UK Health Security Agency

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

Technical briefing 41

6 May 2022

This report provides an update on previous briefings up to 8 April 2022

Contents

Summary

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

Unless stated otherwise, this technical briefing uses a data cut-off of 2 May 2022 to allow time for analyses.

Interpreting variant data

The current testing policy needs to be considered when interpreting all variant data; the targeting of testing at specific groups is likely to delay the detection and characterisation of variants. Specifically:

- the reduction in tests processed through assays which can report S gene target failure (SGTF) has decreased substantially since the change in testing policy on 1 April, and this is no longer a reliable representation of variants in the population – it will no longer be reported following this briefing
- the confidence intervals around growth rates for individual variants are likely to be large, as demonstrated by XE, and this model may not be usable on the national dataset going forwards – assessment of surveillance cohort datasets is being undertaken

A lag in uploading genomic data (31 March to 5 May 2022) from external laboratories to UKHSA was identified and rectified. The resultant analyses will appear in the next technical briefing.

VOC-22JAN-01 (Omicron sub-lineage BA.2)

VOC-22JAN-01 remains dominant in the United Kingdom (UK) based on sequencing data. Some diversity is developing within this variant, based on both lineage and mutation surveillance.

V-22APR-03 (Omicron sub-lineage BA.4) and V-22APR-04 (Omicron sub-lineage BA.5)

These 2 variants are increasing in South Africa and may be associated with the current increase in incidence there. Small numbers of BA.4 sequences continue to be detected in the UK (total 40 genomes). As of 3 May 2022, there were 21 confirmed cases of BA.4 reported in England and 19 cases of BA.5.

Risk assessment

A new risk assessment for V-22APR-03 and V-22APR-04 has been published.

Published information on variants

On 1 April 2022 UKHSA amended its variant classification system. Further details are available in Technical Briefing 39.

SARS-CoV-2 Routine variant data update covers surveillance data and sequencing coverage data on all other VOCs and VUIs up to 25 March 2022. The latest COVID-19 variants: genomically confirmed case numbers are published on GOV.UK.

The collection page gives content on variants, including prior technical briefings. 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 to identify variant and mutation profiles from genotype assay mutation profiles.

The Public Health England repository from 5 March 2021 contains the previous genomic definitions for VOCs and variants under investigation (VUIs).

Part 1. Surveillance overview

World Health Organization (WHO) nomenclature from 24 January 2022 is incorporated. Tables 1a and 1b show the current VOCs, variants (V-date-number), and signals in monitoring detected and not detected in the UK incorporating WHO designations with Phylogenetic Assignment of Named Global Outbreak Lineages (Pangolin lineages).

Table 1a. Variants detected in the UK in the past 12 weeks

Variants of concern	Variants (Vs)	Signals in monitoring
Omicron (B.1.1.529) sub-lineage BA.1 VOC-21NOV-01	V-21OCT-01 (AY.4.2)†	BA.3
Omicron (B.1.1.529) sub-lineage BA.2 VOC-22JAN-01	Alpha (B.1.1.7) V-20DEC-01	Delta and Omicron recombinant lineages (UK)
	Delta (B.1.617.2 and sub-lineages) V-21APR-02	BA.1/BA.2 Recombinant (with unique mutation C3583T)
	XE Recombinant (BA.1 x BA.2) V-22APR-02	XF Recombinant
	Omicron (B.1.1.529) sub-lineage BA.4 V-22APR-03	BA.2.12.1
	Omicron (B.1.1.529) sub-lineage BA.5 V-22APR-04	

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

Table 1b. Variants detected in GISAID, but not in the UK, in the past 12 weeks

Variants of concern	Variants (Vs)	Signals in monitoring
Beta (B.1.351) V-20DEC-02	Mu (B.1.621) V-21JUL-01	AY.119.2/BA.1.1 Recombinant
	(B.1.617.3) V-21APR-03	B.1.640
	XD Recombinant (Delta x BA.1) V-22APR-01	

VOCs and other Variants (V-date-number) 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 Variants 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. Variants and signals in monitoring may also be removed from the grid if they show consistently low growth rates.

