UK Health Security Agency

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

Technical briefing 48

25 November 2022

This report provides an update on previous briefings up to 28 October 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 21 November 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.

Sequencing coverage

Analysis of the mean proportion of sequenced samples originating from different sample groups shows that from the week commencing 22 August 2022 to the week commencing 7 November 2022, 16.8% of samples were from the Office for National Statistics COVID-19 Infection Survey (ONS CIS), 0.8% from VIVALDI (care home study) and 6.8% from AVA (individuals tested because they may be eligible for therapeutics in the community).

Between 25 October 2022 and 20 November 2022, the median age of reported coronavirus (COVID-19) cases was 52 years old. However, during the same period the median age of sequenced COVID-19 cases was 69 years old.

Horizon scanning

The following describes updates to signals/designated variants in horizon scanning.
No new variants have been designated since the last technical briefing.

BA.5, including all sub-lineages, remains the dominant parent lineage in the UK at more than 75% of all sequenced samples in the UK.

BQ.1 (V-22OCT-01) is a BA.5 sub-lineage with additional spike mutations L452R, N460K, and K444T. BQ.1 and its sub-lineages represent greater than 40% of all sequenced UK samples.

XBB (V-22OCT-02) has shown some growth in the UK. However, in the week commencing 7 November 2022, XBB represented only 1.8% of the total number of UK sequenced samples. A total of 345 UK XBB samples have been sequenced so far.

BA.5.2.35 was raised as a signal in monitoring due to a high logistic regression growth rate in the UK data. This lineage is defined the addition of the spike mutation R346T relative to BA.5.2, in addition to 2 synonymous single nucleotide polymorphisms (SNPs) G28423C and C7006T. There have been 848 samples identified in the UK and 447 samples in 29 non-UK countries. We continue to monitor growth.

BN.1 (BA.2.75.5.1), and its sub-lineages, was raised as a signal in monitoring due to a high logistic regression growth rate in the UK data. This lineage is characterised by the addition of spike mutations R346T and F490S to the lineage BA.2.75.5. There have been 190 samples identified in the UK and 1,127 samples in 35 non-UK countries. We continue to monitor growth.

BF.7, BS.1, BA.4.7, BA.2.3.20, and the recombinant XAW have all been de-escalated monitoring due to reduced incidence and low growth rates in the UK.

An international signal has been raised on a cluster of BA.5.7 sequences from Australia, due to more nucleotide synonymous transition mutations (purine to purine or pyrimidine to pyrimidine) than expected. In addition to the mutations defining the BA.5.7 lineage and a number of synonymous mutations, these sequences include 2 mutations resulting in amino acid changes; S:Y453F and Orf1a:A1679T. The cluster currently contains 9 samples. Sequences will be monitored. A further cluster of 9 Australian sequences of lineage BM.2 is also being monitored. This cluster also contains a higher number of transition mutations than expected as well as the following Spike mutations; D111N, S151N, V289I, T549I, D574N, A701V, L841, V1230M. Investigation is ongoing.

Growth rates

Growth rate estimates indicate the lineages BQ.1.1 and BN.1 as the most competitive of the signals in monitoring or designated variants. BQ.1.1 has a 49% weekly growth relative to BA.5.2 (multinomial model), a logistic regression growth rate of 41%, and a generalised additive model growth rate of 24%. BN.1 has a 45% weekly growth relative to BA.5.2 (multinomial model). Due to a lack of ONS samples BN.1 and XBB logistic regression and generalised additive model growth rates could not be accurately estimated.

Published information on variants

On 1 April 2022 the UK Health Security Agency (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 variants of concern (VOCs) and variants under investigation (VUIs) up to 25 March 2022.

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 (PHE) repository from 5 March 2021 contains the previous genomic definitions for VOCs and 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	Designated variants (Vs)	Signals in monitoring
Omicron (B.1.1.529) sub-lineage BA.1 and descendant lineages VOC-21NOV-01	Omicron BA.2.12.1 V-22MAY-01	Delta and Omicron recombinant XBC
Omicron (B.1.1.529) sub-lineage BA.2 and descendant lineages VOC-22JAN-01	Delta (B.1.617.2 and sub-lineages) V-21APR-02	BA.2.75.2
Omicron (B.1.1.529) sub-lineage BA.4 VOC-22APR-03	Omicron XE Recombinant (BA.1 x BA.2) V-22APR-02	BQ.1.1
Omicron (B.1.1.529) sub-lineage BA.5 VOC-22APR-04	Omicron BA.2.75 V-22JUL-01	† BN.1 (BA.2.75.5.1)
	Omicron BA.4.6 V-22SEP-01	† BA.5.2.35
	Omicron BQ.1 V-22OCT-01	
	Omicron XBB Recombinant V-22OCT-02	

†Newly escalated signals in monitoring since the previous technical briefing.

