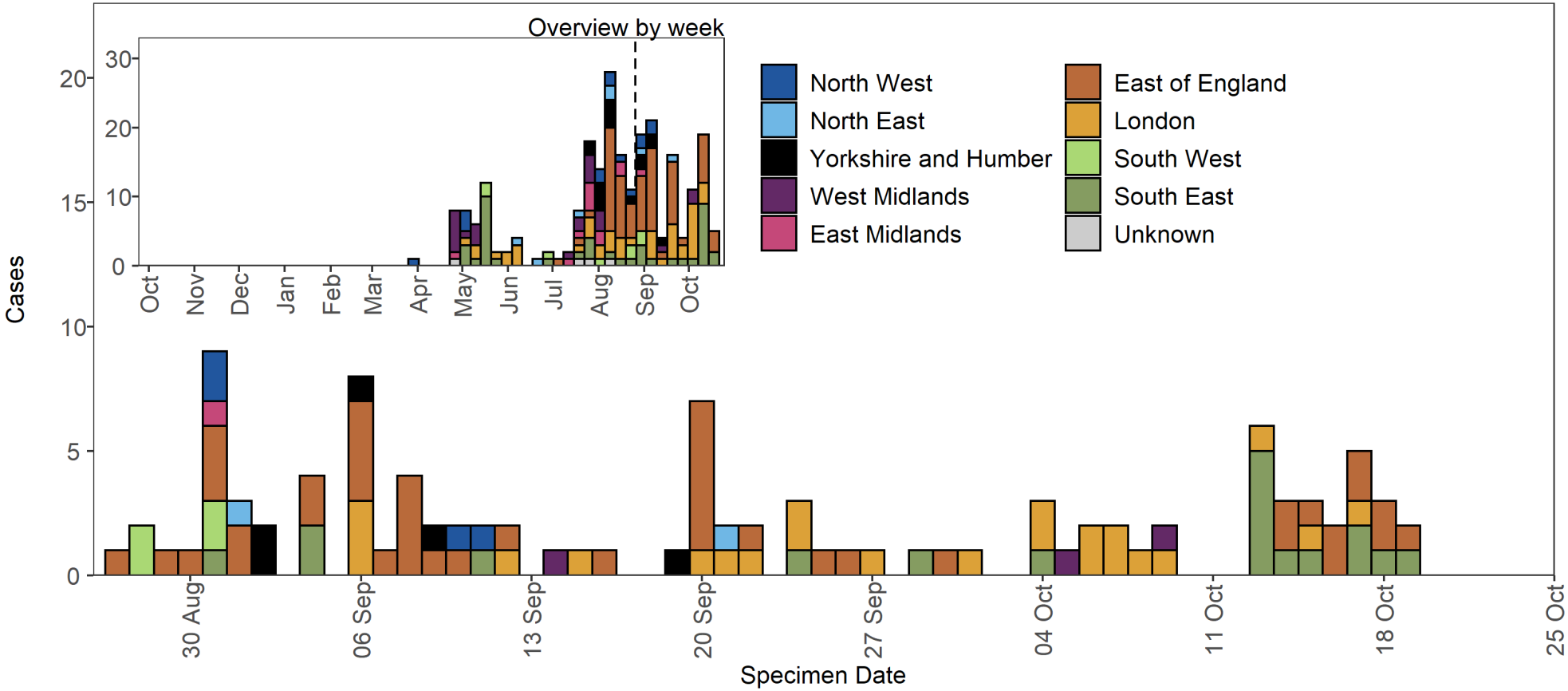
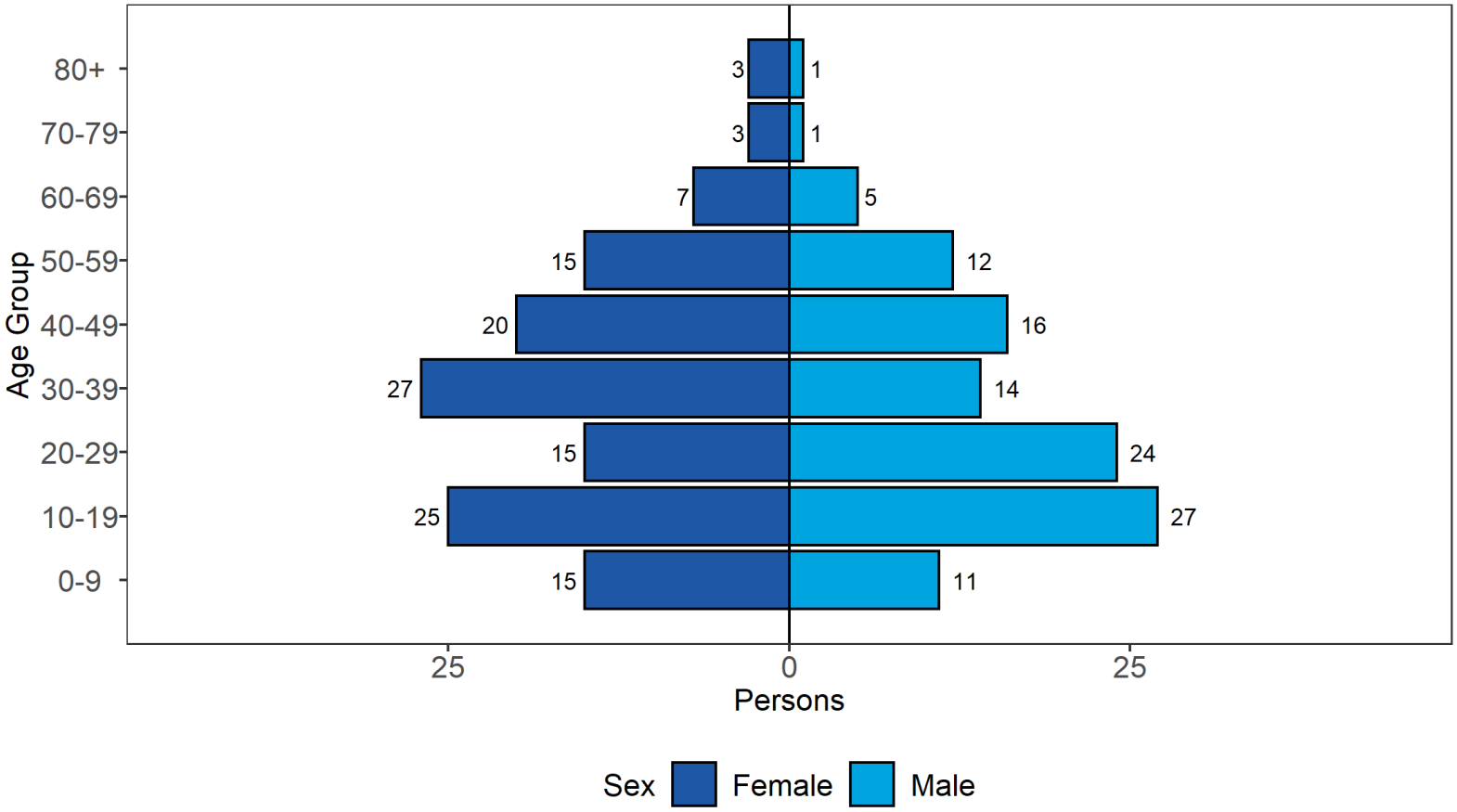


