



UK Health
Security
Agency

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

Technical briefing 39

25 March 2022

This report provides an update on previous [briefings](#) up to 11 March 2022

Contents

Summary.....	3
Changes to variant classification system.....	3
Signals from horizon scanning: Recombinant lineages XD, XE, XF.....	4
VUI-22JAN-01 (BA.2)	4
Published information on variants	5
Part 1. Surveillance overview.....	6
1.1 VOC and VUI overview.....	6
1.2 Variant prevalence.....	7
Part 2. Signals from horizon scanning	12
2.1 Newly designated recombinants.....	12
2.2 Epidemiology of XD	13
2.3 Epidemiology of XF	14
2.4 Epidemiology of XE	17
2.5 Growth rate for XE.....	19
Part 3. Enhanced analysis of VUI-22JAN-01 (BA.2)	21
3.1 Genomic diversity	21
3.2 Epidemiology	27
3.3 Growth rates	30
3.4 Hospitalisation	32
3.5 Update on the SARS-CoV-2 Immunity and Reinfection EvaluationN (SIREN) a cohort study in healthcare workers.....	32
3.6 Reinfections.....	35
Part 4. Enhanced analyses of Omicron VOC-21NOV-01 (BA.1).....	36
4.1 Genomic diversity within Omicron VOC-21NOV-01 (BA.1)	36
Sources and acknowledgments	38
Data sources	38
Repository of human and machine-readable genomic case definitions.....	38
Authors of this report.....	38
Variant Technical Group members.....	39
Acknowledgements	40
About the UK Health Security Agency	41

Summary

This report has been published to share the detailed variant surveillance analyses which contribute to the variant risk assessments and designation of new SARS-CoV-2 variants. This specialist technical briefing contains early data and analysis on emerging variants and findings have a high level of uncertainty.

[SARS-CoV-2 Routine variant data update](#) covers surveillance data and sequencing coverage data on all other Variants of Concern (VOCs) and Variants under Investigation (VUIs). Unless stated otherwise, this technical briefing uses a data cut-off of 21 March 2022 to allow time for analyses.

Changes to variant classification system

UK Health Security Agency (UKHSA) is amending its variant classification system to give a clearer indication of which variants have significant changes in biological properties compared to the current dominant variant(s). These variants may pose a risk to public health in the UK, although at the time of identification it may be difficult to predict the extent of the impact.

In the new system, the Variant of Concern label will be assigned to variants which are currently emerging or circulating, and for which we have confirmed or can predict:

- a detrimental change in biological properties (changes in transmissibility, severity or immune evasion) compared to the current dominant variant(s); and
- a growth rate potentially compatible with maintaining transmission and/or displacing the current dominant variant.

There will be no other categorisation of variants, including no variant under investigation category. UKHSA will continue to designate new variants based on genomic features and growth, and these will receive a variant number (V-date-number) and will have routine characterisation analyses once biological materials are available and/or sufficient cases accrue. Previous variants of concern which no longer meet the criteria above will be redesignated.

These changes will take effect as of 1 April 2022 and will be reflected in full in future technical briefings.

Signals from horizon scanning: Recombinant lineages XD, XE, XF

Three recombinant lineages have been designated by Pangolin.

Two are a combination of Delta and BA.1 (XD and XF). XD, which has an Omicron S gene incorporated into a Delta genome, requires biological characterisation. It is present in several European countries but has not been detected in the UK. XF caused a small cluster in the UK but has not been detected since 15 February.

XE is a BA.1/BA.2 recombinant, with the majority of the genome including the S gene belonging to BA.2. XE shows evidence of community transmission within England, although it is currently <1% of total sequenced cases. Early growth rates for XE were not significantly different from BA.2, but using the most recent data up to 16 March 2022, XE has a growth rate 9.8% above that of BA.2. As this estimate has not remained consistent as new data have been added, it cannot yet be interpreted as an estimate of growth advantage for the recombinant. Numbers were too small for the XE recombinant to be analysed by region.

VUI-22JAN-01 (BA.2)

BA.2 rarely contains the spike gene deletion at position 69-70 and is S-gene target positive (SGTP) on diagnostic assays with targets in this area. SGTP is a reasonable proxy for BA.2, which accounts for >99% of sequenced SGTP cases. The proportion of SGTP cases has increased: the overall proportion of SGTP amongst cases tested by the relevant assay in England on 20 March 2022 is 93.7% compared to 82.6% on 6 March 2022. The proportion of BA.2 in sequenced data from 13 March to 20 March 2022 was 88.8%. This is compatible with the known lag in sequence data compared to test data.

Growth rate

BA.2 has demonstrated an increased growth rate compared to BA.1 in all regions of England. Since mid-February, the growth rate has settled at approximately 75% greater relative growth for BA.2 compared to BA.1.

Hospitalisation

Iterated analysis finds no evidence of a greater risk of hospitalisation following infection with BA.2 compared to BA.1.

Update on the SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) in healthcare workers study

In the SIREN study, a large cohort of healthcare workers are tested regularly by polymerase chain reaction (PCR) to detect asymptomatic infection in addition to normal testing practices for symptomatic infection. Updated analysis shows that PCR positivity has started to increase during March 2022. The rate of reinfections per month has decreased slightly since the peak seen at the end of 2021, but the number remains higher than seen before this peak.

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](#).

UKHSA, formerly Public Health England (PHE), has curated a repository from 5 March 2021 containing the up-to-date genomic definitions for all VOCs and VUIs. [The repository is accessible here](#).

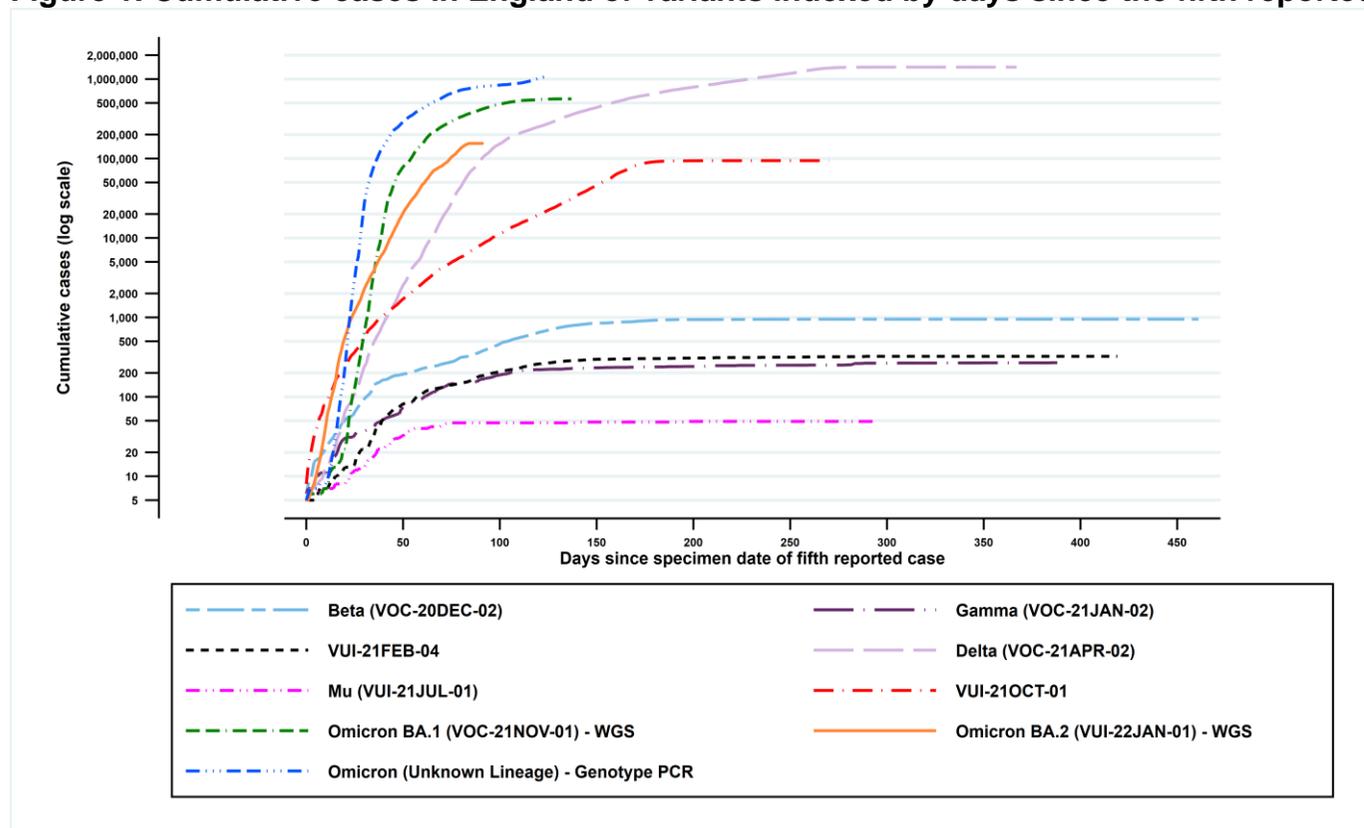
[Technical briefings](#) are published periodically. From technical briefing 15, briefings include variant diagnoses identified by whole-genome sequencing and a genotyping PCR test, including the categorisation of sequenced and genotyped variant results and a rules-based decision algorithm to identify variant and mutation profiles from genotype assay mutation profiles.

Part 1. Surveillance overview

1.1 VOC and VUI overview

[Summary epidemiology for each variant and case numbers](#) are updated online. Figure 1 shows the cumulative number of cases per variant indexed by days since the first report.

Figure 1. Cumulative cases in England of variants indexed by days since the fifth reported case as of 20 March 2022



Find accessible data used in this graph in [underlying data](#).

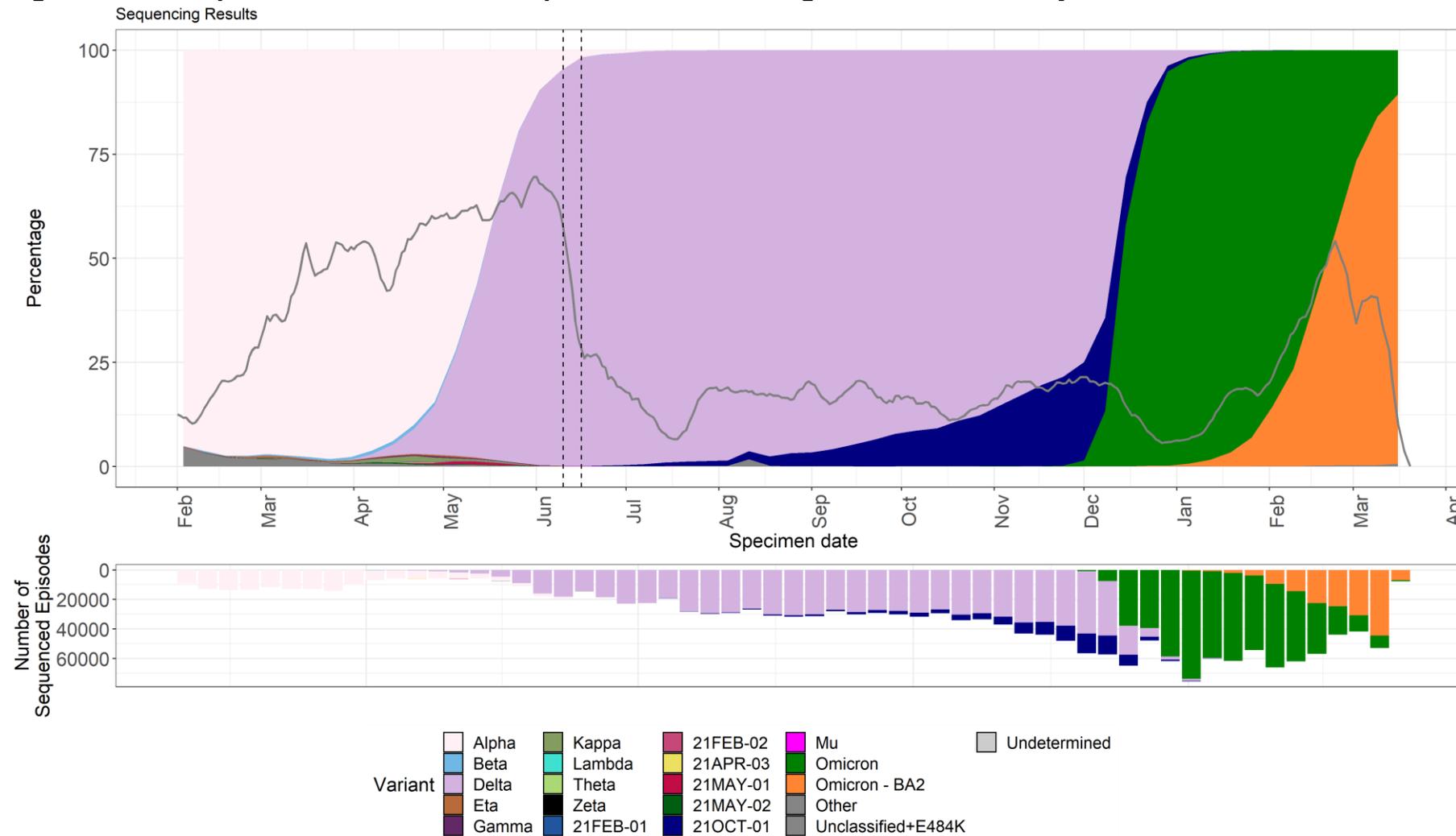
1.2 Variant prevalence

The prevalence of different variants amongst sequenced episodes is presented in Figure 2. Of the sequenced episodes from 13 March to 20 March 2022, 88.8% were Omicron lineage BA.2 (VUI-22JAN-01), 10.5% were Omicron BA.1 (VOC-21NOV-01), and 0.7% were other variants.

The 'Other' category in Figure 2 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.