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

Variants of concern	Designated variants (Vs)	Signals in monitoring
		Cluster of BA.5.7 samples with high number of additional mutations

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 variant 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 individuals who tested positive whilst in hospital.
The data on people who tested positive whilst in hospital is derived from the Hospital-Onset COVID-19 dataset (HO-COVID), which links confirmed COVID-19 episodes to admissions data from the Emergency Care Data Set (ECDS) and Secondary Uses Service (SUS) as provided by NHS Digital (Bhattacharya and others, 2021). The vertical dashed red line indicates the 1 April 2022 when free testing for the general public ended.

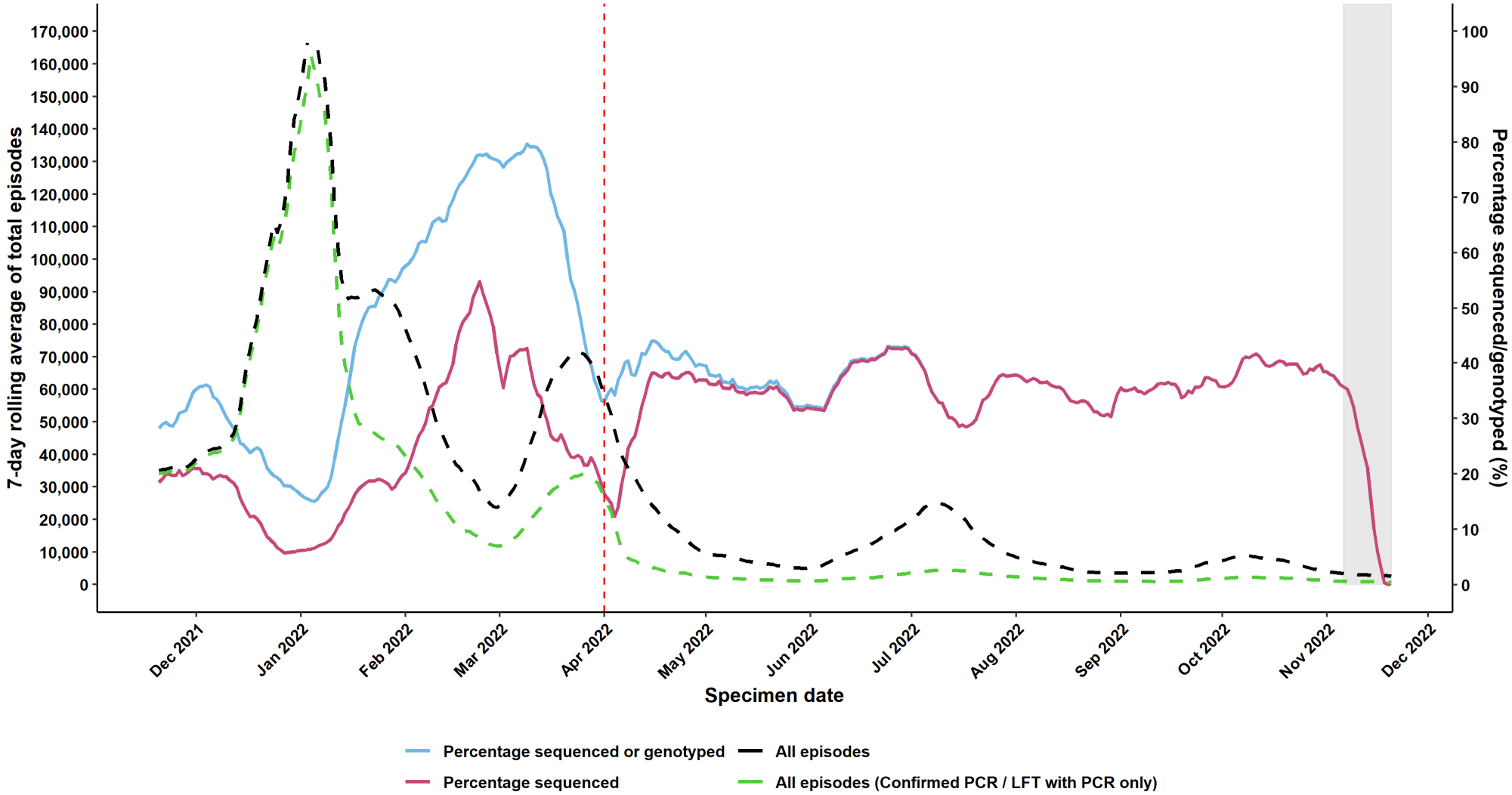
Sequencing coverage of PCR confirmed cases was high during March 2022 (Figure 1). However, this needs to be interpreted with care as PCR tests have declined substantially since mid-February 2022 and case ascertainment is reduced.