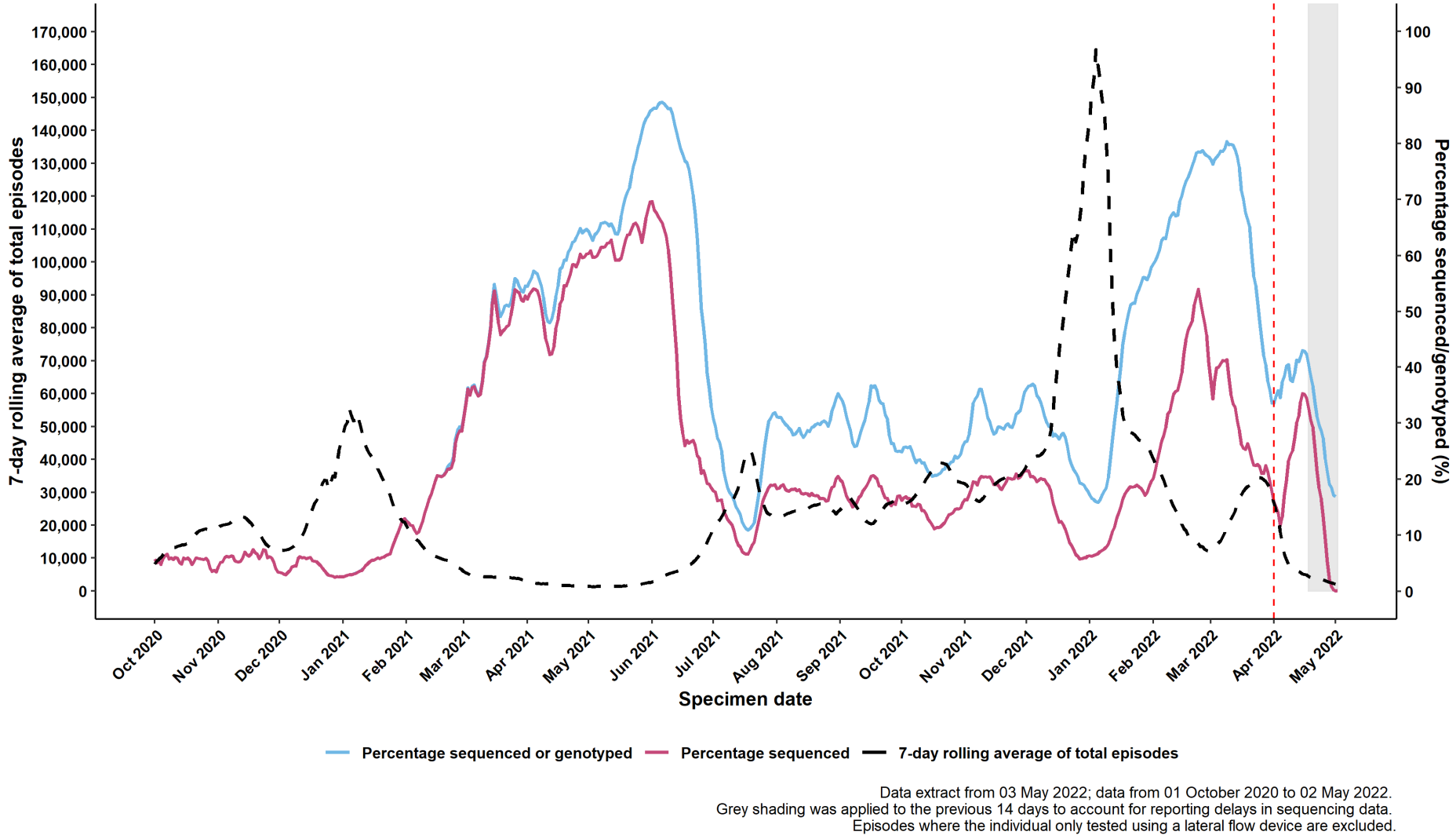
1.1 Sequencing coverage

Figure 1 shows the proportion of coronavirus (COVID-19) cases as detected by PCR that have linked to a valid sequencing result (sequences included have 50% of the genome with sufficient read coverage) or genotyping PCR result over time. Figure 2 shows the proportion of cases sequenced and genotyped over time by regions. Figure 3 shows the proportion of cases sequenced and genotyped amongst cases who tested positive while in hospital.

Sequencing coverage of PCR confirmed cases was high during March 2022 (Figure 1) however, this needs to be interpreted with care as PCR tests have declined substantially since mid-February 2022 and case ascertainment is reduced.

Currently, the sequencing strategy prioritises hospitalised cases, patients who are receiving specific antiviral therapy, and national core priority studies.

Figure 1. Coverage of sequencing with a valid result and genotyping over time (1 October 2020 to 2 May 2022)

