UK Health Security Agency

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

Technical briefing 28

12 November 2021

This briefing provides an update on previous briefings up to 29 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 variants of concern (VOC) and variants under investigation (VUI). 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 VOCs and 9 variants under investigation (VUIs) (Table 1). There are no new VOCs or VUIs in the United Kingdom (UK) classification since the last briefing.
2. Delta remains the predominant variant accounting for approximately 99.8% of sequenced cases in England from 10 October to 8 November 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 11.2% of Delta cases in the most recent complete week of sequencing (17 October 2021 to 23 October 2021). In more recent weeks, sequencing data is incomplete, however AY.4.2 accounts for 13.0% of Delta cases in the week 24 October 2021 to 30 October 2021 and 14.7% in the week 31 October 2021 to 6 November 2021.
4. Vaccine effectiveness analysis does not suggest a significant reduction in vaccine effectiveness for AY.4.2 compared to other Delta viruses. Analysis using the standard test negative case control study does not indicate reduction in vaccine effectiveness for AY.4.2 as compared to non AY.4.2.
5. Preliminary viral neutralisation studies with post-vaccination sera against AY.4.2 virus shows a 2.8 fold drop in comparison the wild-type virus, similar to Delta which showed a 3.2 fold drop in neutralisation (Genotype to Phenotype consortium)
6. A new risk assessment for AY.4.2 has been published and is available here.

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 (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 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 8 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	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
	C.36.3††		Monitoring
	B.1.427/B.1.429		Monitoring
	B.1.620		Monitoring
	R.1		Monitoring
	C.1.2		Monitoring
	B.1.640		Monitoring
	Delta + E484K Phylogenetic Cluster 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
	B.1.1.318	VUI-21FEB-04	VUI
Lambda	C.37*		Monitoring
	A.27		Monitoring
	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		Monitoring
	C.37 (S:L5F, G75V, D614G, L452Q, E484K, P499R, N501T, H655Y, P681R, T859N)		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 and are now WHO variants under monitoring.

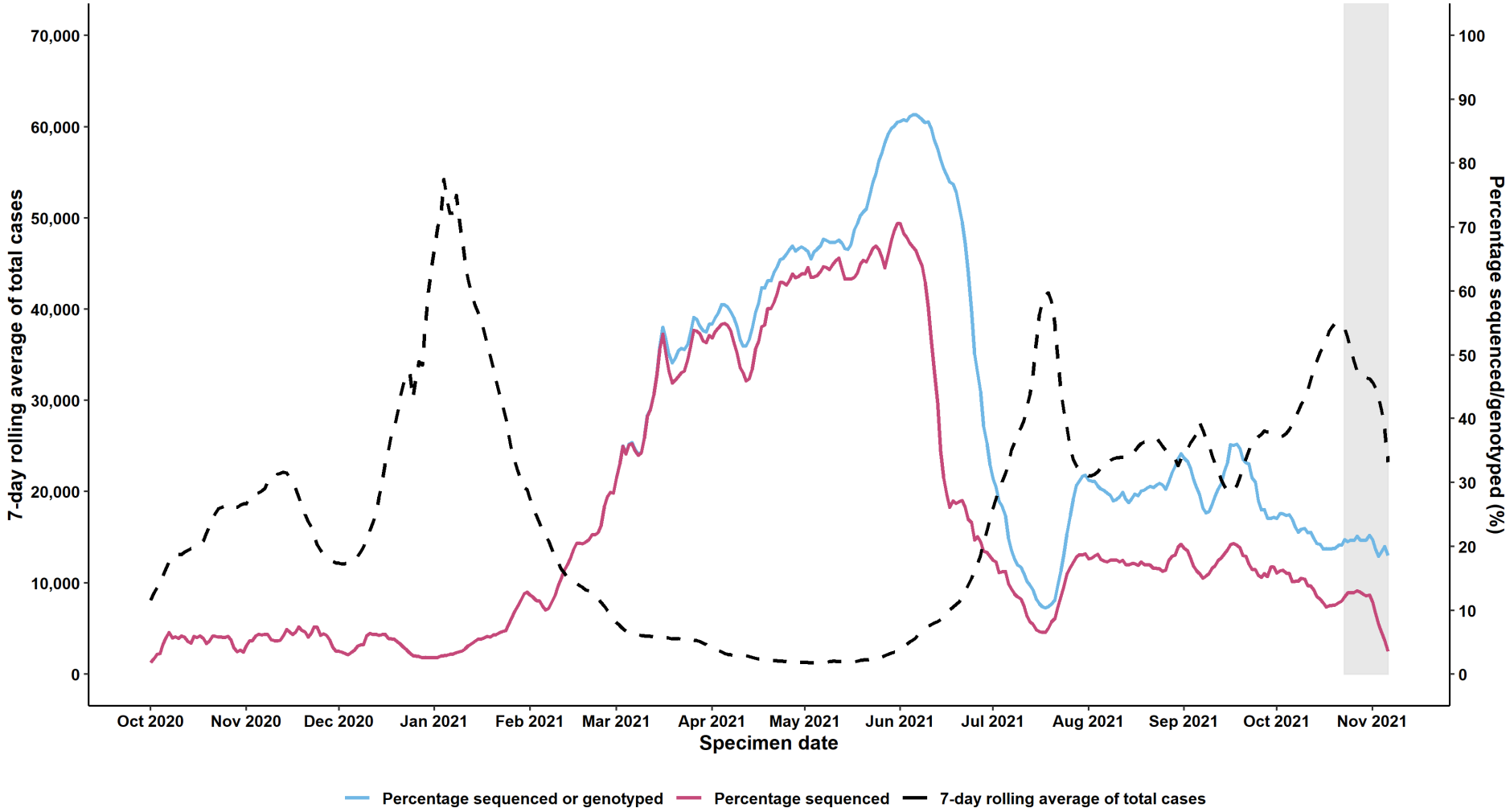
1.2 Sequencing coverage

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. 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. At the current time, 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 6 November 2021)

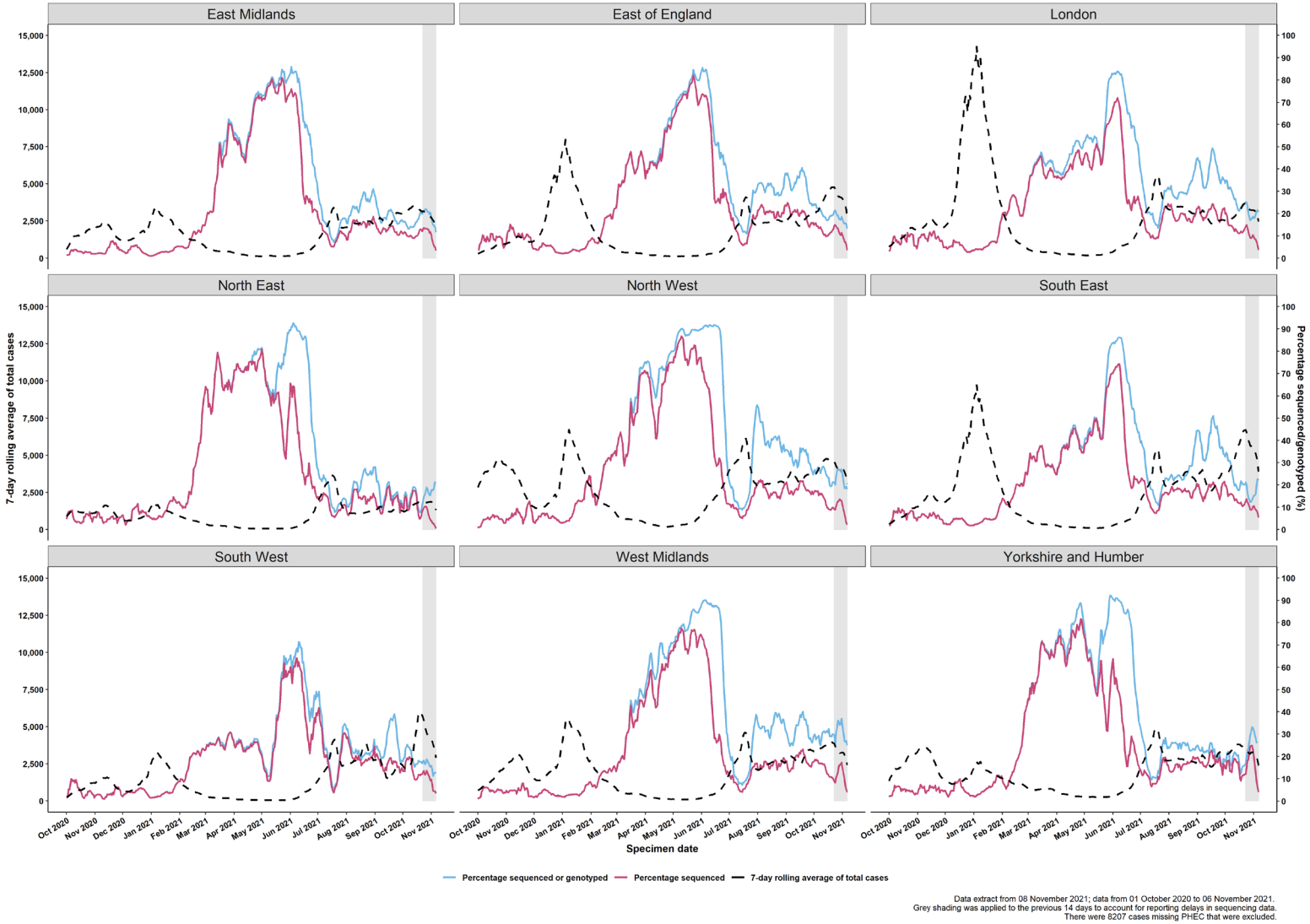


Data extract from 08 November 2021; data from 01 October 2020 to 06 November 2021.
Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

(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.

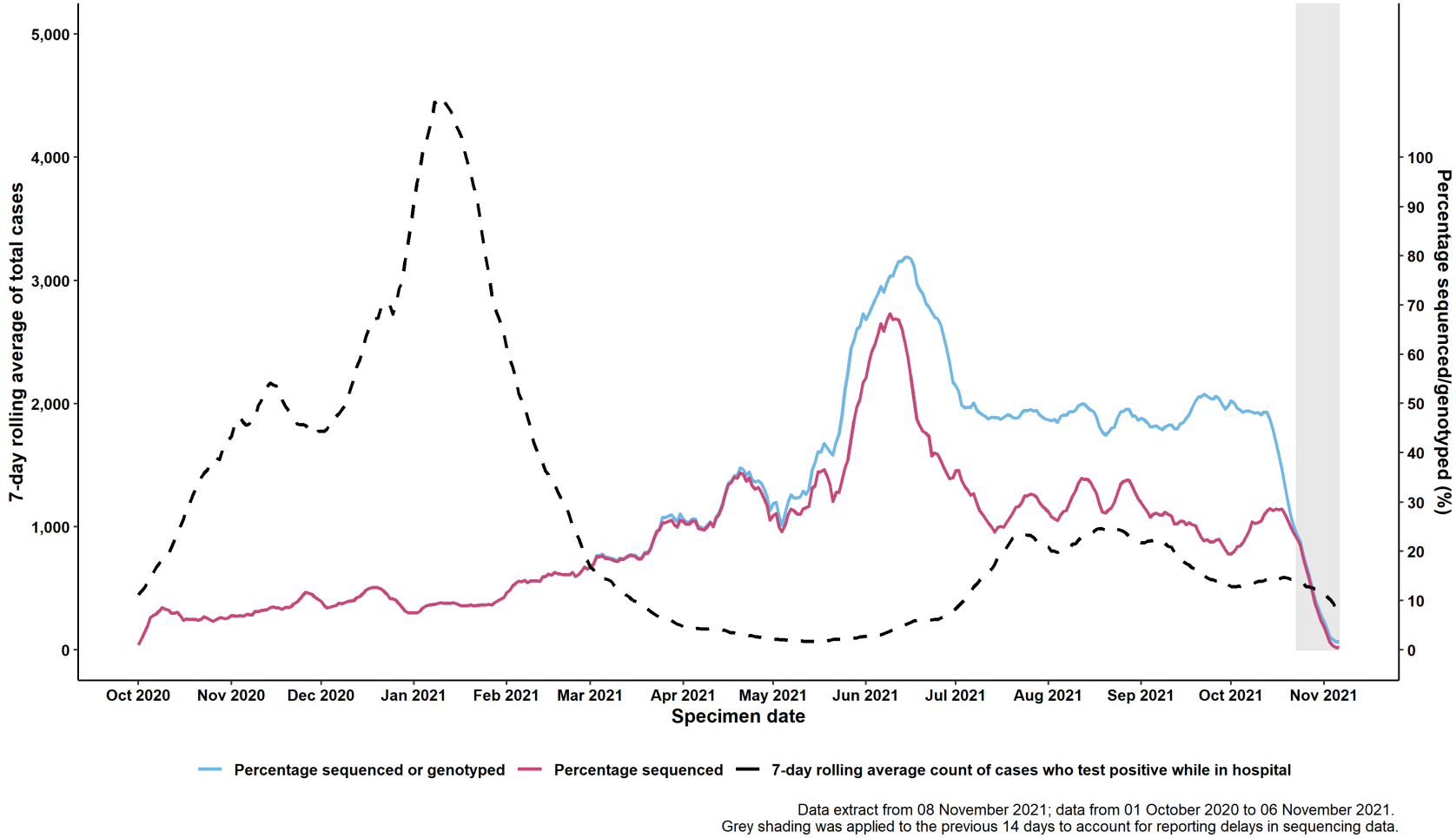
Figure 2. Coverage of sequencing with a valid result and genotyping over time by region (1 October 2020 to 6 November 2021)



(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.

