UK Health Security Agency

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

Technical briefing 24

1 October 2021

This briefing provides an update on previous briefings up to 17 September 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:

- there are 4 current variants of concern (VOCs) and 10 variants under investigation (VUIs) (Table 1)
- there are no new VOCs or VUIs since the last briefing in the UK classification
- Delta remains the predominant variant accounting for approximately 99.7% of sequenced cases as of 27 September 2021
- variants Zeta (VUI-21JAN-01, P.2), VUI-21APR-03 (B.1.617.3), Eta (VUI-21FEB-03, B.1.525), Theta (VUI-21MAR-02, P.3), VUI-21MAY-01 (AV.1), and VUI-21MAY-02 (C.36.3) have not been detected in the UK for 12 weeks and have moved to international monitoring. The variants VUI-21FEB-01 (A.23.1 with E484K), VOC-21FEB-02 (B.1.1.7 with E484K) and VUI-21MAR-01 (B.1.324.1 with E484K) have not been detected either in the UK or in GISAID for 12 weeks and are listed as provisionally extinct
- data on spike mutations occurring on Delta, and epidemiological and phylogenetic summaries of Delta cases with mutations E484K and E484Q are provided – absolute numbers of cases with E484K and E484Q are very small, but new cases continue to occur regularly and there is some evidence of clustering suggesting that such variants can transmit

All risk assessments are published separately, 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) 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 (or B.1.621), Delta, and Gamma. 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 shows the current VOC, VUI, and variants in monitoring as of 27 September 2021.

Table 1. Variant lineage and designation as of 27 September 2021

WHO nomenclature	Lineage	Designation	Status	UK or international (not currently detected in UK)
Alpha	B.1.1.7	VOC-20DEC-01	VOC	UK
Beta	B.1.351	VOC-20DEC-02	VOC	UK
Gamma	P.1	VOC-21JAN-02	VOC	UK
Delta	B.1.617.2, AY.1, AY.2, AY.3, AY.33	VOC-21APR-02	VOC	UK
Eta	B.1.525	VUI-21FEB-03	VUI	International
	B.1.1.318	VUI-21FEB-04	VUI	UK
Kappa	B.1.617.1	VUI-21APR-01	VUI	UK
Theta^	P.3	VUI-21MAR-02	VUI	International
	B.1.617.3	VUI-21APR-03	VUI	International
	AV.1	VUI-21MAY-01	VUI	International
	C.36.3	VUI-21MAY-02	VUI	International
Lambda	C.37	VUI-21JUN-01	VUI	UK
Mu	B.1.621	VUI-21JUL-01	VUI	UK
Zeta	P.2	VUI-21JAN-01	VUI	International
Epsilon^	B.1.427/B.1.429		Monitoring	
	B.1.1.7 with S494P		Monitoring	
	A.27		Monitoring	
Iota	B.1.526		Monitoring	
	B.1.1.7 with Q677H		Monitoring	
	B.1.620		Monitoring	
	B.1.214.2		Monitoring	

WHO nomenclature	Lineage	Designation	Status	UK or international (not currently detected in UK)
	R.1		Monitoring	
	B.1 with 214insQAS		Monitoring	
	AT.1		Monitoring	
	A.30		Monitoring	
	B.1.633		Monitoring	
	P.1 + N501T and E484Q		Monitoring	
	B.1.629		Monitoring	
	B.1.619		Monitoring	
	C.1.2		Monitoring	
	B.1.630		Monitoring	
	B.1.631/B.1.628		Monitoring	
	P.1.8		Monitoring	

^ 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.

Provisionally extinct variants are excluded from this table.

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

The last documented UK cases of VUI-21JAN-01 was on 14 April 2021, VUI-21APR-03 on 17 May 2021, VUI-21FEB-03 on 19 June 2021, VUI-21MAR-02 on 25 May, VUI-21MAY-01 on 21 June 2021, and VUI-21MAY-02 on 26 June 2021, these variants have been moved to international monitoring as of the 27 August 2021.

VUI-21FEB-01 (A.23.1 with E484K), VOC-21FEB-02 (B.1.1.7 with E484K) and VUI-21MAR-01 (B.1.324.1 with E484K) have not been observed in the UK or within the international GISAID dataset within the last 12 weeks. These variants are no longer included in the data update.

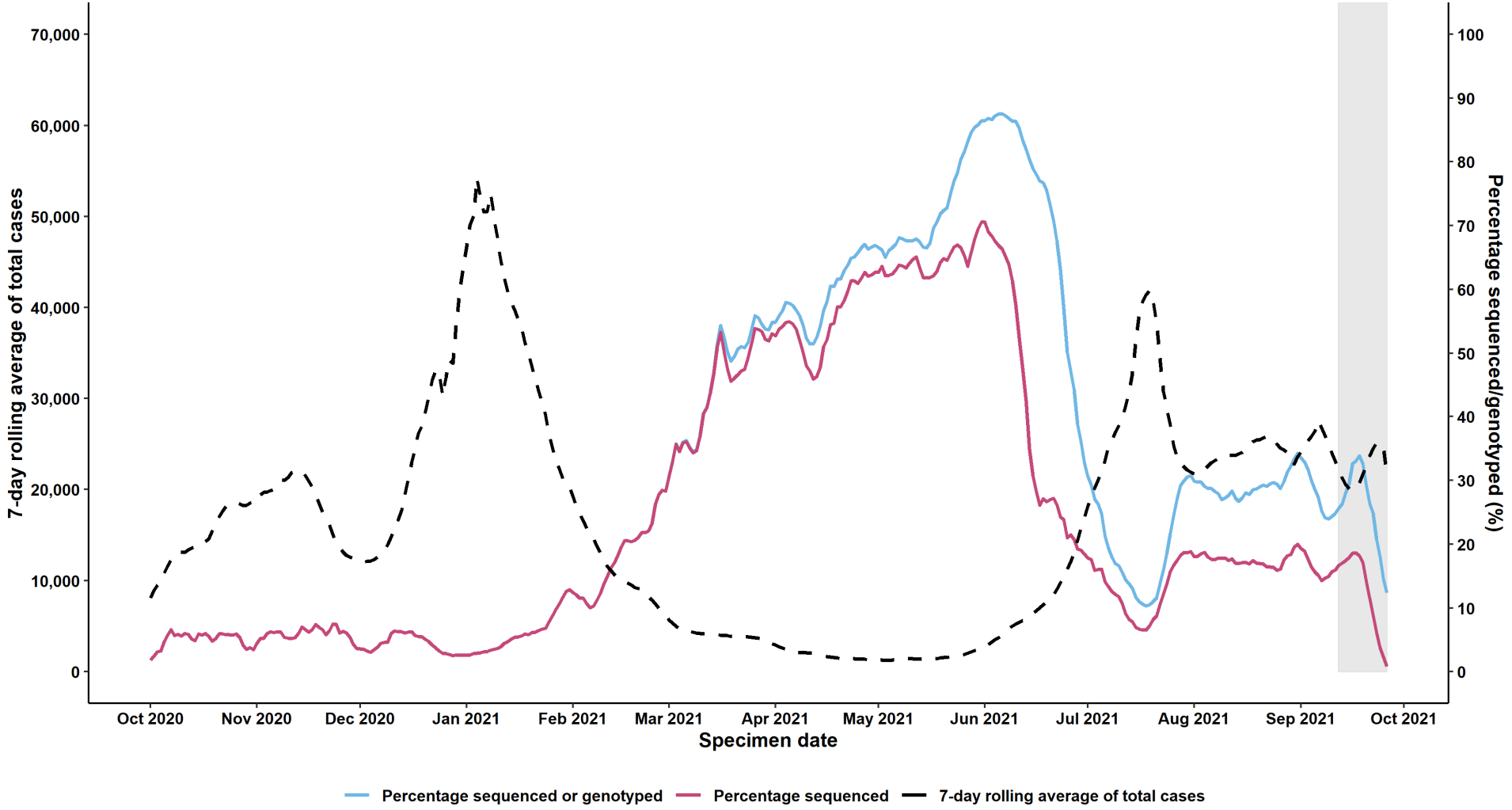
1.2 Sequencing coverage

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 improving (Figure 1). 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

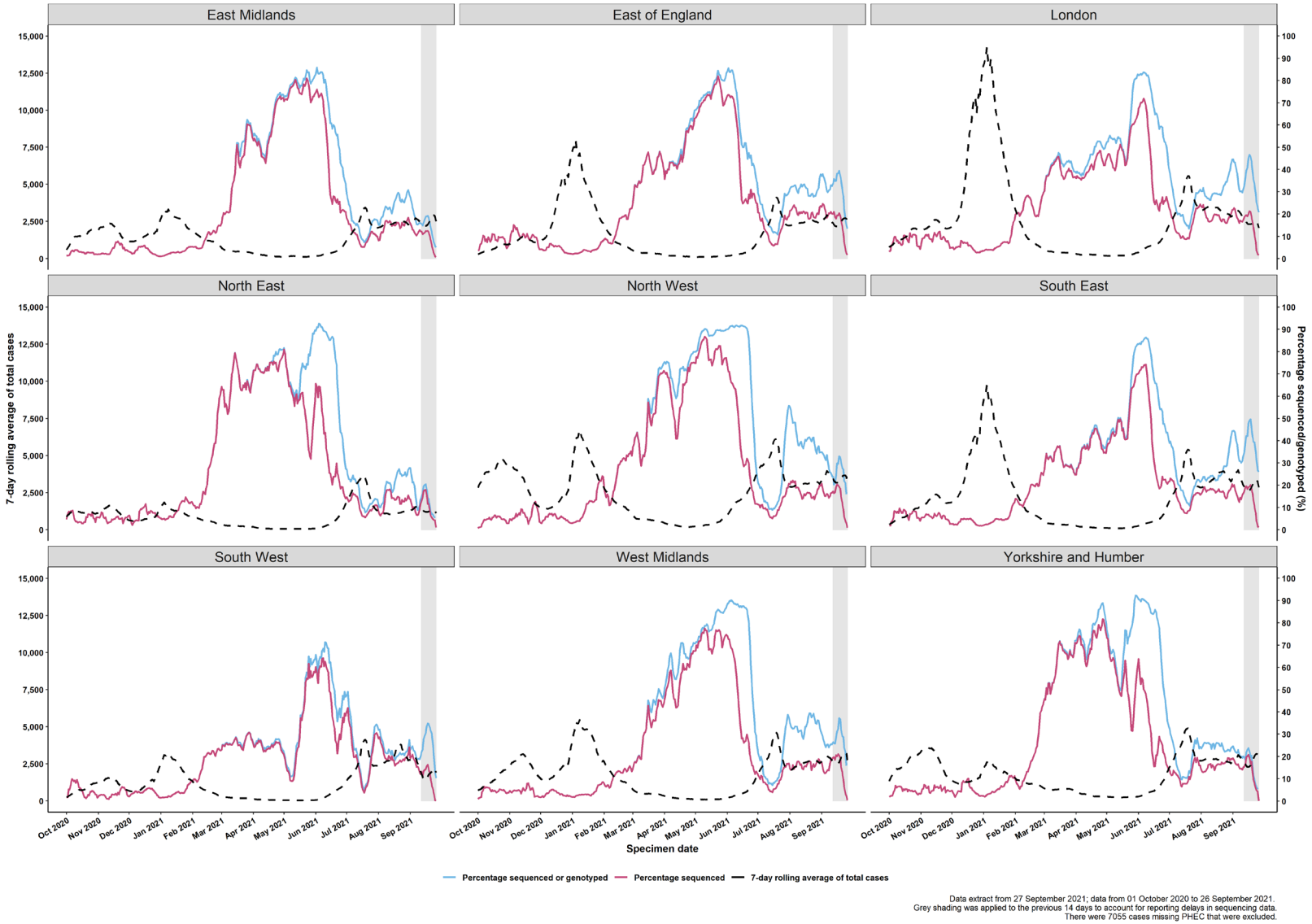
Figure 1. Coverage of sequencing with a valid result and genotyping over time (1 October 2020 to 26 September 2021)
(Find accessible data used in this graph in underlying data.)