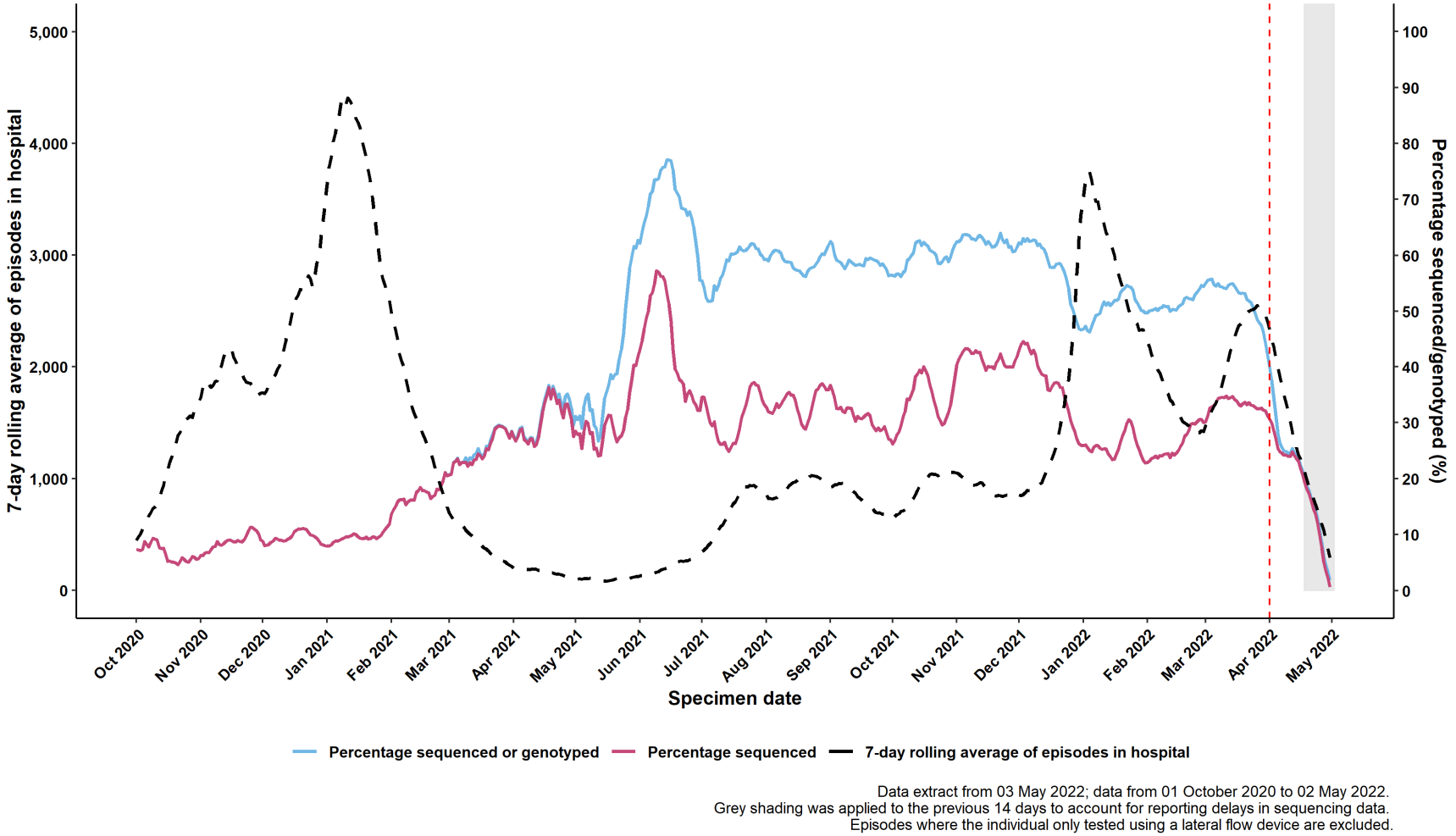


Episodes where the individual only tested using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. The red dash line denotes the start of England's 'Living with COVID' Plan. (The data used in this graph can be found in the accompanying spreadsheet.)

Figure 2. Coverage of sequencing with a valid result and genotyping over time by region (1 October 2020 to 2 May 2022)

Episodes where the individual only tested positive using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. The red dash line denotes the start of England's 'Living with COVID' Plan. (The data used in this graph can be found in the accompanying spreadsheet.)

Figure 3. Coverage of sequencing with valid result and genotyping for cases who test positive in hospital (1 October 2020 to 2 May 2022)

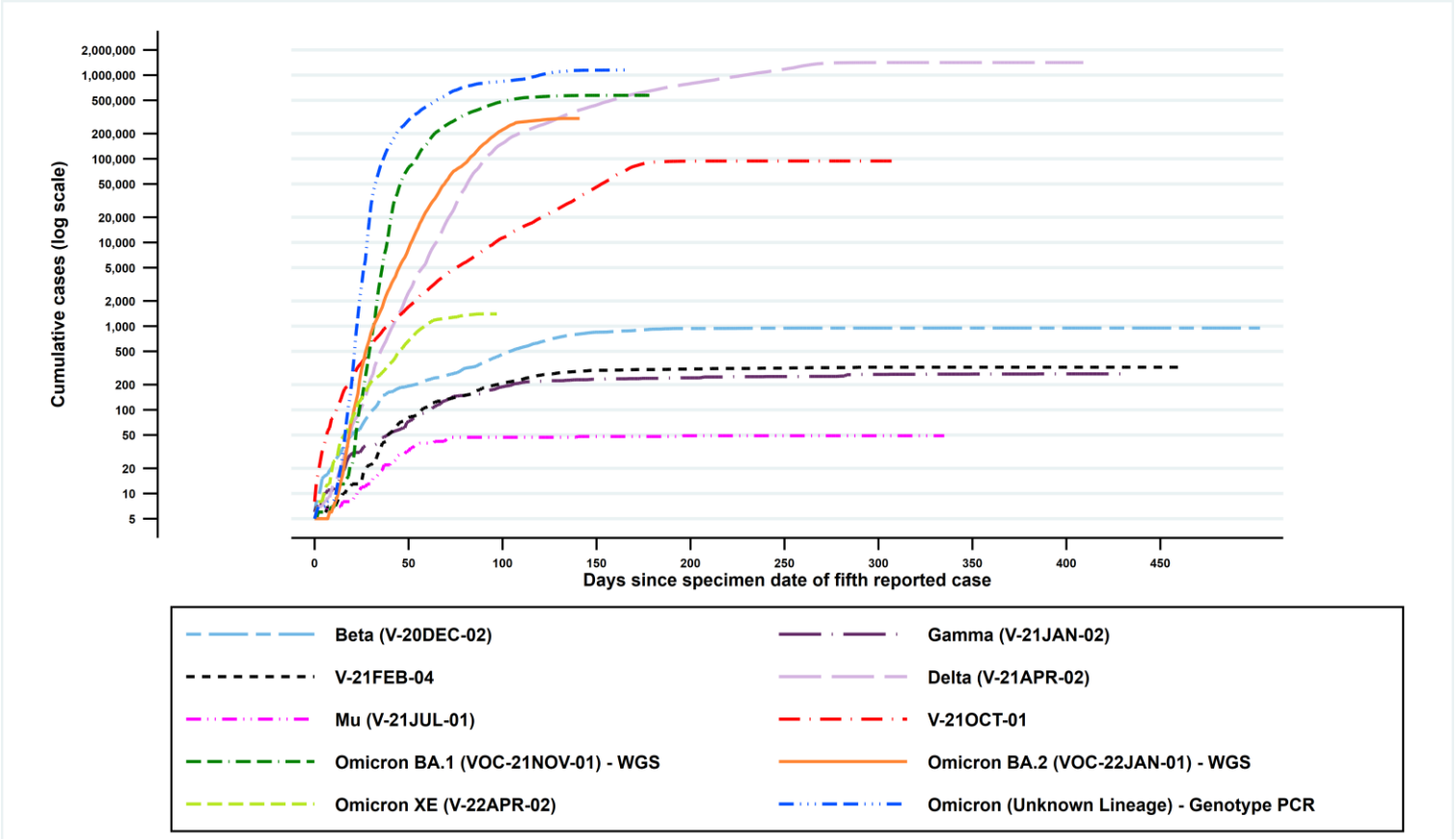


Episodes where the individual only tested positive using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. The red dash line denotes the start of England's 'Living with COVID' Plan. (The data used in this graph can be found in the accompanying spreadsheet.)

1.2 VOC and Variant overview

Summary epidemiology for each variant and case numbers are updated online. Figure 4 shows the cumulative number of cases (including whole genome sequenced and genotyped) per variant indexed by days since the first report.

Figure 4. Cumulative cases* in England of variants indexed by days since the fifth reported case as of 2 May 2022



*includes whole genome sequenced cases and, where available, genotyped PCR cases. Genotyping results are available for Beta, Mu, Delta and Omicron.
Find accessible data used in this graph in underlying data.