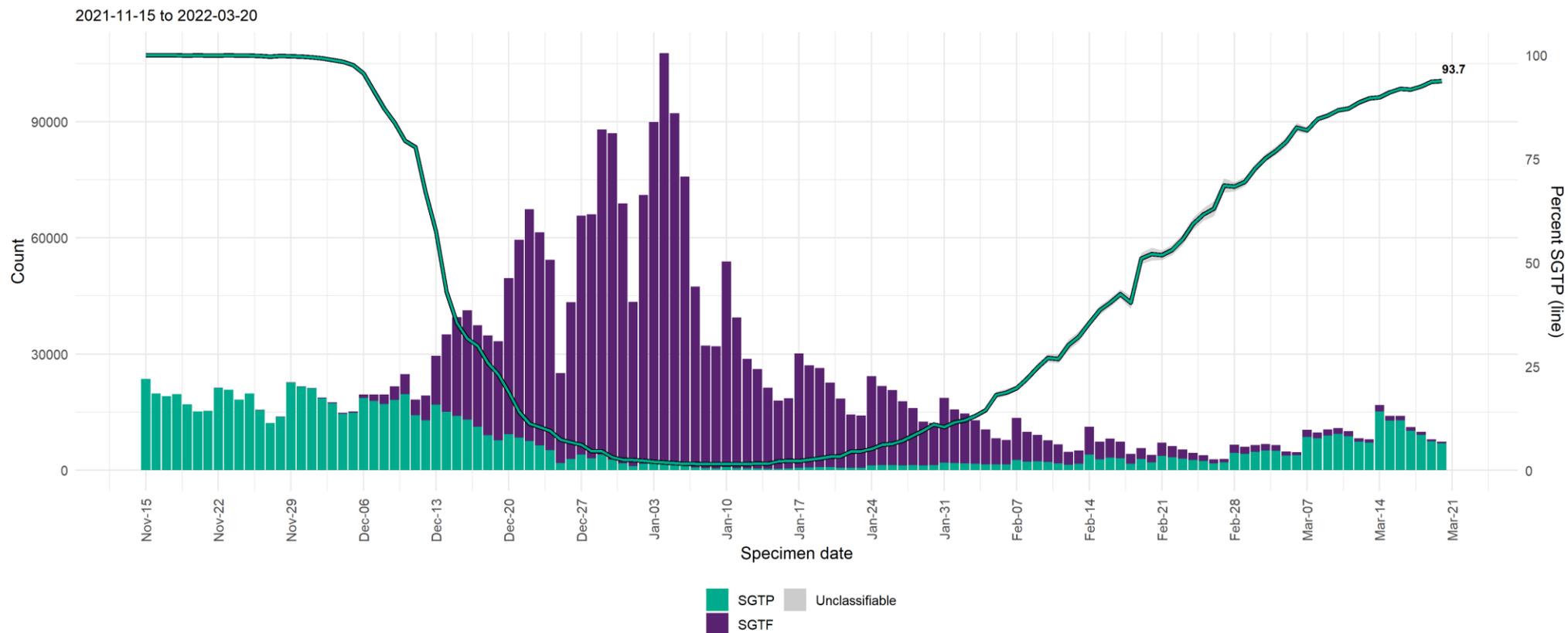
The Omicron genome (lineage BA.1) contains the spike deletion at position 69-70 which is associated with S-gene target failure (SGTF) in some widely used PCR tests. Such PCR tests evaluate the presence of 3 SARS-CoV-2 genes: Spike (S), nucleocapsid (N) and ORF1ab. SGTF is defined as a PCR test where the N and ORF1ab genes are detected (with Ct values less than or equal to 30) but the S-gene is not. SGTF patterns can be used to assess the spread of Omicron lineage BA.1. The Omicron lineage BA.2, VUI-22JAN-01, does not generally contain the spike gene deletion and is S-gene target positive (SGTP). The number of coronavirus (COVID-19) cases with SGTP/SGTF by day, among those tested in TaqPath labs is shown in Figure 3. There is significant variability across the country in SGTF varying from 3.6% in the South East to 8.9% in the East Midlands (Figure 4).

Figure 2. Variant prevalence of available sequenced cases for England from 1 February 2021 as of 22 March 2022



Find accessible data used in this graph in [underlying data](#). Dashed lines indicate period incorporating issue at a sequencing site. Grey line indicates proportion of cases sequenced. Note recombinants such as XE are not specified but are largely within the 'other' group; however this will depend on specific mutations contained within the lineage and how these compare to the variant definitions used within UKHSA.

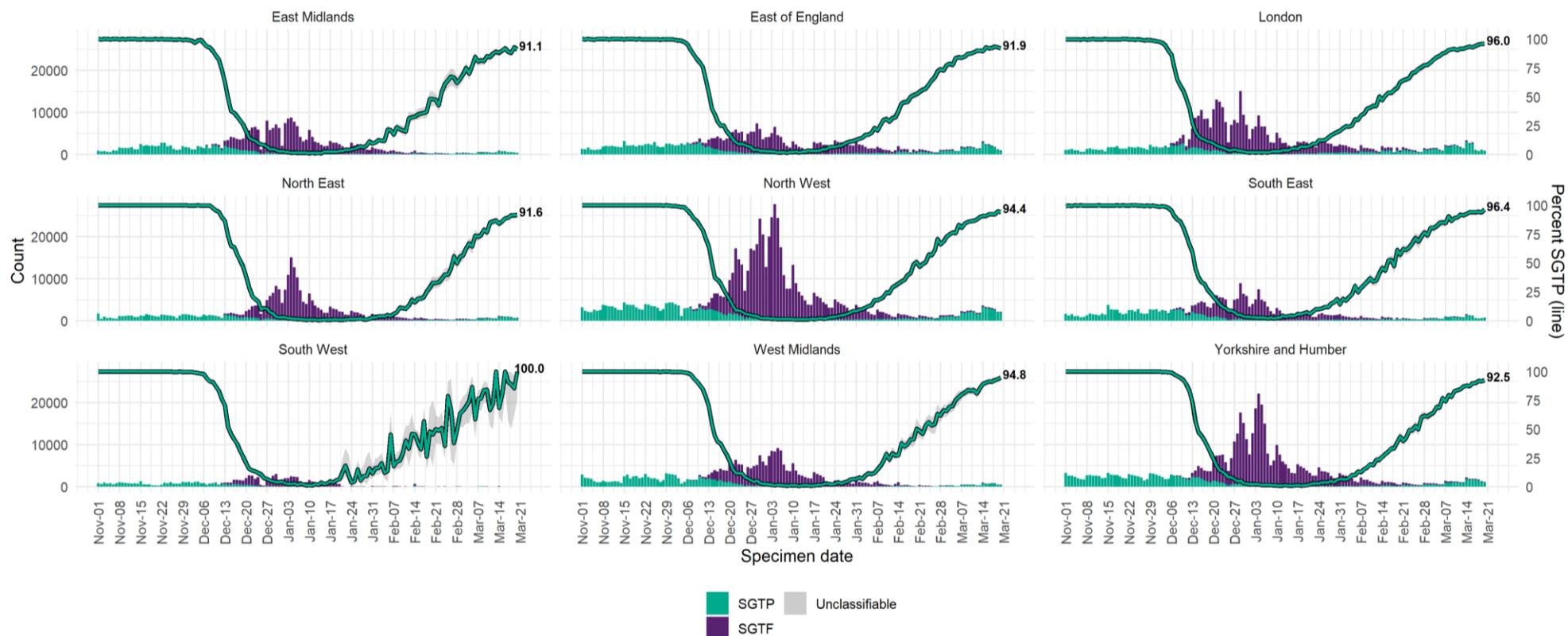
Figure 3. Number of COVID-19 cases with SGTP/SGTF by day, among those tested in TaqPath labs as of 22 March 2022



SGTF (S gene target failure) has been proxy for VOC-21NOV-01 since December 2021. SGTP (S gene target positive) has been a reliable proxy for Omicron BA.2 since January 2022, and before this since April 2021 was a Delta proxy. Local trends in these data may be affected by decisions to direct the processing of samples via a TaqPath laboratory. Only tests carried out with the TaqPath PCR assay and with SGTF or SGTP results included, from Newcastle, Alderley Park, Milton Keynes and Glasgow Lighthouse Labs. SGTF refers to non-detectable S gene target and ≤ 30 CT values for N and ORF1ab gene targets. SGTP refers to ≤ 30 CT values for S, N, and ORF1ab gene targets. Produced by Outbreak Surveillance Team, UKHSA.

Ninety-five percent confidence intervals indicated by grey shading. Percentage for most recent day shown. Find accessible data used in this graph in [underlying data](#).

Figure 4. Number of COVID-19 cases with SGTP/SGTF by day, among those tested in TaqPath labs by region of residence as of 22 March 2022

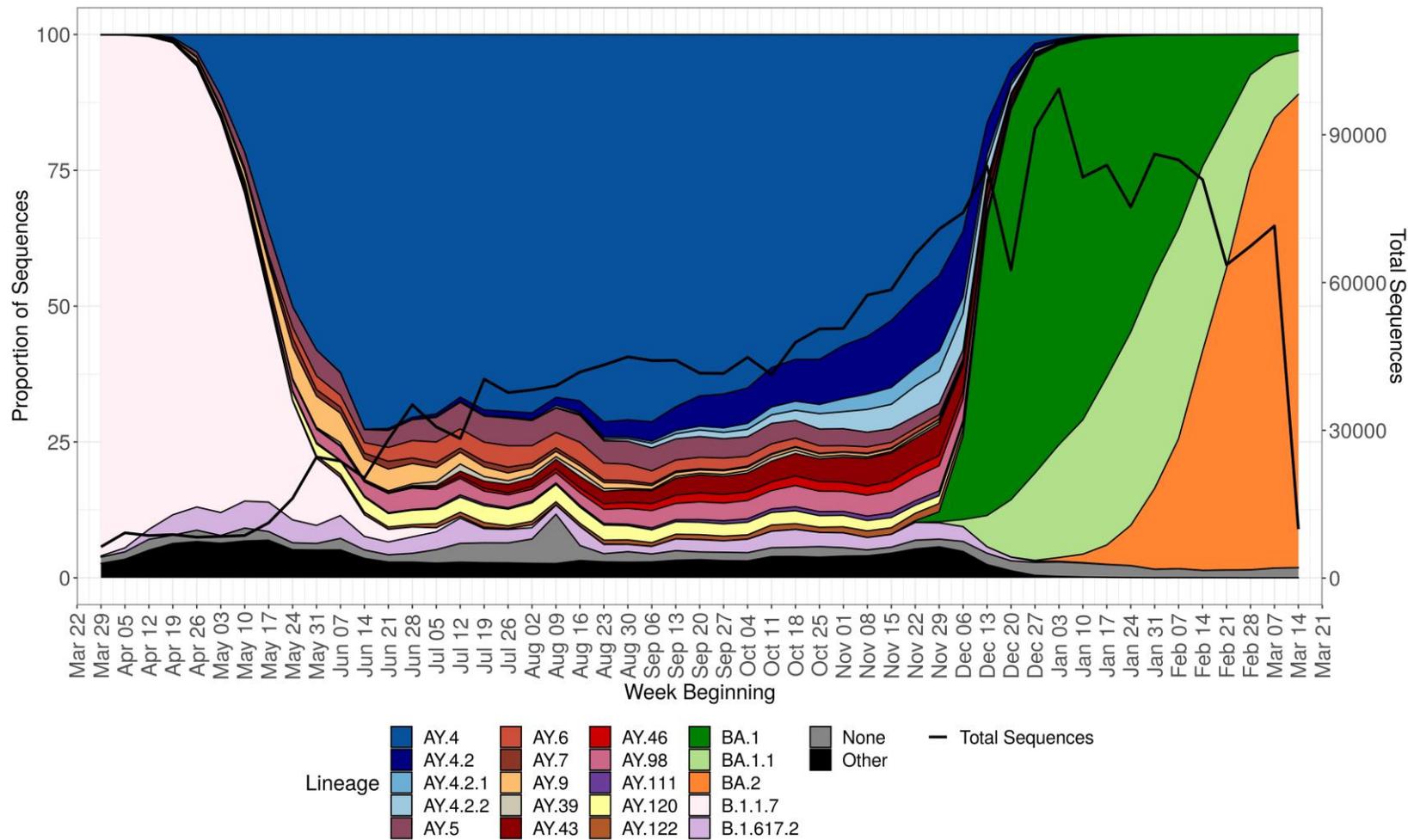


SGTF (S gene target failure) has been proxy for VOC-21NOV-01 since December 2021. SGTP (S gene target positive) has been a reliable proxy for Omicron BA.2 since January 2022, and before this since April 2021 was a Delta proxy. Local trends in these data may be affected by decisions to direct the processing of samples via a TaqPath laboratory. Only tests carried out with the TaqPath PCR assay and with SGTF or SGTP results included, from Newcastle, Alderley Park, Milton Keynes and Glasgow Lighthouse Labs. SGTF refers to non-detectable S gene target and ≤ 30 CT values for N and ORF1ab gene targets. SGTP refers to ≤ 30 CT values for S, N, and ORF1ab gene targets. Produced by Outbreak Surveillance Team, UKHSA.

Ninety-five percent confidence intervals indicated by grey shading. Percentage for most recent day shown.

Find accessible data used in this graph in [underlying data](#).

Figure 5. Prevalence of Pangolin lineages in the United Kingdom (UK) with sequence data from 1 April 2021 to 20 March 2022



The total number of valid sequence results per week is shown by the black line. Only lineages with more than 5,000 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'. Sequences where Pangolin could not assign a lineage due to poor quality data are assigned 'None' in this plot. XE is not currently assigned by Pangolin so these sequences will be included in None on this plot. Find accessible data used in this graph in [underlying data](#).