Figure 24. Age-sex pyramid of confirmed (sequencing) and probable (genotyping) Delta cases with K417N mutation cases as of 25 October 2021

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



2 cases excluded where sex or age not reported

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

The lineage B.1.617.2 was escalated to a variant of concern 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 Vaccine Effectiveness

An assessment of VUI-21OCT-01 vaccination status within Delta cases for weeks 25 to 41 2021 was undertaken. Sequenced samples linked to the National Immunisation (NIMS) data set were used in the analyses. Where individuals had multiple test results the first Delta variant sample was used as long as not within 14 days of a sample taken that was of a different variant. Samples with low quality sequence, those that were non Delta or indeterminant for the VUI-21OCT-01 were excluded. Samples taken from week 25 2021 when VUI-21OCT-01 was first detected in England. VUI-21OCT-01 status was compared by vaccine dose (unvaccinated, day 1 to 13 days post first dose, day 14 to day 27 post first dose, day 28 to day 0 of second dose, day 1 to day 13 post second dose, day 14+ post second dose). Logistic regression analysis was performed with adjustment for travel, ethnicity, sex, age (5 year bands), index of multiple deprivation quintile, at risk or clinically extremely vulnerable categories (as recorded in NIMS), health and social care worker (as recorded in NIMS), region of England and week of test. For the analyses including all cases vaccination status was assigned according to status on the date of the test because date of onset is only available in those reporting symptoms in the community testing (pillar 2 data set) and not the NHS (pillar 1) data set. For the analysis with the symptomatic pillar 1 cases date of onset was used to assign vaccination status.

An odds ratio (OR) of greater than 1 for VUI-21OCT-01 would suggest a lower vaccine effectiveness compared to non AY4.2 cases. After adjustment for the potential confounding variables there was no evidence that AY4.2 differed significantly compared to non-AY4.2 Delta cases, both symptomatic and asymptomatic, across the 3 vaccines in circulation. The adjusted OR point estimate Pfizer BioNTech 14 days after the second dose was 1.08 (95% confidence interval 1.00 to 1.16) for all cases and 1.12 (1.00-1.26) for symptomatic cases, so was close to being increased as the bottom end of the 95% confidence intervals were at 1.00. The most recent vaccine effectiveness (from the test negative case control study) for this vaccine after dose 2 for Delta was 83%. An OR of 1.12 would suggest a minimal reduction in vaccine effectiveness from 83% to 81%, if this was a true difference in effect.

Table 9. Vaccine effectiveness against VUI-21OCT-01 and non- VUI-21OCT-01 (2 doses at least 14 days before sample / onset date)

	Non- VUI-21OCT-01	VUI-21OCT-01	Adjusted* OR (95%CI) Pillar 2 symptomatic only	Adjusted* OR (95%CI) Pillar 1 and 2
Unvaccinated	86,988	2,338	Base	base
Astra Zeneca	96,826	3,688	0.98 (0.89-1.08)	1.02 (0.95-1.09)
Pfizer BioNTech	39,160	1,594	1.12 (1.00-1.26)	1.08 (1.00-1.16)
Moderna	663	37	1.14 (0.66-1.98)	0.96 (0.69-1.35)
All vaccines, 14+ days after the second dose	136,648	5,319	1.03 (0.94-1.13)	1.04 (0.97-1.11)

* Travel, ethnicity, sex, age (5 year bands), index of multiple deprivation quintile, at risk or clinically extremely vulnerable categories health and social care worker (as recorded in NIMS), region of England and week of test.