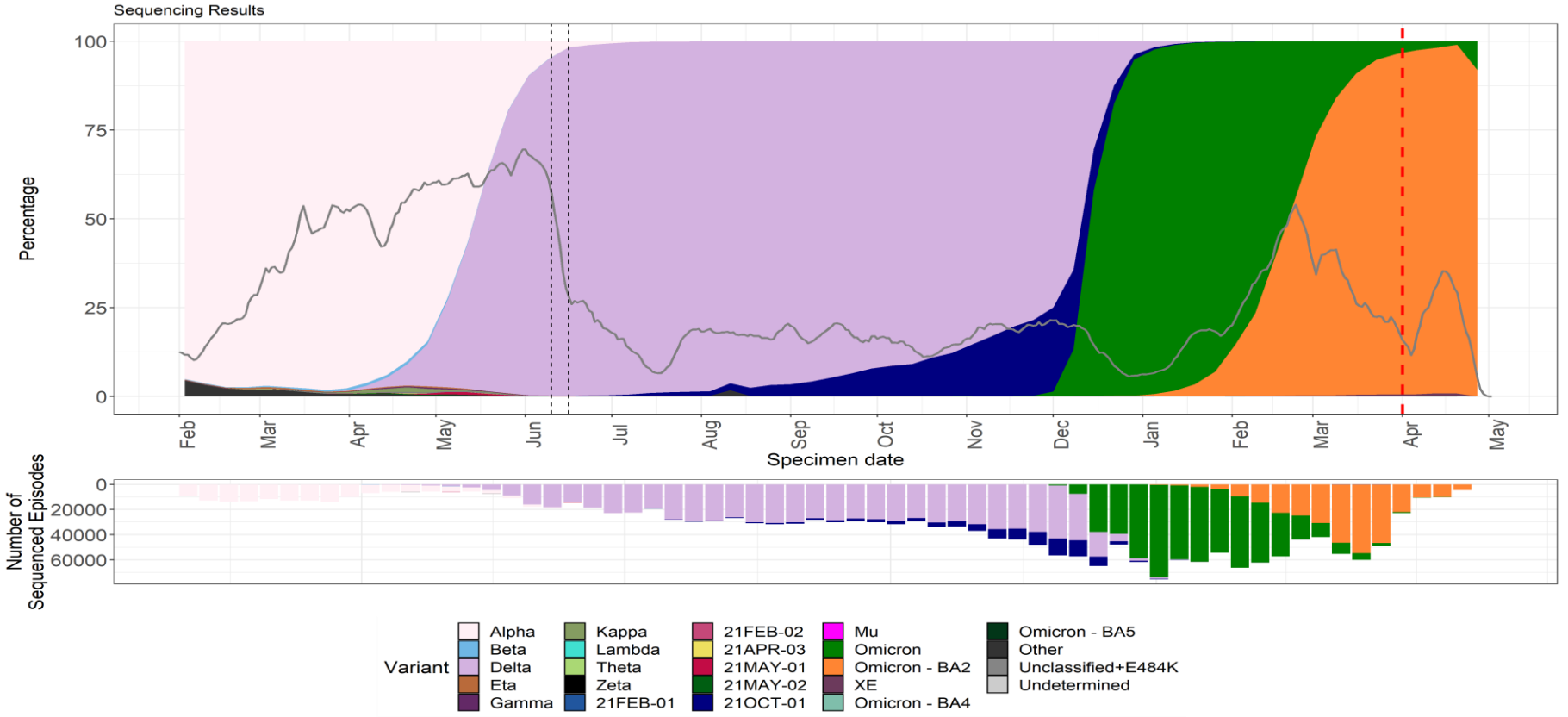
1.3 Variant prevalence

The prevalence of different UKHSA-designated variants amongst sequenced episodes is presented in Figure 5 and by Pango designation in Figure 6. Of the sequenced episodes from 24 April to 1 May 2022, 91.9% were Omicron lineage BA.2 (VOC-22JAN-01) and 8.1% were Omicron lineage BA.1 (VOC-21NOV-01).

S gene target failure/positive (SGTF or SGTP) data has previously been presented here as a way of monitoring the spread of the Omicron sub-lineages. SGTF is defined as a PCR test where the N and ORF1ab genes are detected (with cycle threshold (Ct) values less than or equal to 30) but the S-gene is not (BA.1 usually SGTF; BA.2 usually SGTP).