Data extract from 27 September 2021; data from 01 October 2020 to 26 September 2021.
Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

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

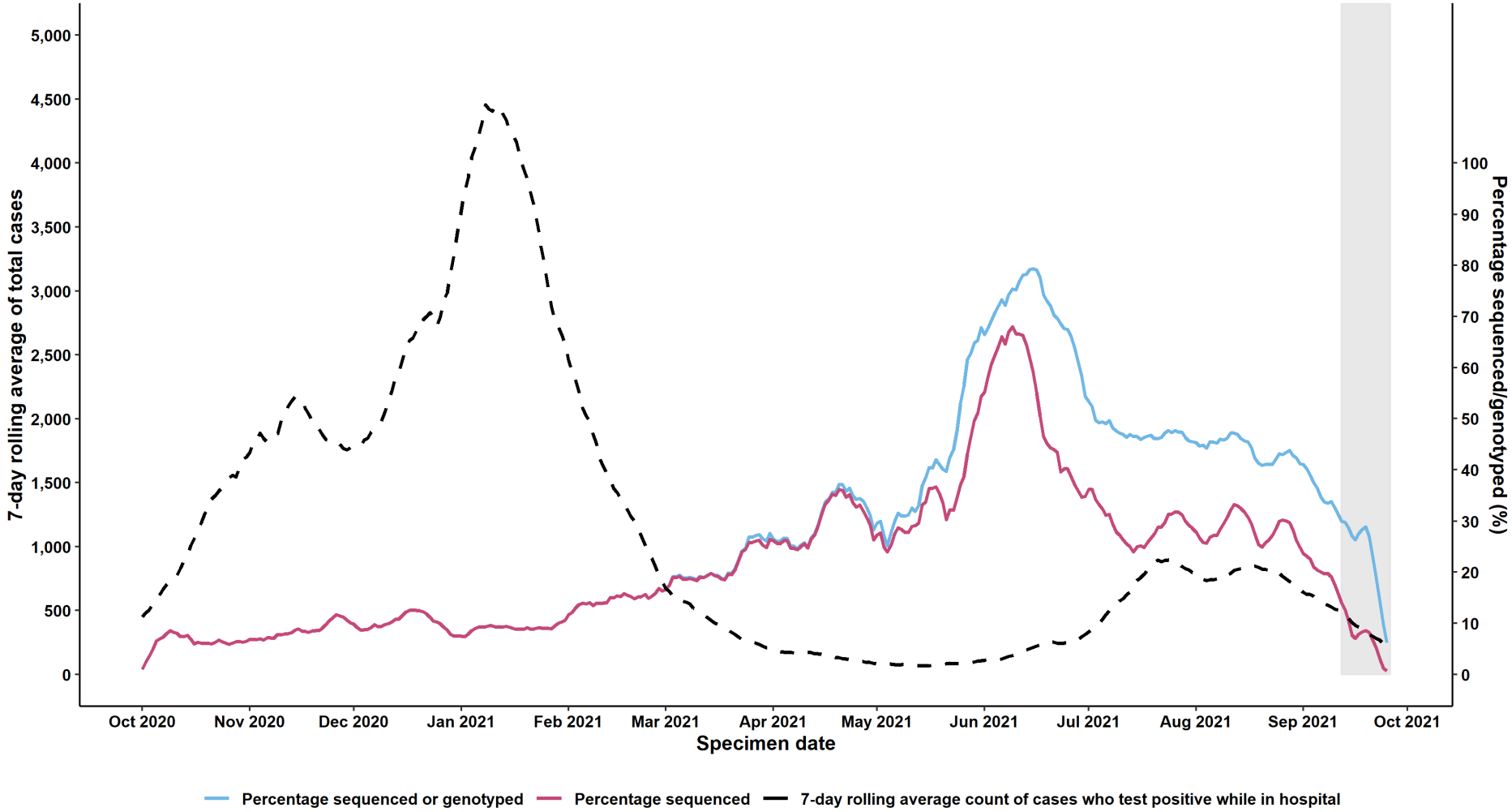
Figure 2. Coverage of sequencing with a valid result and genotyping over time by region (1 October 2020 to 26 September 2021) (Find accessible data used in this graph in underlying data.)



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 26 September 2021)

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



Data extract from 27 September 2021; data from 01 October 2020 to 26 September 2021.
Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

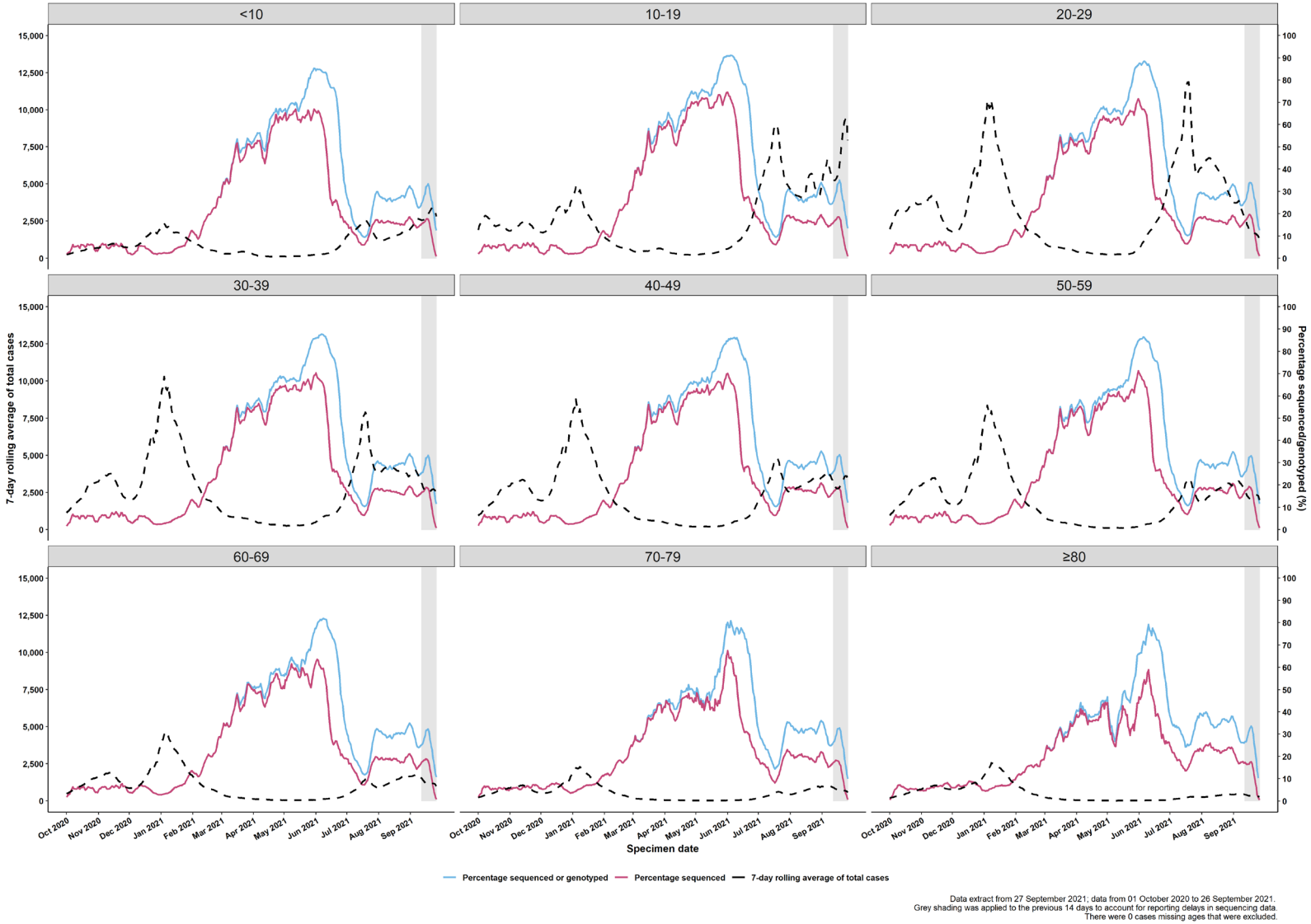
Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data.

Notes to Figure 3

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

From 14 to 18 June 2021 an operational issue at a sequencing site resulted in a reduction in the number of samples with sequencing data of sufficient quality for variant assignment. There were 19,502 samples reported to PHE as impacted by the incident. PHE has received approximately 10,000 sample identifiers from the list of those affected of which sequencing data has been obtained for approximately 4,300 and genotyping data for 3,300 have a reflex assay result. For approximately 2,400 samples variant assignment is not possible. This issue resulted in a reduction in genome coverage for specimen dates 10 to 15 June 2021 and may impact variant counts in figures and tables for this limited period. The unusable samples were from locations distributed around the UK and the proportions of different variants by region should be correct. In addition, the genotyping results means that this has limited impact in the interpretation of the overall data.

Figure 4. Coverage of sequencing with valid result and genotyping for cases by age group (1 October 2020 to 26 September 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 on Delta is shown in Table 2 and 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.

Information on attendance to emergency care is derived from the Emergency Care Data Set (ECDS), provided by NHS Digital. These data only show 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 reporting is lagged as NHS trusts routinely provide monthly data by the 21st of the following month. However, some trusts report daily data, and the linkage between coronavirus (COVID-19) cases and ECDS data is updated twice-weekly.

The crude analysis indicates that the proportion of Delta cases who present to emergency care is greater than that of Alpha, but a more detailed analysis of 43,338 COVID-19 cases indicates that the risk of hospitalisation among Delta cases is 2.26 times greater compared to Alpha[1].