3.2 Surveillance case definitions

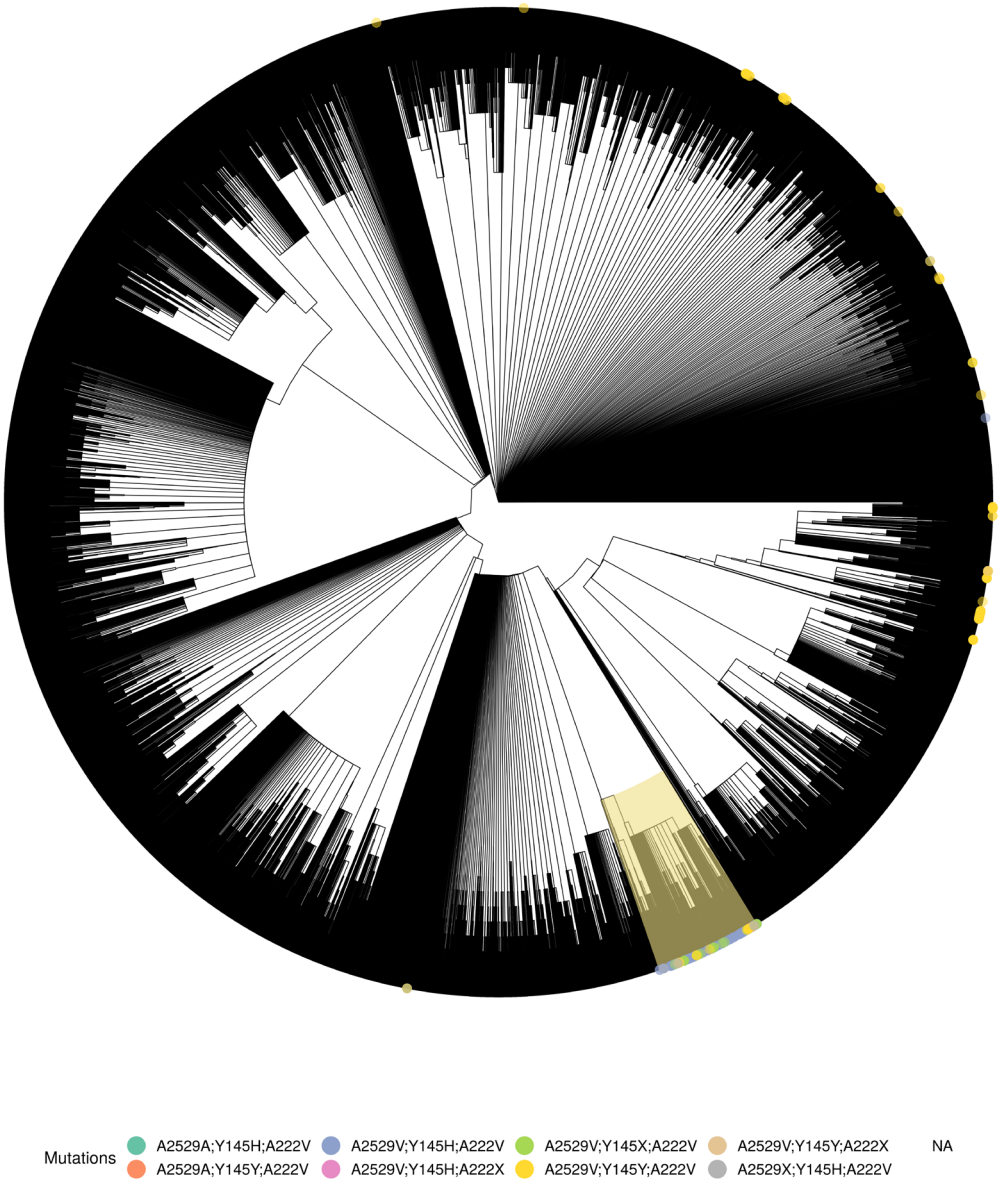
AY.4.2 includes the spike mutations A222V and Y145H, as well as the mutations seen in Delta and the AY.4 lineage. Y145H is in an area of the genome which has lower sequencing coverage with some primer sets. A222V is present in other clades outside AY.4.2.

A variant definition was developed based on sequencing data from England (in Technical Briefing 26), the current surveillance case definition is a genome meeting the existing Delta genome case definition plus any 2 of the 3 mutations (orf1ab: A2529V; S: Y145H; S: A222V) where none of the positions are wild-type. To evaluate the case definition among (non-UK) GISAID sequences, 1,095 sequences from GISAID that each had at least 2 of the AY.4.2 mutations (A222V, Y145H, A2529V) were downloaded. These sequences were added to the UK Delta subsampled phylogeny (Figure 25). 77.8% of them fell within the UK AY.4.2 clade. The majority of those that did not fall within the clade (225 out of 242, 93.0%) had the A222V and A2529V mutations but were wild-type at position 145. The sensitivity of the case definition in correctly placing GISAID sequences within or outside the AY.4.2 clade is 95.2% and the specificity is 97.5%.

Figure 25. Maximum likelihood sub-sampled phylogenetic tree of Delta variants from England with sequences from GISAID that contain at least 2 of the VUI-21OCT-01 defining mutations

Supplementary data is not available for this figure.

This tree was built using Fasttree and Usher with a sub-sample of n=115,097 Delta sequences with image edge coloured by key mutations. To generate the sub-sample, Delta sequences were grouped by Pangolin lineage and week of sample. Where the group was 4 or more sequences, 25% of the group was selected at random to be included, where the group was smaller than 4 sequences, the whole group was included. Only mutation combinations for sequences from GISAID (non-UK) are indicated. The clade containing VUI-21OCT-01 sequences is highlighted in yellow.