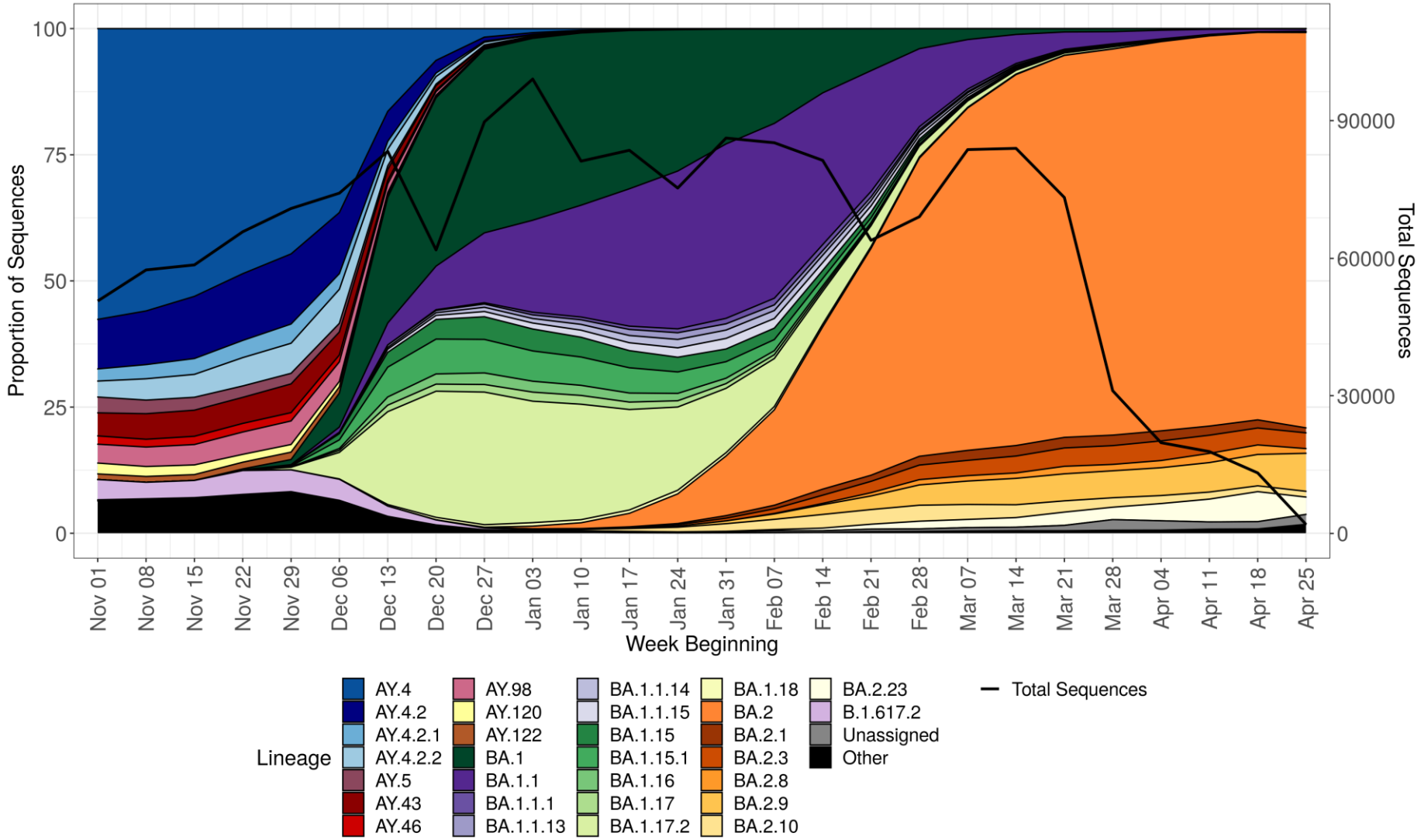
After the change in community testing policy, most Pillar 2 laboratories using the TaqPath assay and submitting data to UKHSA ceased operations, leading to a significant decrease in the number of specimens with SGTF/SGTP results. Consequently, S gene target data is currently not a robust proxy for SARS-CoV-2 variants and will no longer be reported.

Figure 5. Variant prevalence of available sequenced cases for England from 1 February 2021 as of 3 May 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. The red dash line denotes the start of England's 'Living with COVID' Plan. Note recombinants, such as XD, are not specified but are largely within the 'other' group currently as numbers are too small.

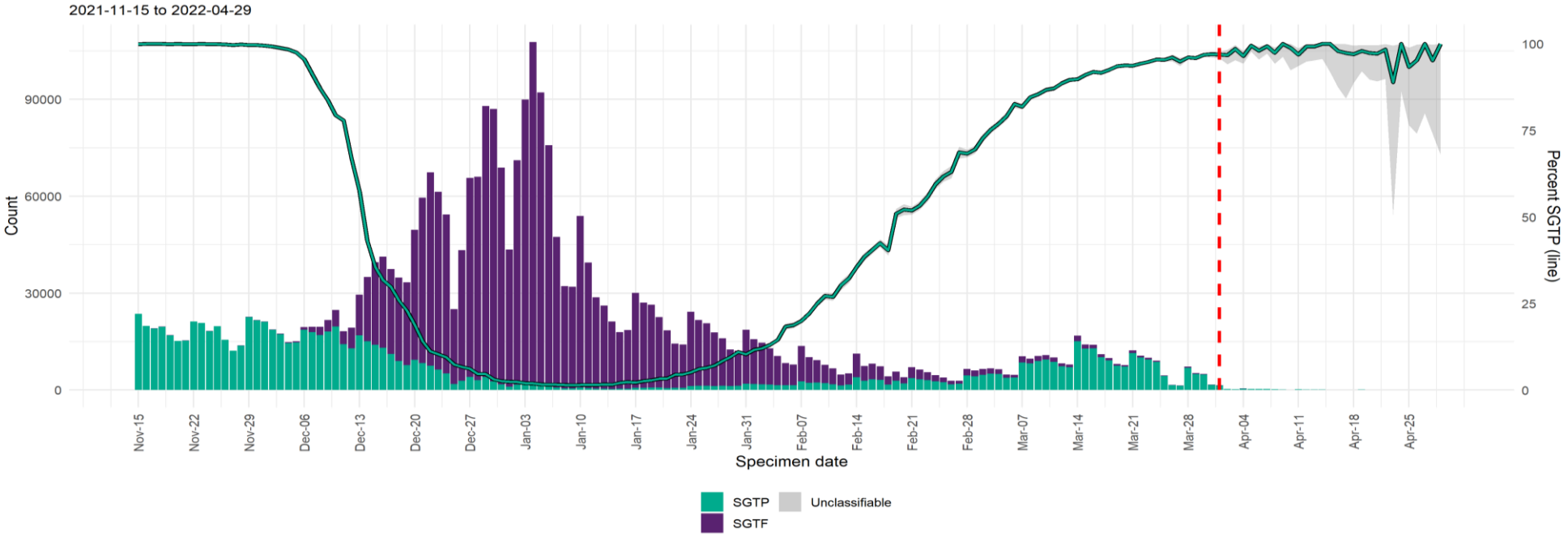
Figure 6. Prevalence of Pangolin lineages in the UK with sequence data from 1 November 2021 to 1 May 2022



The ‘Other’ category in Figure 6 includes genomes where the total number of genomes for that lineage and relevant sub-lineages is less than 5,000. The ‘Unassigned’ category includes genomes where the quality is insufficient to determine a lineage using Pangolin.