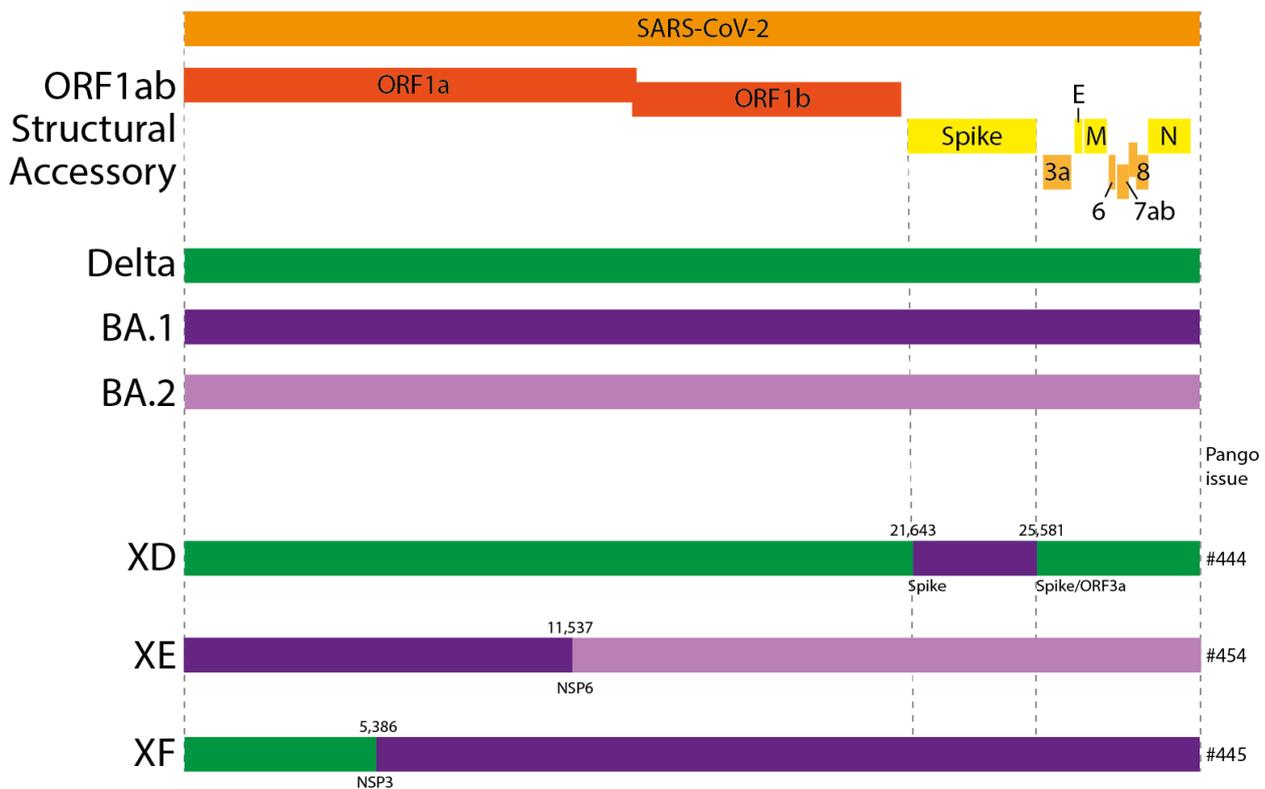
Part 2. Signals from horizon scanning

2.1 Newly designated recombinants

There are currently 3 recombinant lineages being monitored as part of horizon scanning: XD, XE, and XF (Figure 6). XD and XF are Delta and BA.1 recombinants. XE is a BA.1 and BA.2 recombinant and has 3 mutations that are not present in all BA.1 or BA.2 sequences: NSP3 C3241T and V1069I, and NSP12 C14599T. XF and XE are associated with UK sequenced samples. XD is predominantly associated with France. XD contains the unique mutation NSP2: E172D.

Figure 6 shows the SARS-CoV-2 genomes full length (first tier, orange), gene locations across the genome (second tier, dark orange, yellow, and orange). Reference genomes colours: fourth tier Delta (Green), fifth tier BA.1 (purple), and sixth tier BA.2 (lilac). XD, XE and XF are in tiers 7 to 9 are coloured by the associated references, annotated with break points and the gene location of their break points. On the right hand side, the GitHub Pangolin lineage request number is listed.

Figure 6. XD, XE and XF – newly designated recombinant lineages

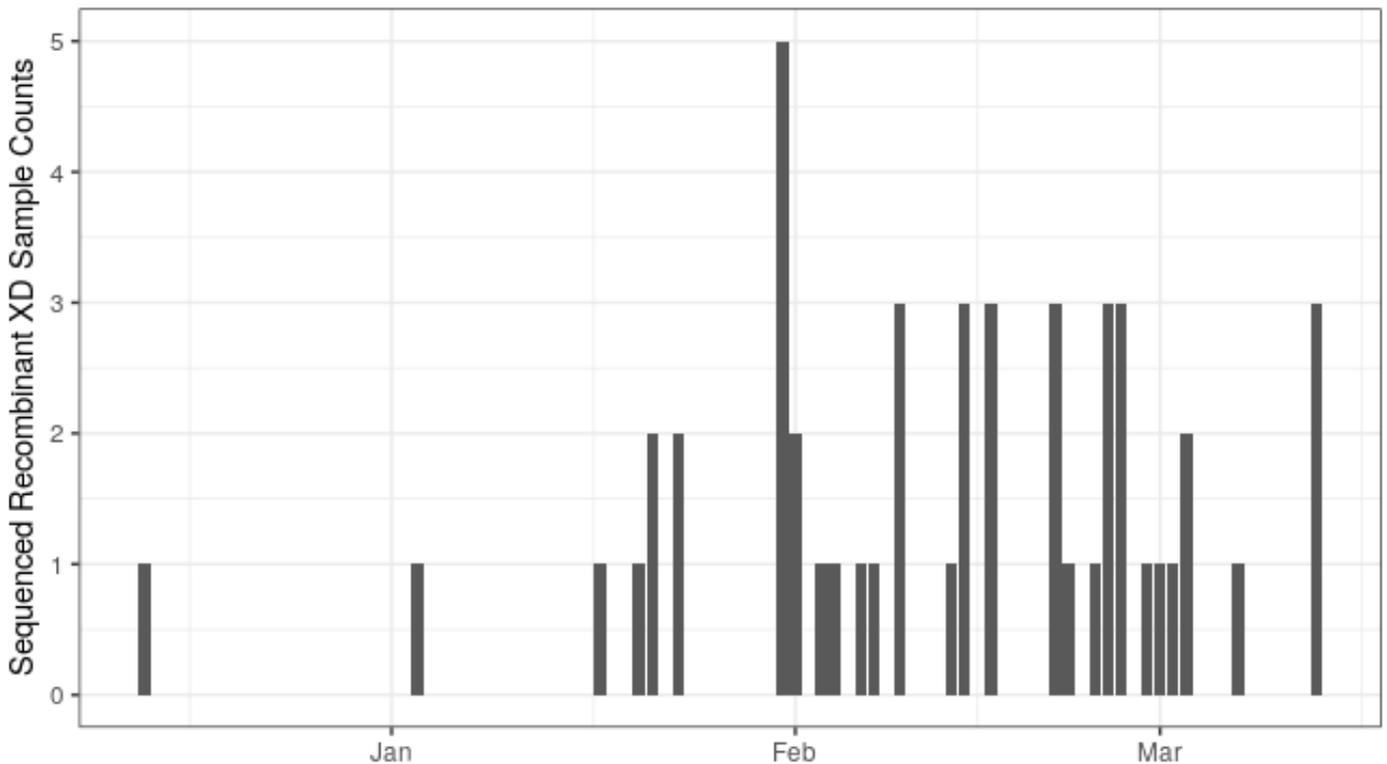


Supplementary data is not available for this figure.

2.2 Epidemiology of XD

The XD recombinant lineage is a Delta AY.4 genome that has acquired a BA.1 spike sequence (nucleotide positions 21,643 to 25,581). As of 22 March 2022, XD has not been detected in the UK. Screening GISAID indicates that there are 49 samples that meet the XD definition and show no signs of contamination. The earliest collection date for these samples is the 13 December 2021 and the most recent collection date is 13 March 2022 (Figure 7). Forty samples have been identified from France, 8 from Denmark, and 1 from Belgium (Table 1).

Figure 7. Sample collection date distribution for XD samples identified in GISAID



Find accessible data used in this graph in [underlying data](#).

Table 1. Summary of geographic distribution of sequenced samples for the XD recombinant in GISAID

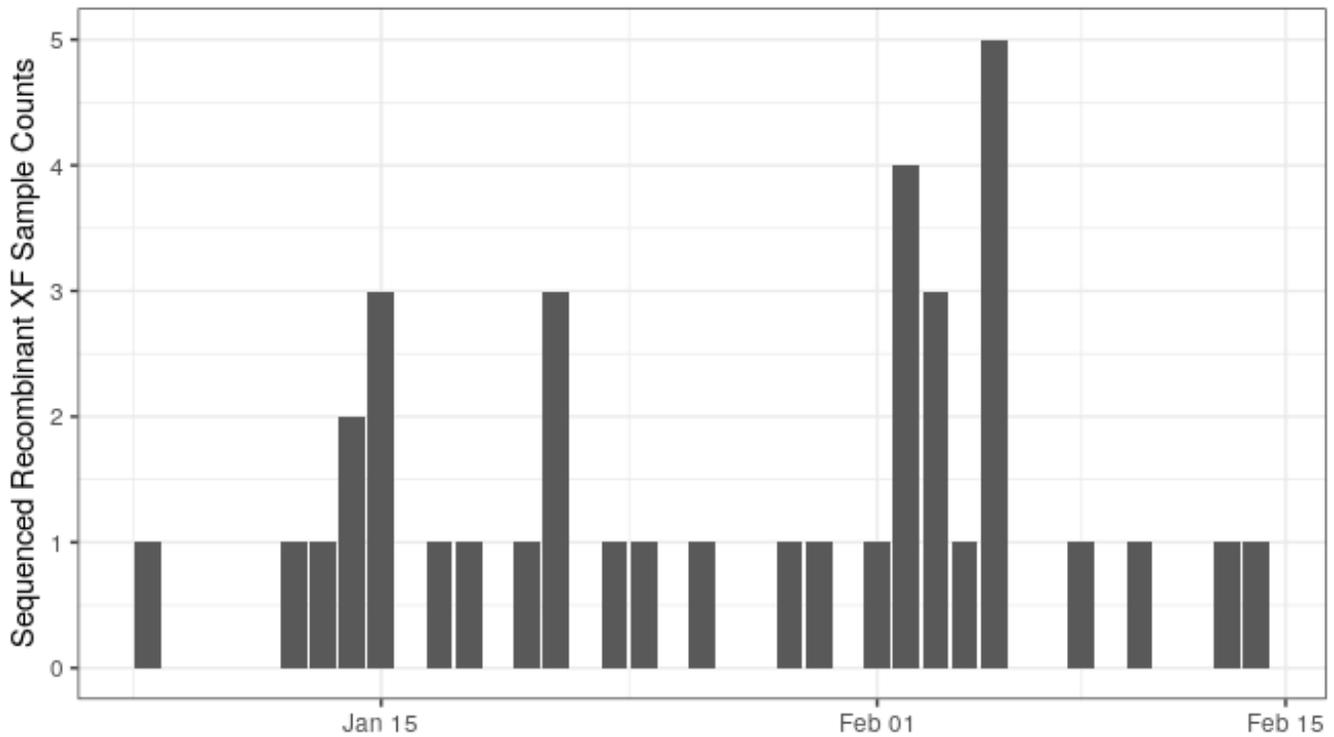
Country	Region	Samples
Belgium	Hainaut	1
Denmark	Hovedstaden	1
	Sjaelland	7
France	Auvergne-Rhone-Alpes	8
	Bourgogne-Franche-Comte	1
	Bretagne	1
	Grand Est	3
	Hauts-de-France	18
	Ile-de-France	2
	Normandie	3
	Occitanie	1
	Provence-Alpes-Cote d'Azur	3

2.3 Epidemiology of XF

The XF lineage is a recombinant of Delta and BA.1 with a break point near the end of NSP3 (nucleotide 5,386).

In total 39 UK sequenced samples were identified and validated as part of the XF recombinant lineage. The earliest known sample date in the UK dataset is 7 January 2022 and the most recent sample to date is 14 February 2022 with no recent evidence for growth (Figure 8). Given the lack of evidence for recent UK samples from this lineage it is unlikely to be associated with sustained community growth. There is currently no evidence for samples from non-UK countries on GISAID for this lineage.