3.3 Epidemiology of VUI-21OCT-21 in England

As of 25 October 2021, there are 23,830 VOC-21OCT-01 genomes in the UK data set, of which 16,876 linked to cases in England. VUI-21OCT-01 accounts for 4.2%, 5.2%, and 5.6% of Delta cases in England in the weeks beginning 20 September, 27 September, and 4 October 2021 respectively. Data is incomplete for more recent weeks.

Variant prevalence for all cases in England as of 21 October 2021 is shown by region in Figure 26 and travel status in Figure 27.

Figure 7 shows AY.4.2 as a proportion of all Delta cases (Pangolin lineage call).

Cases have been detected across all regions in England (Table 5 and Figure 26). Of the 15,120, 420 had a recent travel history. At least 32 countries of travel have been reported. Age data is shown in Figure 9.

Severity outcomes

In the previous technical briefing (Technical Briefing 26), severe outcomes associated with VUI-21OCT-01 were assessed by comparing hospital admission and mortality outcomes for VUI-21OCT-01 cases against Delta cases for the period between 15 May 2021 and 23 September 2021.

This analysis has been updated to include data up to 24 October 2021. Minor reductions in percentage of VUI21-OCT-01 cases with severe outcomes have been noted since the previous analysis. A 0.4% reduction in hospitalisation and 0.23% reduction in mortality was observed.

Information on attendance to emergency care is derived from the Emergency Care Data Set (ECDS) and Secondary Uses Service (SUS), provided by NHS Digital. This data only shows whether a case has attended emergency care at an NHS hospital and was subsequently admitted as an inpatient. The data does not include cases who were directly admitted without first presenting to emergency care.

ECDS and SUS reporting is lagged, where NHS trusts routinely provide monthly data by the 21st of the following month. However, some trusts report daily data, and the linkage between COVID-19 cases and ECDS data is updated twice-weekly.

These initialanalyses produced overlapping confidence intervals between rates of hospitalisation or death among VUI-21OCT-01 and Delta, suggesting that rates are similar and differences observed are not statistically significant. However, these crude analyses do not adjust for crucial factors that can influence outcomes such as age and vaccination status and should be interpreted with caution.

Table 9. Attendance to emergency care and inpatient admission of cases in England (15 May 2021 to 24 October 2021)

Variant	Number of cases since 15 May 2021#	Cases with an A&E visit or where presentation to A&E resulted in inpatient admission* (exclusion‡)	
	n	n	%
Delta	728,088	1,789	(0.25%, 95% CI 0.23-0.26)
VUI-21OCT-01	10,024	27	(0.27%, 95% CI 0.18-0.39)
Total	738,112	1,816	(0.25%, 95% CI 0.23-0.26)

Data sources: Emergency care attendance and admissions from ECDS and SUS. NHS trusts are required to submit emergency care attendances by the 21st of each month. As a result, the number of cases with attendances may show substantial increases in technical briefs prepared after the monthly cut-off, compared with other briefs from the same month.
¥ Cases without specimen dates and unlinked sequences (sequenced samples that could not be matched to individuals) are excluded from this table.
* Cases are assessed for any emergency care attendance within 14 days of their positive specimen date.
# Inclusion: Including cases where 28 days has elapsed since their positive specimen date.
‡ Exclusion: Excluding cases with the same specimen and attendance dates. Cases where specimen date is the same as date of emergency care visit are excluded to help remove cases picked up via routine testing in healthcare settings whose primary cause of attendance is not COVID-19. This underestimates the number of individuals in hospital with COVID-19 but only includes those who tested positive prior to the day of their emergency care visit. Some of the cases detected on the day of admission may have attended for a diagnosis unrelated to COVID-19.

Table 10. Deaths of cases in England (15 May 2021 to 24 October 2021)

Variant	Number of cases since 15 May# (Exclusion‡)	Deaths^	
	n	n	%
Delta	727,986	3,813	(0.53%, 95% CI 0.53-0.56)
VUI-21OCT-01	10,023	64	(0.49%, 95% CI 0.49-0.82)
Total	738,009	4,031	(0.53%, 95% CI 0.53-0.56)

Data sources: deaths from UKHSA daily death data series (deaths within 28 days).
¥ Cases without specimen dates and unlinked sequences (sequenced samples that could not be matched to individuals) are excluded from this table.
Inclusion: Including cases where 28 days has elapsed since their positive specimen date.
‡ Exclusion: Excluding cases who tested positive at post-mortem.
^ Total deaths in any setting (regardless of hospitalisation status) within 28 days of positive specimen date.

Table 11. Number of confirmed and provisional VUI-21OCT-01 cases, by region of residence as of 25 October 2021

Region	Total case number	Case Proportion
East Midlands	1,083	6.4%
East of England	1,713	10.2%

Region	Total case number	Case Proportion
London	2,410	14.3%
North East	357	2.1%
North West	1,874	11.1%
South East	3,284	19.5%
South West	1,999	11.8%
West Midlands	2,598	15.4%
Yorkshire and Humber	1,496	8.9%
Unknown region	62	0.4%
?Total	16,876	-

Figure 26. Confirmed and provisional VUI-21OCT-01 cases by specimen date and region of residence as of 25 October 2021
(Find accessible data used in this graph in underlying data.)