The total number of valid sequence results per week is shown by the black line. Only lineages with more than 5,000 sequences and accounts for >=2% of sequences within at least one week 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 ‘Unassigned’ in this plot. Lineages XE, BA.4 and BA.5 are not currently at a high enough prevalence to meet the 5,000 sequence cut-off so are included in Other in this plot. Find accessible data used in this graph in underlying data.

Figure 7. Number of COVID-19 cases with SGTP/SGTF by day, among those tested in TaqPath labs as of 3 May 2022



Ninety-five percent confidence intervals indicated by grey shading. Percentage for most recent day shown. The red hashed line denotes the start of England's 'Living with COVID' Plan. Find accessible data used in this graph in underlying data.

Part 2. V-22APR-03 (BA.4)

Omicron sub-lineage BA.4 was identified as part of horizon scanning on 4 April 2022. On 6 April 2022, the Variant Technical Group classified Omicron sub-lineage BA.4 as V-22APR-03.

The genomic case definition for V-22APR-03 is available in Technical Briefing 40. Following further work on the lineage, it has been corrected as follows: BA.4 shares all mutations/deletions with the BA.2 lineage except the following: S: 69/70 deletion, R408 (WT, wild type)*, L452R, F486V, Q493 (WT); ORF 7b: L11F; N: P151S; synonymous SNP G12160A.

* Note, only a subset of BA.4 samples have the S: R408S mutation.

2.1 Epidemiology of V-22APR-03 (BA.4) in England

Thirty-nine sequences assigned to the BA.4 in the UK genomics dataset, of these 26 were associated England, 21 of which were linked to patient information. Cases are geographically distributed across England with most cases in the South East and West Midlands.

2.2 International Epidemiology

The earliest BA.4 sample in GISAID was from South Africa with a sample collection date of 10 January 2022. Countries reporting BA.4 genomes via GISAID now include South Africa (395), Austria (36), United Kingdom (24), USA (20), Denmark (17), Belgium (9), Israel (8), Germany (5), Italy (4), Canada (3), France (3), Netherlands (3), Australia (2), Switzerland (2), and Botswana (1). Although the number of total genomes is low, the apparent geographic spread suggests that the variant is transmitting successfully. Apart from South Africa, Austria currently has the highest proportion of BA.4 amongst its uploads. Sampling strategies for many countries are unknown.

Part 3. Enhanced analyses of V-22APR-04 (BA.5)

Omicron sub-lineage BA.5 was identified as part of horizon scanning on 4 April 2022. On 6 April 2022, the Variant Technical Group classified Omicron sub-lineage BA.5 as V-22APR-04.

The genomic case definition for V-22APR-04 is available in Technical Briefing 40. Following additional work on the lineages, it has been corrected as follows: BA.5 shares all mutations/deletions with the BA.2 lineage except the following: S: 69/70 deletion, R408 (WT), L452R, F486V, Q493 (WT); ORF6: D61 (WT); M: D3N; synonymous SNPs: G12160A, A27038G, and C27889T.

3.1 Epidemiology of V-22APR-04 (BA.5) in England

Thirty-one sequences assigned to the BA.5 in the UK genomics dataset, of these 24 were associated with England, 19 of which were linked to patient information. Cases are geographically distributed across England with most cases in the South East and South West.

3.2 International epidemiology

Countries reporting BA.5 genomes via GISAID include: South Africa (134), Portugal (57), Germany (52), United Kingdom (17), USA (6), Denmark (3), France (3), Austria (2), Belgium (2), Hong Kong (2), Australia (1), Canada (1), Israel (1), Norway (1), Pakistan (1), Spain (1), and Switzerland (1). Although the number of total genomes is low, the apparent geographic spread suggests that the variant is transmitting successfully. This lineage shows sample dates between 3 January and 25 April 2022. Sampling strategies for many countries remain unknown.

Part 4. Updated epidemiology of XE (V-22APR-02)

XE is a BA.1 and BA.2 recombinant (containing BA.1 mutations for NSP1-6 and BA.2 mutations for the rest of the genome). It also has 3 mutations that are not present in all BA.1 or BA.2 sequences: NSP3 V1069I (non-synonymous) and C3241T (synonymous), and NSP12 C14599T (synonymous).

As of 3 May 2022, there are 1,880 XE sequences in the UK data with 1,569 XE cases in England. Cases are geographically distributed across England, with the first case detected via sequencing on 19 January 2022, and most cases in the East of England, London, and the South East. As of 3 May 2022, a total of 1,399 episodes of V-22APR-02 have been reported in England. XE remains at a low prevalence. Between 3 April 2022 and 3 May 2022, XE accounted for 0.7% of sequenced cases reported in England.

Part 5. Omicron VOC-22JAN-01 (BA.2)

The mutation profile of the Omicron sub-lineages was previously reported in Technical Briefing 31.

BA.2 has been reclassified as a VOC under the new classification on 1 April 2022.