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

Figure 4 shows the proportion of sequenced samples that originate from different sample groups, assigned as ‘AVA’ (individuals tested because they may be eligible for therapeutics in the community), ‘VIVALDI’ (care homes study) and ‘ONS’ (Office for National Statistics COVID-19 Infection Survey) over time. Samples not assigned to a specific group are denoted as ‘other’ and will include samples submitted from NHS and UKHSA routine laboratories and routine testing from care homes. Over the past 12 complete weeks of data (week commencing 22 August 2022 to week commencing 7 November 2022), mean proportions were 16.8% ONS, 0.8% VIVALDI and 6.8% AVA.

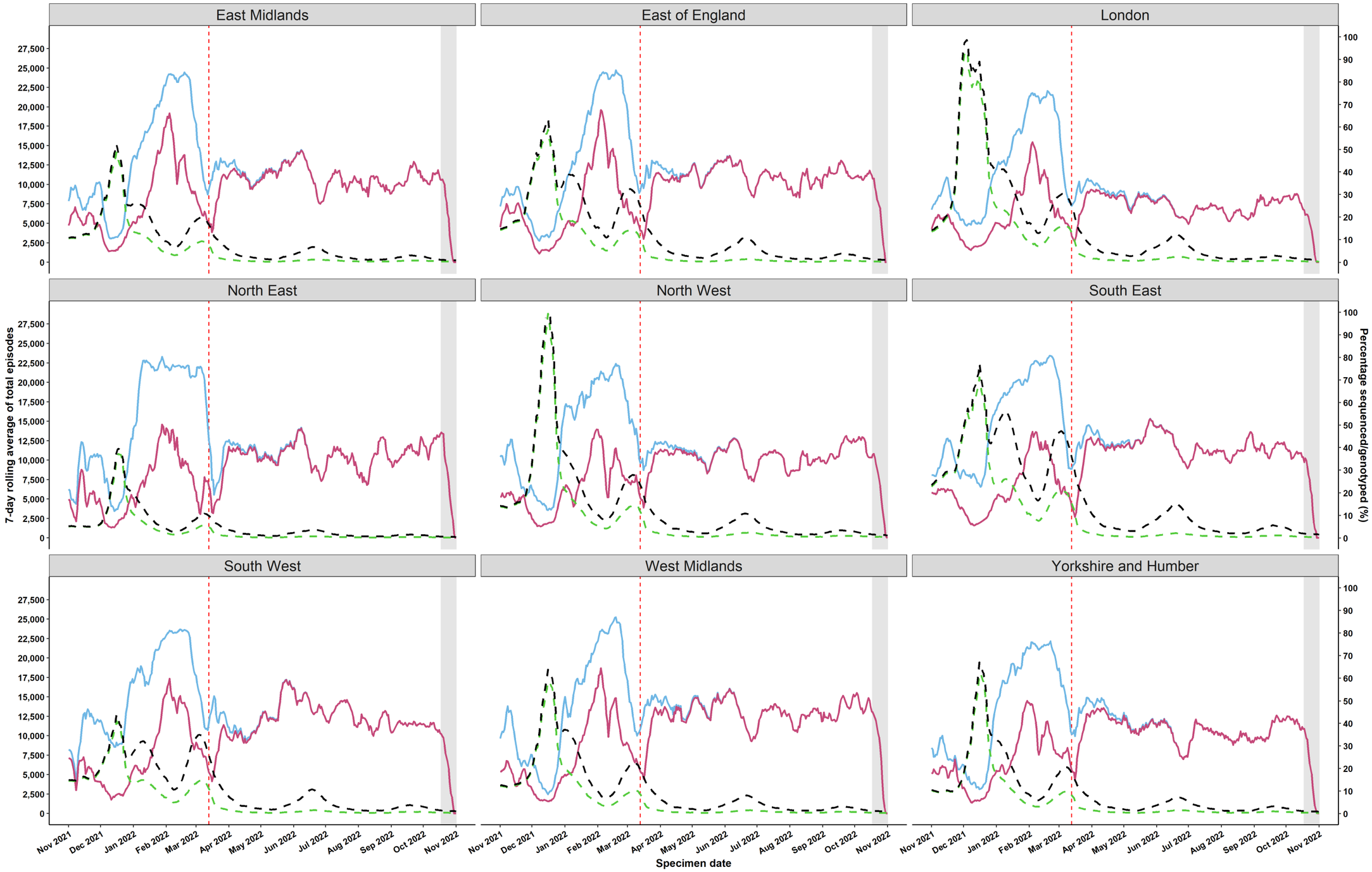
Between 24 October 2022 and 13 November 2022, a total of 19,802 SARS-CoV-2 sequences have been generated. Of these, 3,093 samples are from ONS (15.6%). This is a random sample of community cases which can be used for lineage growth modelling.