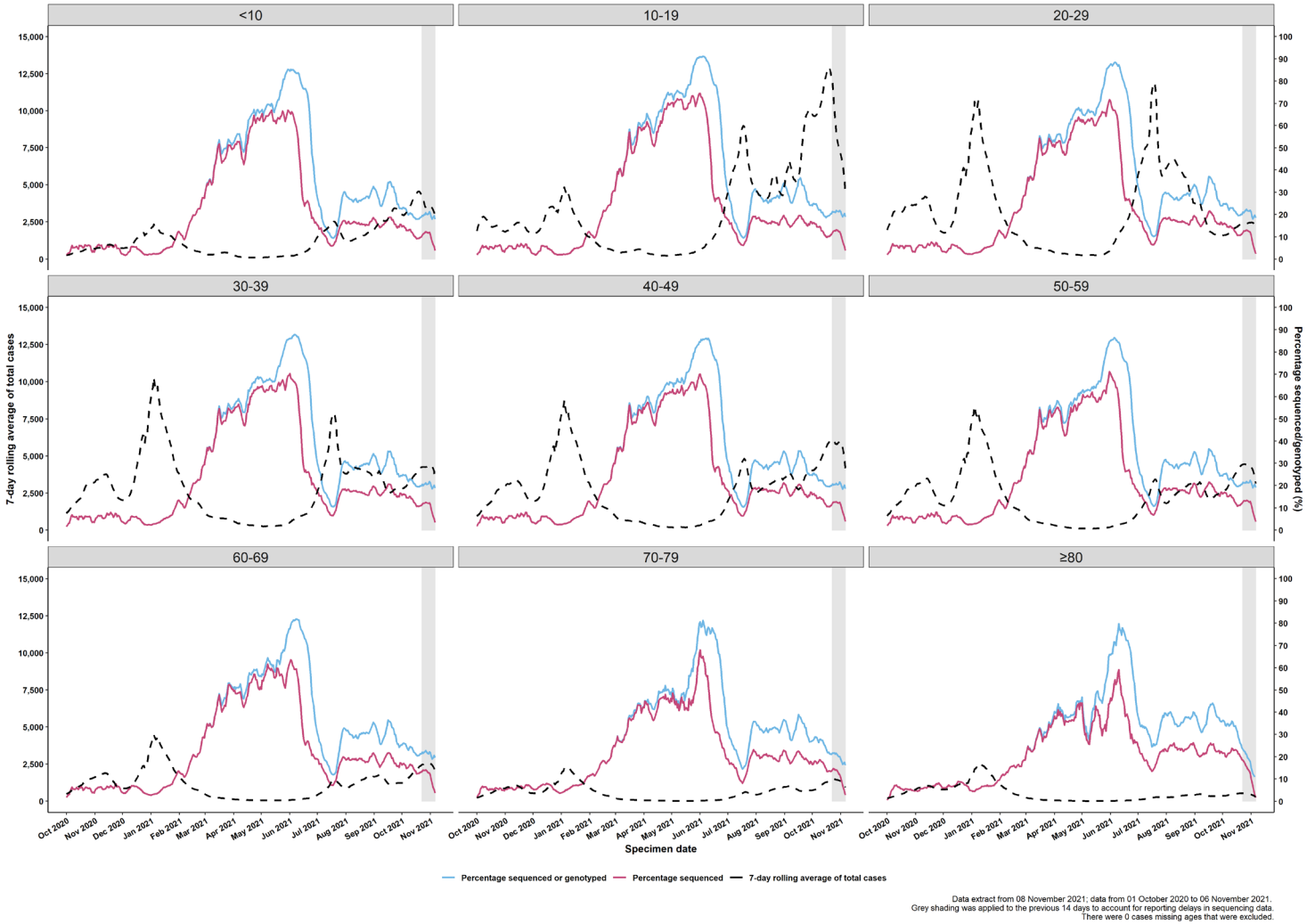
Figure 3. Coverage of sequencing with valid result and genotyping for cases who test positive in hospital (1 October 2020 to 6 November 2021)



(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 4. Coverage of sequencing with valid result and genotyping for cases by age group (1 October 2020 to 6 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 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. These tables will be reinstated in the technical briefing for new VOC when they are identified.

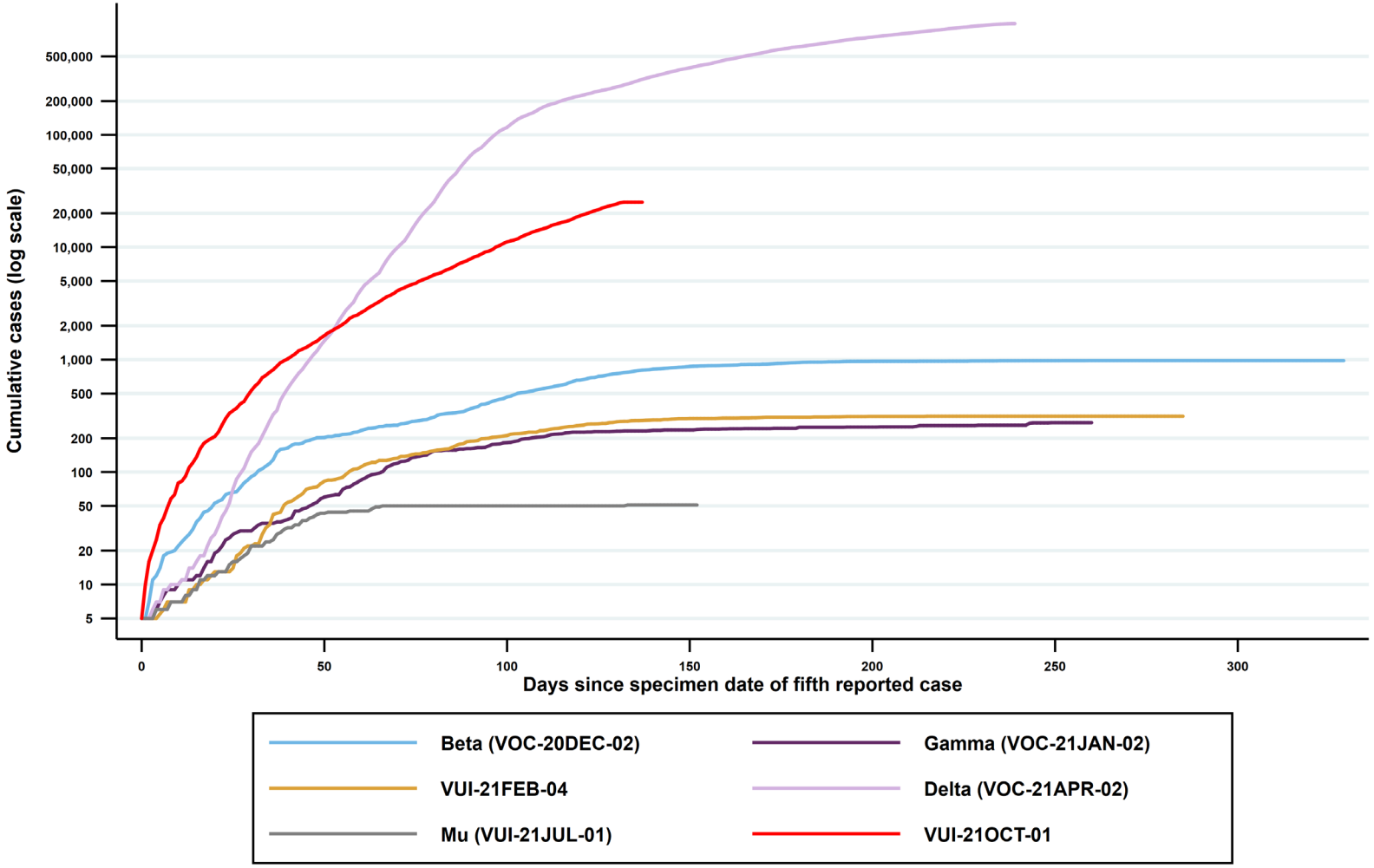
Table 3. Number of confirmed and probable cases by variant as of 8 November 2021

Variant	Confirmed (sequencing) case number	Probable (genotyping) case number[1]	Total case number	Case proportion	Deaths
Alpha	221,159	5,685	226,844	18.4%	4,323
Beta	929	61	990	0.1%	12
Delta	574,952	402,722	977,674	79.3%	5,066
Eta	462	0	462	0.0%	12
Gamma	211	68	279	0.0%	0
Kappa	474	0	474	0.0%	2
Lambda	8	0	8	0.0%	0
Mu	51	0	51	0.0%	0
Theta	7	0	7	0.0%	0
VOC-21FEB-02	45	0	45	0.0%	1
VUI-21APR-03	15	0	15	0.0%	0
VUI-21FEB-01	79	0	79	0.0%	2
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	25,116	0	25,116	2.0%	110
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 and genotyped cases identified as Delta before 1 May 2021 were excluded.

Figure 5. Cumulative cases in England of variants indexed by days since the fifth reported case as of 8 November 2021



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

1.4 Variant prevalence

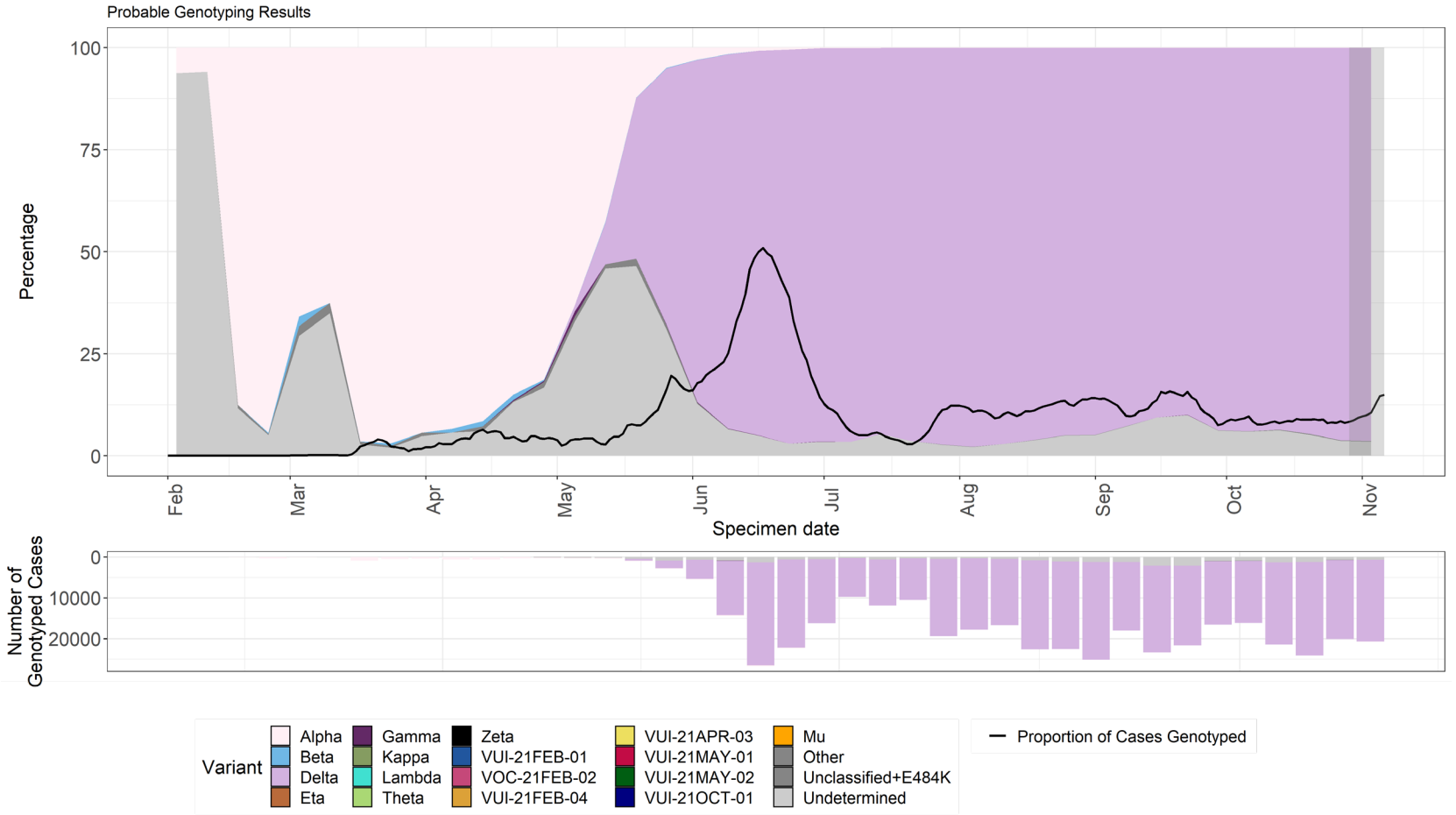
The prevalence of different variants amongst genotyped and sequenced cases is presented in Figure 6 and Figure 7 and split by region in Figure 8 and Figure 9 and by travel in Figure 10.

Genotyping provides probable variant results with a shorter turnaround time of 12 to 24 hours after initial confirmation of coronavirus (COVID-19) 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 7 to 10 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.

Figure 6. Variant prevalence for all England available genotyped cases from 1 February 2021 as of 8 November 2021 (excluding 472 case where the specimen date was unknown).

(Find accessible data used in this graph in underlying data.) Genotyped cases identified as Delta before 1 May 2021 were excluded.



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 8 November 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.