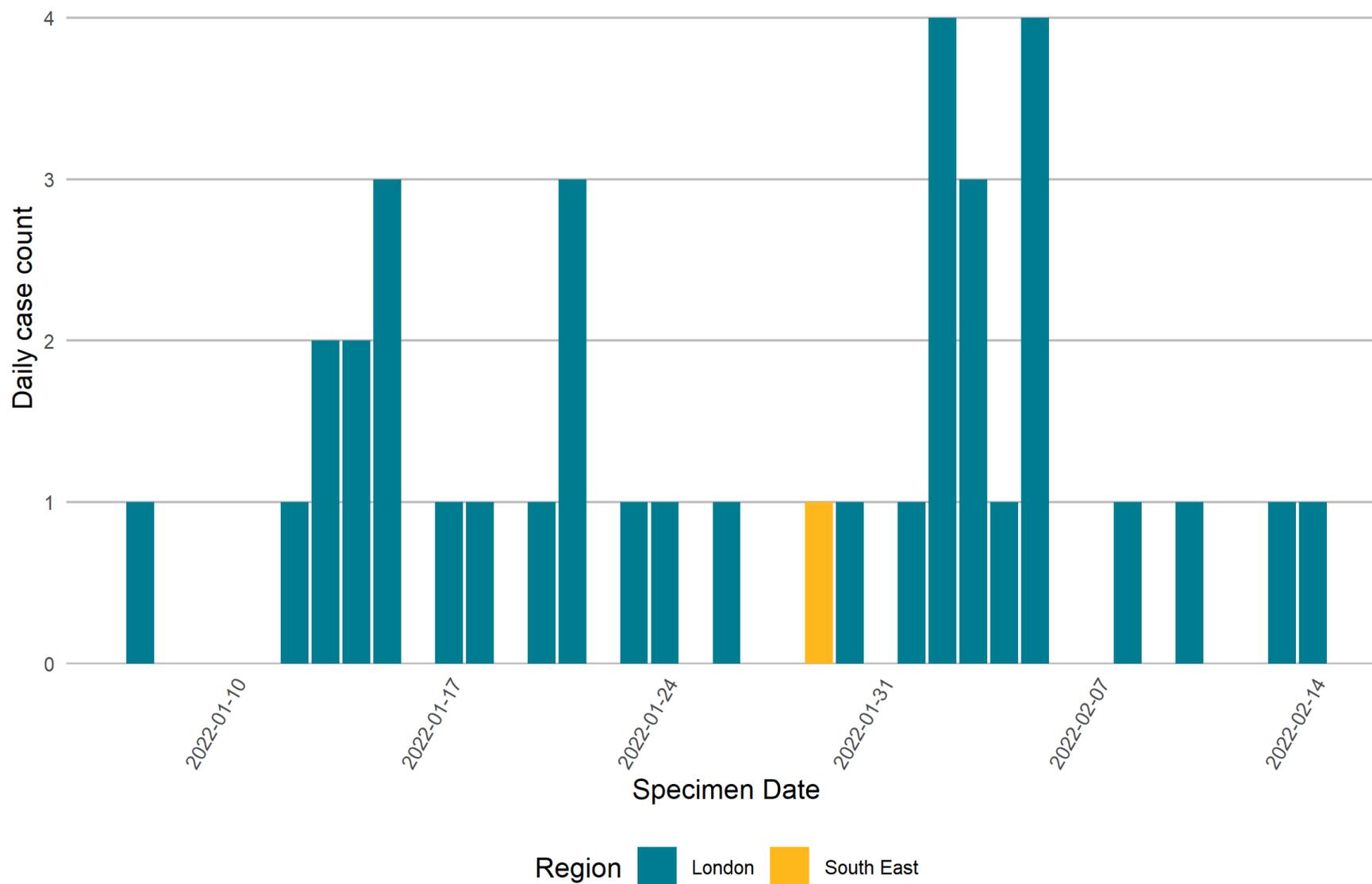
Figure 8. UK Sequenced sample counts for Delta and BA.1 recombinant over time



Find accessible data used in this graph in [underlying data](#).

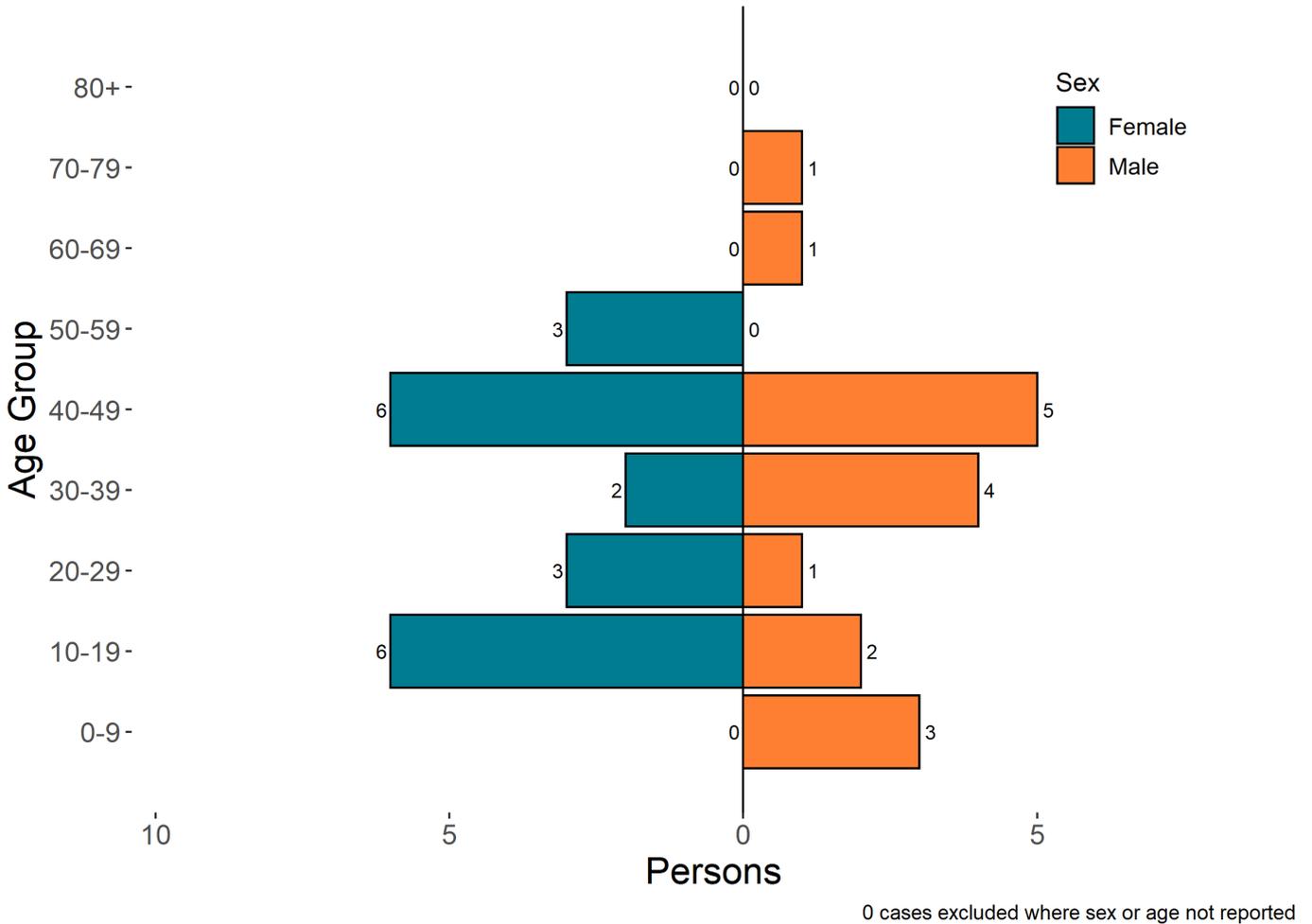
Thirty-seven cases with the XF recombinant have been detected with specimen dates since 7 January 2022 (Figure 9). Of these, 36 are London residents, who live across 19 different local authorities.

Figure 9. Epicurve of recombinant XF cases in England by region of residence – data as of 22 March 2022



Find accessible data used in this graph in [underlying data](#).

Figure 10. Age-sex pyramid of recombinant XF cases in England – data as of 22 March 2022

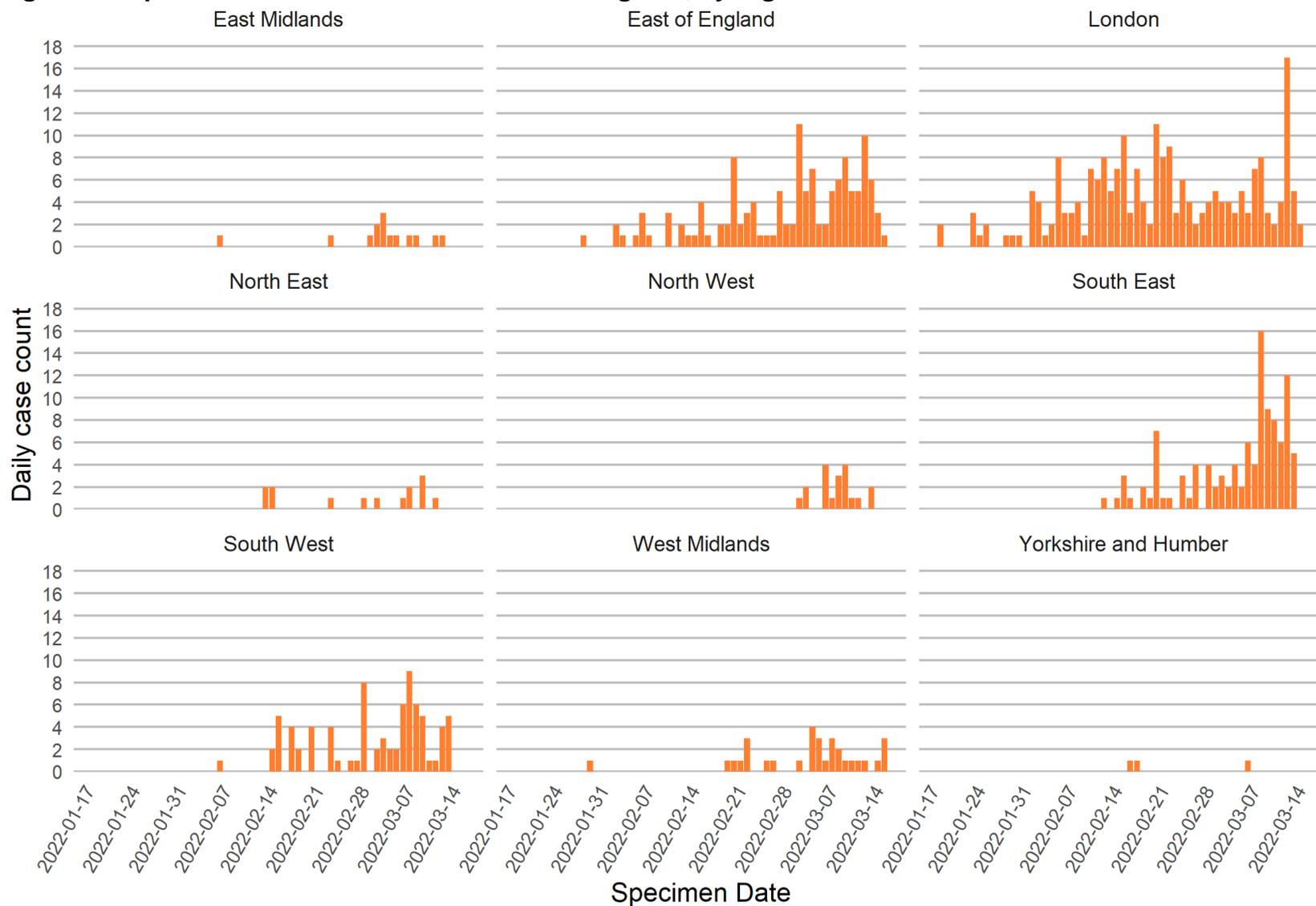


Find accessible data used in this graph in [underlying data](#).

2.4 Epidemiology of XE

The XE recombinant contains BA.1 mutations for NSP1-6 and then BA.2 mutations for the remainder of the genome. As of 22 March 2022, there are 763 XE sequences in the UK data. As of 22 March 2022, there are 637 XE cases in England. These are geographically distributed across England and increasing in number, with the first case detected via sequencing on 19 January 2022, and most cases in East of England, London, and the South East (Figure 11).

Figure 11. Epicurve of recombinant XE cases in England, by region of residence – data as of 22 March 2022



Find accessible data used in this graph in [underlying data](#). Fifteen cases not included due to missing geography.

2.5 Growth rate for XE

The growth rate of a novel variant is calculated relative to a matched control. Matched controls are samples of other circulating variants selected from the same time and location. For XE, genomes identified as XE using a draft mutation-based definition are compared to co-circulating BA.2 only

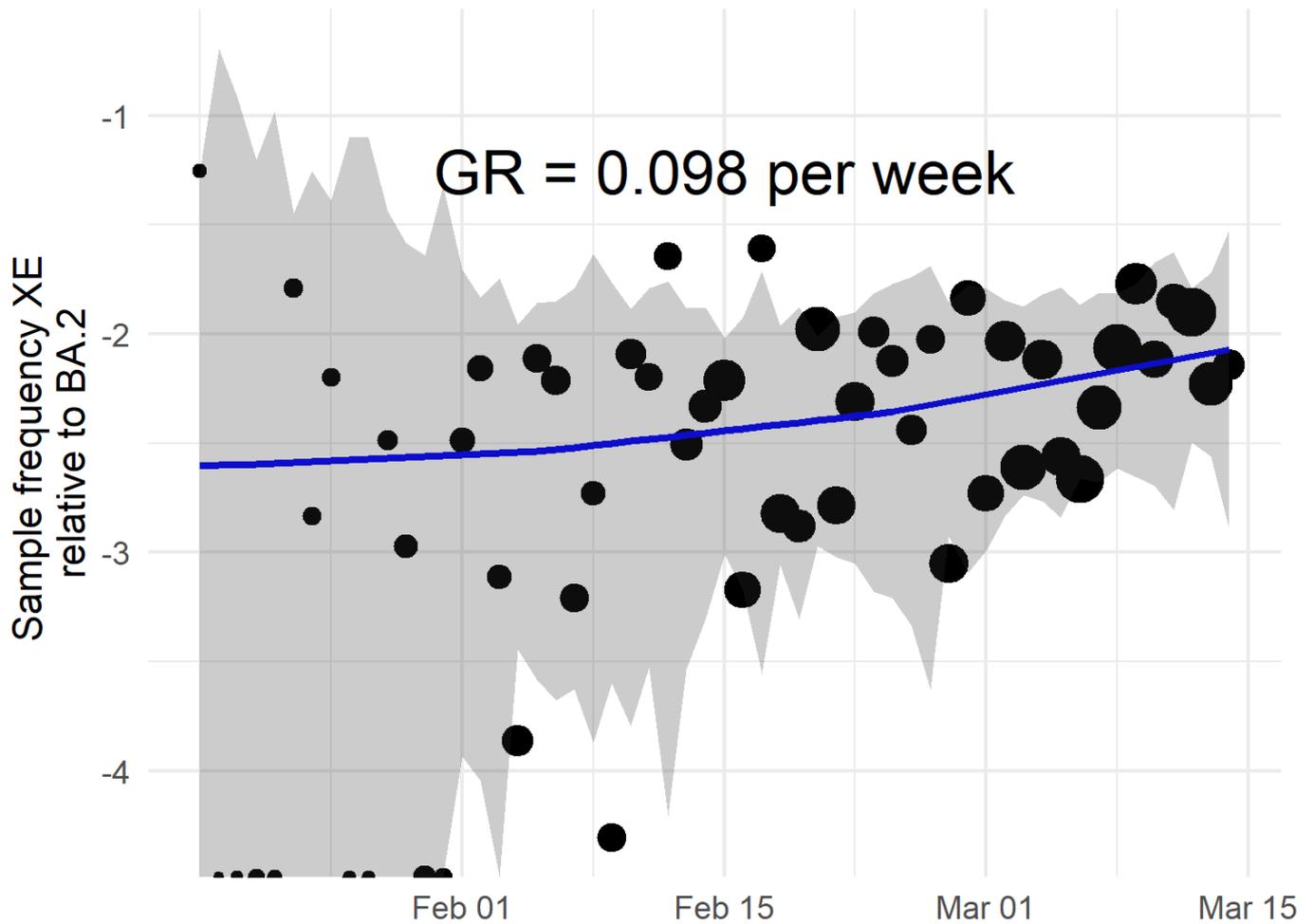
We run a statistical model to calculate the probability of a sampled genome being from the novel variant vs from the control over time. Growth rates are calculated per week or per day and are expressed on a log scale. A logistic growth rate of 0.5 per week indicates that the variant is increasing by a multiplicative factor of $\exp(0.5) = 1.65$ per week in comparison to the control. A logistic growth rate of zero would indicate no difference in growth rates between the 2 variants.