Cases, hospitalisation, attendance and deaths by vaccination status are now presented in the COVID-19 vaccine surveillance report and 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 2. Sequenced and genotyped Delta cases by region from 1 October 2020 as of 27 September 2021

Region	Sequenced case	Genotyped cases[2]	Total Delta cases	Case proportion per region
East Midlands	29,839	16,274	46,113	6.7%
East of England	42,320	24,347	66,667	9.6%
London	60,283	42,762	103,045	14.9%
North East	20,822	13,287	34,109	4.9%
North West	75,525	72,242	147,767	21.3%
South East	53,239	40,154	93,393	13.5%
South West	45,574	10,174	55,748	8.0%

[1] 'Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study' (The Lancet Infectious Diseases)

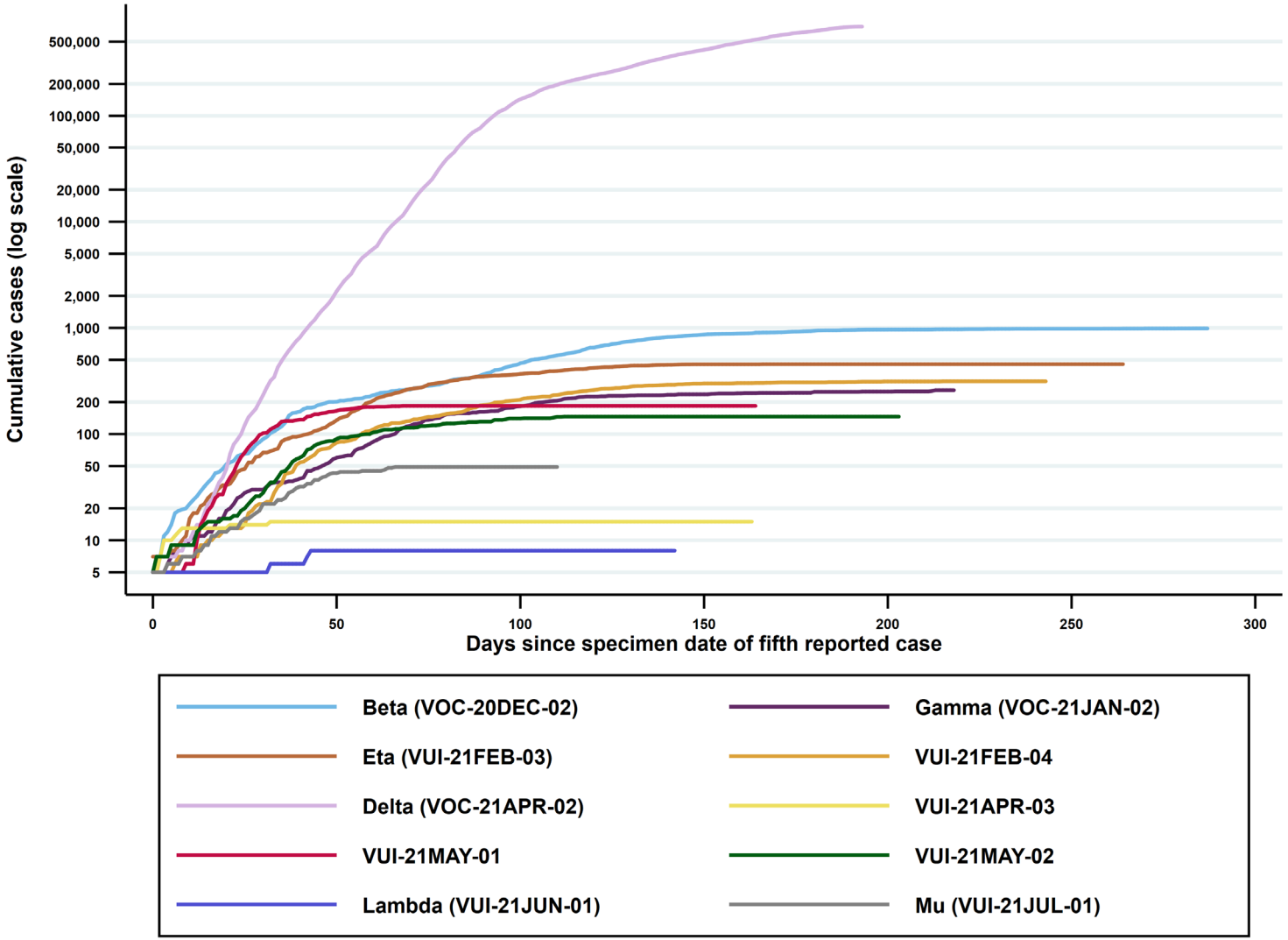
Region	Sequenced case	Genotyped cases[2]	Total Delta cases	Case proportion per region
West Midlands	37,936	35,073	73,009	10.5%
Yorkshire and Humber	43,708	25,485	69,193	10.0%
Unknown region	2,528	1,779	4,307	0.6%
Total	411,774	281,577	693,351	-

Table 3. Number of sequenced and genotyped cases by variant from 1 October 2020 as of 27 September 2021

Variant	Sequenced cases	Genotyped cases[2]	Total case number	Case proportion	Deaths
Alpha	221,646	5,706	227,352	24.6%	4,364
Beta	929	74	1,003	0.1%	13
Delta	411,774	281,577	693,351	75.1%	3,216
Eta	460	0	460	0.0%	12
Gamma	209	54	263	0.0%	0
Kappa	473	0	473	0.1%	2
Lambda	8	0	8	0.0%	0
Mu	49	0	49	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	147	0	147	0.0%	0
Zeta	54	0	54	0.0%	1

[2] 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 5. Cumulative cases in England of variants indexed by days since the fifth reported case as of 26 September 2021
(Find accessible data used in this graph in underlying data.)



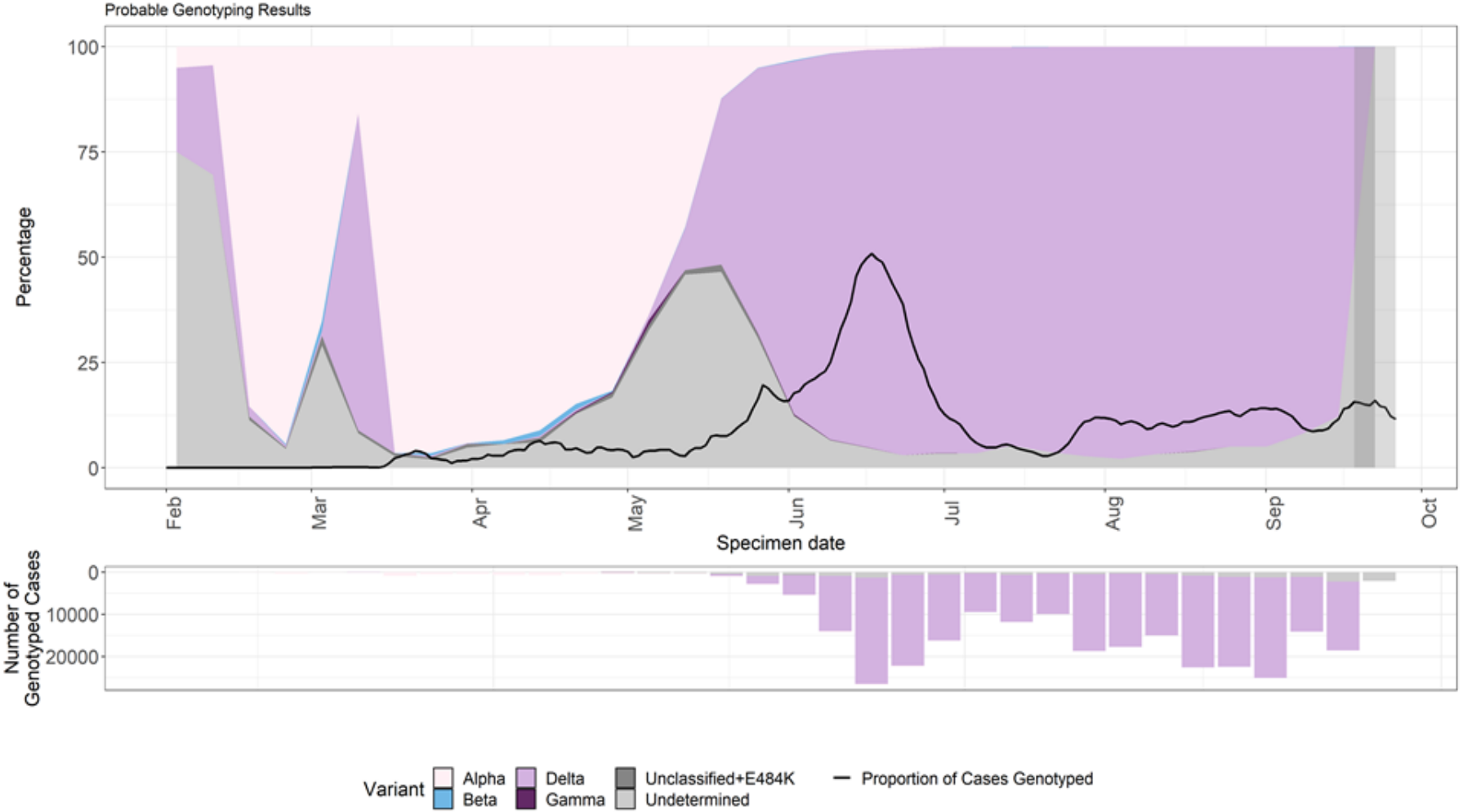
1.4 Variant prevalence

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. Genotyping provides probably variant result with a shorter turnaround time of 12 to 24 hours after initial confirmation of 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 are available.

Delta variant accounted for approximately 99.7% of sequenced and 88.6% genotyped cases from 29 August 2021 as of 27 September 2021.

Figure 6. Variant prevalence for all England available genotyped cases from 1 February 2021 as of 27 September 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 VUI-21JUL-01 (B.1.621) with an additional K417N mutation.

Figure 7. Variant prevalence for all England available sequenced cases from 1 February 2021 as of 27 September 2021 (excluding 340 cases where the specimen date was unknown)

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

Dashed lines indicate period incorporating issue at a sequencing site.