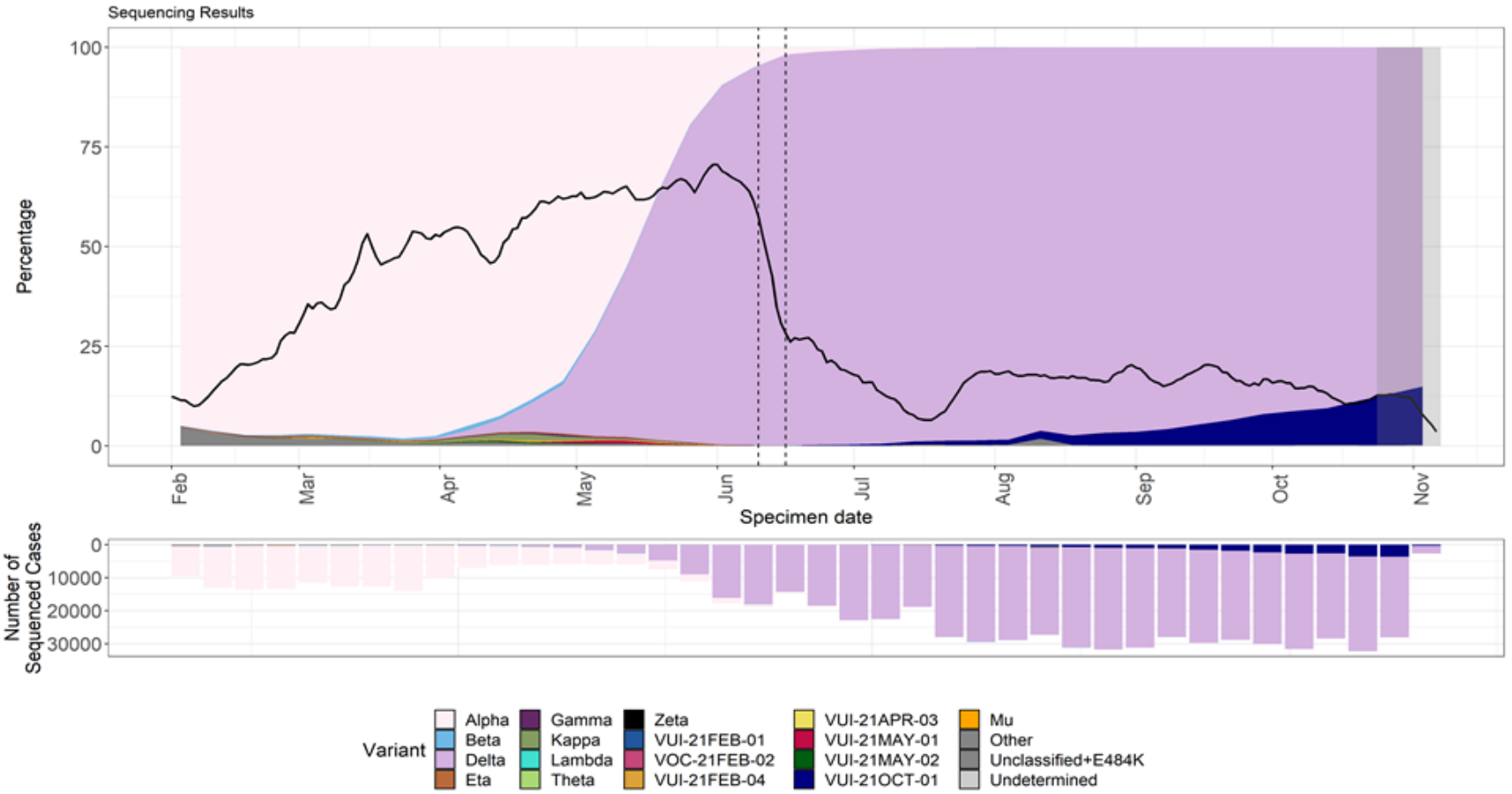


Figure 8. Variant prevalence from 1 February 2021 as of 8 November 2021 by region for all genotyped cases in England (excluding 3,541 cases where the region or specimen date were unknown).

(Find accessible data used in this graph in underlying data.) Genotyped cases identified as Delta before 1 May 2021 were excluded

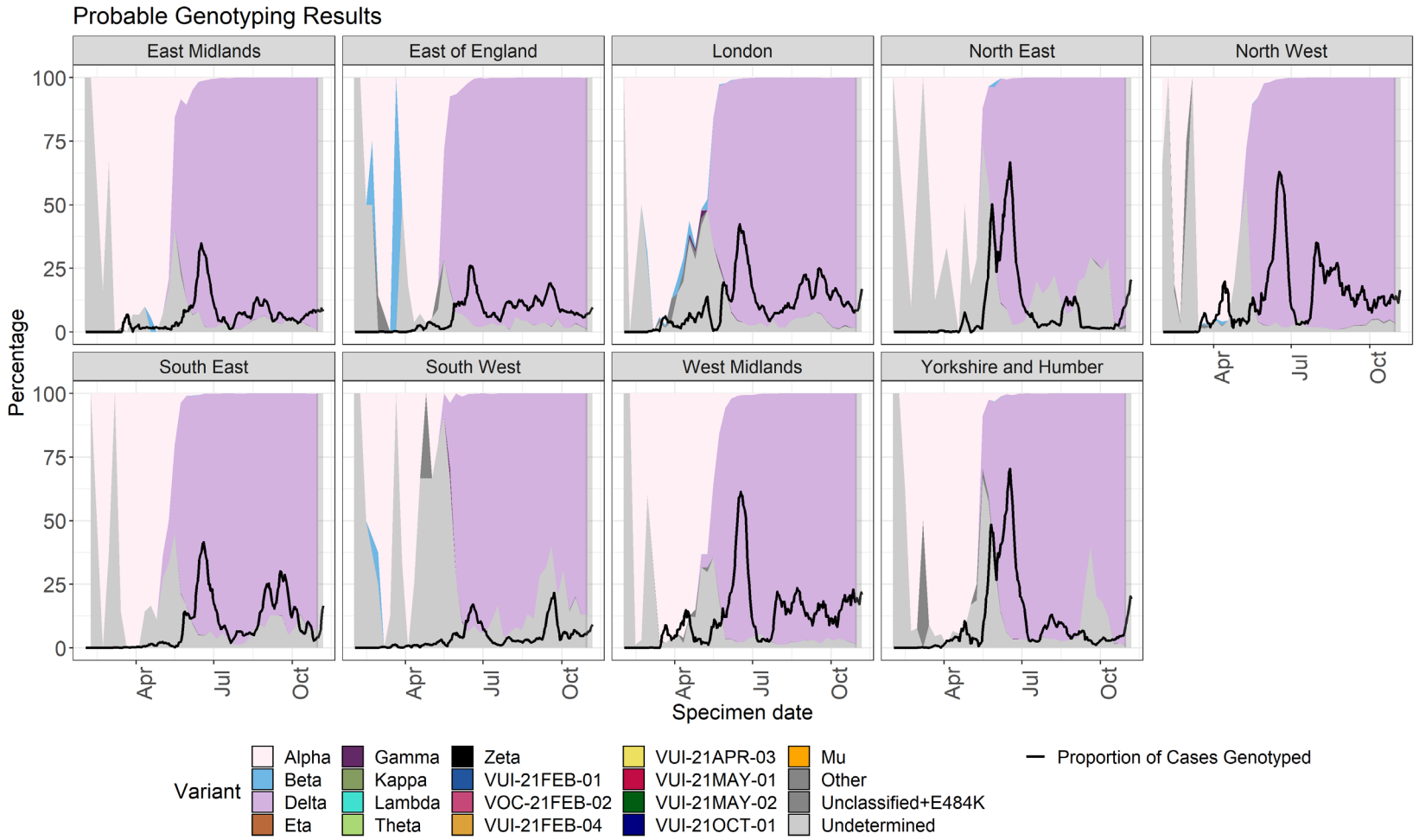


Figure 9. Variant prevalence from 1 February 2021 as of 8 November 2021 by region for all sequenced cases in England (excluding 4,342 cases where the region or specimen date were unknown).

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

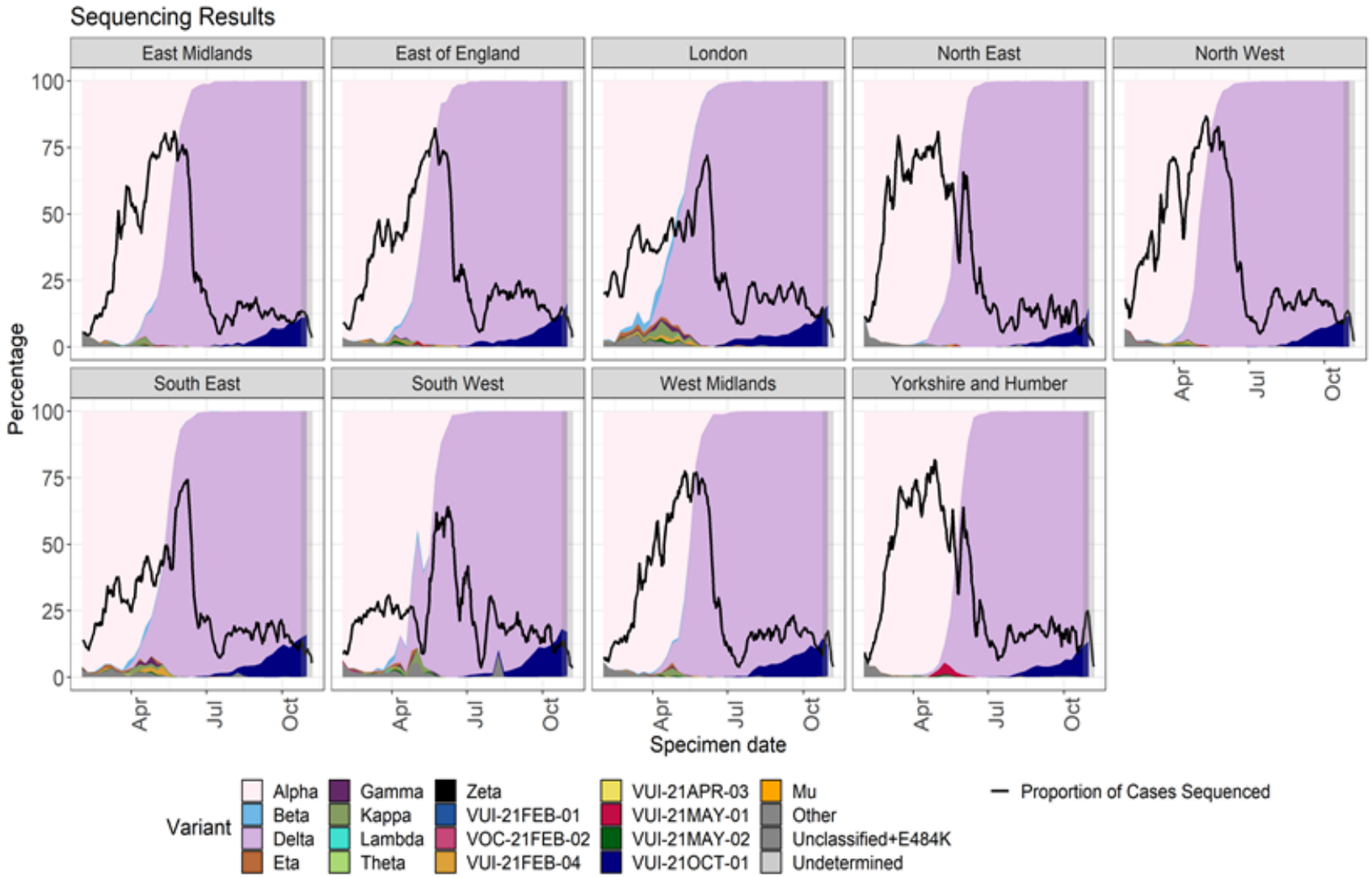
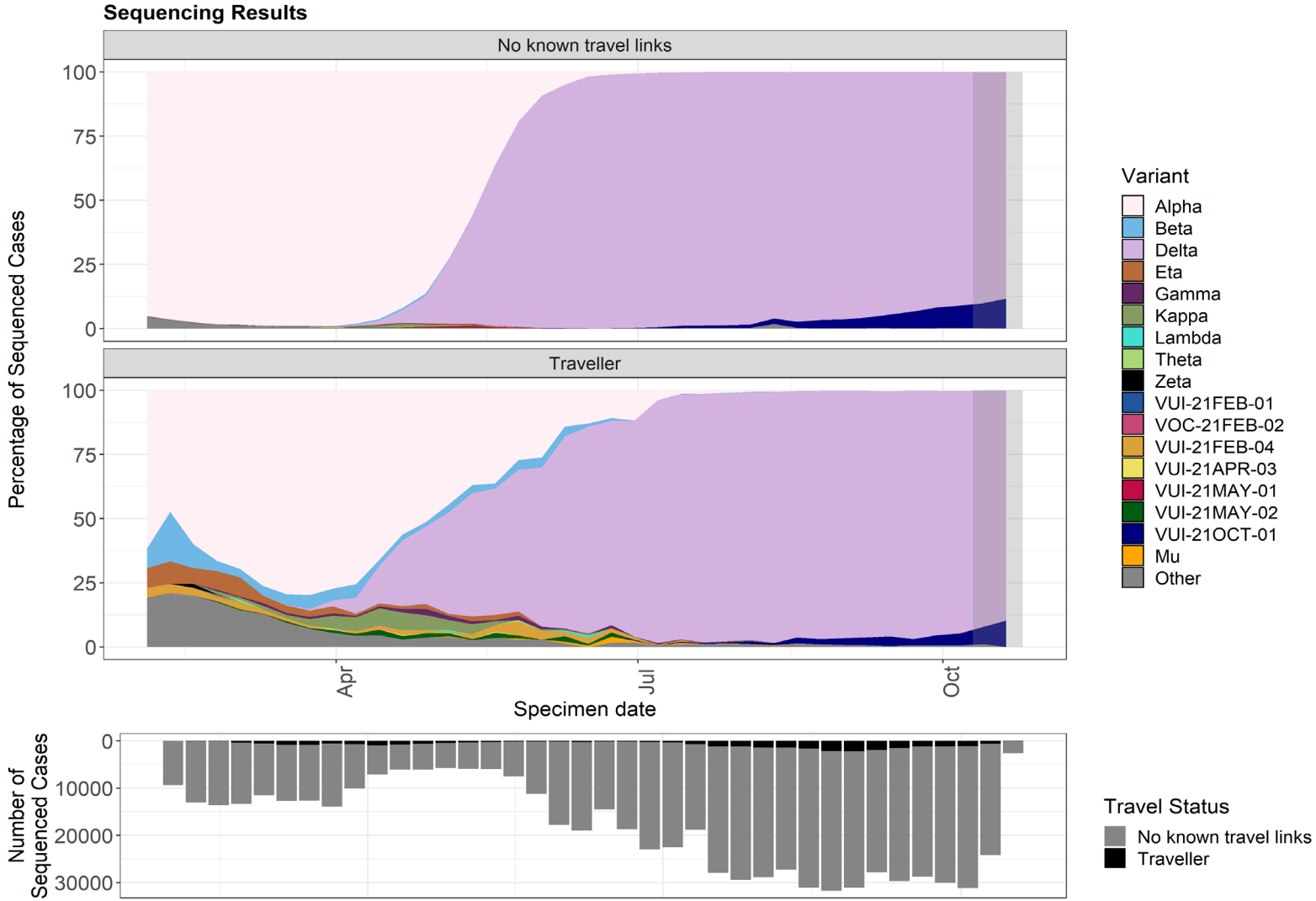


Figure 10. Prevalence of variants over time: all sequenced cases in England, split by travel status as of 8 November 2021

(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 and the mutation is seen in more than 100 sequences.