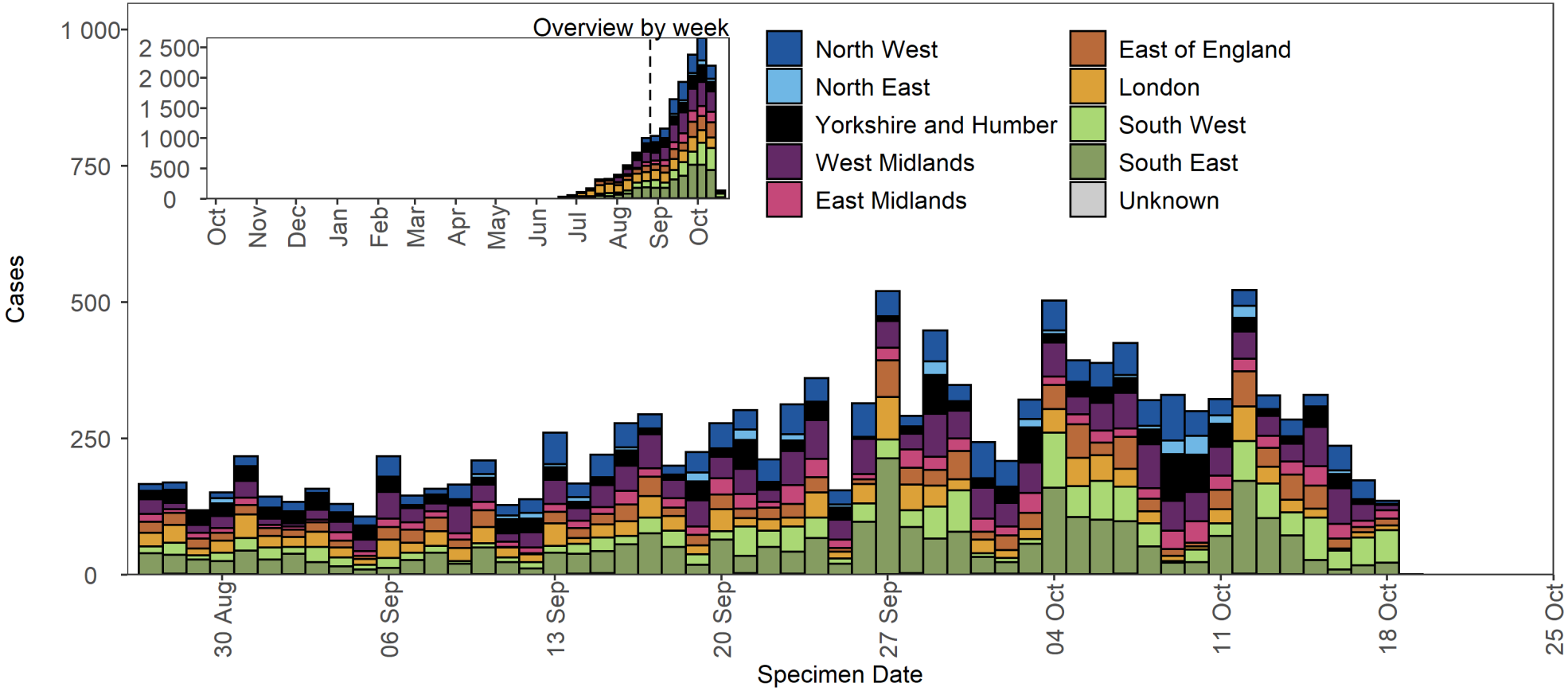
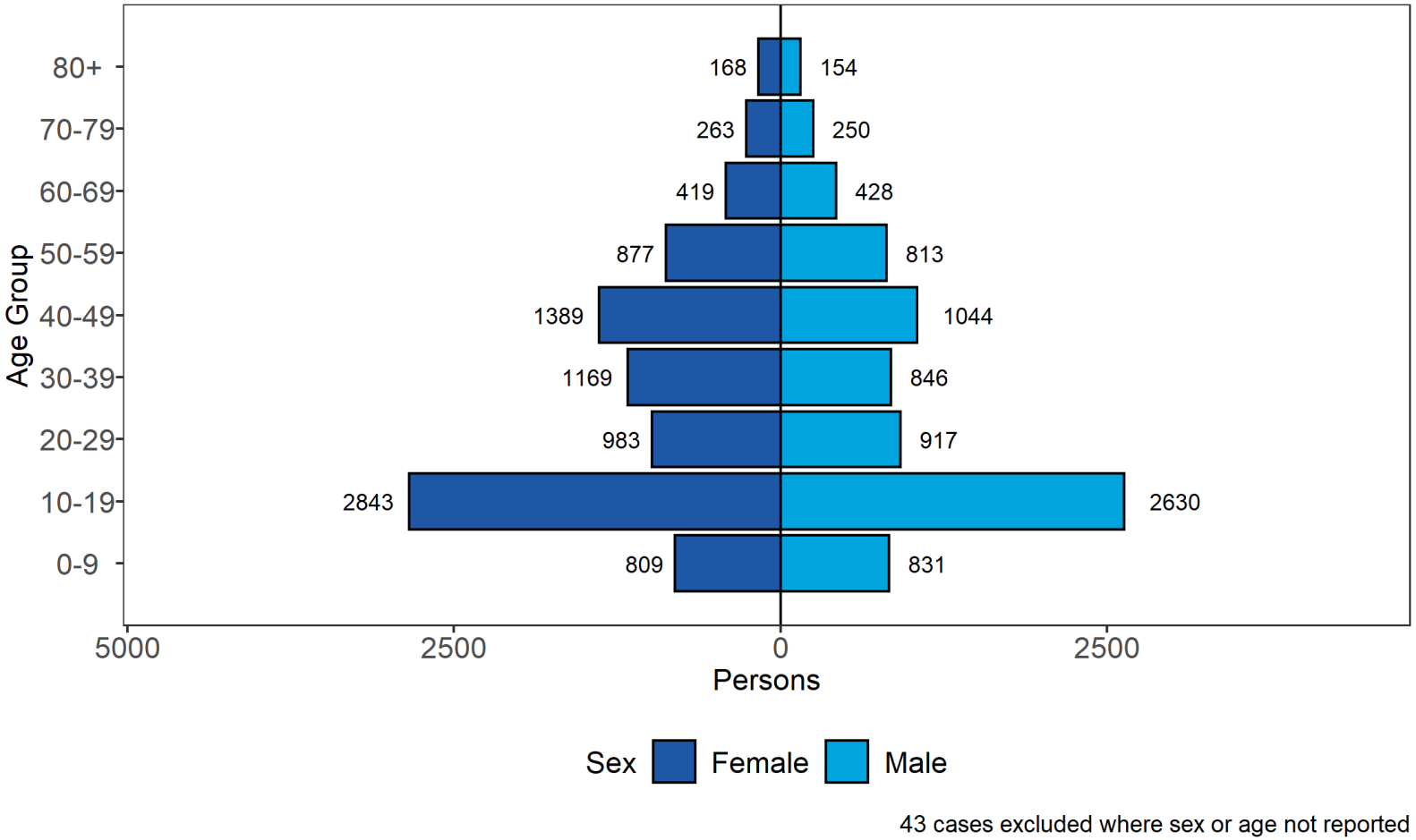