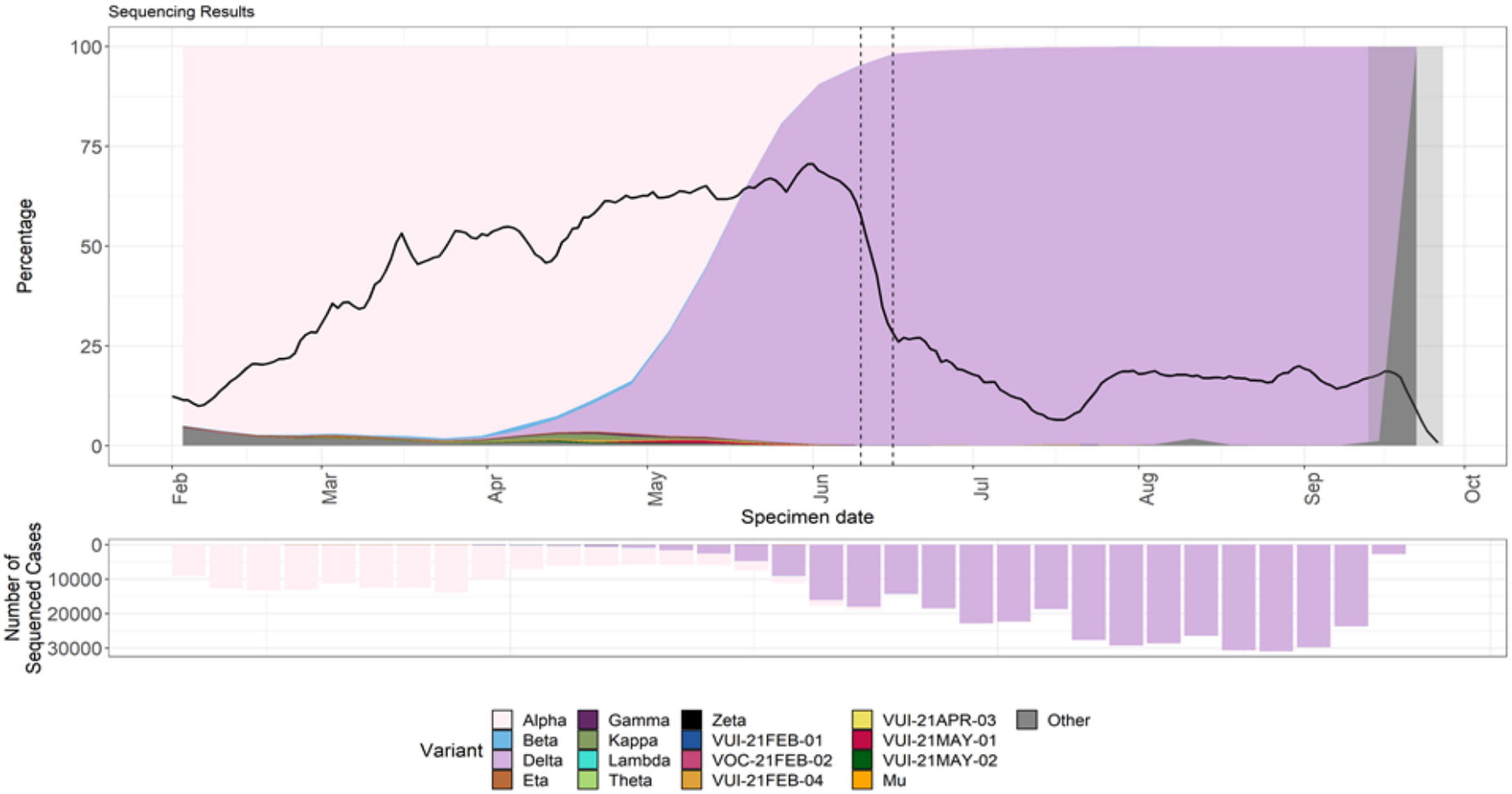


Figure 8. Variant prevalence from 1 February 2021 as of 27 September 2021 by region for all genotyped cases in England (excluding 2,116 cases where the region or specimen date were unknown)

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

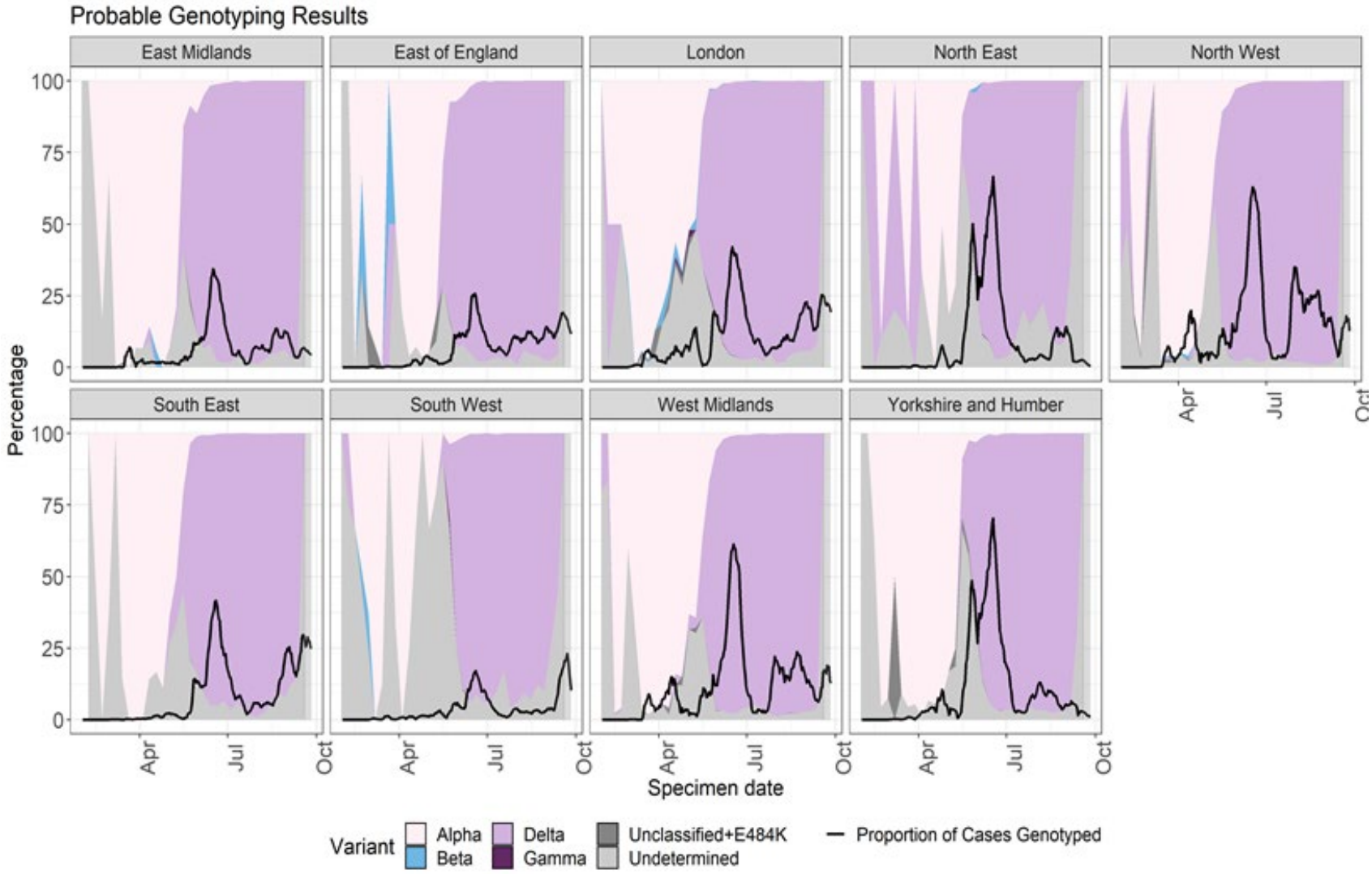
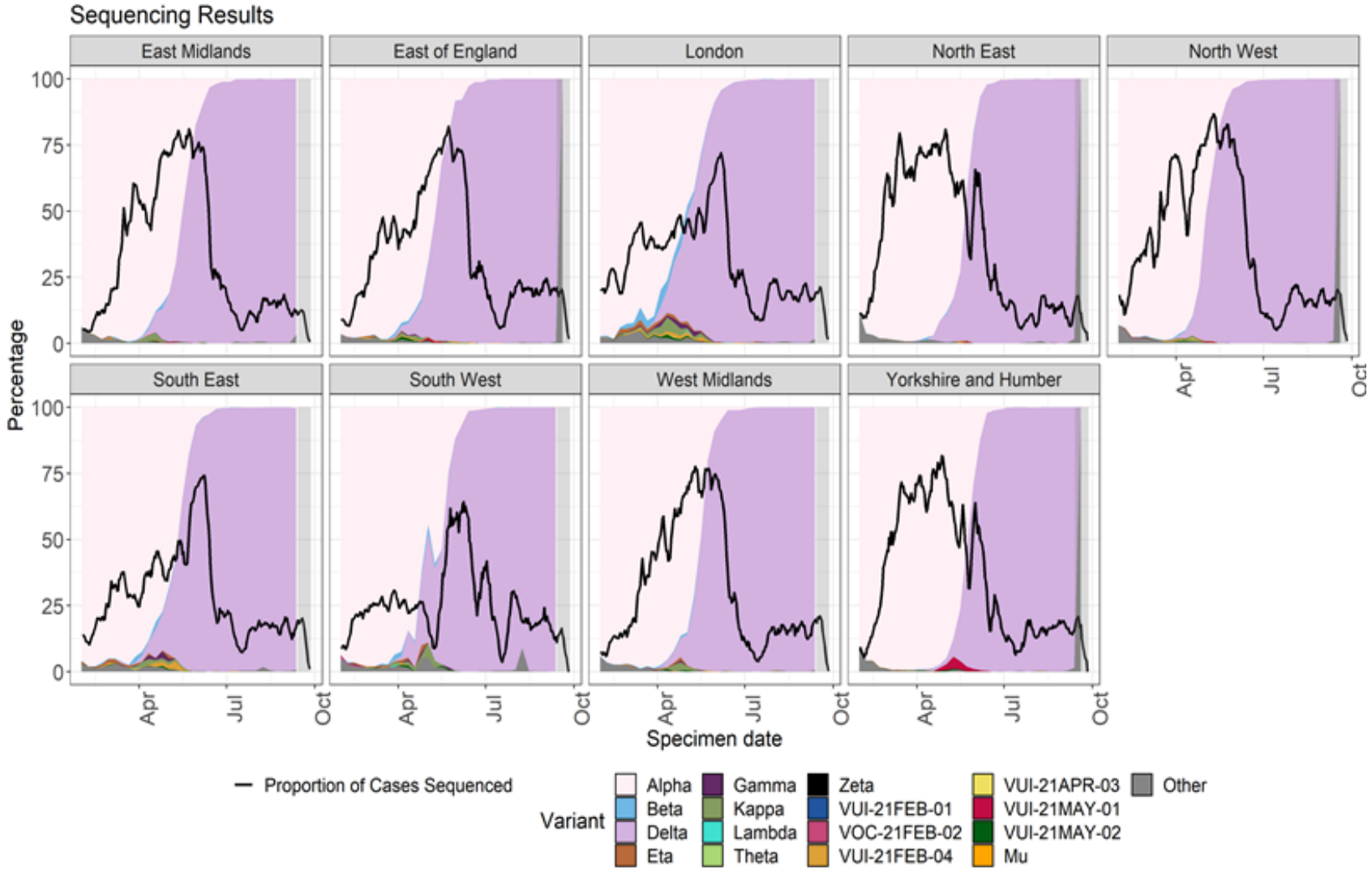


Figure 9. Variant prevalence from 1 February 2021 as of 27 September 2021 by region for all sequenced cases in England (excluding 2,984 cases where the region or specimen date were unknown).