Figure 11. Prevalence of Pangolin lineages within Delta from 1 March 2021 to 6 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.)

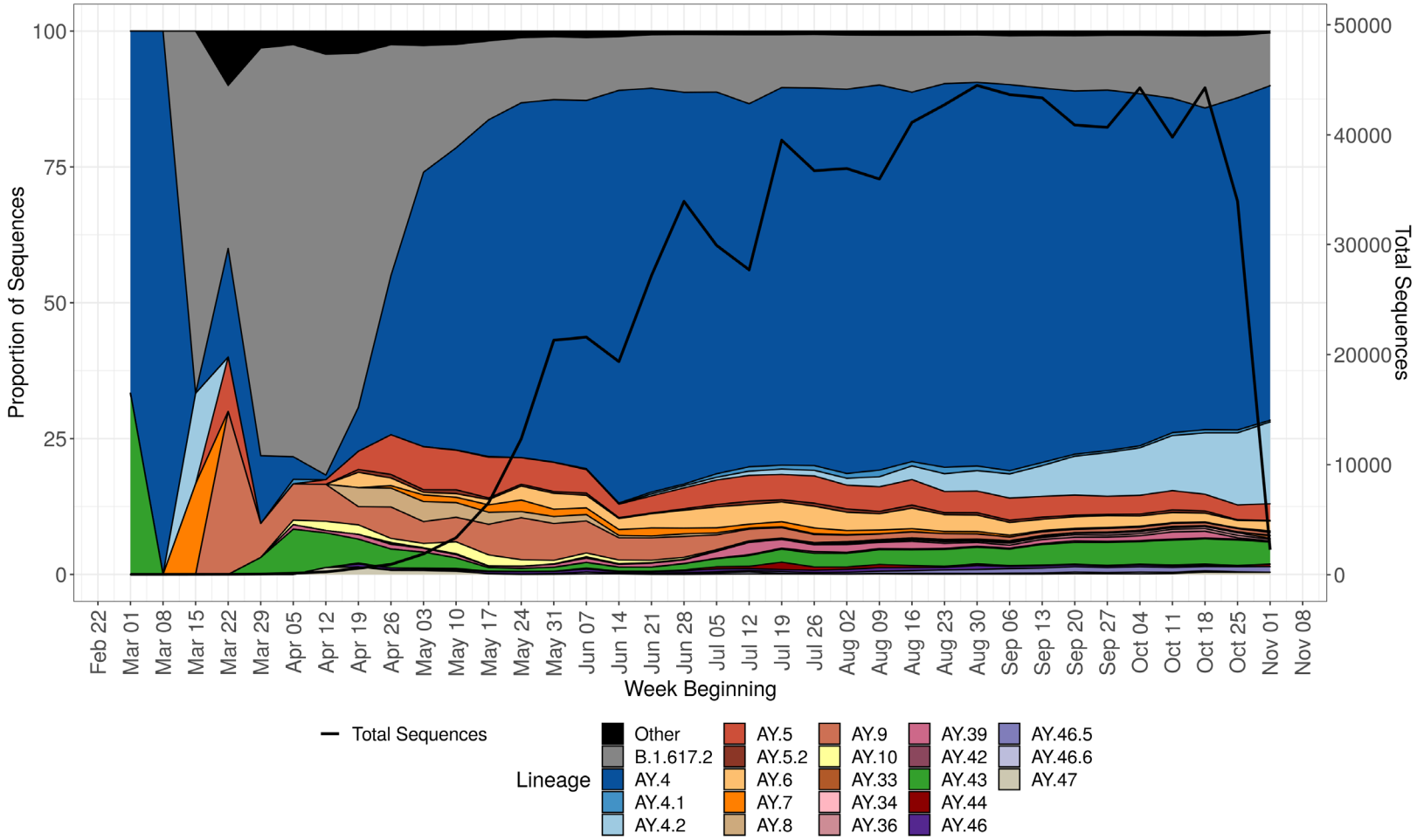


Figure 12. Proportion of Delta sequences (excluding VUI-21OCT-01 sequences) from England containing mutations in spike, restricted to those mutations which are observed in at least 1,000 sequences

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. 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.

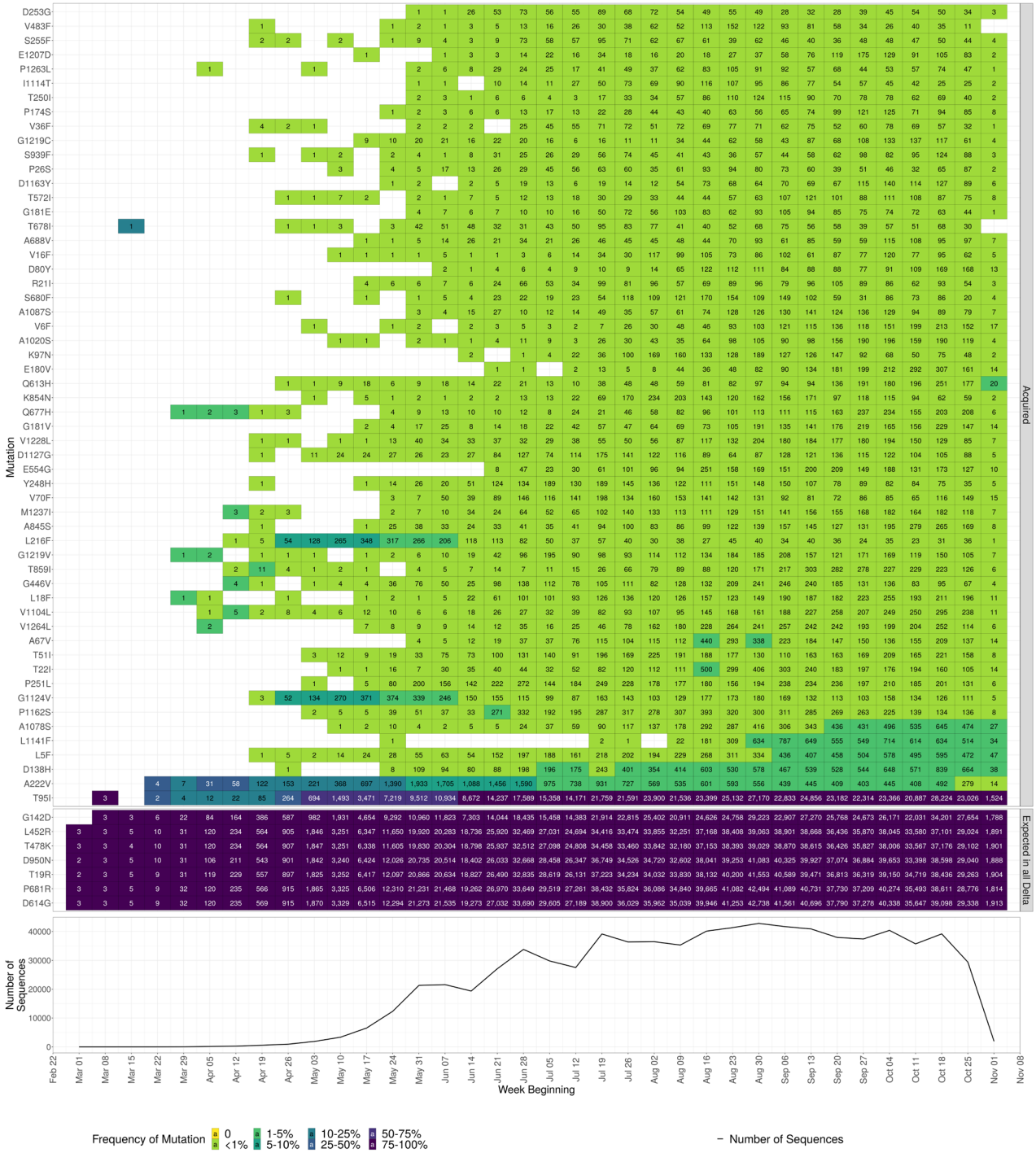


Figure 13. Proportion of VUI-21OCT-01 sequences from England containing mutations in spike, restricted to those mutations which are observed in at least 100 sequences

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. 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.)

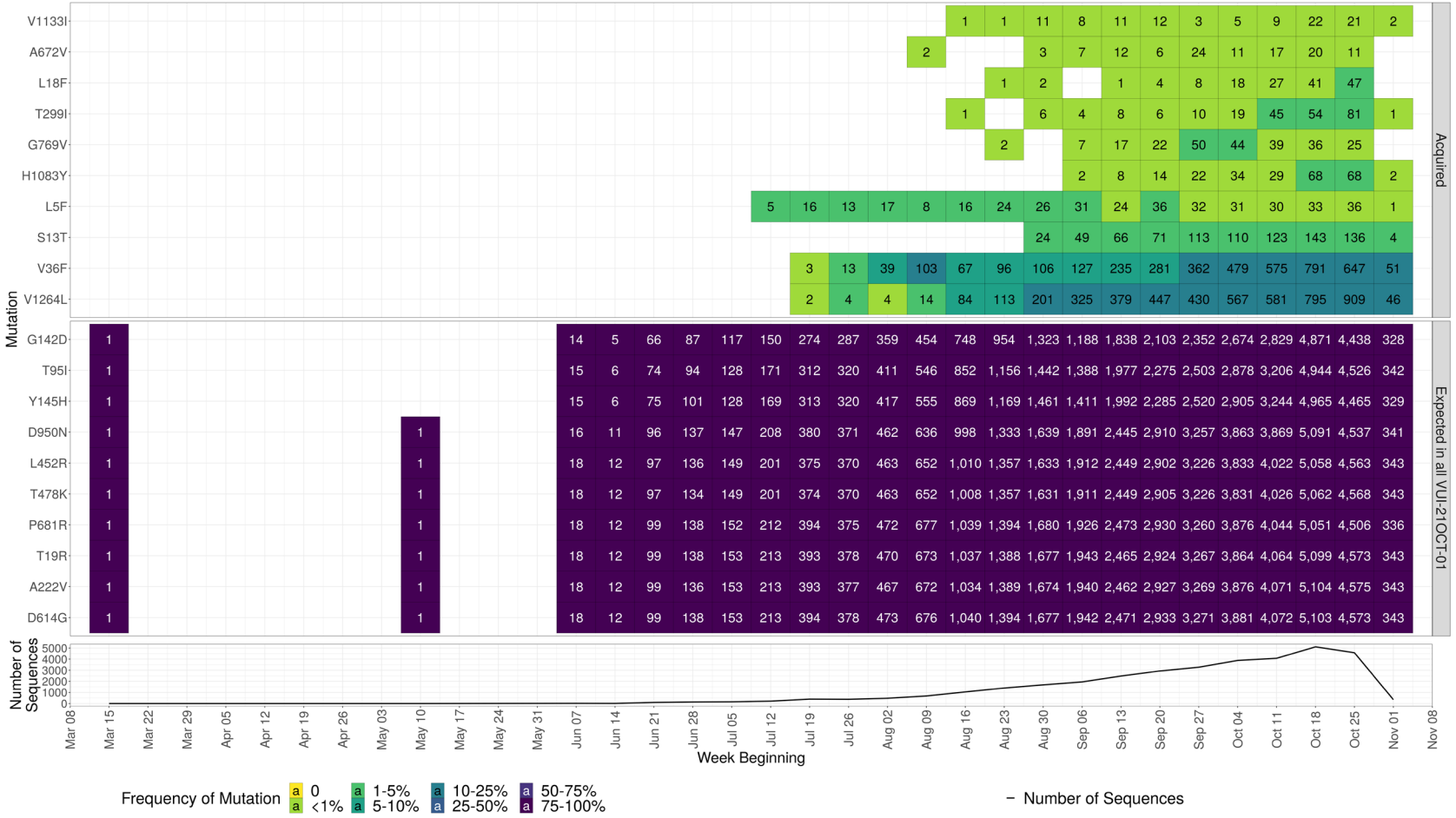


Table 4. Additional spike mutations of possible functional significance detected in Delta genomes in the UK as of 9 November 2021

Amino Acid Change	Delta sequences in UK data set	Delta sequences outside UK (GISAID)	Delta sequences 10 August to 9 September 2021		Delta sequences 10 September to 9 October 2021		Delta sequences 10 October to 9 November 2021	
			England	Outside UK	England	Outside UK	England	Outside UK
P251L	4,484	17,092	541	5,993	591	3,266	405	983
G446V	2,894	3,229	411	1,020	448	927	226	327
Q613H	2,013	23,670	308	11,858	555	5,762	614	1,309
V483F	1,029	773	128	285	82	247	34	53
Q493E	408	232	166	58	50	23	6	4
S494L	446	706	125	324	101	136	90	80
E484Q	494	2,876	85	774	108	631	166	441
K417N	280	5,523	61	1,195	22	381	66	72
L455F	232	613	59	193	49	204	21	36
V445I	107	53	26	26	6	13	0	0
F490L	157	372	51	161	9	89	45	50
K444N	119	348	28	126	21	88	8	19
S494P	130	452	9	176	14	120	27	36
N501Y	93	616	17	40	15	28	12	40

F490S	133	238	18	75	41	72	50	44
A475V	64	95	22	34	18	27	5	8
K458N	47	84	10	24	4	15	1	9
R246I	66	153	10	83	17	32	0	3
P681H	67	400	6	120	5	77	16	33
E484K	168	448	16	140	46	102	62	26
K444R	85	164	6	45	29	66	1	20
L452Q	49	175	13	80	13	43	11	10
E484A	50	440	8	74	21	206	5	111
P499L	31	78	6	25	5	26	3	7
V445F	35	71	9	31	16	16	5	6
N439K	19	6	12	2	1	3	0	0
S494A	22	23	9	11	10	1	0	0
N501T	20	71	0	21	3	29	0	10
E484G	18	82	2	33	1	24	3	10
E484V	14	82	4	25	2	26	0	12
Q493L	17	67	2	19	1	5	5	2
D80N	9	76	0	31	1	24	0	5
V483A	9	87	2	28	1	32	2	8
F486L	6	6	1	0	0	4	0	0
V445A	35	68	1	20	9	30	17	2