Figure 1. Coverage of sequenced cases with a valid result and genotyping over time (20 November 2021 to 20 November 2022)



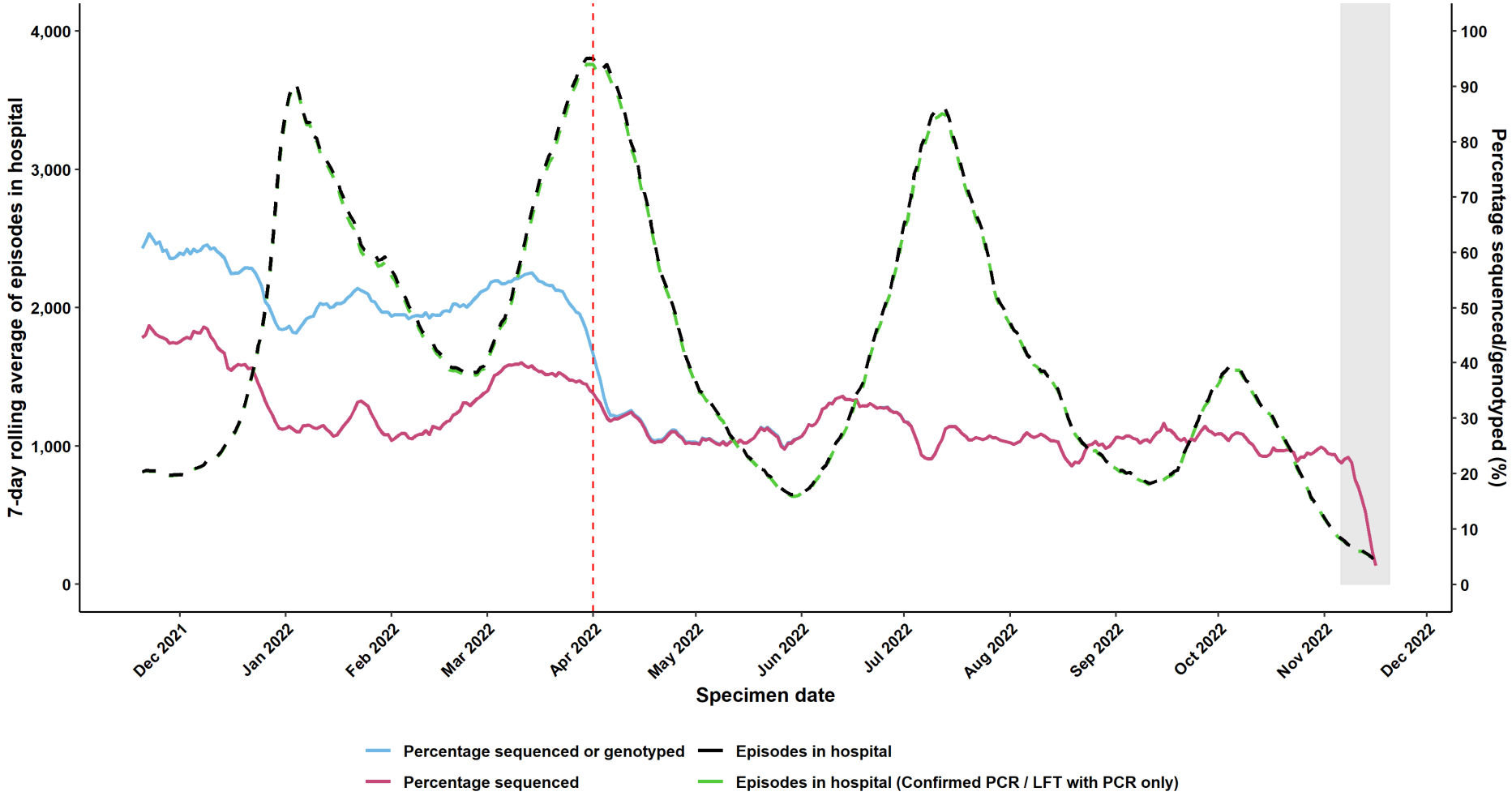
Cases where the individual only tested using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. (The data used in this graph can be found in the accompanying spreadsheet.)