Using a control adjusts for geographic and temporal variation in case numbers, but despite these adjustments, differences in growth rates can be due to epidemiological factors such as founder effects and sampling, especially early on. Over time, the growth rate of a variant will converge towards an estimate of the variant's inherent transmissibility in comparison to other circulating variants.

The growth rate is estimated by logistic regression of the number of genomes sampled with the XE and BA.2 lineages on time of sample collection. Only Pillar 2 testing (community testing) samples are included. To adjust for geographic variation in case growth rates, XE growth rates were estimated relative to a geographically matched sample of BA.2 genomes.

Data sampled between 15 January 2021 and 15 March 2022 were included. The relative frequency of genomes from the BA.2 lineage is shown in Figure 12. The median growth rate is +9.8% per week. Numbers were too small for the XE recombinant to be analysed by region.

Figure 12. Sample frequency of XE relative to Omicron (BA.2) over time sampled through Pillar 2 testing



Supplementary data is not available for this figure.

Part 3. Enhanced analysis of VUI-22JAN-01 (BA.2)

The mutation profile of the Omicron sub-lineages was previously reported in [Technical Briefing 31](#).

BA.2 was designated VUI-22JAN-01 (BA.2) by the UKHSA Variant Technical Group on 19 January 2022.

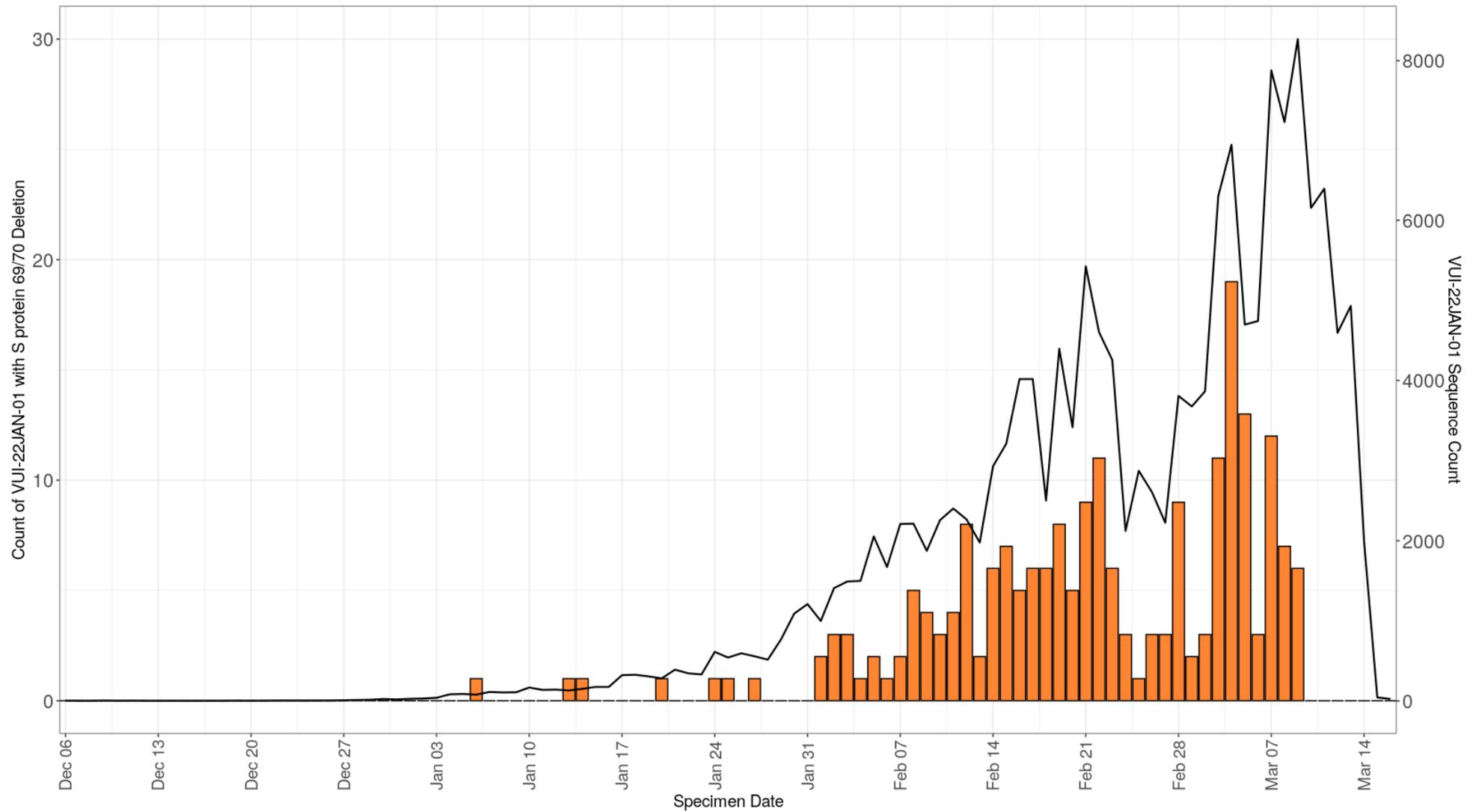
3.1 Genomic diversity

S-gene 69/70 deletion

Currently, SGTF is a suitable proxy for the VOC-21NOV-01 (BA.1) variant due to the deletion of amino acids at position 69 and 70 of the S protein for laboratories using the specific assays. The deletion is not present in VUI-22JAN-01 (BA.2) definition, although recently a number of VUI-22JAN-01 (BA.2) sequences containing the deletion have been identified. As of 2 March 2022, a total of 244 VUI-22JAN-01 (BA.2) sequences were detected with the deletion in the UK genome data, out of a total of 188,947 confirmed or probable VUI-22JAN-01 (BA.2) sequences.

This represents 0.13% of the VUI-22JAN-01 (BA.2) sequences. A graph of English sequences, where specimen date is available is shown in Figure 13. The frequency of detections of VUI-22JAN-01 (BA.2) sequences with 69/70 deletion tracks the total number of sequences available. When analysed phylogenetically, these comprise one main phylogenetic cluster and a number of individual sequences which do not cluster together. The correlation between the S-gene target results, deletion and Omicron lineages will be monitored. The 244 sequences are from 205 cases, who are distributed across England but most concentrated in the East Midlands, East of England, and the South East.

Figure 13. Daily count of confirmed VUI-22JAN-01 (BA.2) sequences in England containing S-gene 69/70 deletion that can be called (bar), alongside the number of England VUI-22-JAN-01 sequences (line), where specimen dates are available



Find accessible data used in this graph in [underlying data](#).

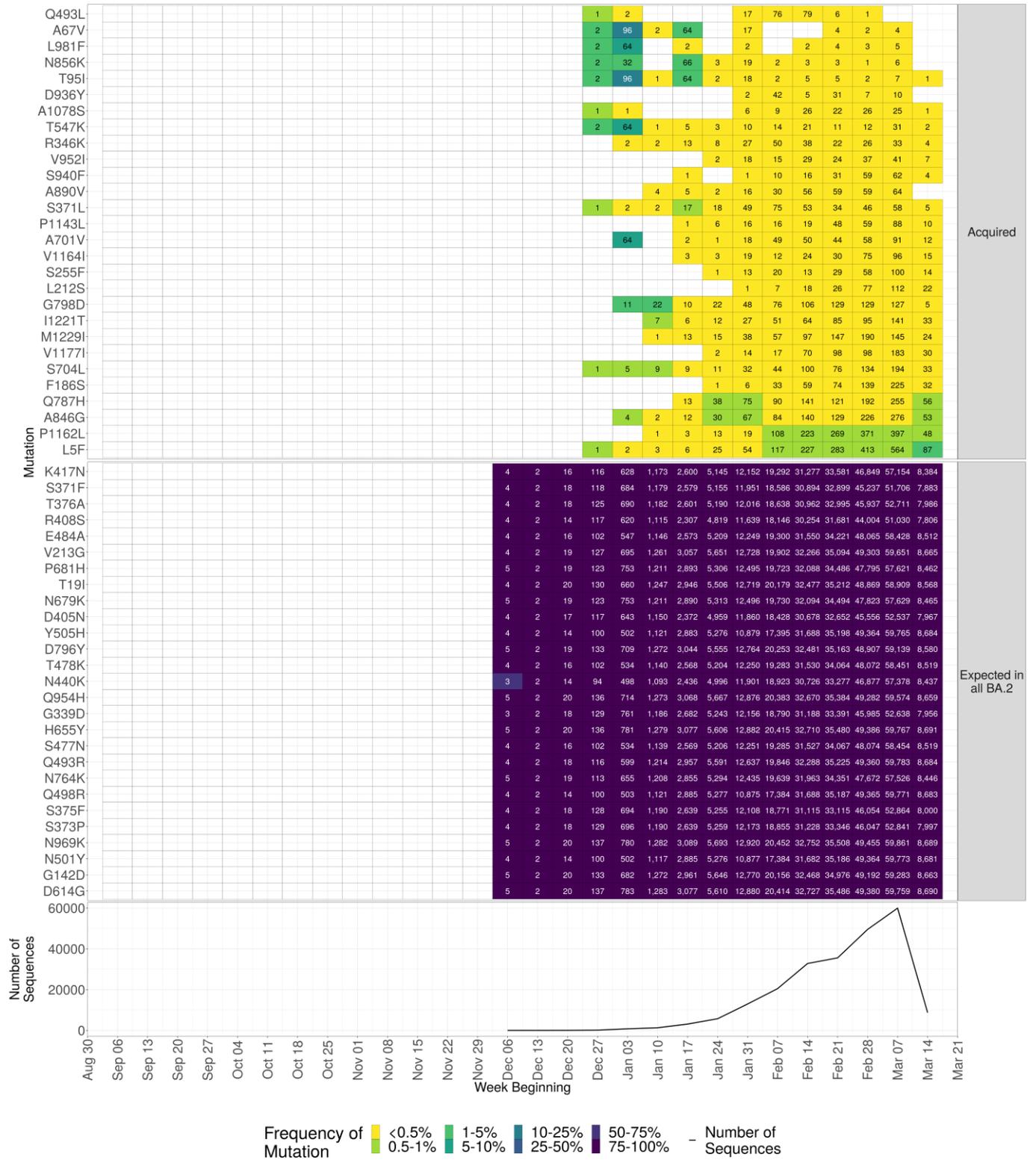
Diversity in Spike

Spike mutations are monitored within BA.2 using 4 criteria (Table 2). A mutation is investigated further if it meets more than one of these criteria and is present in at least 10 sequences. Twenty-eight additional mutations have been observed in BA.2 sequences according to the criteria in Table 2 (Figure 14). The criteria for mutation monitoring are currently being reviewed and amended.

Table 2. Criteria used to assess emerging mutations

Criteria	Threshold
Cumulative count	Running total for the number of sequences containing mutation is at least 50
Proportion	1% of sequences classified as this variant contain this mutation within a single week
Difference in proportion	The difference in the proportion of sequences in 2 consecutive weeks is at least 0.25%
Percentage change in the number of sequences	The percentage change between the number of sequences containing the mutation in 2 consecutive weeks is at least 5%