E484D	21	82	0	31	1	18	10	8
G446D	6	25	2	7	0	10	0	1
G485D	5	3	2	1	0	1	1	0
T478I	3	18	0	11	0	4	0	0
Y453F	3	30	1	5	2	14	0	8
Q498R	5	51	0	10	0	21	0	4
Q493H	3	22	0	8	0	8	0	0
D80A	4	222	1	27	1	13	0	3
K444E	3	6	0	1	0	2	0	0
I472V	4	11	0	4	0	4	0	1
R246G	23	35	0	12	5	9	9	3
Q493R	2	13	0	5	1	7	1	0
Q493K	2	3	1	0	1	0	0	0
N450K	1	19	0	3	1	13	0	0
K458Q	1	7	1	2	0	5	0	0
K417T	2	21	1	10	1	4	0	2
K417E	3	16	0	10	0	2	0	0
V483G	1	17	0	5	0	4	0	0
V503L	1	2	0	2	0	0	0	0
Y144N	1	3	0	1	0	0	0	0
N501H	1	9	0	5	0	3	0	0

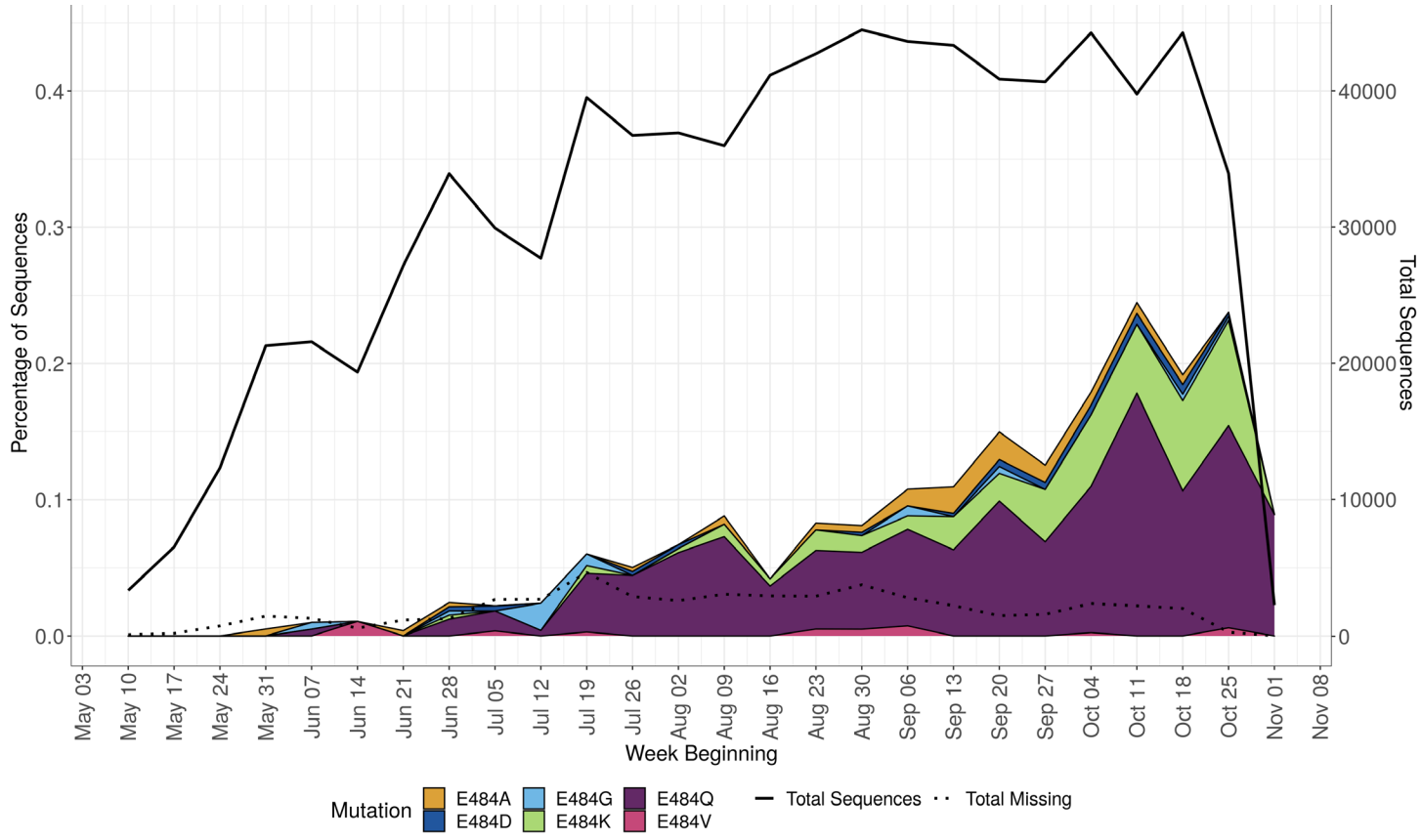
Total	825,404	1,569,615	135,449	560,519	127,287	337,978	105,224	95,615

*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 mutations at Spike:484

Changes at position 484 in spike are potentially antigenically significant. Figure 14 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 14: 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 8 November 2021, 477 sequences have been identified with 446 from England, 21 from Scotland, 8 from Wales and 2 from Northern Ireland. This is an increase of 114 sequences since the last report and a prevalence of 0.06% of Delta genomes in the UK to date (where the mutation can be called). The prevalence of Delta with E484Q in the most recent complete week of sequencing data (week beginning 18 October 2021) is 0.11% (where the mutation can be called). Internationally, as of 8 November 2021 the prevalence of Delta with E484Q mutations is 0.15% of Delta genomes on GISAID (including the UK).

Epidemiology in England

As of 8 November 2021, there are 478 Delta with E484Q sequences in the UK, 382 of which were linked to epidemiological data in England. This is an increase of 113 since the briefing of 25 October 2021. Cases have been detected across all 9 English regions, with most cases in the London (125, 32.7%) as shown by region in Table 5 and Figure 15 and age in Figure 16. Of the 382 cases 129 have history of travel.

Table 5. Number of confirmed (sequencing) Delta cases with E484Q mutation, by region of residence as of 8 November 2021

Region	Confirmed (sequencing) case number	Case proportion
East Midlands	19	5.0%
East of England	34	8.9%
London	125	32.7%
North East	41	10.7%
North West	26	6.8%
South East	47	12.3%
South West	13	3.4%
West Midlands	23	6.0%
Yorkshire and Humber	35	9.2%
Unknown region	19	5.0%
Total	382	-

382 of the 478 Delta + E484Q sequences linked to a case.

Figure 15. Confirmed (sequencing) and probable (genotyping) Delta with E484Q mutation cases by specimen date and region of residence as of 8 November 2021

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

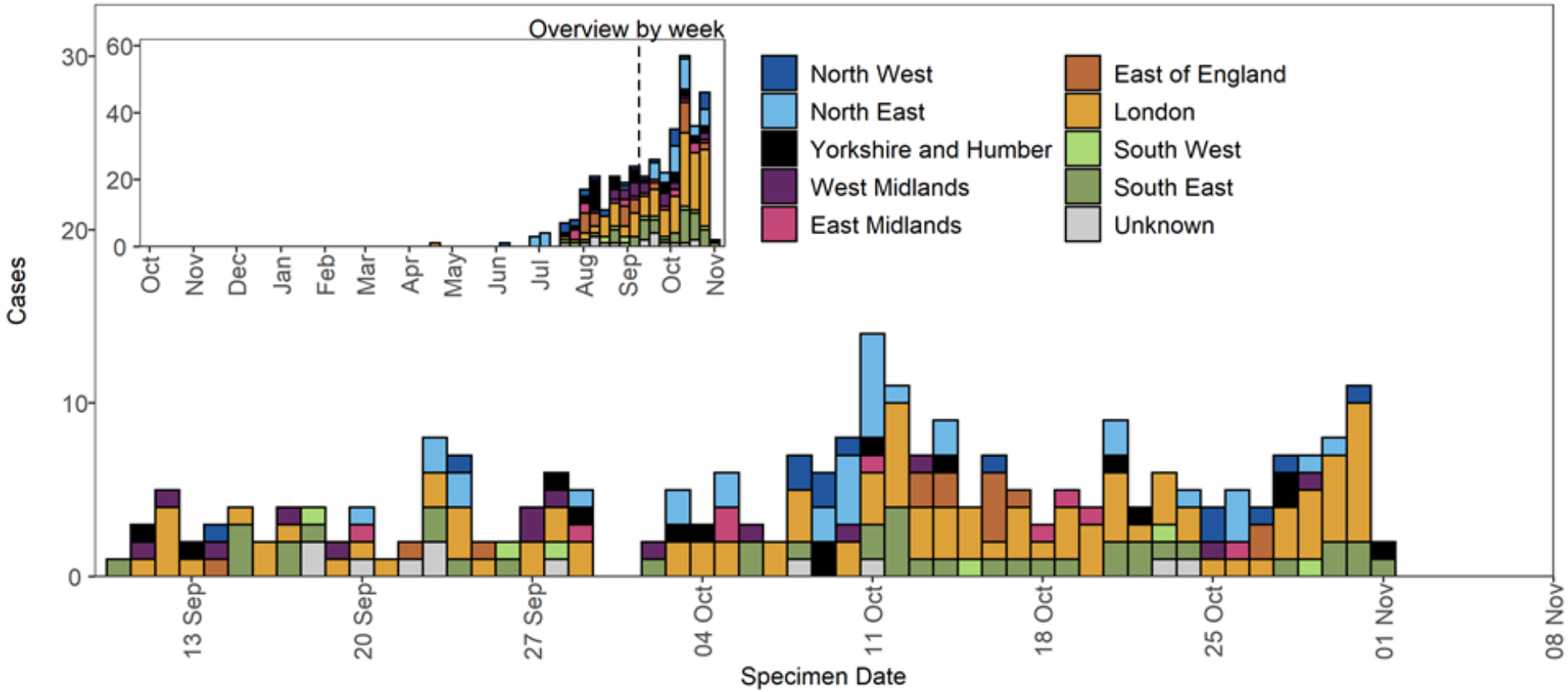
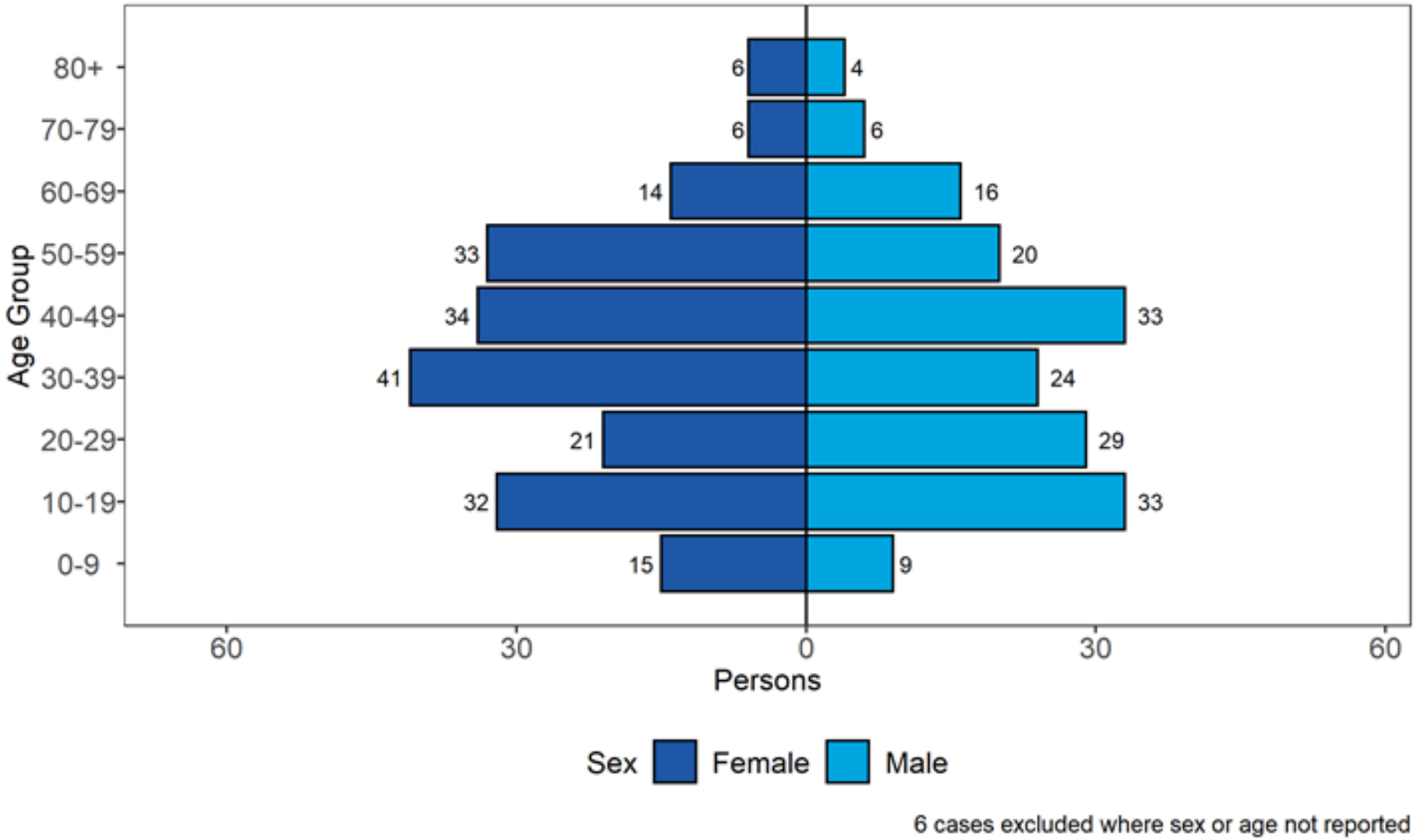


Figure 16. Age-sex pyramid of confirmed (sequencing) and probable (genotyping) Delta with E484Q mutation cases as of 8 November 2021