Figure 2. Coverage of sequencing with a valid result and genotyping over time by region (20 November 2021 to 20 November 2022)



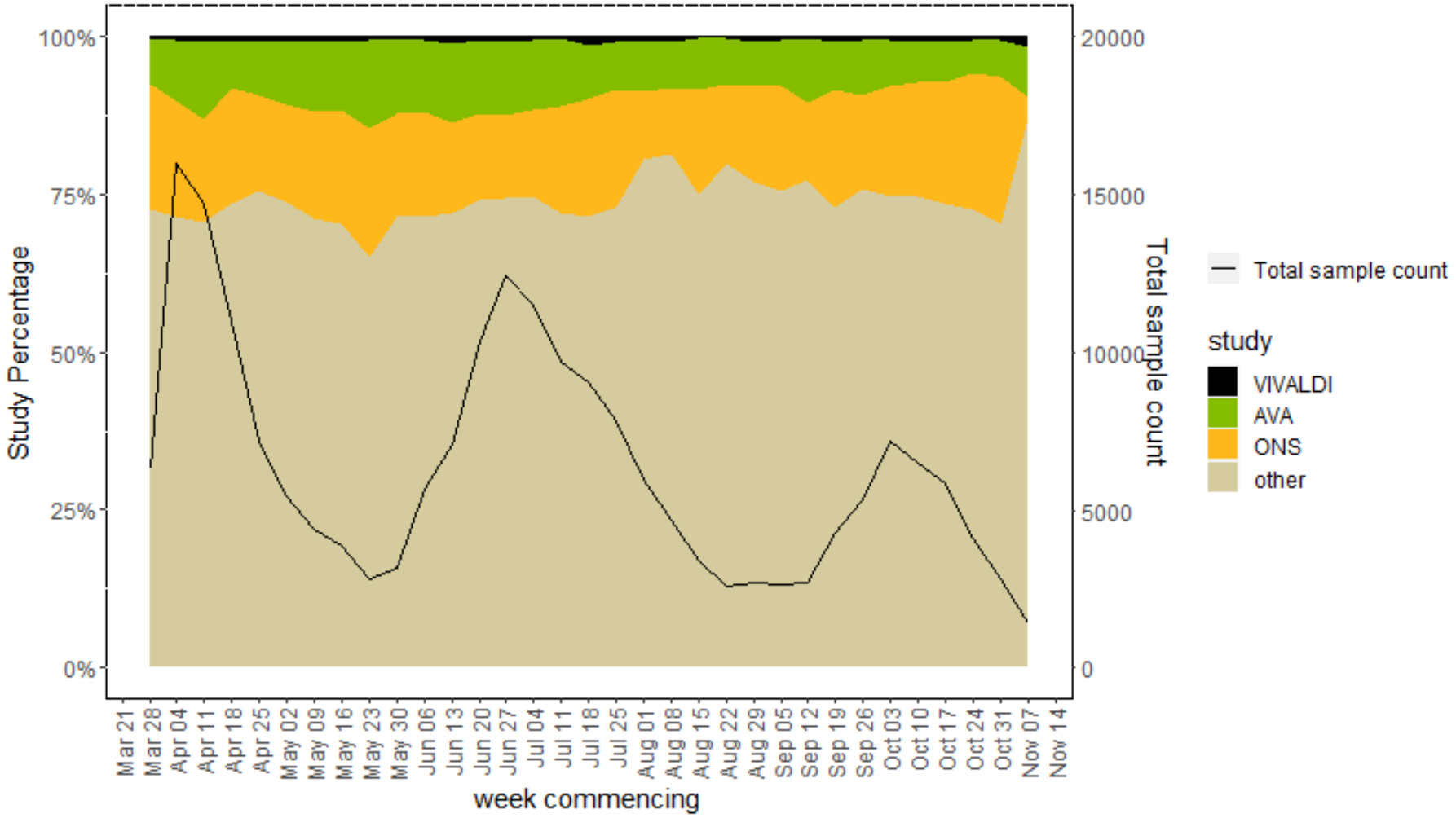
Cases where the individual only tested positive using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. (The data used in this graph can be found in the accompanying spreadsheet.)