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



1.5 Secondary attack rates

This section includes secondary attack rates for traveller and non-traveller cases, and separate household contact rates, including new analysis of rates for household and non-household contacts of non-traveller cases over time for Delta and Alpha variants.

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. Variant cases are identified using sequencing results supplemented with genotyping results and exclude low-quality results.

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 4 shows secondary attack rates for all variants between 5 January 2021 and 5 September 2021, which was a period chosen to capture data for all variants. Direct comparisons between variants using this table are not valid as factors including vaccination levels and social restrictions in England have varied over this period. (See Figure 10 for such comparison over time for Alpha and Delta.) Estimates of secondary attack rates for travel-related contacts with VOCs or VUIS were considerably lower than non-travel cases due to differences in contact definitions.

Figure 10 shows the secondary attack rates amongst household and non-household contacts of non-travel cases with Delta and Alpha between 4 January 2021 to 5 September 2021. This period has been extended to provide comparability with Table 4 for these 2 variants. Overall general trends over time of secondary attack rates for both variants and in both household and non-household settings are downward. However, secondary attack rates amongst household contacts of cases with Delta rose between mid-July and end of August 2021, with estimate of 12.2% (95% CI: 12.0% to 12.4%) for household contacts in week commencing 23 August 2021, dropping in the most recent week, with an estimate of 10.9% (95% CI: 10.7% to 11.2%) in week commencing 30 August 2021. Secondary attack rates among non-household contacts of cases with Delta were 3.7% (95% CI: 3.5% to 4.0%) in week commencing 30 August 2021. Secondary attack rate estimates for contacts of cases with variants are only available for time periods with sufficient contacts of cases for analysis.

Table 4. Secondary attack rates for all variants
(5 January 2021 to 5 September 2021, variant data as of 20 September 2021, and contact tracing data as of 28 September 2021. Direct comparisons between variants using this table are not valid as factors including vaccination levels and social restrictions in England have varied over period of study.)

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 or contacts]	Secondary attack rate in household contacts of non-travel or unknown cases (95% CI) [secondary cases or contacts]	Secondary attack rate in non-household contacts of non-travel or unknown cases (95% CI) [secondary cases or contacts]
Alpha	4,878 (75.1% with contacts)	185,271 (75.0% with contacts)	2.6%	1.5% (1.4% - 1.6%) [1,346/89,515]	10.2% (10.1% - 10.3%) [34,625/338,655]	5.6% (5.5% - 5.8%) [3,307/58,686]
Beta	360 (69.4% with contacts)	435 (67.4% with contacts)	45.3%	1.8% (1.5% - 2.2%) [114/6,208]	9.9% (7.9% - 12.2%) [75/761]	2.9% (1.3% - 6.2%) [6/206]
Gamma	87 (62.1% with contacts)	155 (72.3% with contacts)	36.0%	1.1% (0.6% - 1.9%) [12/1,123]	10.6% (7.4% - 15.0%) [27/254]	3.3% (1.1% - 9.2%) [3/91]
Eta	211 (67.8% with contacts)	197 (73.1% with contacts)	51.7%	1.1% (0.8% - 1.4%) [47/4,339]	9.9% (7.2% - 13.6%) [33/332]	Unavailable [1/43]

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 or contacts]	Secondary attack rate in household contacts of non-travel or unknown cases (95% CI) [secondary cases or contacts]	Secondary attack rate in non-household contacts of non-travel or unknown cases (95% CI) [secondary cases or contacts]
VUI-21FEB-04	135 (66.7% with contacts)	159 (79.2% with contacts)	45.9%	0.5% (0.3% - 0.8%) [18/3,429]	8.4% (5.8% - 12.0%) [26/309]	6.5% (3.0% - 13.4%) [6/93]
Theta	5 (40.0% with contacts)	1 (100.0% with contacts)	83.3%	Unavailable [0/5]	Unavailable [0/3]	Unavailable [0/0]
Delta	15,165 (65.0% with contacts)	549,162 (72.4% with contacts)	2.7%	1.8% (1.8% - 1.9%) [3,345/181,991]	10.6% (10.5% - 10.7%) [96,214/907,281]	5.2% (5.1% - 5.3%) [15,669/300,682]
VUI-21APR-03	9 (22.2% with contacts)	5 (100.0% with contacts)	64.3%	Unavailable [2/204]	Unavailable [1/12]	Unavailable [0/0]
VUI-21MAY-01	2 (0.0% with contacts)	175 (85.1% with contacts)	1.1%	Unavailable [0/0]	8.0% (5.8% - 11.1%) [33/411]	2.4% (0.8% - 6.9%) [3/124]

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 or contacts]	Secondary attack rate in household contacts of non-travel or unknown cases (95% CI) [secondary cases or contacts]	Secondary attack rate in non-household contacts of non-travel or unknown cases (95% CI) [secondary cases or contacts]
VUI-21MAY-02	76 (75.0% with contacts)	51 (82.4% with contacts)	59.8%	1.0% (0.6% - 1.7%) [15/1,439]	8.4% (4.5% - 15.2%) [9/107]	Unavailable [0/13]
Lambda	9 (66.7% with contacts)	0 (0 with contacts)	100.0%	Unavailable [1/196]	Unavailable [0/0]	Unavailable [0/0]
Mu	21 (47.6% with contacts)	22 (68.2% with contacts)	48.8%	Unavailable [10/297]	Unavailable [2/30]	Unavailable [1/9]

Notes to table

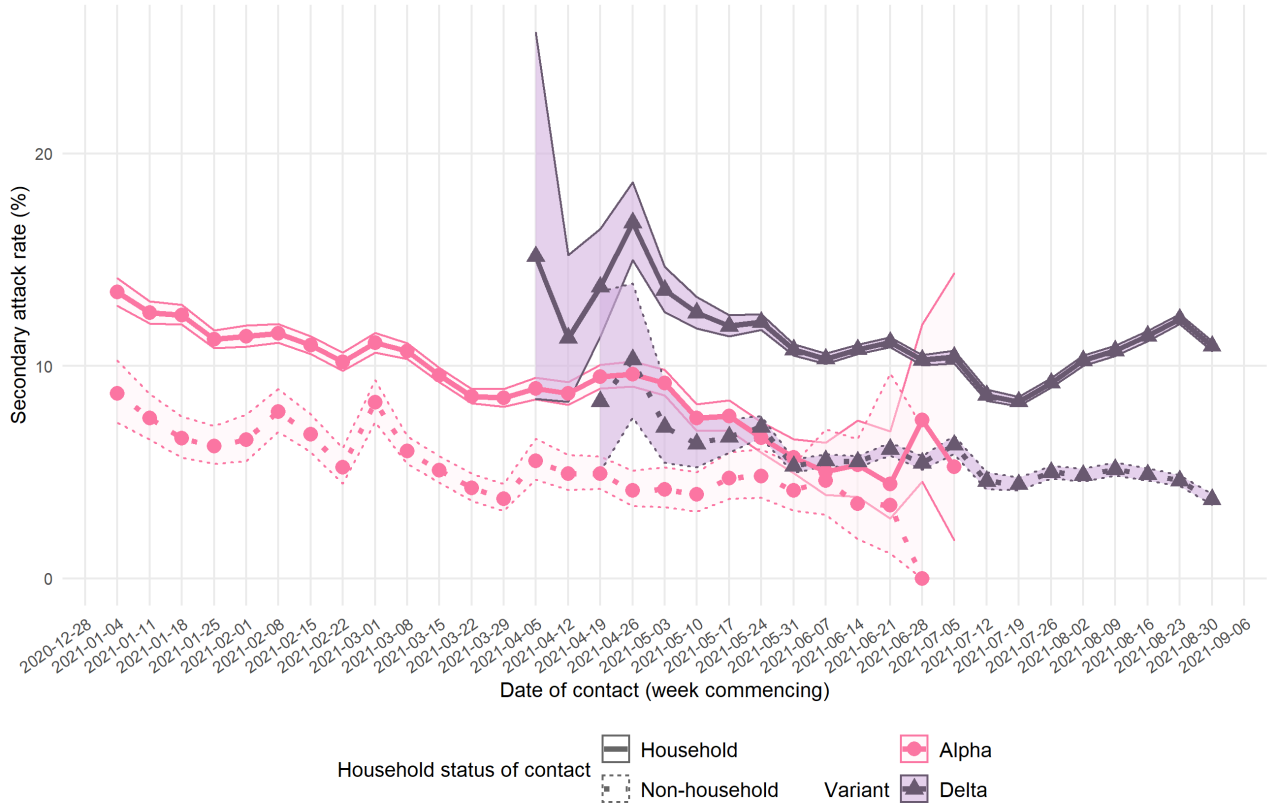
Secondary attack rates are marked as ‘Unavailable’ when count of contacts is fewer than 50 or count of cases is fewer than 20. Travel-linked cases for secondary attack rates are identified positively in NHS Test and Trace data using multiple PHE sources. A case is considered as being travel-linked if EpiCell or Health Protection Teams have found evidence of international travel, their NHS Test and Trace record mentions an event associated with international travel, their NHS Test and Trace record was created after notification via International Health Regulations National Focal Point, their contacts were traced by the international contact tracing team, or they have been marked for priority contact tracing in NHS Test and Trace for reasons of travel. Some travel-linked cases may be missed by these methods and would be marked as non-travel-linked or unknown.

Secondary attack rates from NHS Test and Trace should generally be considered lower bounds due to the nature of contact tracing and testing. Data provided is for period until 5 September 2021 in order to allow time for contacts to become cases, hence case counts are lower than other sources. Cases are included in case counts if their onset or (if asymptomatic) test is during the period of study,

contacts are included in secondary attack rates if their exposure date or onset or test of exposing case if the contact is a household contact is during the period of study. Secondary attack rates are suppressed when count of contacts is less than 50 or count of cases is less than 20. Probable (genotyping) results are included, low quality genomic results are not.

Figure 10. Secondary attack rates in household and non-household contacts of non-travel Alpha and Delta cases, with 95% confidence intervals

4 January 2021 to 5 September 2021, variant data as of 20 September 2021 and contact tracing data as of 28 September 2021 (Find accessible data used in this graph in underlying data)



Please see footnote from Table 4.