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

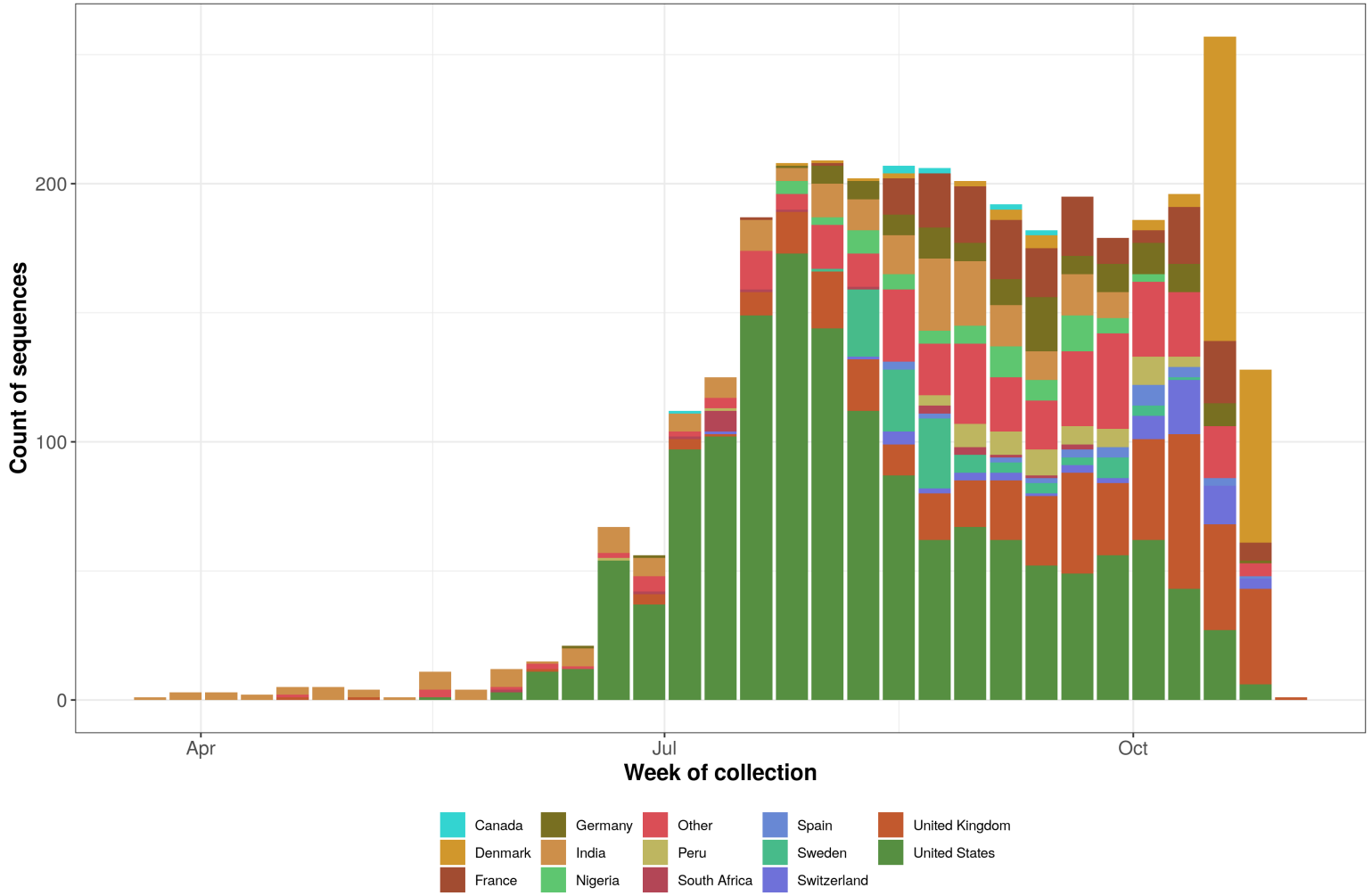


International epidemiology

As of 8 November 2021, 3,479 GISAID sequences have been assigned to the B.1.617.2 and AY sub-lineages with the additional E484Q mutation, of those 3,383 sequences had appropriate date information. Sequences have been uploaded from USA (1468), India (242), Denmark (210), France (192), Germany (126), Sweden (109), Nigeria (78), Switzerland (70), Peru (63), Spain (32), South Africa (24), and 51 other countries with 20 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 8 November 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.

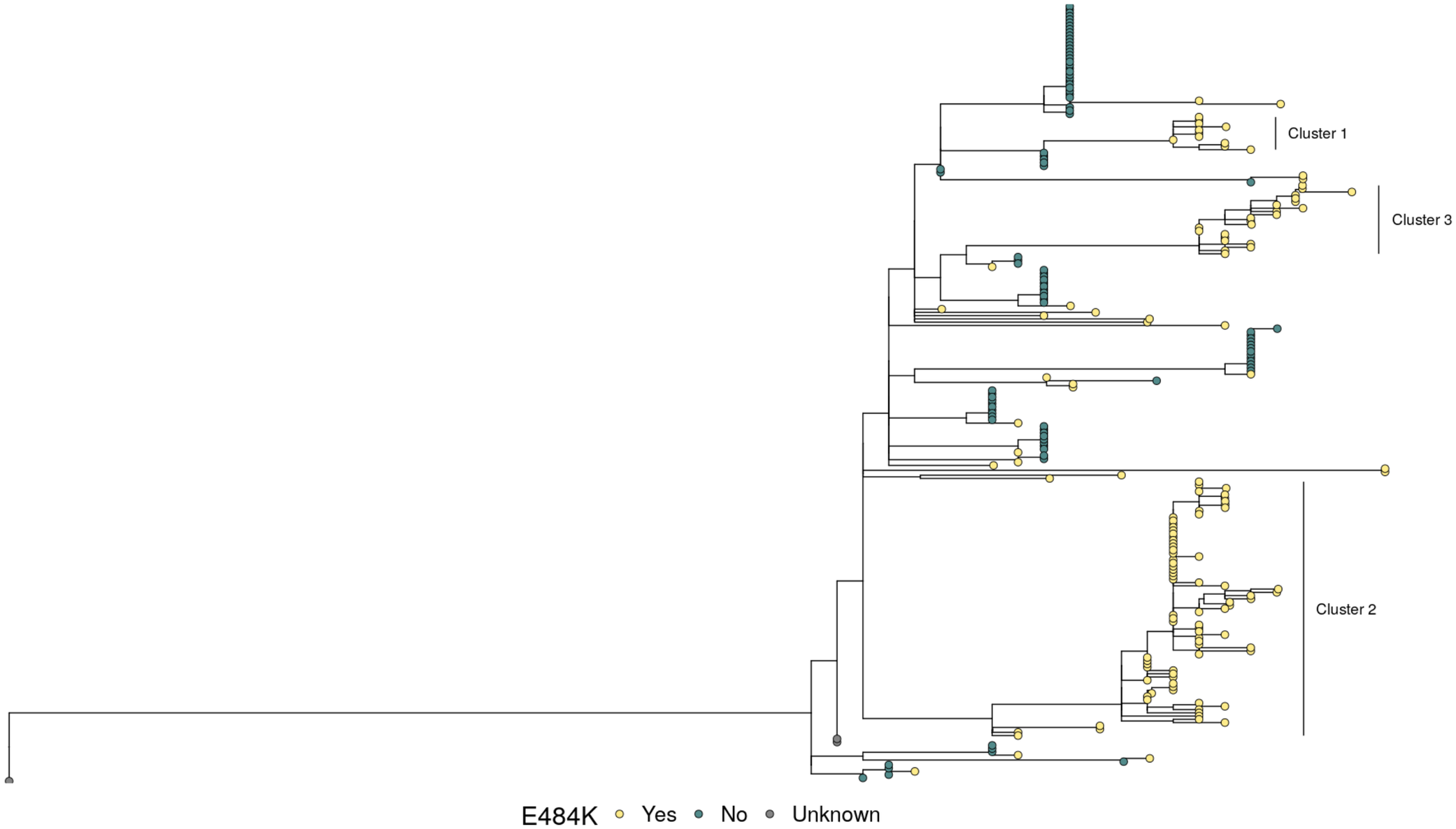


Delta with E484K was first detected on 8 July 2021 in a UK sequence with a collection date of 28 June 2021. As of 8 November 2021, 152 sequences have been identified with 141 from England, 8 from Scotland and 3 from Wales, an increase of 59 since the briefing of 15 October 2021. The prevalence of this mutation is 0.02% of all Delta genomes in the UK and 0.07% of Delta sequences (where the mutation could be called) for the week beginning 18 October 2021, which is the last complete week of sequencing data. Internationally, as of 08 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 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 8 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 38 sequences and cluster 3 by 16 sequences since the last report. Seven 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 8 November 2021, there are 152 Delta with E484K sequences, a subset of which have been identified as belonging to 3 separate clusters. Cluster 1 contains 12 sequences, cluster 2 contains 87 sequences and cluster 3 contains 21 sequences in the UK. Of the 87 Delta with E484K sequences in in cluster 2 the UK, 70 could be linked to epidemiological data in England. Cases have been detected across 7 English regions, with most cases in the North West (57, 81.4%) as shown by region in Table 6, Figure 19 and by age in Figure 20. Of the 70 cases, 9 have history of travel.

Table 6. Number of confirmed (sequencing) cluster 2 Delta cases with E484K mutation, by region of residence as of 8 November 2021

Region	Confirmed (sequencing) case number	Case proportion
East Midlands	0	0.0%
East of England	3	4.3%
London	2	2.9%
North East	2	2.9%
North West	57	81.4%
South East	0	0.0%
South West	4	5.7%
West Midlands	0	0.0%
Yorkshire and Humber	1	1.4%
Unknown region	1	1.4%
Total	70	-

70 of the 87 cluster 2 Delta + E484K sequences linked to a case.

Figure 19. Confirmed (sequencing) cluster 2 Delta with E484K mutation cases by specimen date and region of residence as of 8 November 2021

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

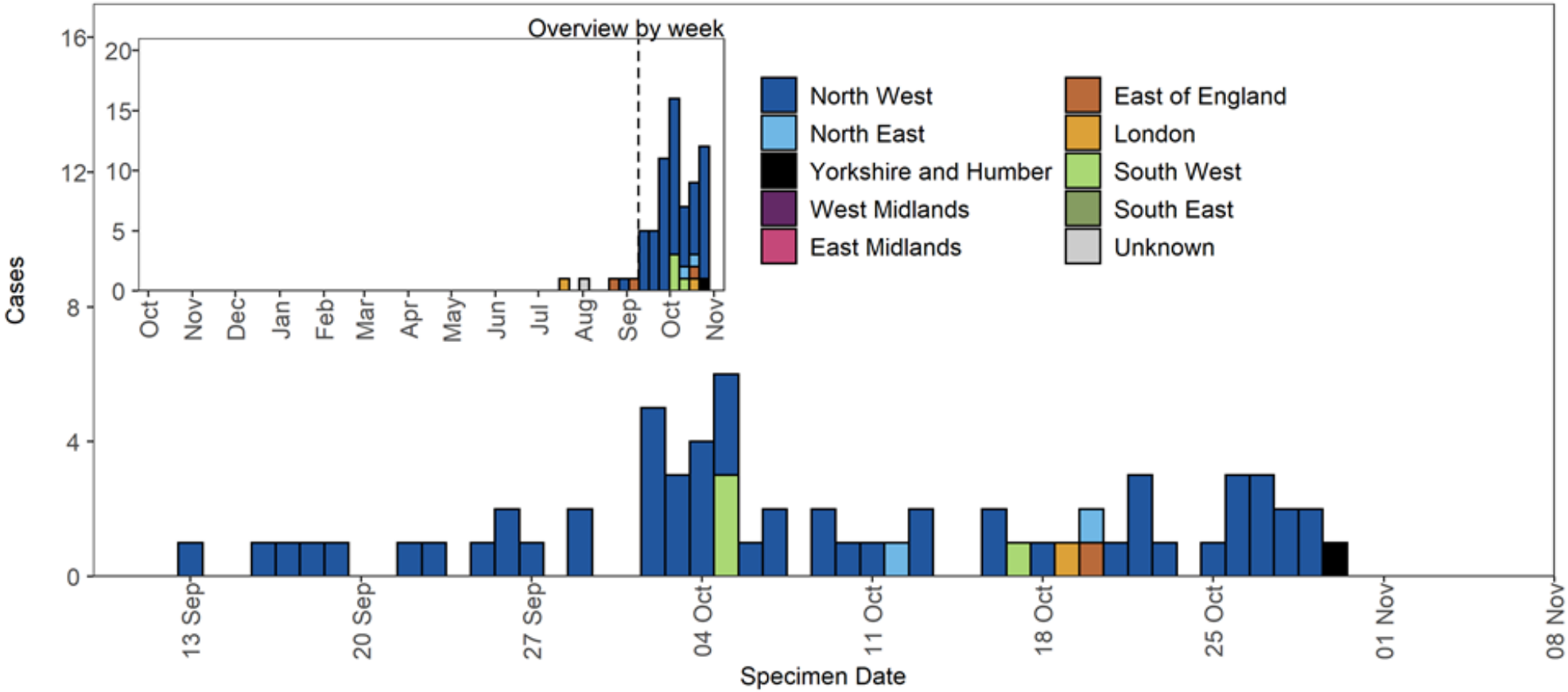
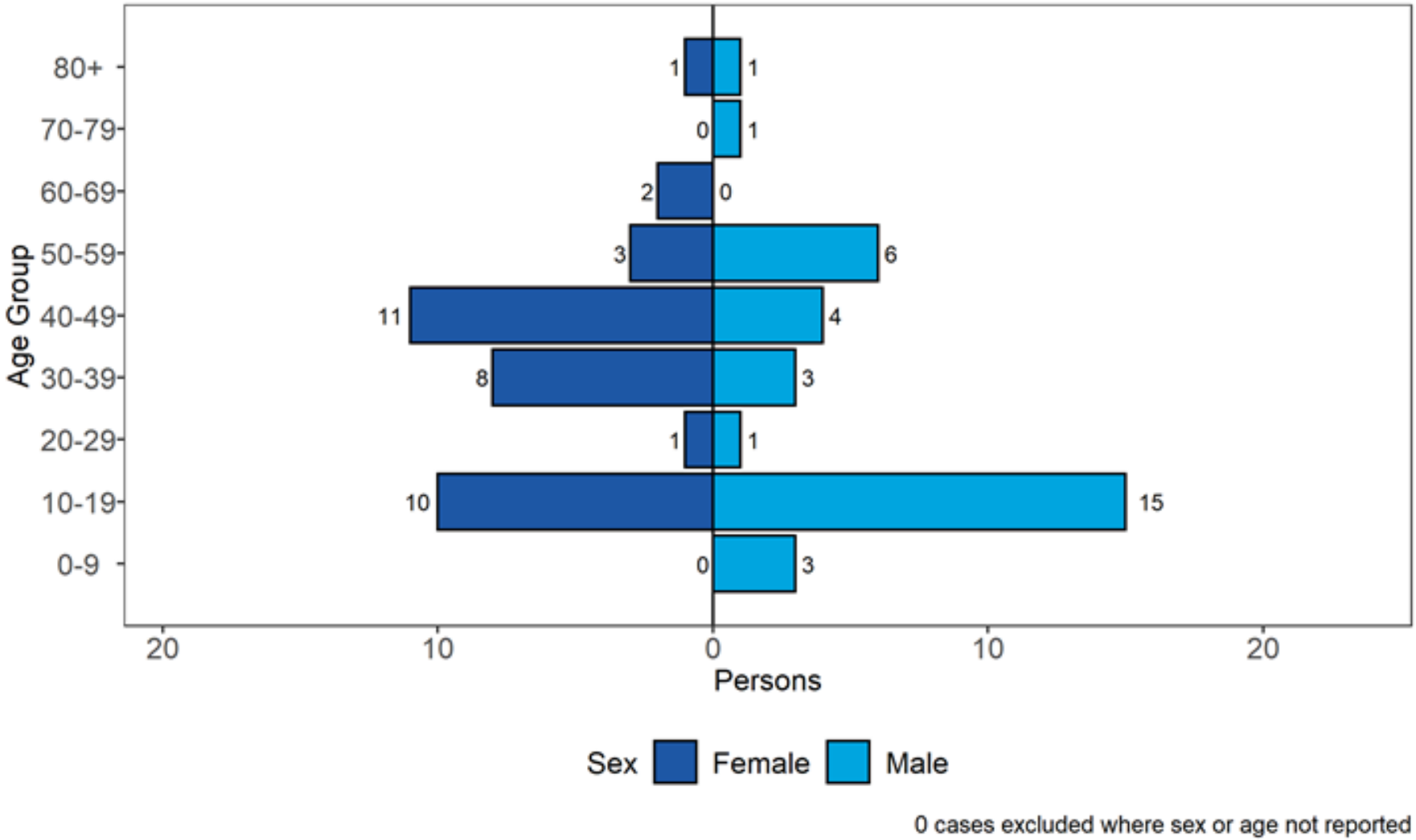