Figure 3. Coverage of sequencing with valid result and genotyping for cases who test positive in hospital (20 November 2021 to 17 November 2022)



Cases 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 data used in this graph can be found in the accompanying spreadsheet.)

Figure 4. Proportion of sequenced sample assigned to studies 'AVA' (community therapeutics), 'VIVALDI' (care home study) and 'ONS' (COVID-19 Infection Survey) from 28 March 2022 to 14 November 2022



Other category denotes all sequenced samples that are not assigned to one of the listed studies (ONS, AVA, VIVALDI)
The data used in this graph can be found in the accompanying spreadsheet.

Due to prioritisation of samples for sequencing from hospitalised patients and care homes, sequenced cases are significantly older than reported cases. Between 25 October 2022 and 20 November 2022, the median age of reported COVID-19 cases was 52 years old. However, during the same period the median age of sequenced COVID-19 cases was 69 years old (Figures 5A and 5B).

Figure 5A. Age-sex distribution of all COVID-19 cases for the past 4 weeks (25 October 2022 to 20 November 2022)

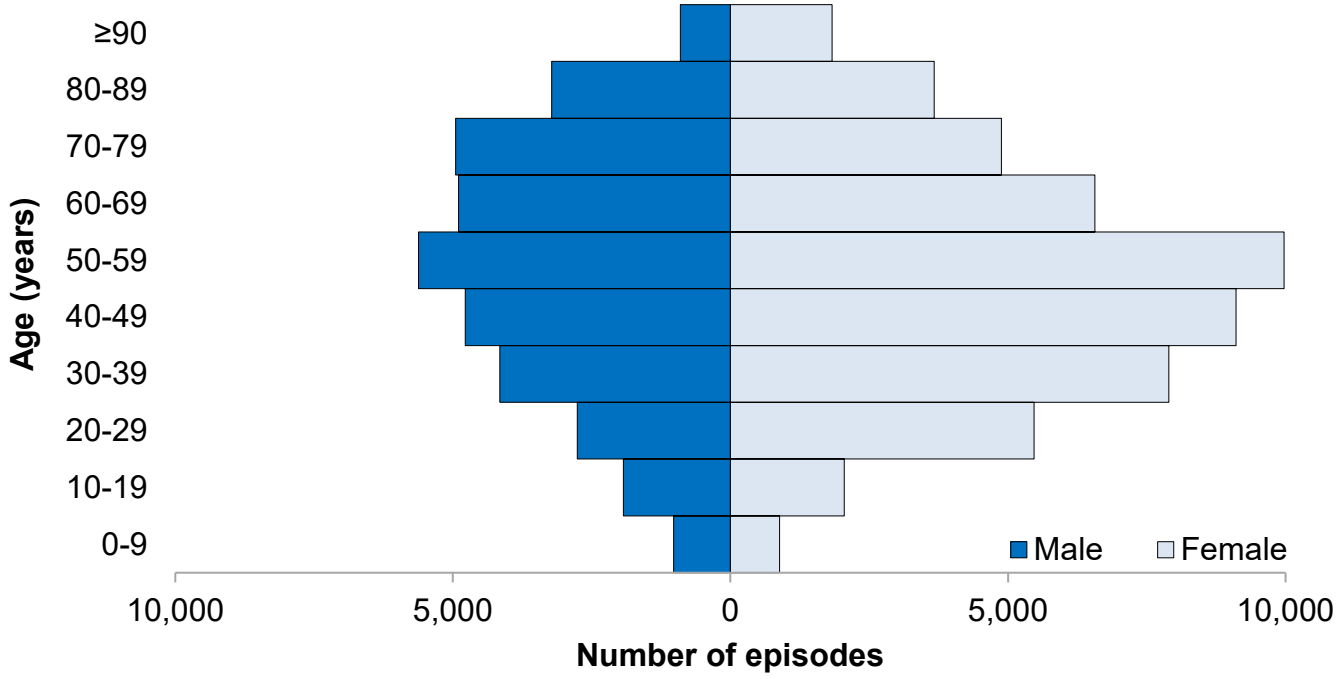
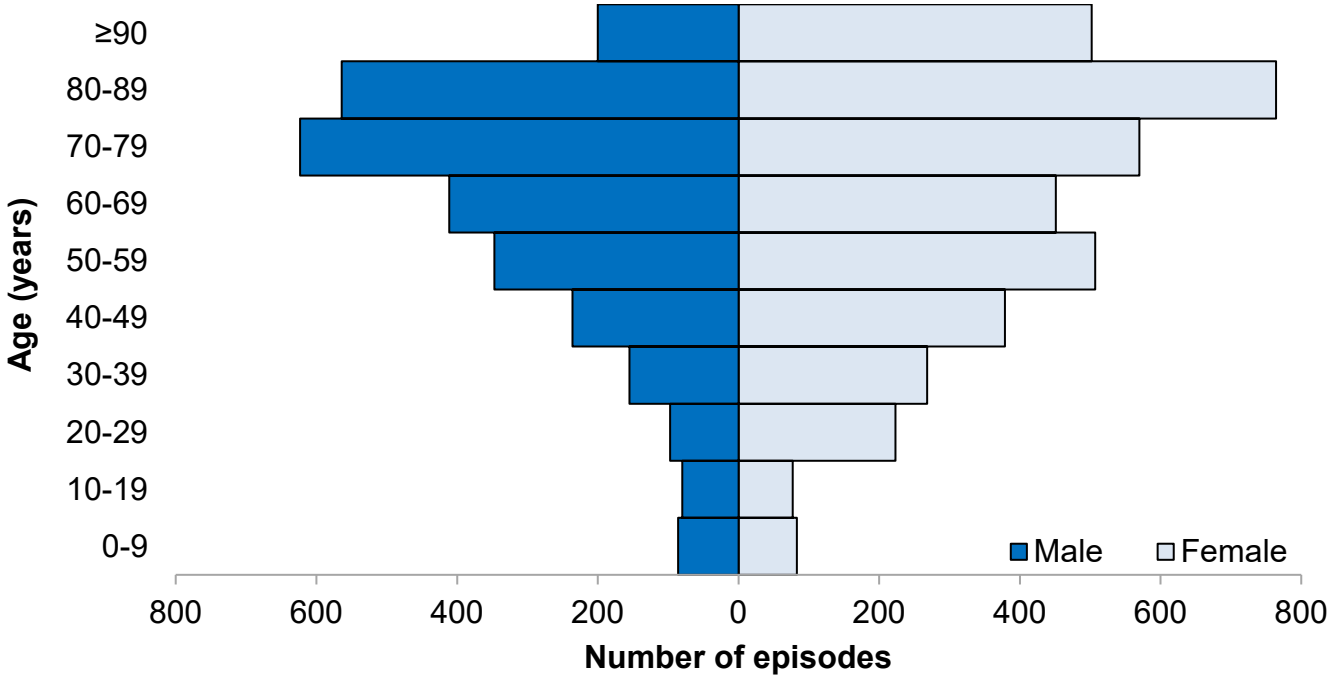


Figure 5B. Age-sex distribution of sequenced COVID-19 cases for the past 4 weeks (25 October 2022 to 20 November 2022)



The data used in this graph can be found in the accompanying spreadsheet.