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 – mutation scan

Table 6 shows spike mutations with a potential impact on antigenicity, avidity, or the furin cleavage site significance acquired by Delta in the UK. This data uses the numbers of genomes in the national genomic data set rather than case numbers. Only mutations associated with antigenic change are presented here, such as those identified by published research. 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 PHE.

Table 5. Additional spike mutations of interest detected in Delta genomes in the UK as of 28 September 2021

Amino acid change	Delta sequences in UK dataset	Delta sequences outside UK (GISAID)	Delta sequences 29 June to 28 July		Delta sequences 29 July to 28 August		Delta sequences 29 August to 28 September	
			England	Outside UK	England	Outside UK	England	Outside UK
P251L	3,095	10,899	465	4,046	534	5,111	386	1,396
G446V	1,978	1,511	192	424	316	674	347	253
Q613H	751	21,854	76	2,884	235	14,352	248	4,036
V483F	673	337	67	82	112	166	91	43
Q493E	365	175	60	66	172	58	67	12
S494L	260	311	23	56	107	185	89	36

Amino acid change	Delta sequences in UK dataset	Delta sequences outside UK (GISAID)	Delta sequences 29 June to 28 July		Delta sequences 29 July to 28 August		Delta sequences 29 August to 28 September	
			England	Outside UK	England	Outside UK	England	Outside UK
E484Q	195	1,329	17	428	72	568	66	149
K417N	168	7,702	11	3,040	60	2,254	31	348
L455F	151	562	26	108	73	284	24	86
V445I	103	34	36	3	40	10	11	17
F490L	98	405	16	18	50	252	14	102
K444N	85	346	8	90	32	154	14	48
S494P	59	209	19	38	12	100	4	49
N501Y	58	528	16	98	21	288	3	9
F490S	45	87	2	19	12	38	28	24
A475V	43	41	4	10	19	17	14	11
K458N	42	47	14	8	13	25	5	7
R246I	39	91	12	11	14	49	5	21
P681H	38	223	2	35	12	135	2	18
E484K	33	247	2	40	11	122	17	52
K444R	33	61	11	13	5	27	11	21
L452Q	26	80	1	14	11	45	6	14
E484A	25	82	2	10	3	29	13	22
P499L	20	27	6	9	3	14	5	3
V445F	19	39	2	6	5	22	11	7

Amino acid change	Delta sequences in UK dataset	Delta sequences outside UK (GISAID)	Delta sequences 29 June to 28 July		Delta sequences 29 July to 28 August		Delta sequences 29 August to 28 September	
			England	Outside UK	England	Outside UK	England	Outside UK
N439K	18	4	2	0	10	2	3	0
S494A	17	18	0	2	5	16	9	0
N501T	16	20	0	2	4	6	0	6
E484G	13	26	7	5	0	16	2	3
E484V	11	24	1	12	1	5	4	6
Q493L	11	102	3	62	4	32	1	8
D80N	9	33	1	6	2	18	1	6
V483A	6	28	1	8	2	14	3	3
F486L	6	2	2	1	0	1	1	0
V445A	6	27	2	10	3	14	0	3
E484D	5	84	2	8	2	64	0	6
G446D	5	12	3	3	1	6	1	2
G485D	4	1	0	1	0	0	2	0
T478I	3	10	1	1	0	6	0	3
Y453F	3	7	0	0	0	4	3	3
Q498R	3	21	0	7	0	9	0	3
Q493H	3	10	2	1	0	5	0	0
D80A	3	130	1	58	0	19	1	1
K444E	3	3	2	0	0	3	0	0

Amino acid change	Delta sequences in UK dataset	Delta sequences outside UK (GISAID)	Delta sequences 29 June to 28 July		Delta sequences 29 July to 28 August		Delta sequences 29 August to 28 September	
			England	Outside UK	England	Outside UK	England	Outside UK
I472V	2	3	0	0	0	0	0	1
R246G	1	21	0	4	1	16	0	0
Q493R	1	1	0	0	0	1	1	0
Q493K	1	1	0	0	0	1	1	0
N450K	1	4	0	1	0	3	1	0
K458Q	1	2	0	0	1	2	0	0
K417T	1	12	0	2	0	4	1	5
K417E	1	14	1	1	0	12	0	1
V483G	1	9	0	3	1	6	0	0
V503L	1	1	0	0	0	0	0	1
Y144N	1	2	1	2	0	0	0	0
N501H	1	5	1	0	0	3	0	2
Total of Delta sequences	**542,319**	**876,771**	**102,516**	**250,715**	**130,801**	**425,099**	**92,130**	**116,322**

Note: column labels of Table 5 in this briefing were incorrectly labelled prior to 1 November 2021 and were corrected in this version published on 1 November 2021.

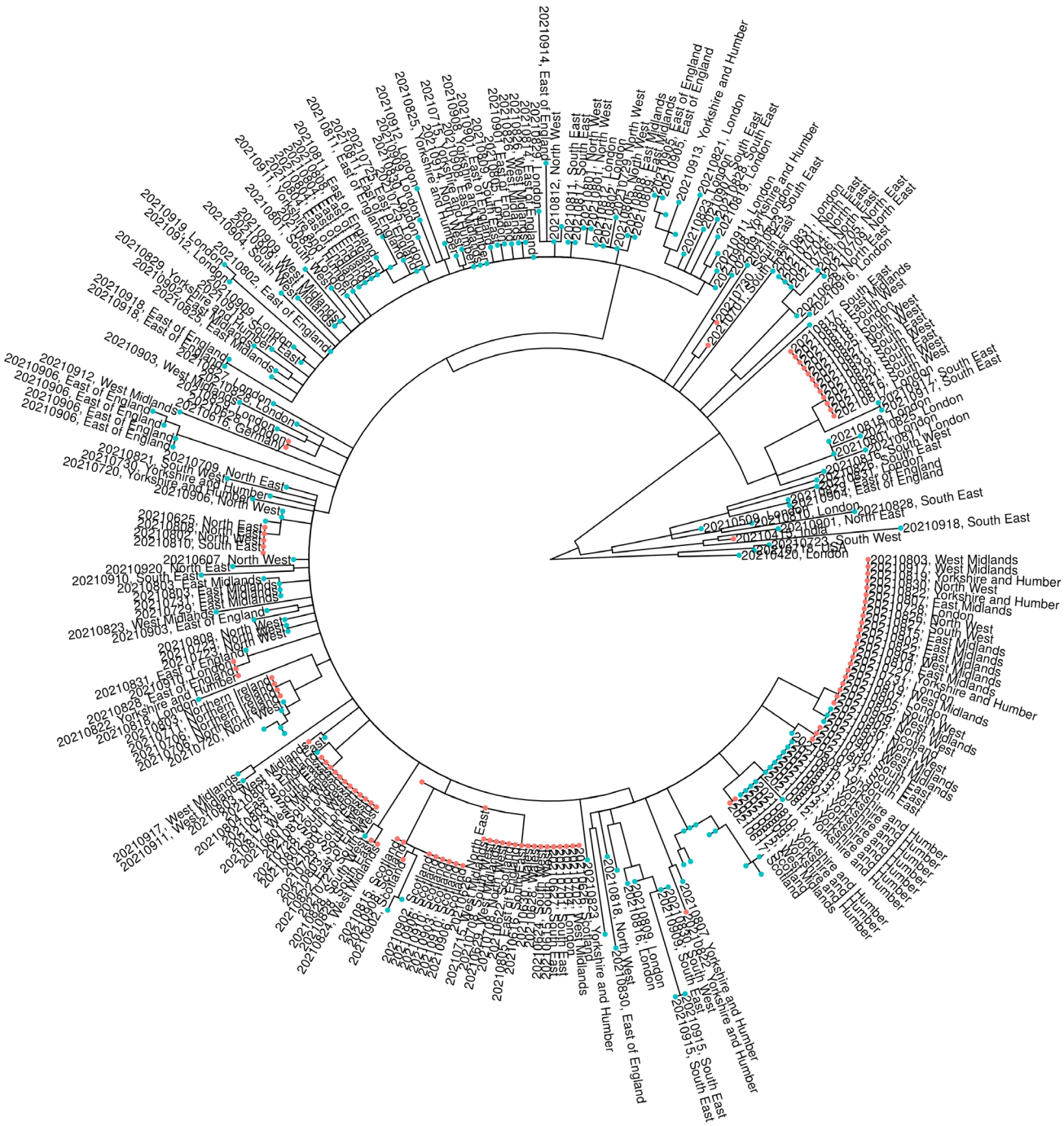
2.2 Monitoring diversity within Delta – Delta with E484Q

Changes at position 484 in spike are potentially antigenically significant. Delta with E484Q was first detailed as a signal under investigation on the 3 August 2021 after being detected in 6 Scottish samples between 22 and 28 July 2021. 195 sequences have been identified as of the 29 September 2021, with 174 from England, 15 from Scotland, and 6 from Wales.

The phylogenetic tree of UK Delta with E484Q cases is shown in Figure 11, which includes a cluster of 11 genetically indistinguishable samples from Yorkshire and Humber (10) and West Midlands (1), a node of 4 samples (3 genetically indistinguishable) from the East Midlands, a large node of diverse (genetically and geographically) samples that are predominantly annotated with the E484Q mutation, and an additional cluster of 5 samples from the North East.