Figure 20. Age-sex pyramid of confirmed (sequencing) cluster 2 Delta with E484K mutation cases as of 8 November 2021

(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 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.

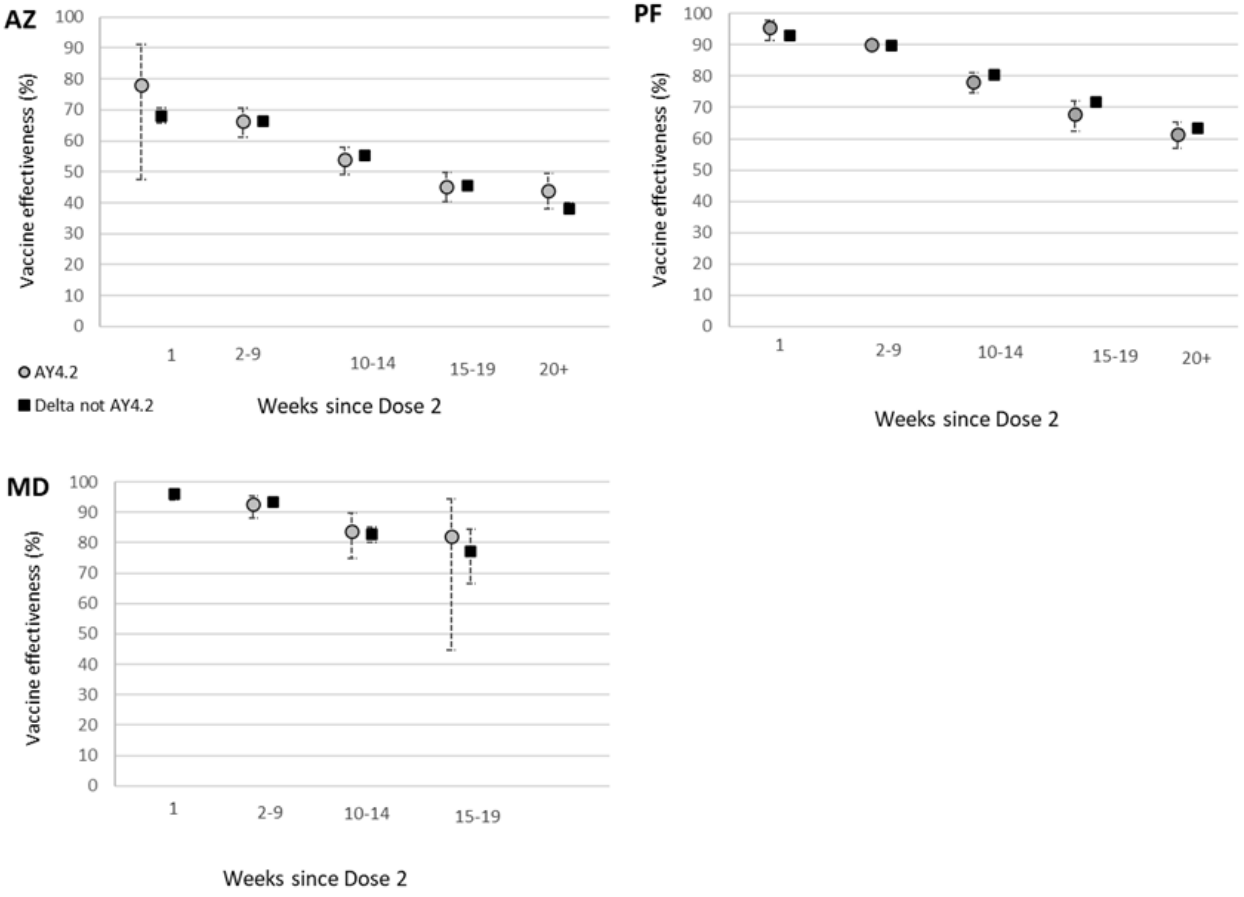
3.1 Vaccine effectiveness

Vaccine effectiveness against symptomatic disease and hospitalisation with AY.4.2 compared to those sequenced as Delta but not AY.4.2 was estimated using a test negative case control design. Adjustments were made for health and social care worker status, care home residents, region, whether cases were in a risk group or clinically extremely vulnerable group, index of multiple deprivation, ethnicity, age group, gender and week of onset. This analysis was based on community testing among individuals reporting symptoms and further linkage to the Emergency Care Dataset for hospital admissions via emergency care. The period covered by the analysis is from 21 June 2021 to 29 October 2021. To allow for lags in hospital admissions to estimate vaccine effectiveness against hospitalisation data were restricted to 15 October 2021.

Vaccine effectiveness by period after the second dose of vaccine are shown in Figure 21. For all the AstraZeneca, Pfizer and Moderna vaccines, vaccine effectiveness against AY.4.2 symptomatic disease is very similar to that seen for Delta not AY.4.2. There may be a marginal reduction in effectiveness with Pfizer vaccine at longer intervals after 2 doses, however this effect if present is extremely small.

Figure 21: Vaccine effectiveness against symptomatic disease by period after vaccination for AY.4.2 and Delta not AY.4.2: AstraZeneca (AZ), Pfizer-BioNTech (PF) and Moderna (MD)

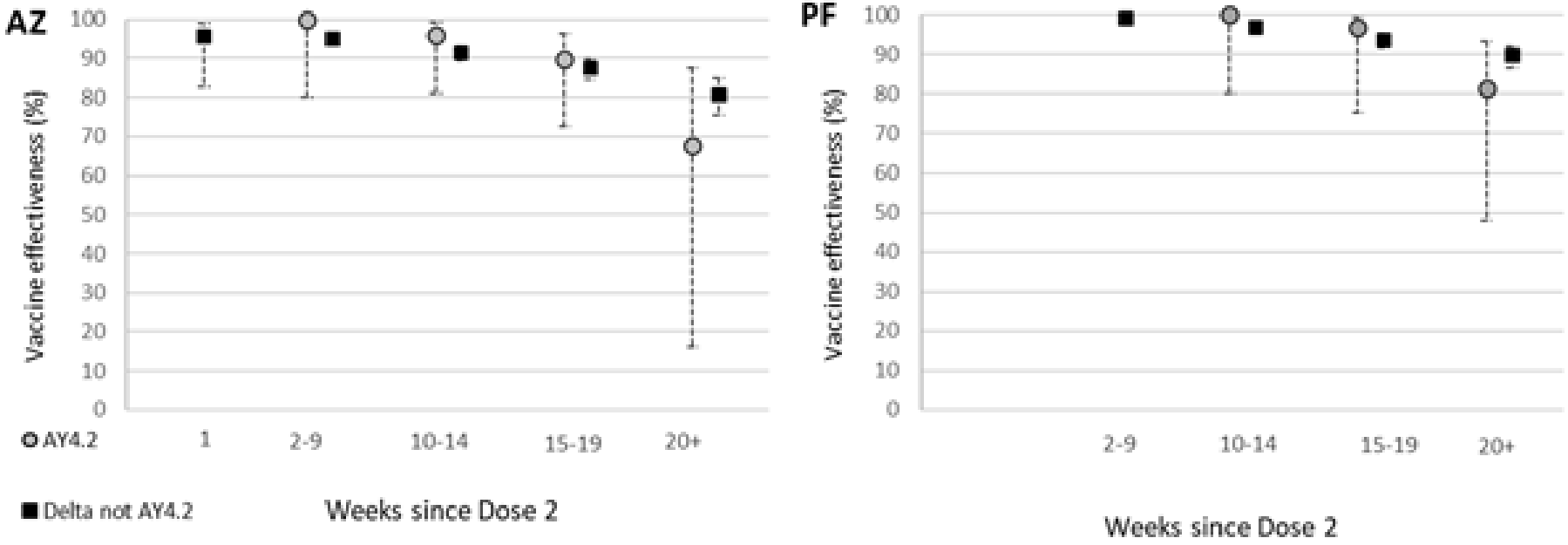
Supplementary data is not available for this figure.



The number of hospitalisations with AY.4.2 is currently relatively small; therefore, confidence intervals are wide for this analysis, nevertheless, again vaccine effectiveness for AY.4.2 looks similar to that seen against Delta not AY.4.2 (Figure 22).

Figure 22: Vaccine effectiveness against hospital admission by period after vaccination for AY.4.2 and Delta not AY.4.2: AstraZeneca (AZ), Pfizer-BioNTech (PF)

Supplementary data is not available for this figure.

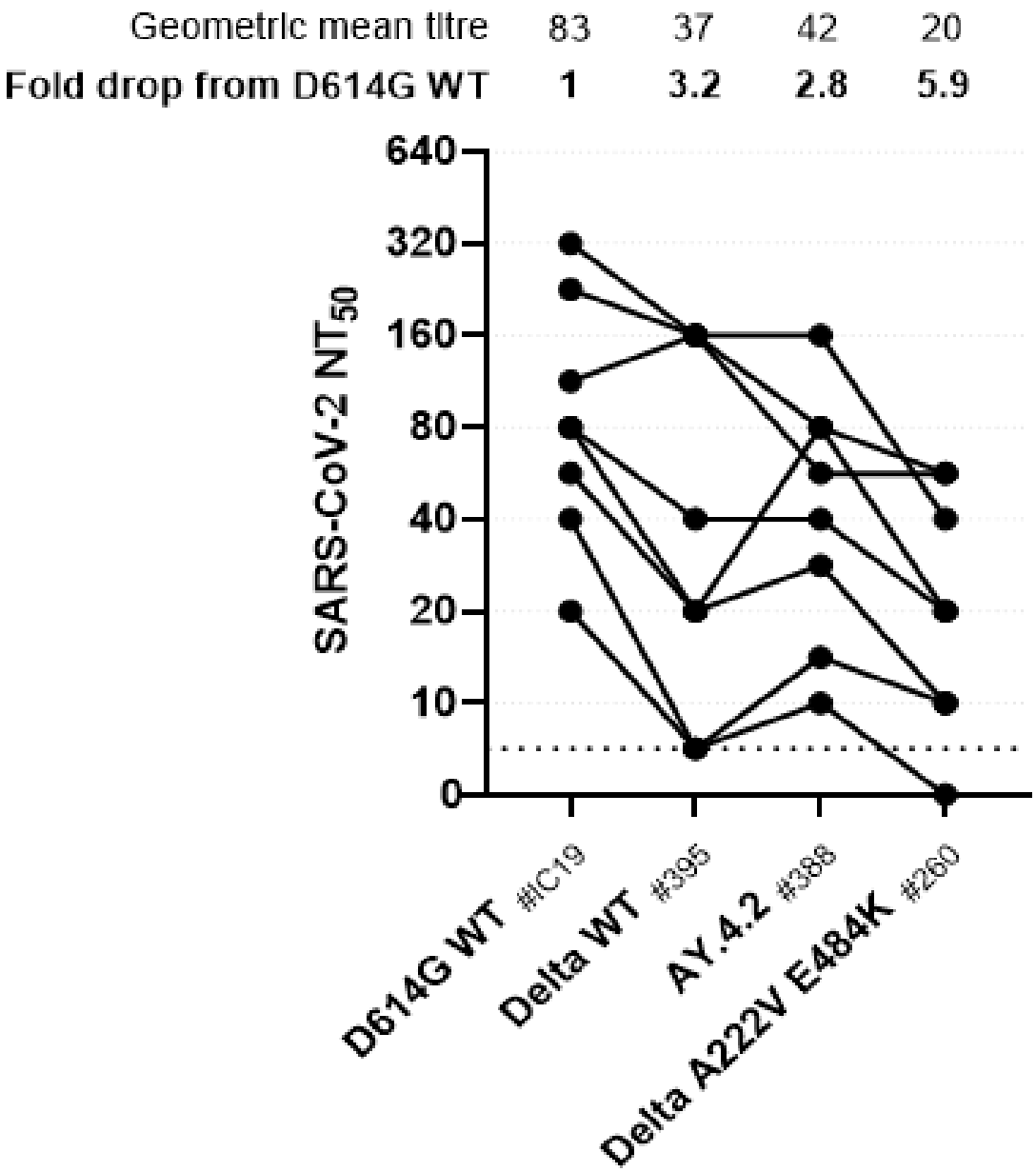


Live virus neutralisation

Preliminary neutralisation (live virus and pseudo virus) assays from the Genotype to Phenotype Consortium UK suggests AY.4.2 is equally, or even more easily neutralised by both post-vaccination antisera. Overall, this data is consistent with the preserved vaccine effectiveness seen in the epidemiological study.