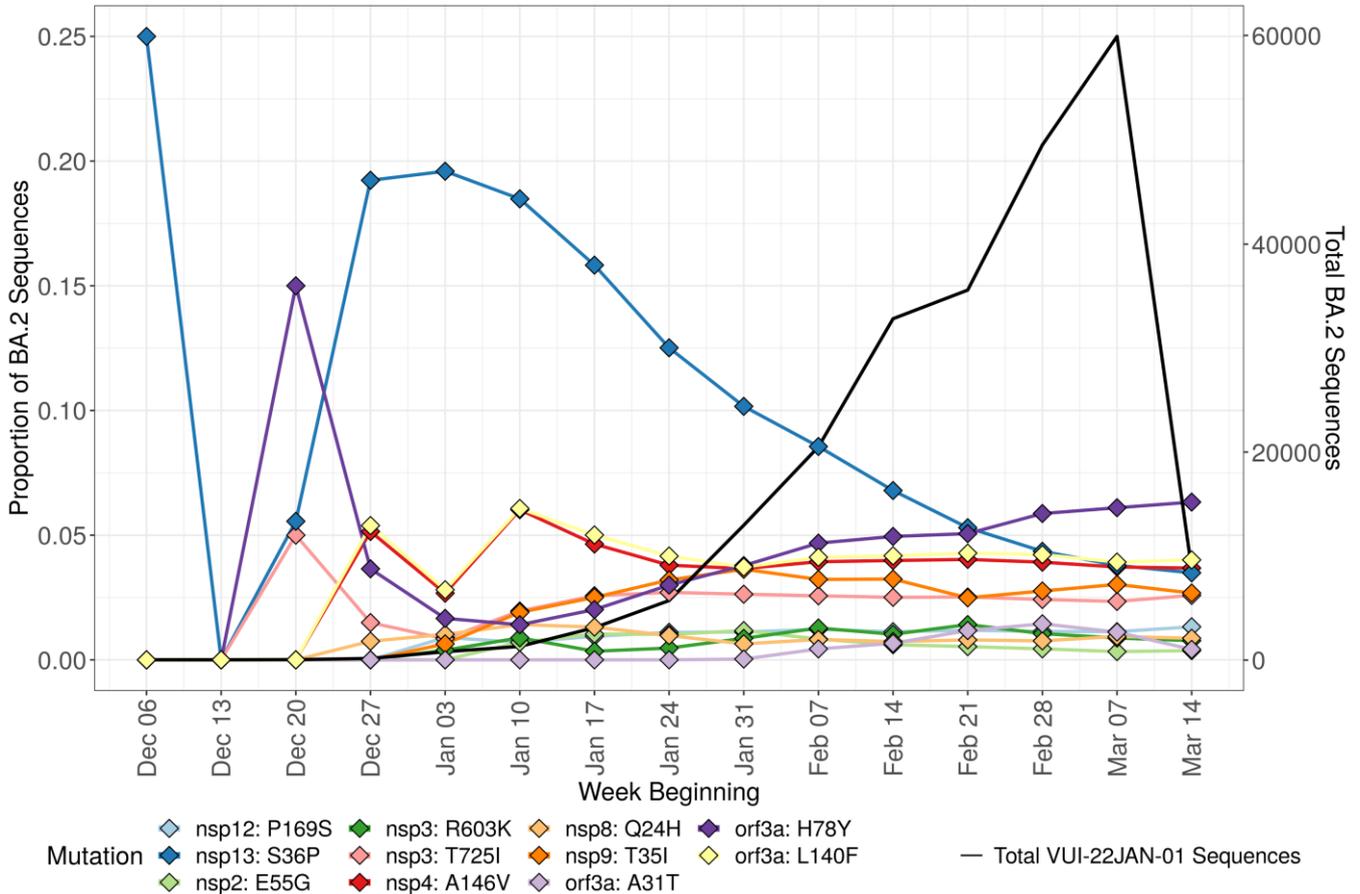
Figure 14. Spike mutations found in BA.2 genomes in the UK dataset relative to the Wuhan sequence NC_045512.2 between 8 November 2021 and 21 March 2022



Supplementary data is not available for this figure. It should be noted all mutations in the sequence alignment are reported in these plots for review purposes.

Outside of Spike, there are 11 mutations that are present in at least 1% of BA.2 sequences for 3 consecutive weeks (Figure 15). One of these (nsp13: S36P) has been declining since December 2021.

Figure 15. Proportion of sequences containing mutations found in BA.2 genomes that are present in at least 1% of sequence for 3 consecutive weeks in the UK dataset relative to the Wuhan sequence NC_045512.2 between 6 December 2021 and 21 March 2022



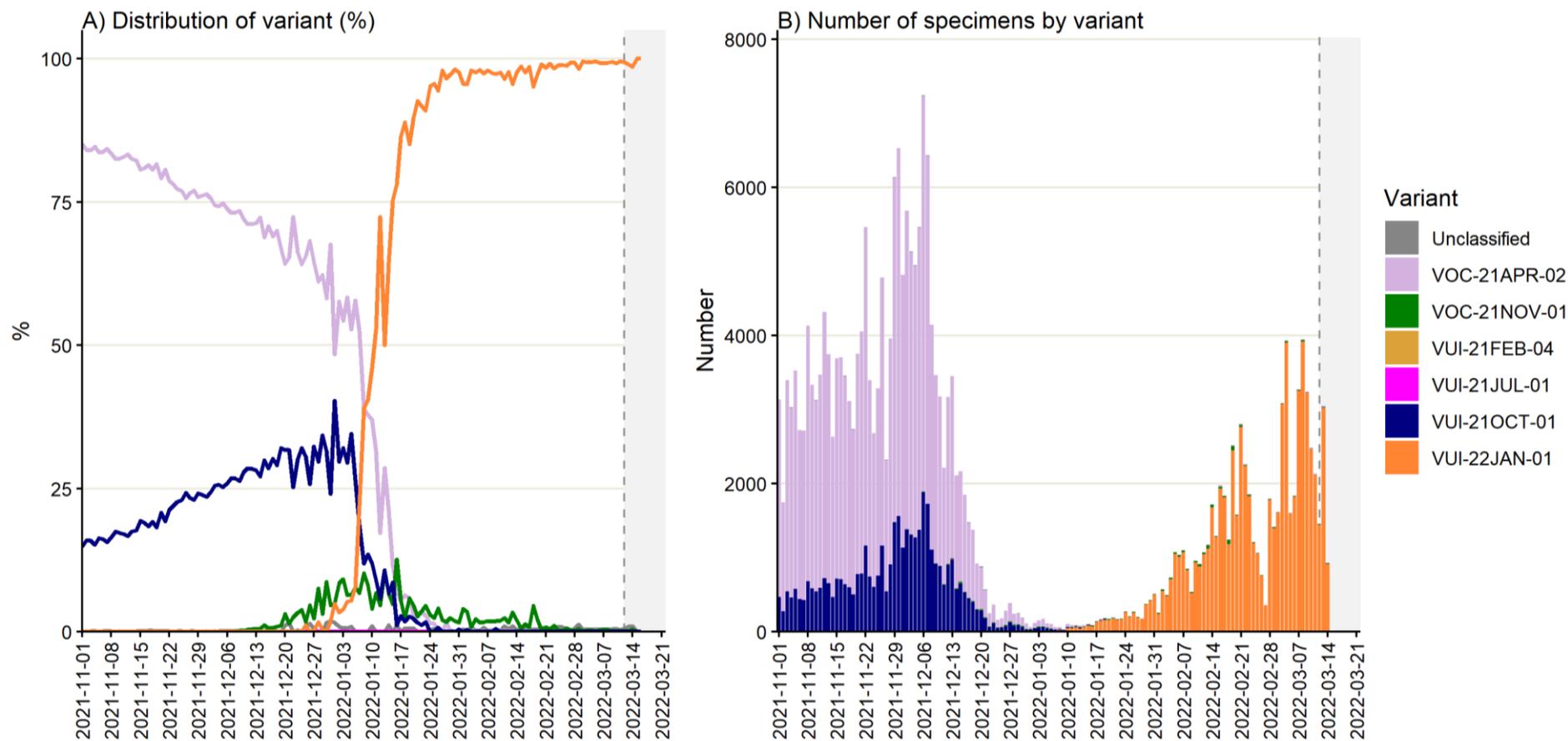
The total number of BA.2 mutations per week are indicated by the black line. (Find accessible data used in this graph in [underlying data](#).)

Epidemiology of SGTP

The Omicron sub-lineage VUI-22JAN-01 (BA.2) rarely contains the spike deletion and therefore is SGTP. VUI-22JAN-01 (BA.2) has accounted for more than 95% of sequenced SGTP from 27 January to 16 March 2022.

Figure 16. Number and distribution of variants per week among sequenced SGTP specimens as of 22 March 2022

Specimen dates within last 11 days shaded in gray due to associated reporting delay; 10 days is median turn-around-time for sequencing.



Source: SGSS and COG-UK sequencing data, restricted to sequenced positive S-gene positive tests from Newcastle, Alderley Park, Glasgow, and Milton Keynes Lighthouse Laboratories. S gene +ve defined as positive SARS-CoV-2 test with CT values ≤ 30 for S, N, and ORF1ab.

Find accessible data used in this graph in [underlying data](#).

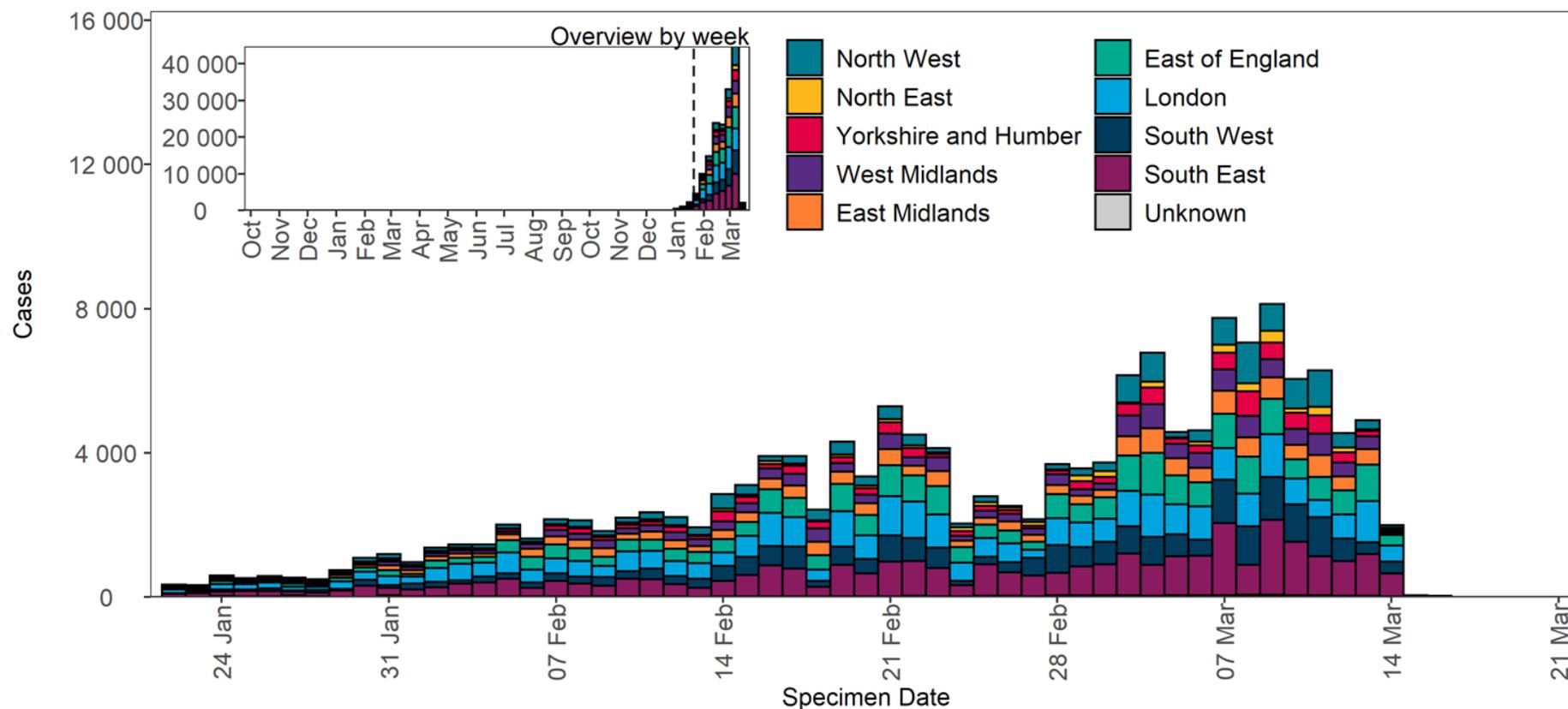
3.2 Epidemiology

As of 22 March 2022, 160,351 sequences of VUI-22JAN-01 (BA.2) have been identified in England. As VUI-22JAN-01 (BA.2) is designated by sequencing only, there is a known time lag of 11 days (interquartile range: 9 to 18) from obtaining a sample to reporting of VUI-22JAN-01 (BA.2) as the cause of infection. This will be reflected in case numbers presented.

Table 3. Number of confirmed VUI-22JAN-01 (BA.2) cases, by region of residence as of 22 March 2022

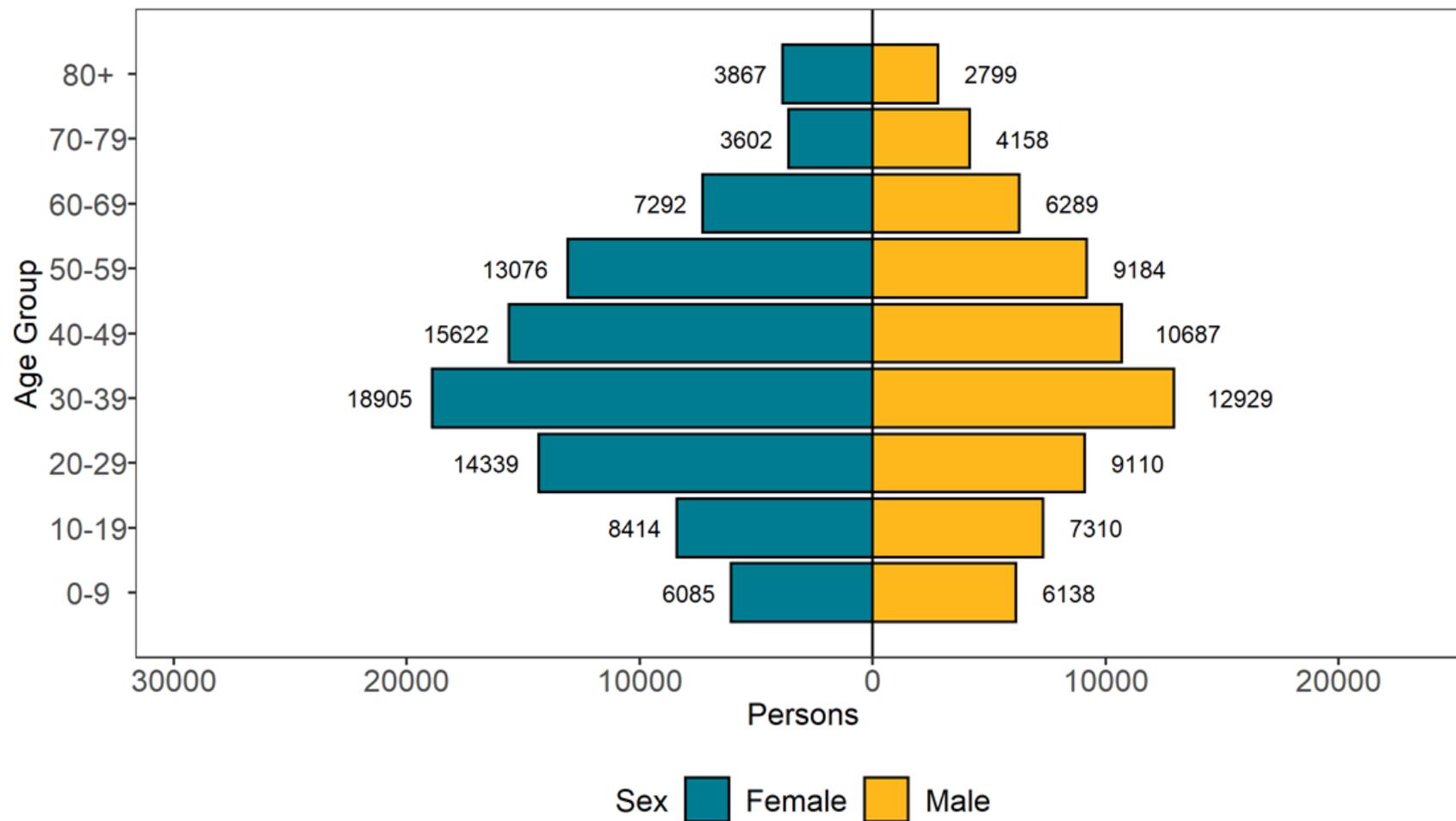
Region	Total case number	Case proportion
East Midlands	13,688	8.5%
East of England	23,616	14.7%
London	29,734	18.5%
North East	3,630	2.3%
North West	13,333	8.3%
South East	33,225	20.7%
South West	20,867	13.0%
West Midlands	12,395	7.7%
Yorkshire and Humber	8,698	5.4%
Unknown region	1,165	0.7%
Total	160,351	-

Figure 17. Confirmed VUI-22JAN-01 (BA.2) cases by specimen date and region of residence as of 22 March 2022



Find accessible data used in this graph in [underlying data](#).