Figure 27. Age-sex pyramid of VUI-21OCT-01 cases as of 25 October 2021
(Find accessible data used in this graph in underlying data.)



43 cases excluded where sex or age not reported

International epidemiology

As of 26 October 2021, 1,366 sequences on GISAID meet the VUI-21OCT-01 definition from 35 countries excluding the United Kingdom (Figure 10), with 1,347 having suitable dates. The case definition has not been validated on international data and will be further assessed; results are provisional.

Using the surveillance case definition. sequences are identified from Germany (319), Denmark (300), Poland (115), USA (113), Italy (88), Ireland (74), Romania (66), Belgium (61), Switzerland (35), Netherlands (30), France (23), India (20), Norway (15), Canada (12), Portugal (10), Luxembourg (9), Lithuania (8), Sweden (8), Czechia (7), Malaysia (7), Slovakia (7) and 13 countries with less than 5 sequences.

Sequences shown before late June 2021 in Figure 29 meet the VUI-21OCT-01 definition, but do not have an amino acid call at the site 145, and therefore could either be wildtype or mutant. Using a stricter definition requiring all 3 mutations from the VUI-21OCT-01 definition results in 995 sequences present on GISAID as of 26 October 2021, from 29 countries. This data is shown in Figure 30, and a later first week of collection is seen.

Figure 28. Count of VUI-21OCT-01 classified sequences by week of collection uploaded to GISAID by week as of 26 October 2021. The first sequence was uploaded by India with a collection date of 28 March 2021.

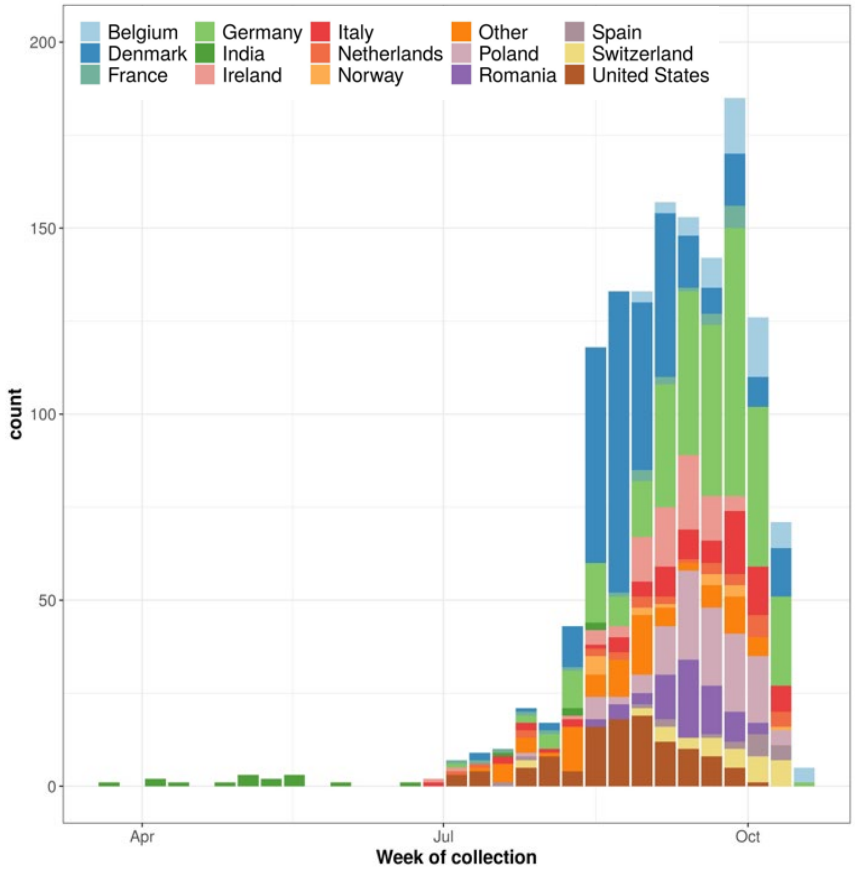
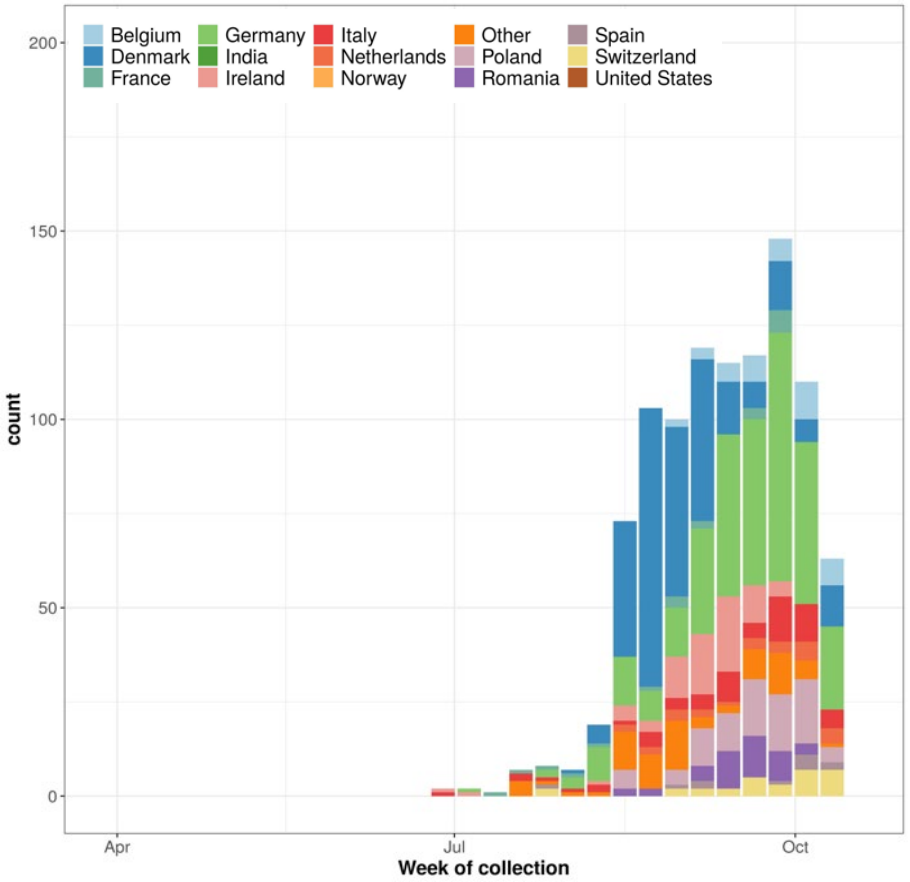