5.1 Genomic diversity

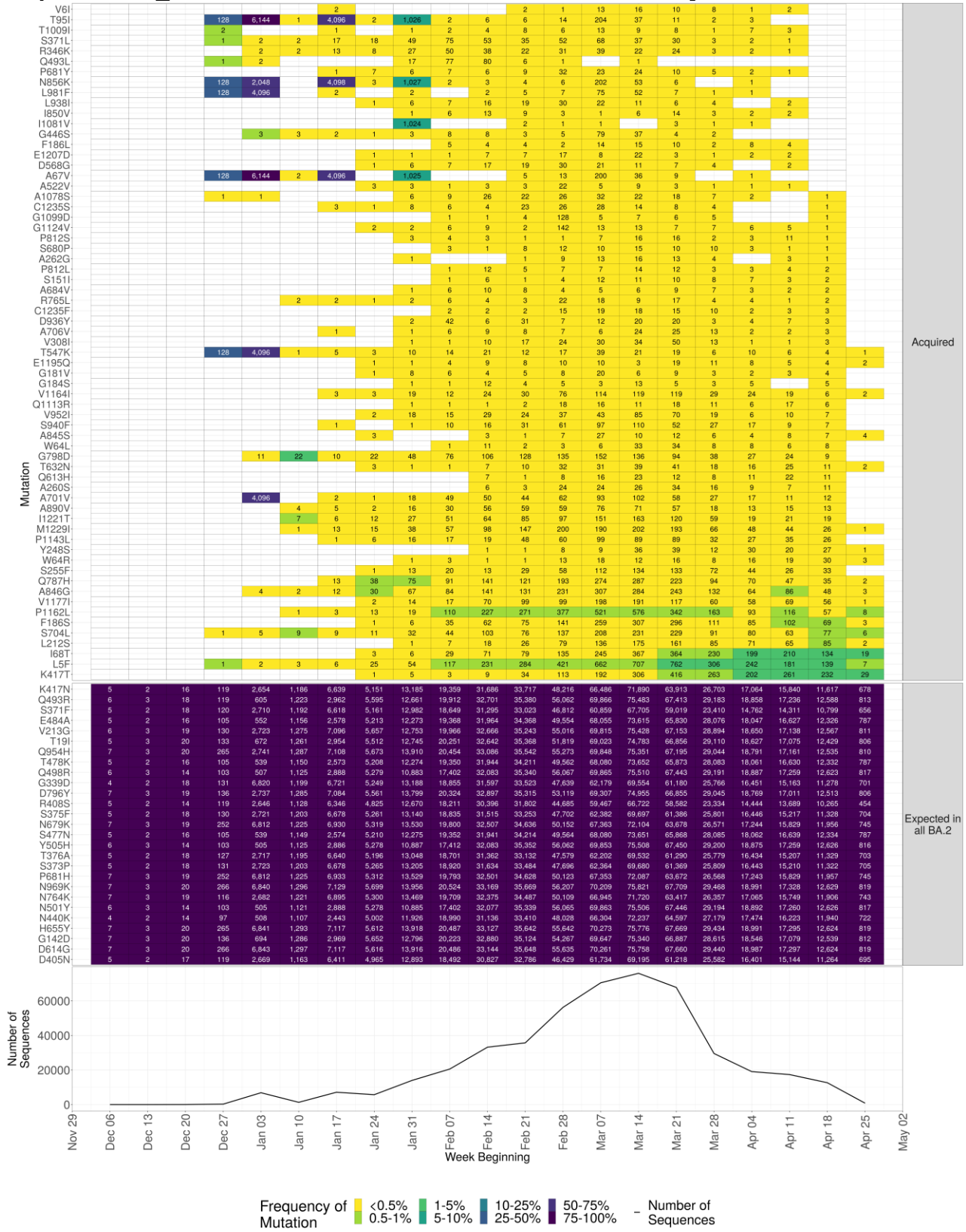
Diversity in Spike

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. Sixty-five additional mutations have been observed in BA.2 sequences according to the criteria in Table 2 (Figure 8). 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 8. Spike mutations found in BA.2 genomes in the UK dataset relative to the Wuhan sequence NC_045512.2 between 8 November 2021 and 1 May 2022