Figure 18. Age-sex pyramid of VUI-22JAN-01 (BA.2) cases as of 22 March 2022



527 cases excluded where sex or age not reported

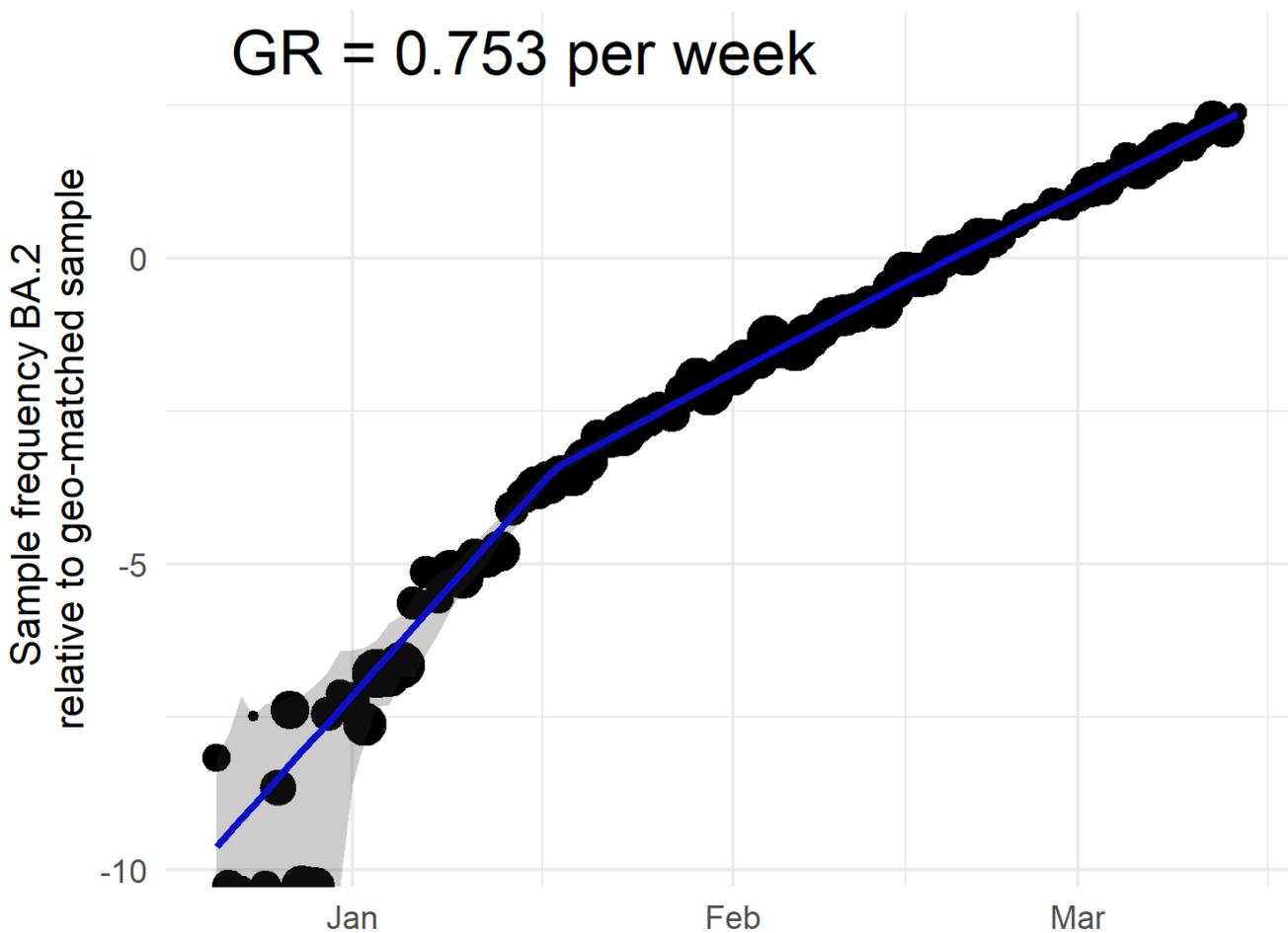
Find accessible data used in this graph in [underlying data](#).

3.3 Growth rates

The growth rate is estimated by logistic regression of the number of genomes sampled with the BA.1 and BA.2 lineages on time of sample collection. Only Pillar 2 testing (community testing) samples are included. To adjust for geographic variation in case growth rates, BA.2 growth rates were estimated relative to a geographically matched sample of BA.1 genomes.

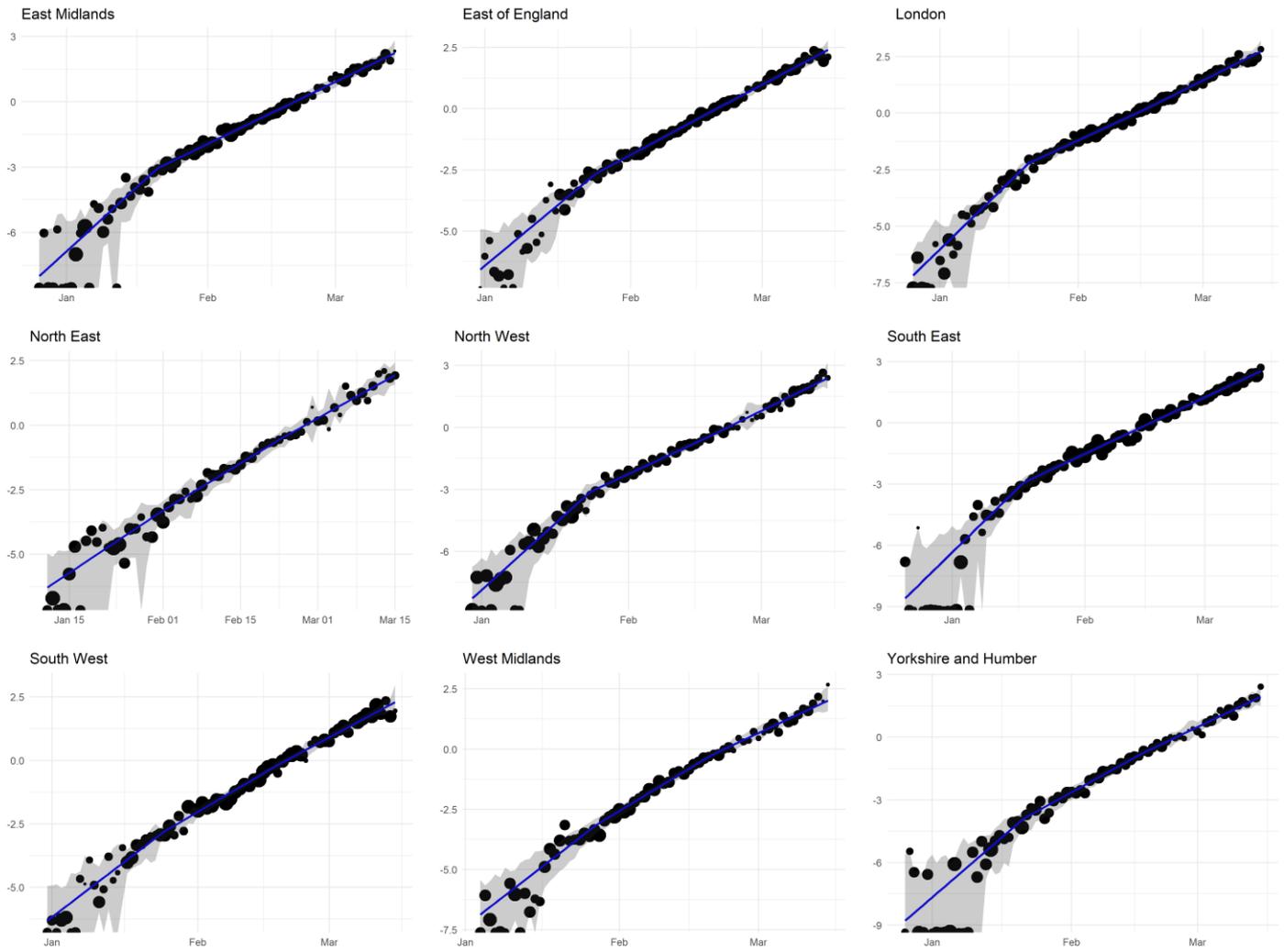
Data sampled between 15 December 2021 and 15 March 2022 were included. The relative frequency of genomes from the BA.2 lineage is shown in Figure 19. The median growth rate is +75.3% per week. The analysis was repeated on data from each region of England and is shown in Figure 20. Current logistic growth rates are consistent across regions, ranging from 67% to 83% per week.

Figure 19. Sample frequency of VUI-22JAN-01 (BA.2) relative to Omicron (BA.1) over time



Supplementary data is not available for this figure.

Figure 20. Sample frequency of VUI-22JAN-01 (BA.2) relative to Omicron (BA.1) over time in regions of England sampled through Pillar 2 testing



Supplementary data is not available for this figure.

3.4 Hospitalisation

Analyses of sequenced cases up to 8 March 2022 have been undertaken to compare the risk of hospitalisation, as defined by admission as an inpatient, or presentation to emergency care that resulted in admission, transfer or death, following BA.2 compared to BA.1. This analysis adjusted for age, reinfection status, sex, ethnicity, local area deprivation and vaccination status. It also controlled for the effect of geography and specimen date. The risk of hospitalisation does not appear to be higher following a BA.2 infection than following a BA.1 infection (hazard ratio 0.94 95% CI: 0.88-1.00).

3.5 Update on the SARS-CoV-2 Immunity and Reinfection EvaluationN (SIREN) a cohort study in healthcare workers

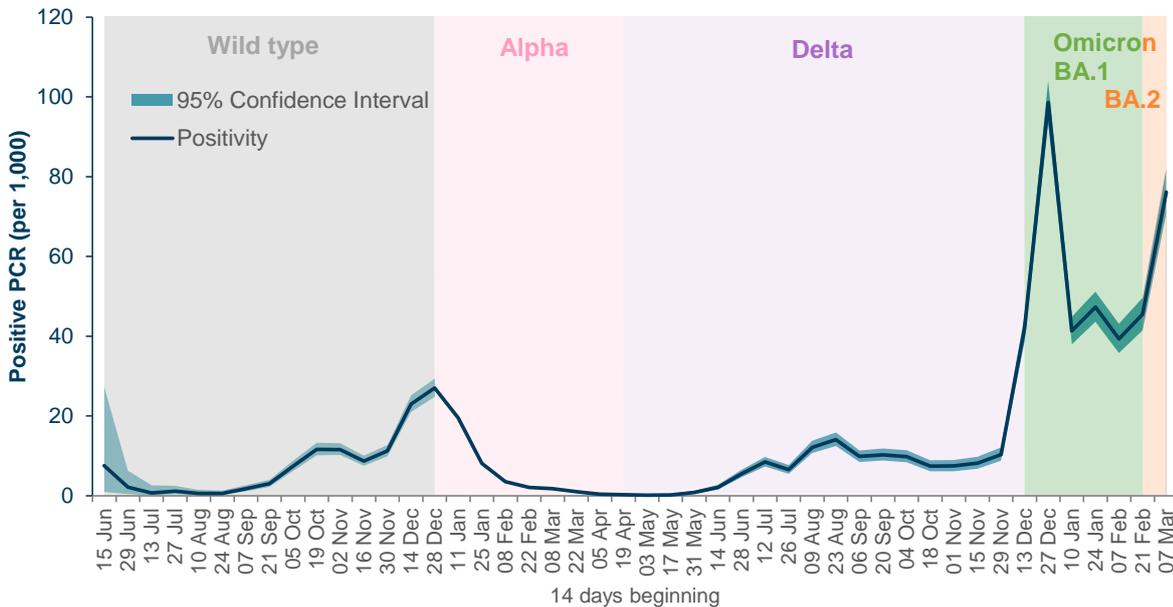
The SARS-CoV-2 Immunity and Reinfection EvaluationN (SIREN) is a cohort over 44,000 National Health Service healthcare workers, recruited from 135 hospital sites UK-wide. Participants under active follow-up undergo asymptomatic SARS-CoV-2 PCR testing every 2 weeks. This cohort had high seropositivity on recruitment (30% before the second wave) and is now highly vaccinated (more than 95%). The incidence of new infections and potential reinfections in SIREN is monitored.