Figure 11. Phylogenetic tree of UK Delta (B.1.617.2) with E484Q cases with a down-sampled international background dataset as of 29 September 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). Sample date and location of case is shown in the label for each tip (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

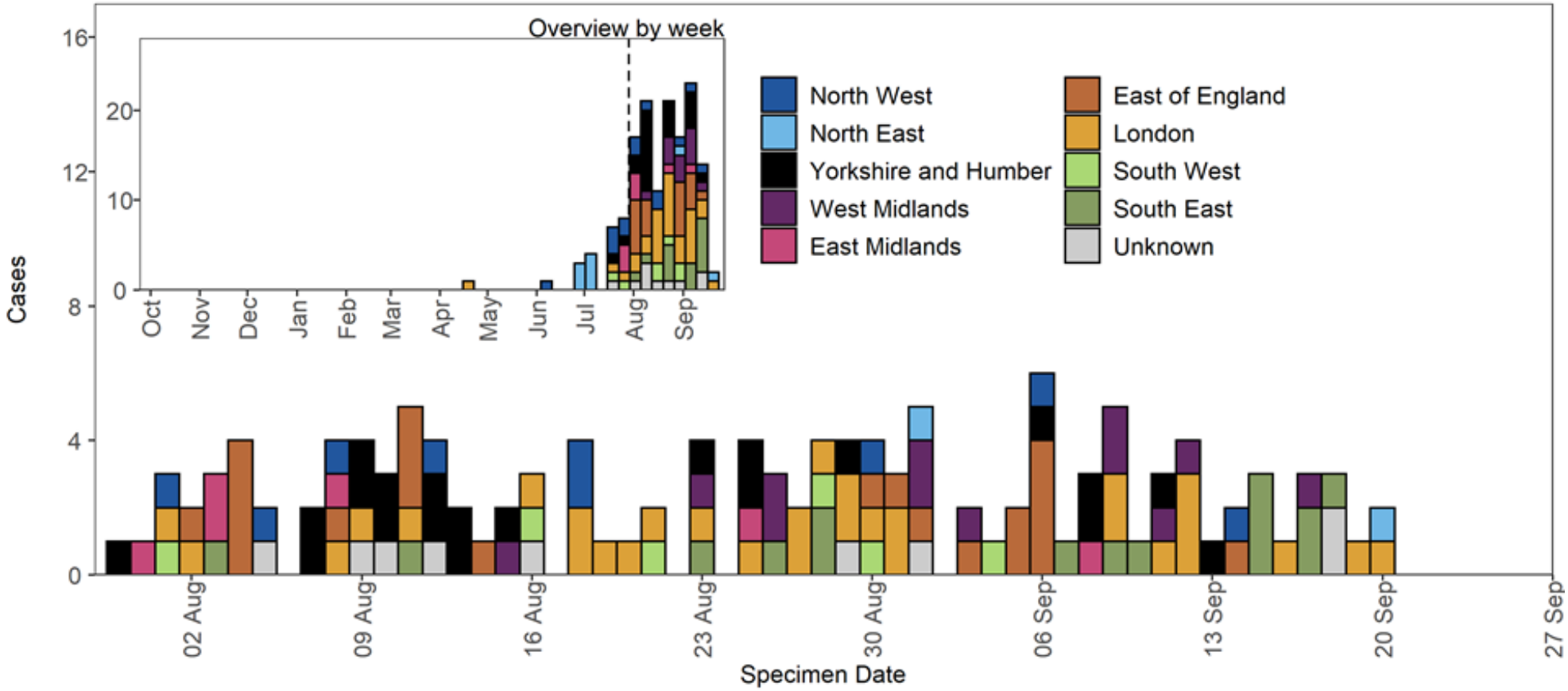
As of 29 September 2021, there are 195 Delta with E484Q sequences in England, 150 of which were linked to epidemiological data. Cases have been detected across all 9 English regions, with most cases in the London (32, 21.3%) as shown in Table 6 and cases by region in Figure 12. The most frequent age group was the 40 to 49 age group, with 32 cases. 14 of the 126 cases have history of travel.

Table 6. Confirmed and provisional Delta with E484Q cases in England by region as of 27 September 2021

Region	Total case number	Proportion of Delta with E484Q cases in England with epidemiological data
East Midlands	8	5.3%
East of England	21	14.0%
London	32	21.3%
North East	9	6.0%
North West	14	9.3%
South East	15	10.0%
South West	7	4.7%
West Midlands	12	8.0%
Yorkshire and Humber	22	14.7%
Unknown region	10	6.7%
Total	150	-

[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.

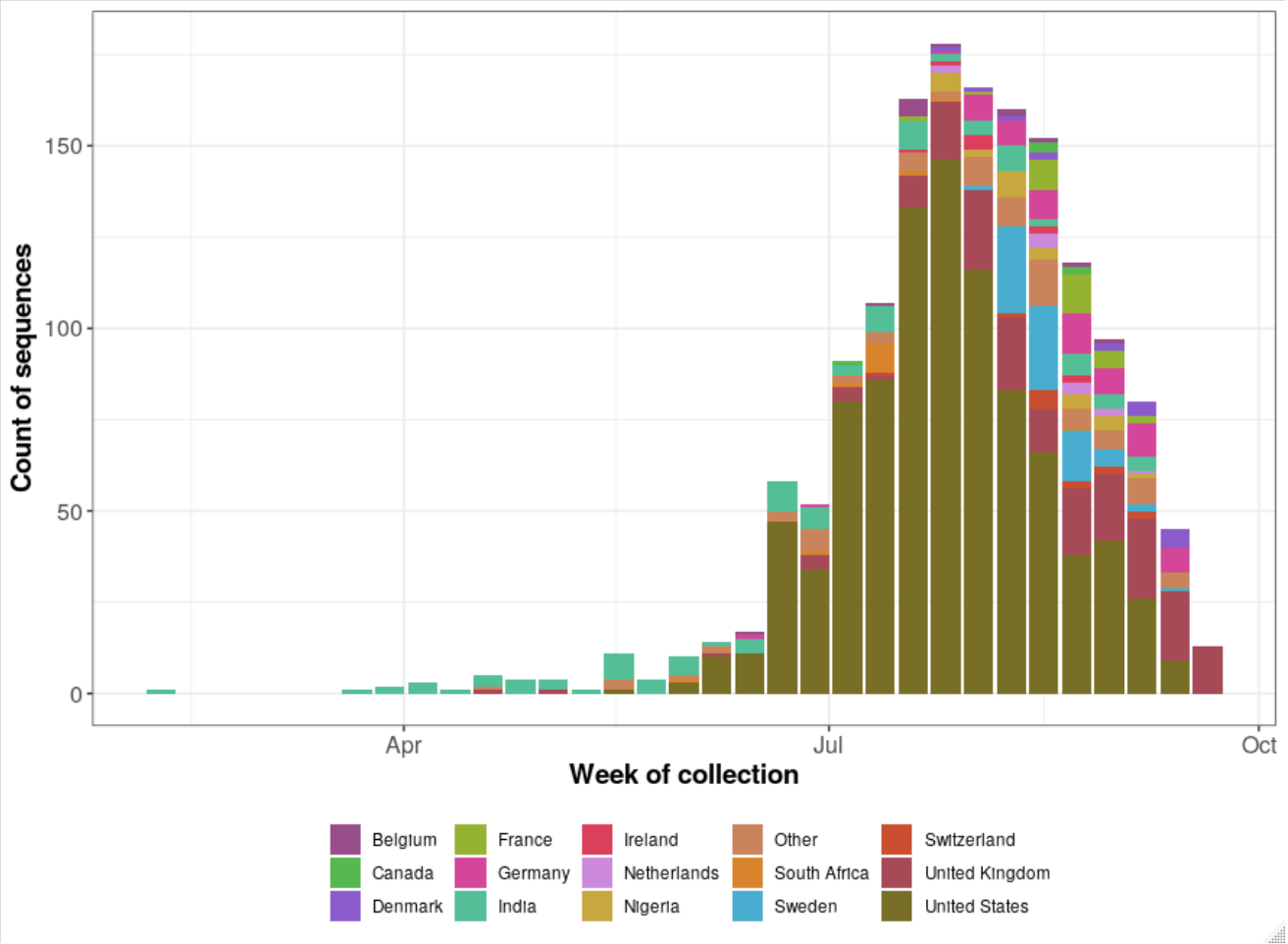
Figure 12. Cases of Delta with E484Q in England by region as of 27 September 2021



International epidemiology

As of 27 September 2021, 1631 GISAID sequences have been assigned to the B.1.617.2 and AY sub-lineages with the additional E484Q mutation, of those 1,558 sequences had appropriate date information. Sequences have been uploaded from USA (932), India (104), France (86), Sweden (70), Germany (59), Nigeria (26), Denmark (16), South Africa (14), Belgium (13), Switzerland (13), Netherlands (12), Canada (11), Ireland (10), Israel (6), Mexico (6), Spain (6), Puerto Rico (5) and 30 other countries with less than 5 samples. Figure 13 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 September 2021.

Figure 13. Count of Delta with E484Q classified sequences by week of collection uploaded to GISAID by week as of 27 September 2021



2.3 Monitoring diversity within Delta – Delta with E484K

Changes at position 484 in spike are potentially antigenically significant. Delta with E484K was detailed as a signal under investigation on 8 September 2021 and was first detected on 22 July 2021 in UK sequences. Both Delta and Delta with E484K are routinely monitored. 33 sequences have been identified as of the 27 September, with 31 from England and 2 from Scotland.

The phylogenetic tree of UK Delta with E484K cases is shown in Figure 14, which includes 2 small clusters and multiple independent occurrences of the mutation (Delta with E484K is shown in yellow on Figure 14).

Figure 14. Maximum likelihood tree of UK Delta (B.1.617.2) with E484K cases

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 111 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. Two clusters of Delta with E484K have been identified with 4 or more sequences, cluster 1 and 2 which are highlighted on the tree. Three 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 27 September 2021, there are 33 Delta with E484K sequences in England, of which 30 could be linked to epidemiological data. Cases have been detected across 9 English regions, with most cases in the East Midlands (10, 33.3%) as shown in Table 7 and cases by region in Figure 15 and by cluster in Figure 16. The most frequent age group was the 60 to 69 age group, with 6 cases. Three of the 29 cases have history of travel.

Table 7. Confirmed and provisional Delta with E484K cases in England by region as of 27 September 2021

Region	Total case number	Proportion of Delta with E484K cases in England with epidemiological data
East Midlands	10	33.3%
East of England	4	13.3%
London	1	3.3%
North East	0	0.0%
North West	7	23.3%
South East	2	6.7%
South West	1	3.3%
West Midlands	0	0.0%
Yorkshire and Humber	4	13.3%
Unknown region	1	3.3%
Total	30	-

[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 15. Cases of Delta with E484K in England by region as of 27 September 2021
(Find accessible data used in this graph in underlying data.)