Figure 29. Count of VUI-21OCT-01 with all three mutations in the definition present, classified sequences by week of collection uploaded to GISAID by week as of 26 October 2021. The first sequence date was uploaded by the UK with a collection date of 15 June 2021.



Countries with 10 or fewer sequences have been grouped together as Other. Note time to upload data into GISAID varies by country and therefore recent weeks are likely to be incomplete. (Find accessible data used in this graph in underlying data).

Growth rates

Logistic growth rates for VUI-21OCT-01 for the country as a whole and for each UK region are shown in Figure 30 and Figure 31. Growth rates are computed relative to non-AY.4.2 variants circulating in the same region (geo-matched sample). Sample inclusion criteria are: 1) A non-traveller as determined by matching each case against passenger locator forms and managed quarantine service test codes 2) Collected from Pillar 2 testing. 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. 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 19% per week for VUI-21OCT-01. Growth rate is context dependent and cannot be interpreted as a change in biological transmissibility.

Figure 30. Sample frequency of VUI-21OCT-01 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 across the UK has increased since the beginning of August 2021.

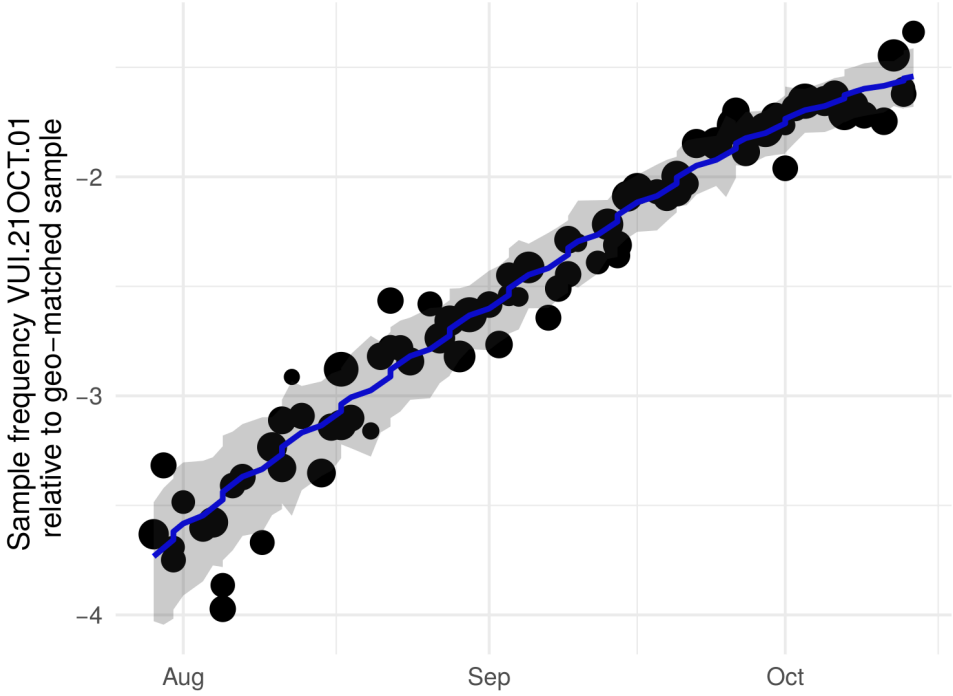
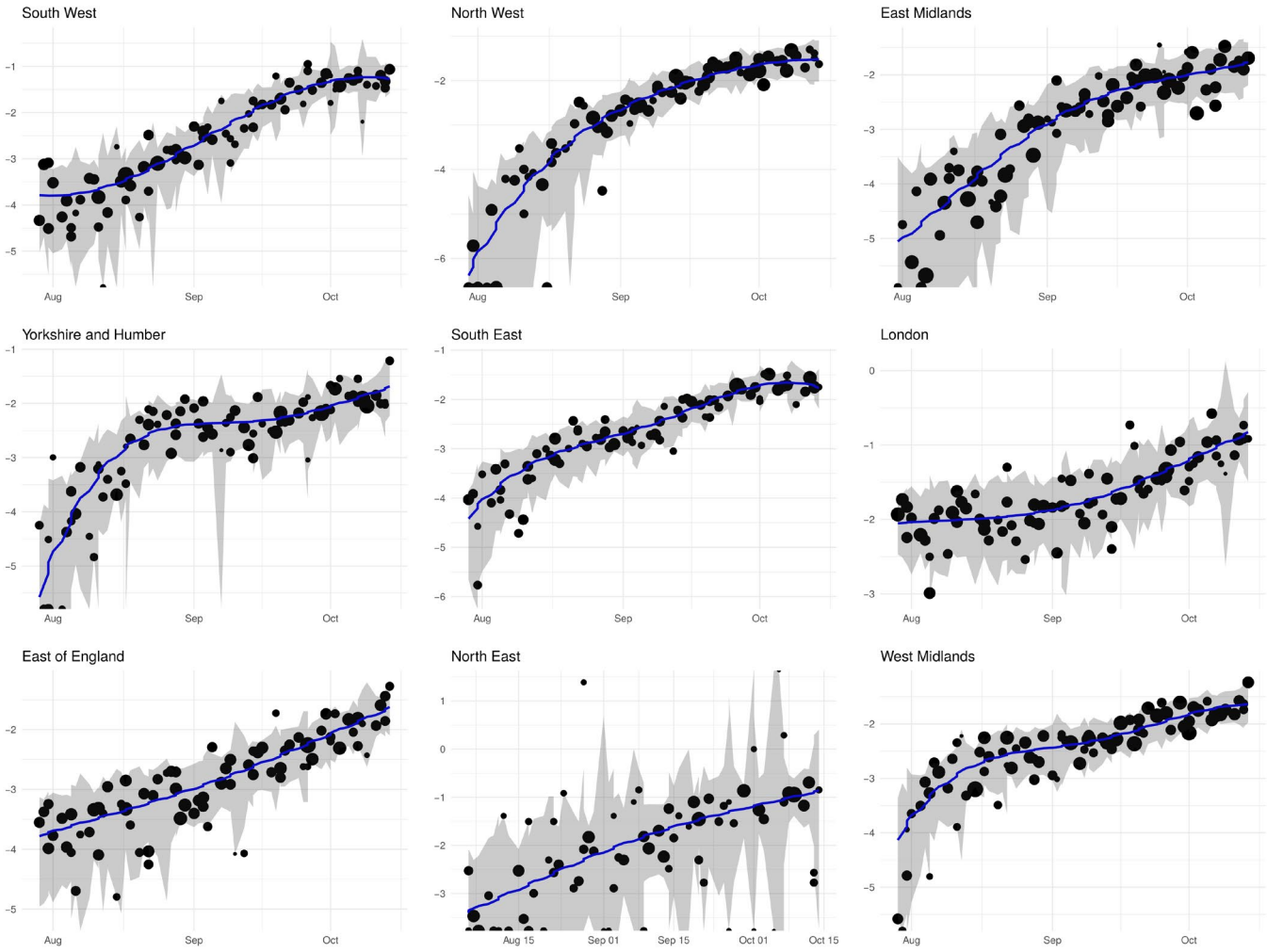


Figure 31. Sample frequency of VUI-21OCT-01 as compared to geography-matched sample of non-AY.4.2 for each UK region