Figure 21 describes fortnightly trends in PCR positivity within the SIREN study from 15 June 2020 to 20 March 2022. Following a steep increase in PCR positivity in December 2021, the rate has decreased slightly since the peak at the end of December. However, the PCR positivity over the last 2 months remains higher than was seen before this peak and has potentially started to increase again during March 2022.

Figure 22 shows the monthly trends in reinfections within SIREN. Reinfections were defined as new PCR positive infections 90 days after a previous PCR positive date or 28 days after antibody positivity consistent with prior infection. Following a similar trend as all infections (Figure 21), the rate of reinfections per month has decreased slightly since the peak seen at the end of 2021, but the number remains higher than seen before this peak.

Figure 23 shows the number of samples sequenced in SIREN by variant and shows the emergence of Omicron BA.2.

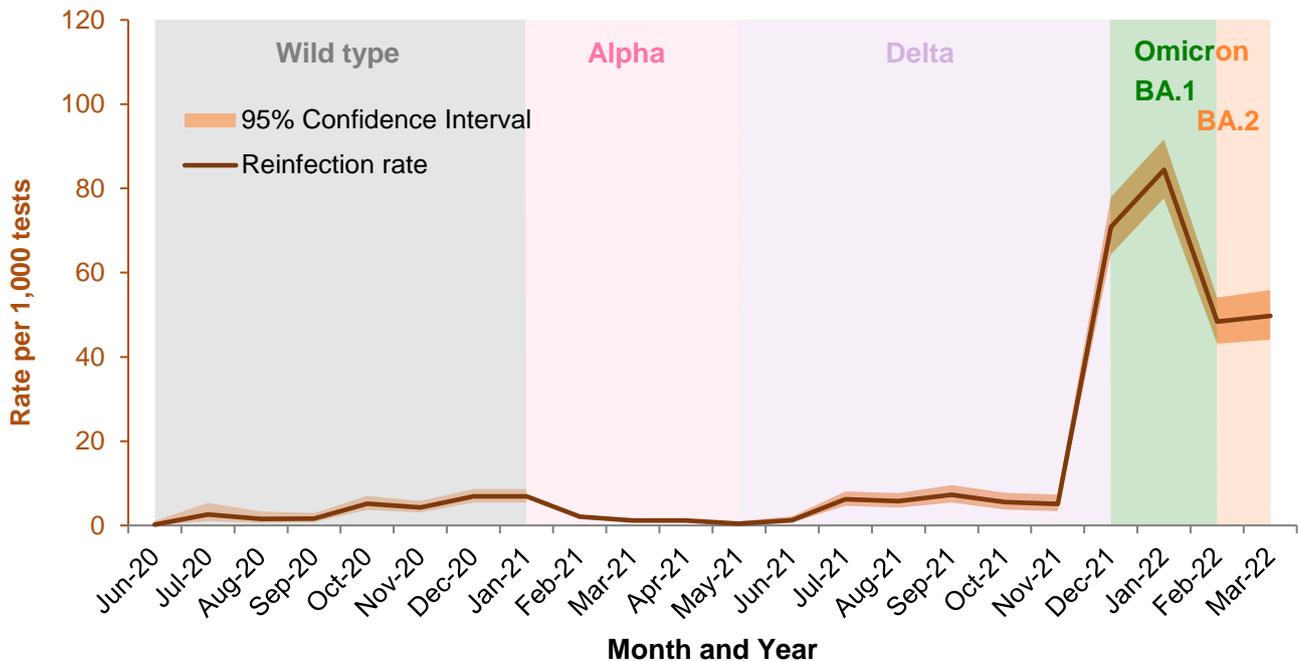
Figure 21. Fortnightly trends in PCR positivity within the SIREN study from 15 June 2020 to 20 March 2022



Supplementary data is not available for this figure.

Note: Data is preliminary and undergoing review. Data at the latest timepoint may be affected by delayed reporting.

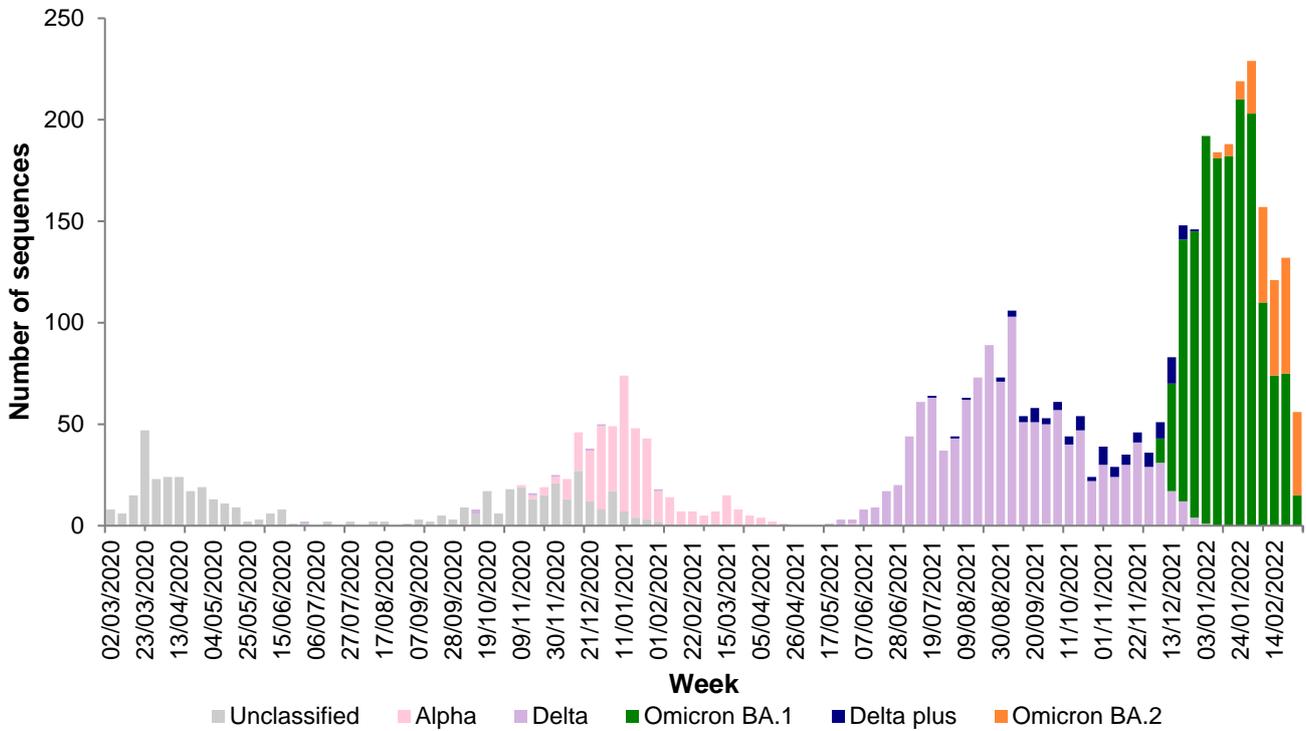
Figure 22. Monthly trends reinfections in SIREN participants in the UK from June 2020 to March 2022



Supplementary data is not available for this figure.

Notes: Data is preliminary, and includes all possible reinfections flagged, but some may subsequently be excluded following clinical review. Data at the latest timepoint may be affected by delayed reporting.

Figure 23. Number of samples sequenced in SIREN March 2020 to March 2022



Supplementary data is not available for this figure.

Note: this figure shows the number of samples that has been sequenced and have the variant data entered onto the UKHSA laboratory reporting database (SGSS), therefore this is an under estimate of the number of samples sequenced in SIREN.

3.6 Reinfections

Preliminary analysis of 496,228 cases of PCR confirmed SARS-CoV-2 infection between 27 December 2021 and 16 January 2022, when Omicron BA.1 was predominant, identified 186,896 BA.1 confirmed cases with genome sequencing. Thirty-one of these cases had another subsequent sequenced sample with an interval of at least 20 days after a previous positive test, with a maximum follow-up period of 72 days. In line with current Omicron BA.2 predominance, 30 of these were BA.2, and one was Delta AY.4.2 at the second positive test, indicative of a short-interval reinfection. There were 21 (68%) female and 10 (32%) male cases with a mean age of 26 years and 12 were unvaccinated children under 12 years of age. In all but one case the initial BA.1 infection was their first episode of SARS-CoV-2 infection. Of those aged 12 years or older, 7 (37%) were unvaccinated.

This analysis is restricted by the limited number of individuals with sequencing available for more than one sample and the short follow-up time to date for these individuals which has not yet reached the 90 day cut-off applied on a population level to determine possible reinfections. We are at the start of the 90 day period for possible reinfection with BA.2 following a BA.1 infection and there is a need for ongoing surveillance but there are no early indications of a specific reinfection issue with this scenario.

National data on SARS-CoV-2 reinfections was published last week in the [National flu and COVID-19 surveillance reports: 2021 to 2022 season – GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/publications/national-flu-and-covid-19-surveillance-reports-2021-to-2022-season) week 11.

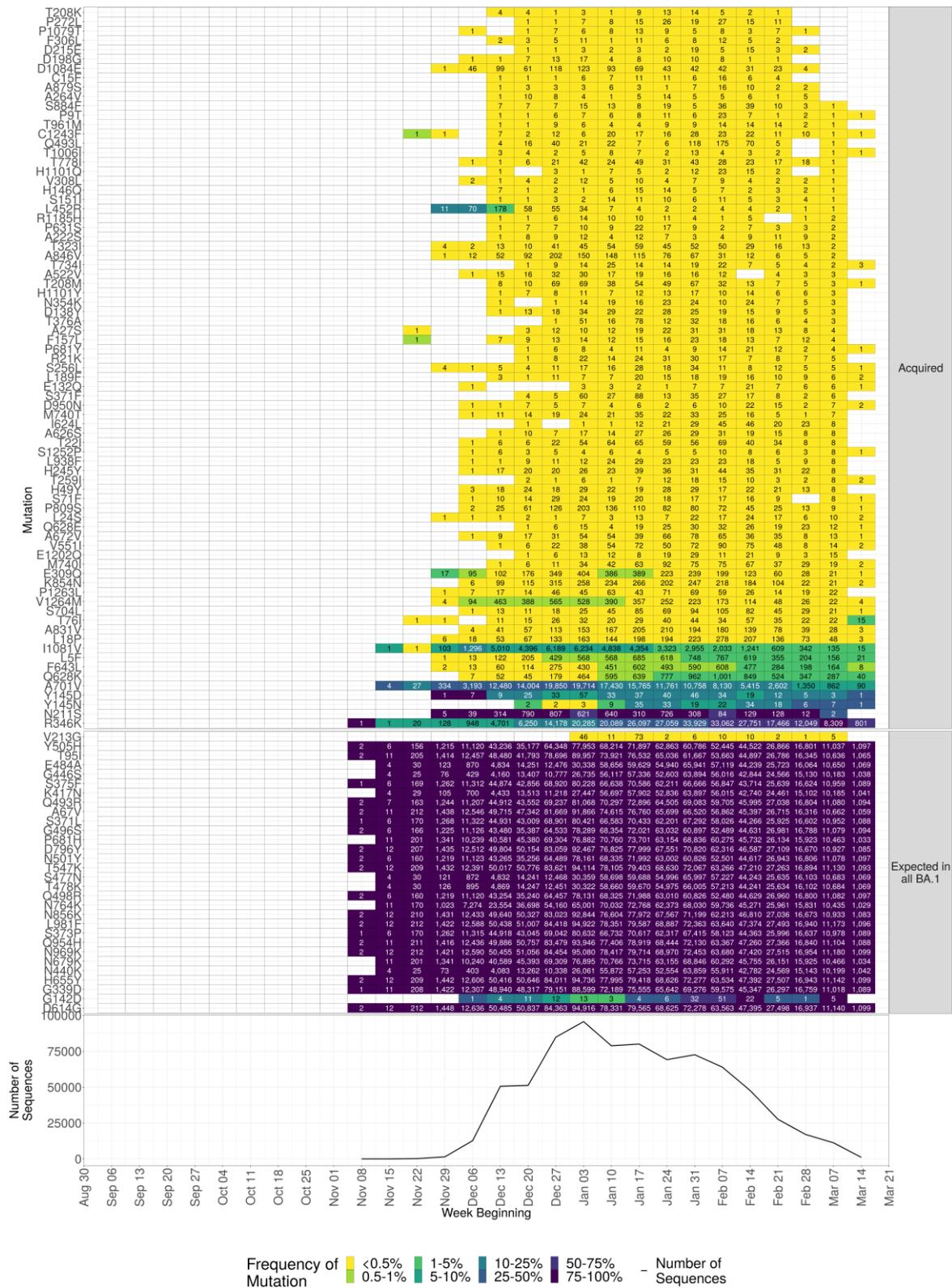
Part 4. Enhanced analyses of Omicron VOC-21NOV-01 (BA.1)

This variant was detected on GISAID on 23 November 2021 and designated B.1.1.529 on 24 November 2021. It was designated VUI-21NOV-01 by the UKHSA Variant Technical Group and on review re-designated as VOC-21NOV-01 on 27 November 2021.

4.1 Genomic diversity within Omicron VOC-21NOV-01 (BA.1)

Spike mutations are monitored within BA.1 using 4 criteria (Table 2). Seventy-seven additional mutations have been observed in BA.1 sequences according to the criteria in Table 2 (Figure 24). The presence of Y145D/N, L452R and N211S may be artefactual. L452R may be due to low level contamination with Delta sequence. The mutations at position 211 and 145 are an alignment artefact caused by the deletions at these positions in Spike. These deletions also reduce the number of sequences where the positions can be called therefore artificially increasing the proportion of sequences where these mutations are present.

Figure 24. Spike mutations found in BA.1 genomes in the UK dataset relative to the Wuhan sequence NC_045512.2 between 8 November 2021 and 20 March 2022



Supplementary data is not available. It should be noted all mutations in the sequence alignment are reported in these plots for review purposes. Those reported here at positions 145 and 211 arise due to base deletions affecting the sequence alignment and are artefactual.

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, the Secondary Uses Service data set, Emergency Care Data Set, the UKHSA Case and Incident Management System and the SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) Study.

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.

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