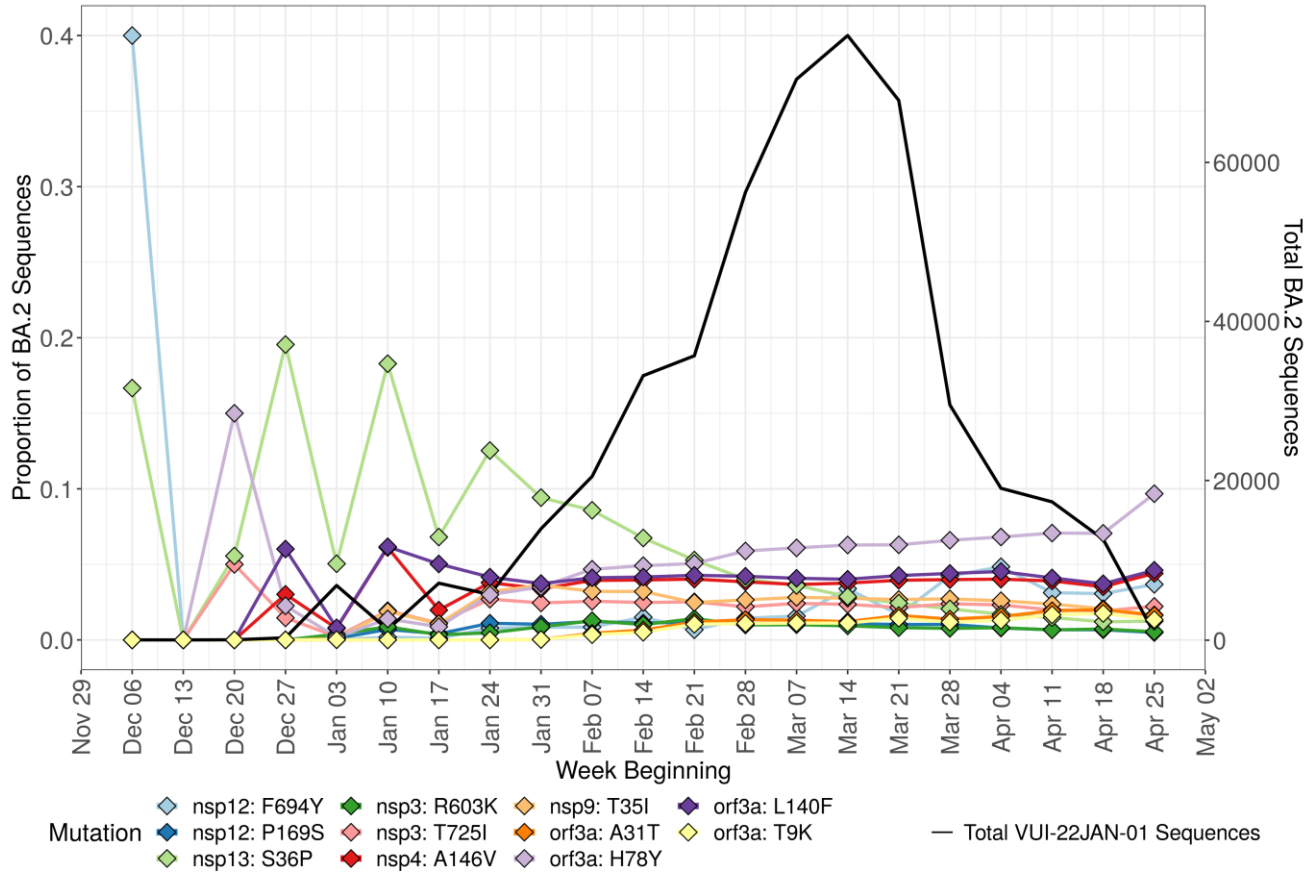


Find accessible data used in this graph in underlying data.

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 9).

Figure 9. Mutations acquired by BA.2, shown as a proportion of total BA.2 sequences (6 December 2021 and 1 May 2022)



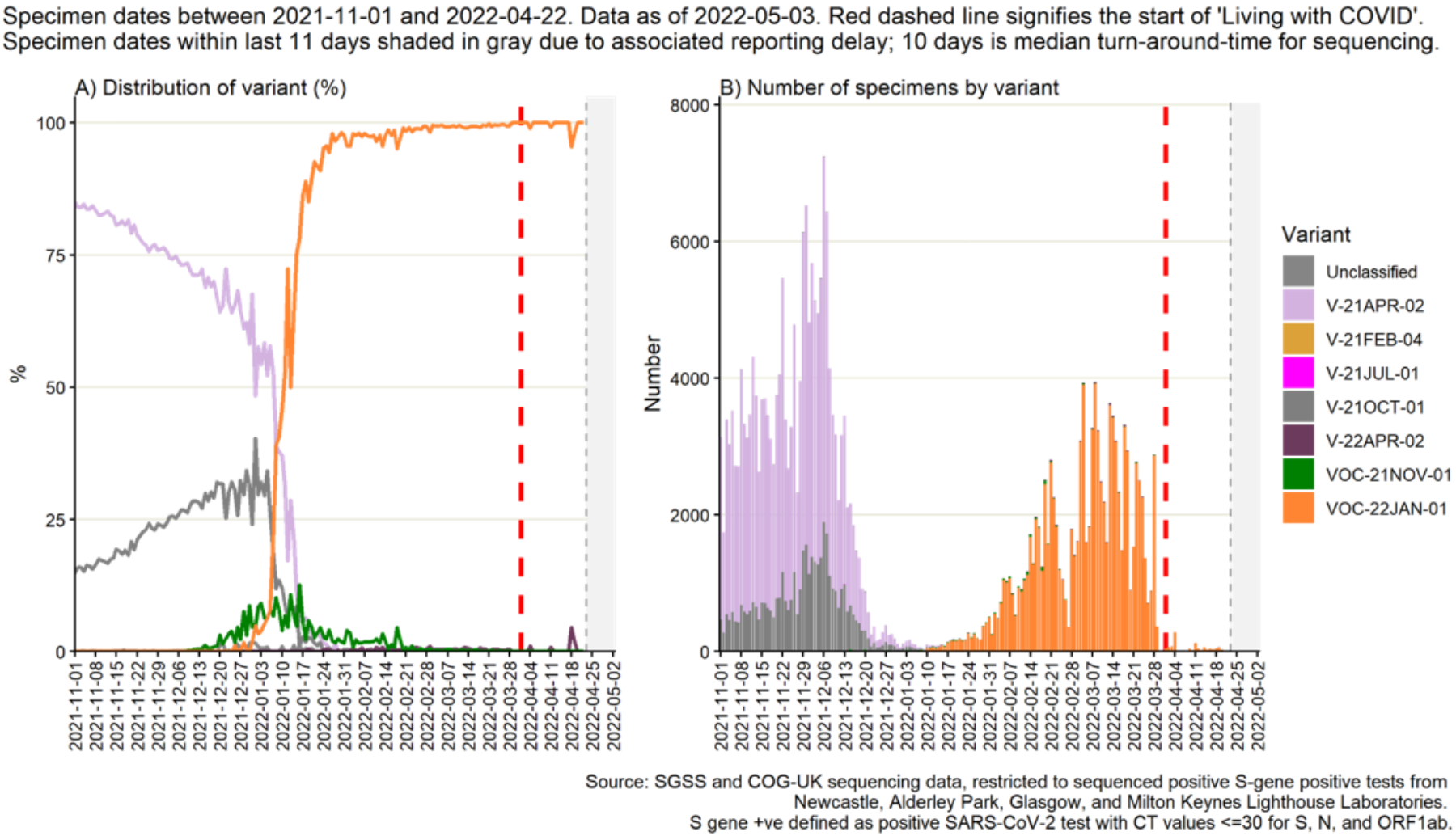
The total number of BA.2 sequences per week are indicated by the black line. Mutations for each genome are called relative to reference Wuhan NC_045512.2 and acquired mutations are those additional to the ancestral BA.2 mutation set. Those that are considered additional, and that are present in at least 1% of BA.2 sequences for 3 consecutive weeks in the UK dataset, are included in Figure 9 as a proportion of total BA.2 sequences.
(Find accessible data used in this graph in underlying data.)

Epidemiology of SGTP

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

Figure 10. Number and distribution of variants per week among sequenced SGTP specimens as of 3 May 2022

Find accessible data used in this graph in underlying data.



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.

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 and the UKHSA Case and Incident Management System.

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