Figure 23: AY.4.2 live virus neutralisation with sera from double vaccinated individuals

Supplementary data is not available for this figure.



3.3 Epidemiology of VUI-21OCT-21 in England

As of 8 November 2021, there are 29,396 VOC-21OCT-01 genomes in the UK data set, of which 26,184 linked to cases in England. VUI-21OCT-01 accounts for 11.2%, 13.0%, 14.7% of Delta cases in England in the weeks beginning 17 October, 24 October, and 31 October 2021 respectively.

Variant prevalence for all cases in England as of 21 October 2021 is shown by region in 4.

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 24). Of the 25,116 cases in England, 971 had a recent travel history. At least 97 countries of travel have been reported.

Age data is shown in Figure 25. The risk assessment for AY.4.2 can be found here.

Table 11. Number of confirmed and provisional 21OCT-01 (AY.4.2) cases, by region of residence as of 8 November 2021

Region	Total case number	Case proportion
East Midlands	1,659	6.6%
East of England	2,768	11.0%
London	3,205	12.8%
North East	520	2.1%
North West	2,621	10.4%
South East	4,865	19.4%
South West	3,344	13.3%
West Midlands	3,496	13.9%
Yorkshire and Humber	2,551	10.2%
Unknown region	87	0.3%
Total	25,116	-

Figure 24. Confirmed and provisional VUI-21OCT-01 cases by specimen date and region of residence as of 8 November 2021

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

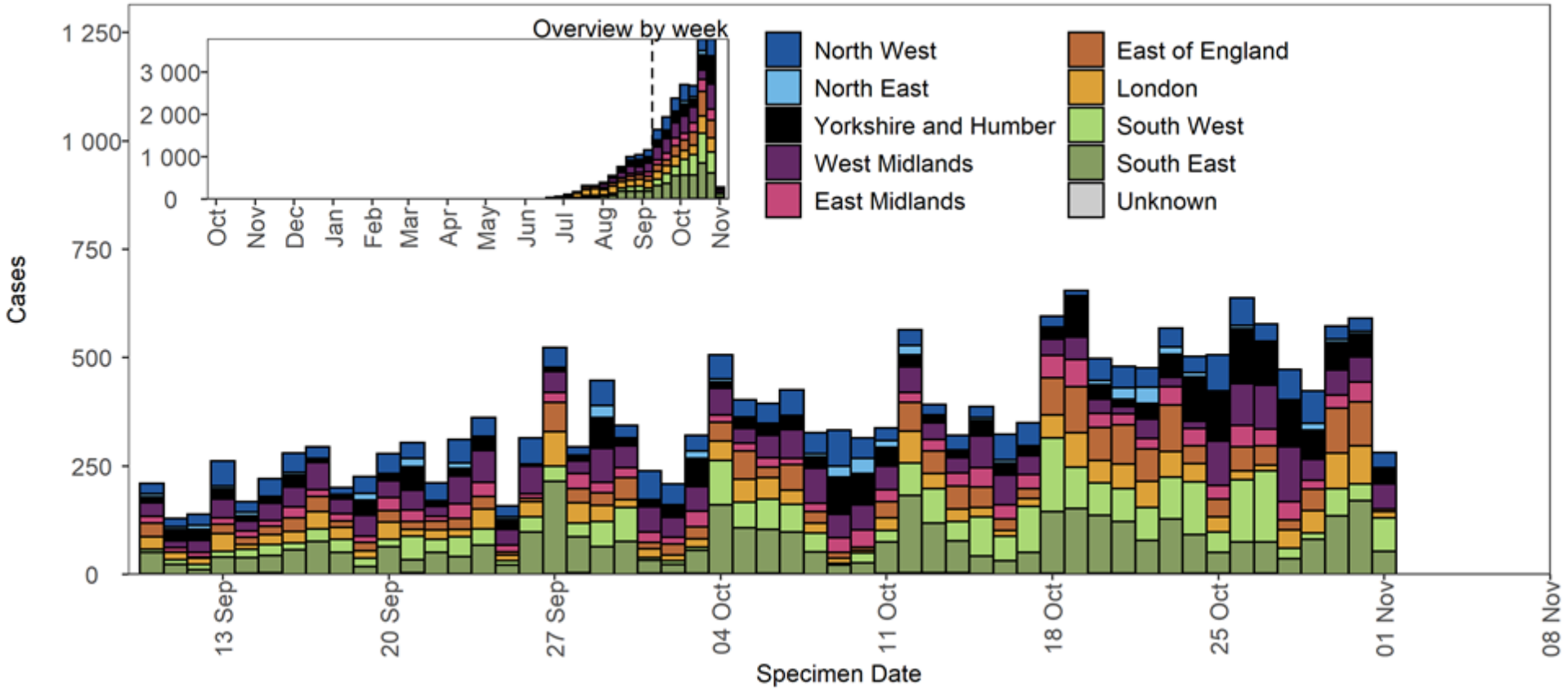
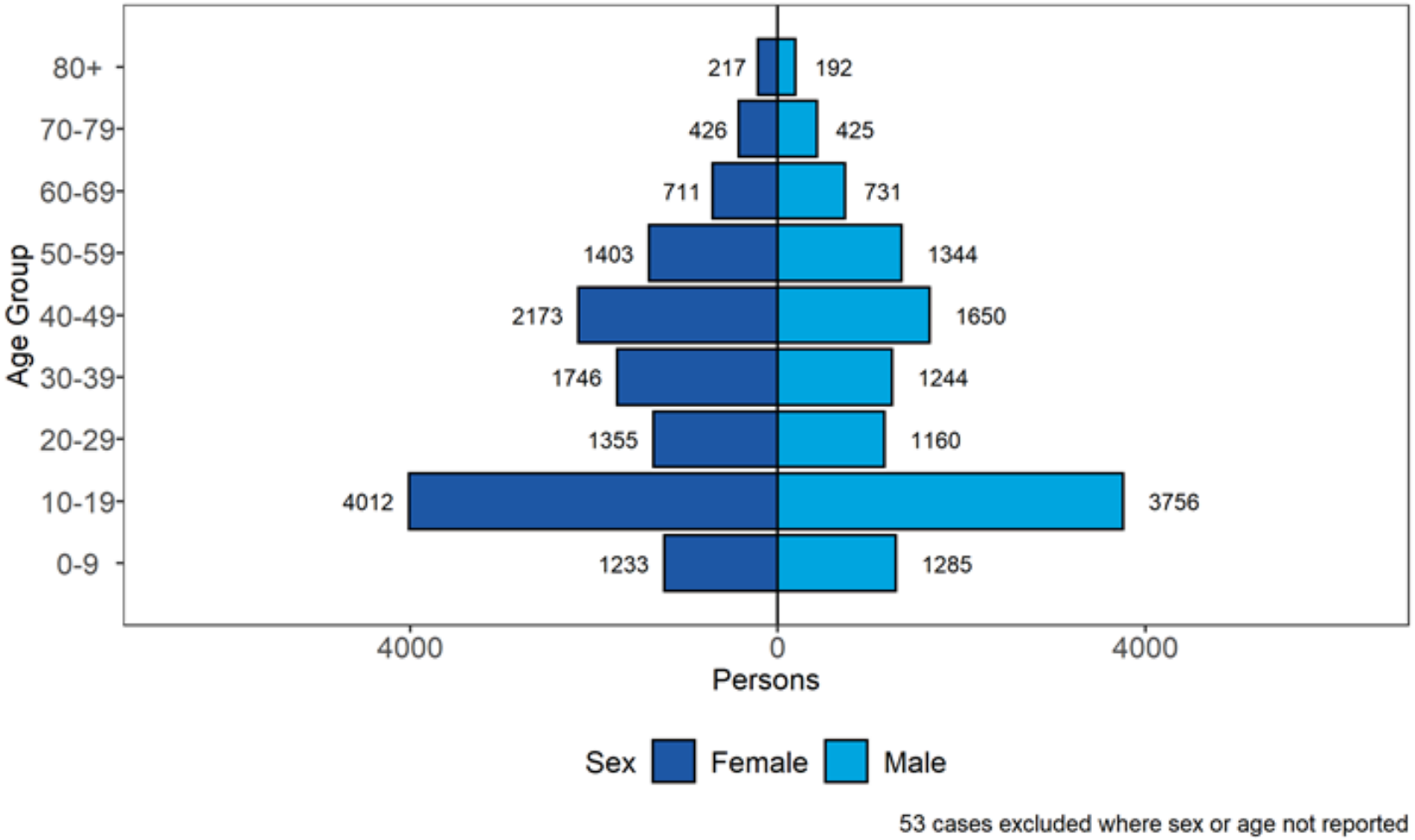


Figure 25. Age-sex pyramid of VUI-21OCT-01 cases as of 8 November 2021

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



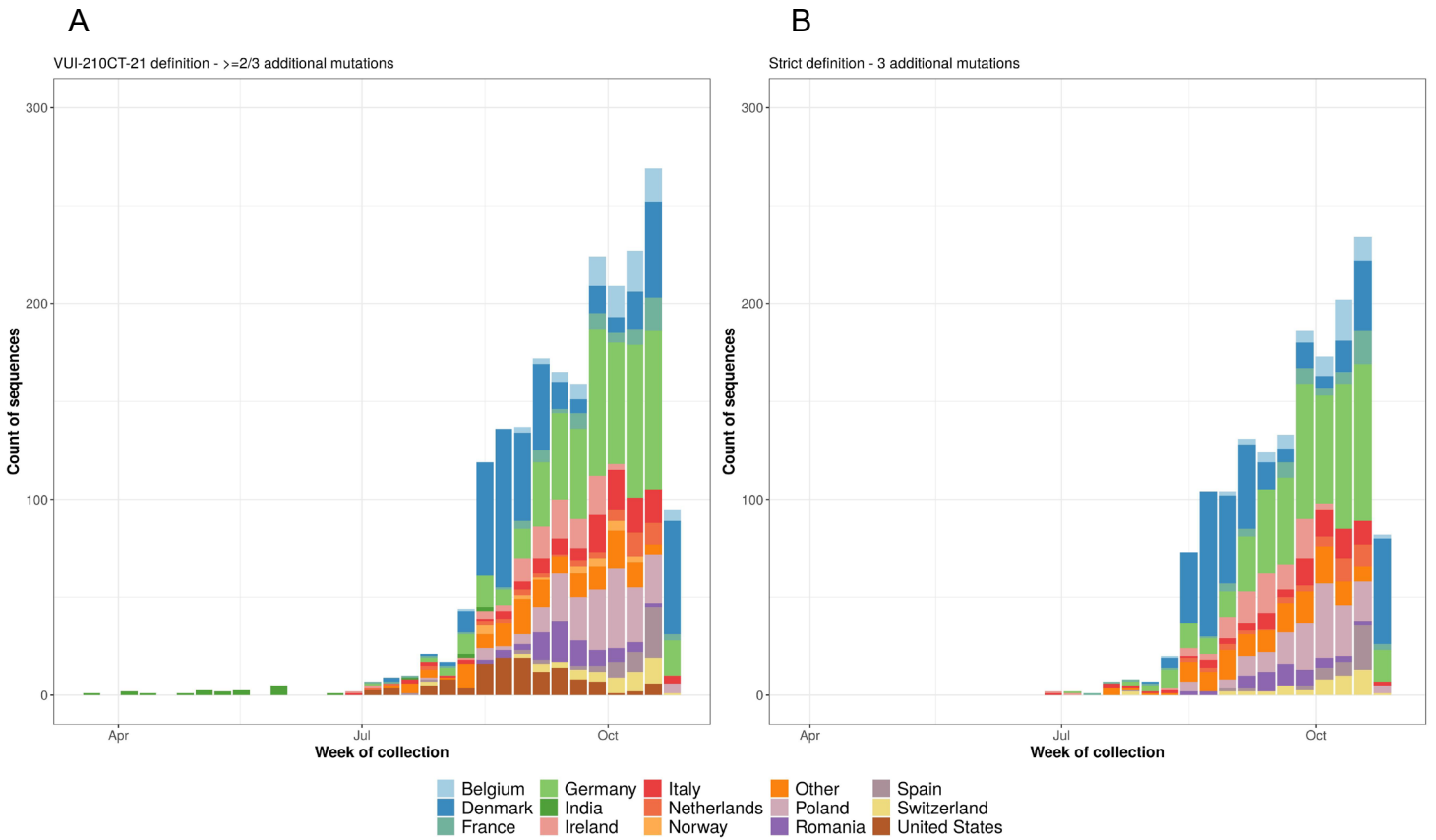
International epidemiology

As of 8 November 2021, 2,072 sequences on GISAID meet the VUI-21OCT-01 definition from 41 countries excluding the UK (Figure 10), with 2,041 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 (493), Denmark (413), Poland (203), United States (128), Italy (117), Ireland (96), Belgium (95), Romania (79), France (68), Spain (55), Switzerland (53), Netherlands (49), India (24), Norway (24), Bulgaria (16), Slovakia (14), Canada (13), Czechia (11), Portugal (10), Lithuania (10) and 21 other countries with fewer than 10 sequences.

Sequences shown before late June 2021 in 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 1,593 sequences present on GISAID as of 8 November 2021, from 35 countries. See Figure 26.

Figure 26. Count of VUI-21OCT-01 classified sequences by week of collection uploaded to GISAID by week as of 8 November 2021. A) (Find accessible data used in this graph in underlying data).



The first sequence was uploaded by India with a collection date of 28 March 2021. B) Count of VUI-21OCT-01 with all 3 mutations in the definition present, classified sequences by week of collection uploaded to GISAID by week as of 08 November 2021. The first sequence date was uploaded by the UK with a collection date of 15 June 2021, outside of the UK the first sequence was uploaded by Ireland with a collection date of 29 June 2021. Countries with 20 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.

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 is 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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Contributions from the Variant Technical Group Members including Imperial College London

Variant Technical Group members and contributors

The UK Health Security Agency Variant Technical Group includes members and contributors from the following organisations: UKHSA, Public Health Wales, Public Health Scotland, Public Health Agency Northern Ireland, the Department of Health and Social Care, Imperial

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