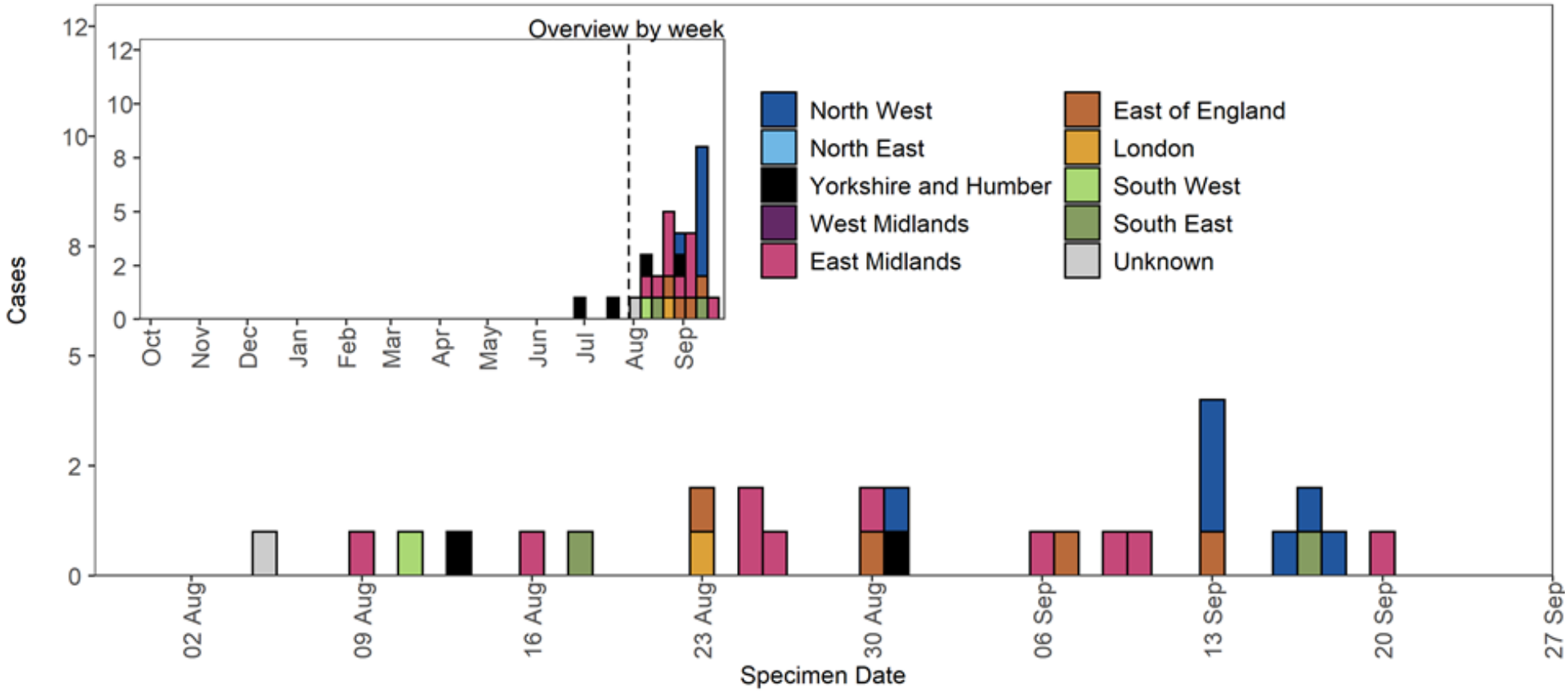
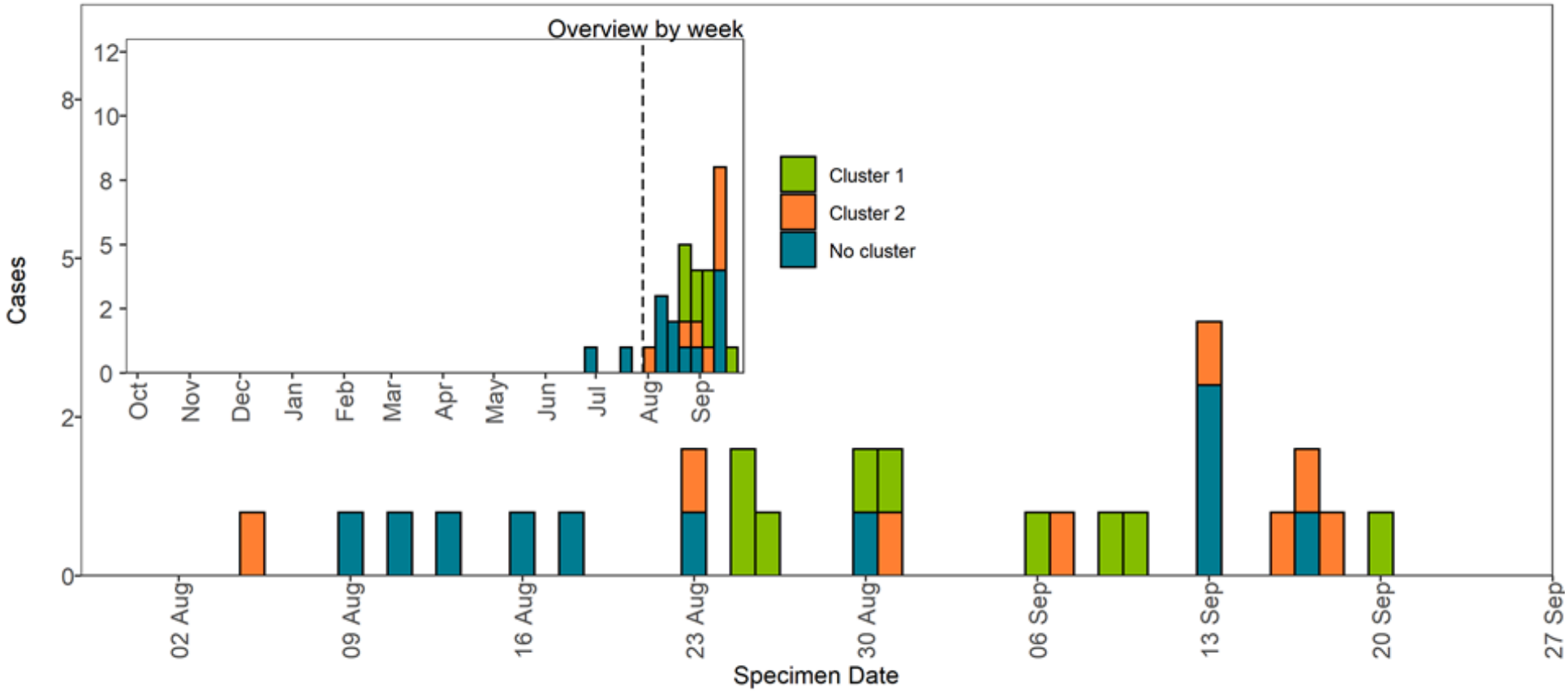


Figure 16. Cases of Delta cases with E484K mutation by detected cluster as of 27 September 2021

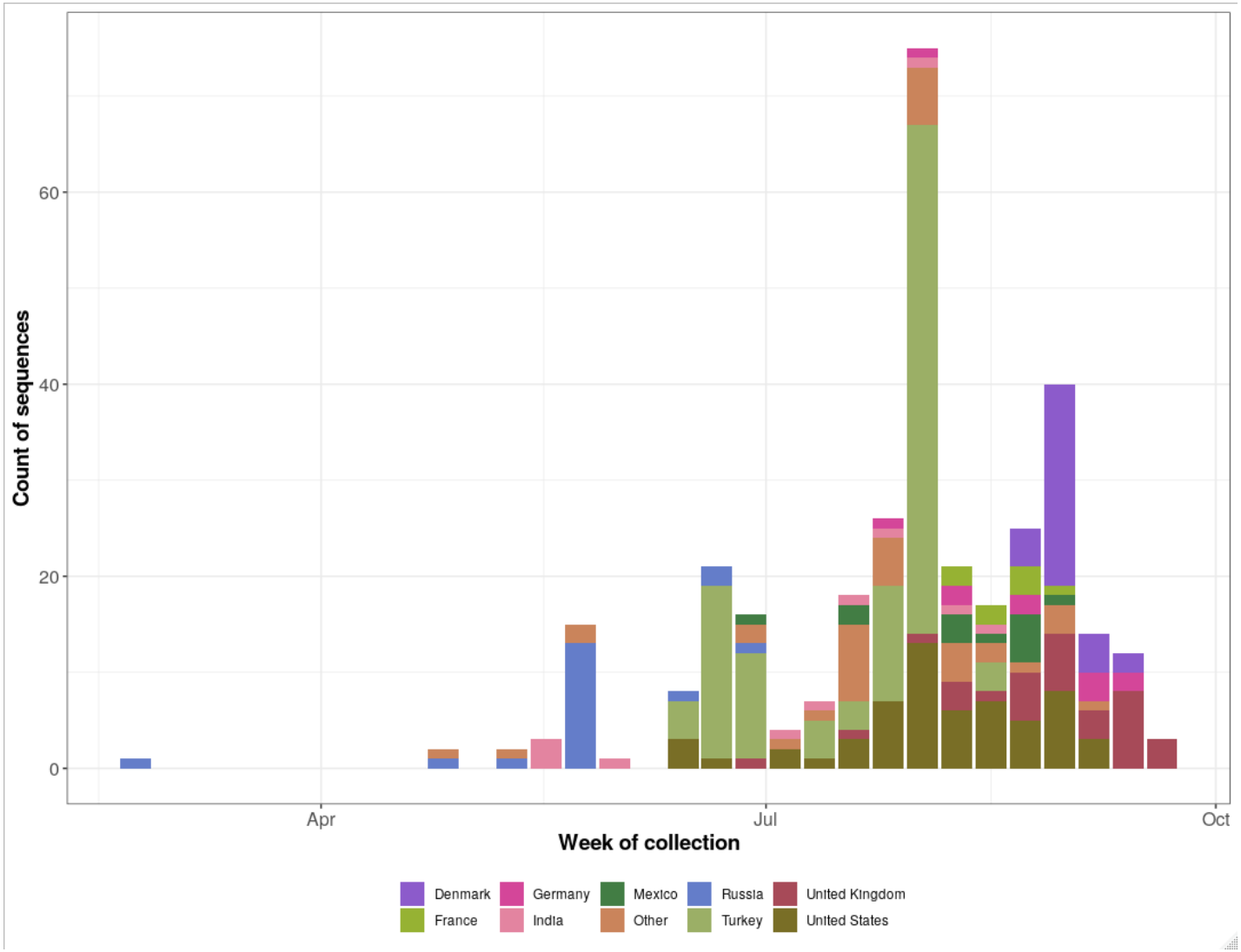
(Find accessible data used in this graph in underlying data.)



International epidemiology

As of 27 September 2021, 345 sequences on GISAID have been assigned to the B.1.617.2 and AY sub-lineages with the additional E484K mutation, of those 332 had appropriate date information. Sequences have been uploaded from Turkey (108), USA (62), Denmark (31), Russia (20), France (16), Mexico (13), Germany (11), India (11), Italy (9), Spain (4), Belgium (3), Netherlands (3), South Africa (2), Sri Lanka (2), Australia (1), Botswana (1), Botswana (1), Canada (1), Ecuador (1), Indonesia (1), Japan (1), Kenya (1), Lebanon (1), Lithuania (1), Luxembourg (1), Malta (1), Mozambique (1), Nigeria (1), Paraguay (1), Poland (1), Portugal (1), Switzerland (1), Ukraine (1). Figure 21 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.

Figure 17. Count of Delta with E484K classified sequences by week of collection uploaded to GISAID by week as of 27 September 2021
Countries with less than 10 sequences have been grouped together as Other.



Sources and acknowledgments

Data sources

Data used in this investigation is derived from the COG-UK dataset, the PHE Second Generation Surveillance System (SGSS), NHS Test and Trace, the Secondary Uses Service (SUS) dataset, Emergency Care Data Set (ECDS), and the PHE Case and Incident Management System (CIMS). Data on international cases are derived from reports in GISAID, the media and information received via the International Health Regulations National Focal Point (IHRNFP) and Early Warning and Response System (EWRS).

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 PHE. 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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