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



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 from the period 1 August 2021 to 5 October 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 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 12 shows the secondary attack rates split by type of contact. Secondary attack rate for household contacts of cases with VUI-21OCT-01 was 12.2% (95% CI: 11.8% - 12.7%), higher than that observed for other Delta cases where it was 11.2% (95% CI: 11.1% - 11.3%). In non-household settings, the secondary attack rate was higher for VUI-21OCT-01 than other Delta cases, but this difference was not significant.

Table 12. Secondary attack rates for contacts of non-travel cases with VUI-21OCT-01 and other Delta
(1 August 2021 to 5 October 2021, variant data as of 25 October 2021 and contact tracing data as of 26 October 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]
Delta except VUI-21OCT-01	15,922 (67.0% with contacts)	407,063 (69.5% with household, 17.5% with non-household contacts)	3.8%	1.5% (1.5% - 1.6%) [3,461/228,660]	11.2% (11.1% - 11.3%) [76,911/686,204]	4.0% (3.9% - 4.1%) [8,076/201,171]
VUI-21OCT-01	356 (69.7% with contacts)	11,414 (73.1% with household, 18.3% with non-household contacts)	3.0%	1.6% (1.3% - 2.0%) [75/4,639]	12.2% (11.8% - 12.7%) [2,593/21,218]	4.5% (3.9% - 5.0%) [257/5,775]

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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