1.2 Variant prevalence

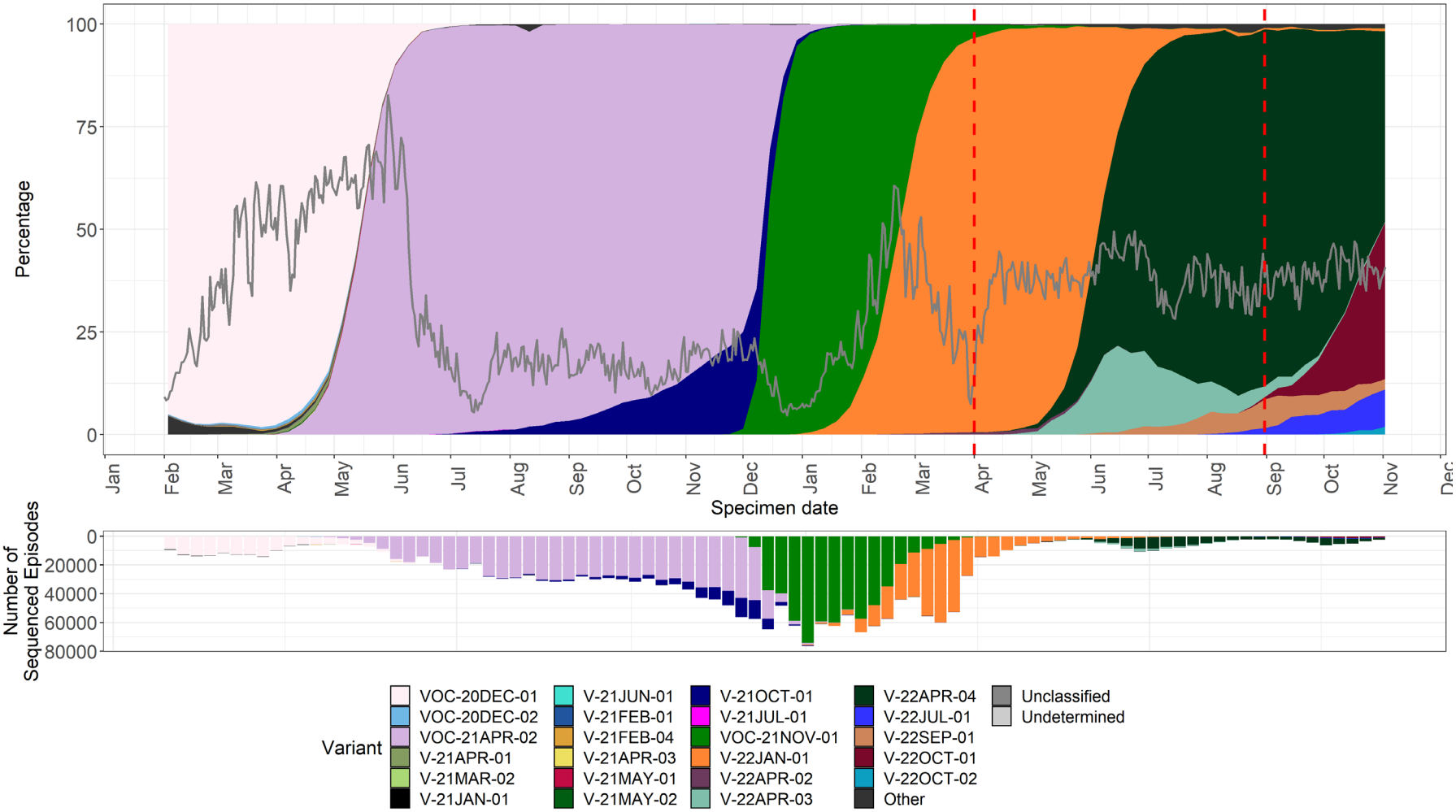
The prevalence of different UKHSA-designated variants amongst sequenced cases is presented in Figure 6. UKHSA designated variants are those assigned for more comprehensive epidemiological studies and may incorporate multiple sub-lineages.

Of the sequenced cases from 30 October 2022 to 5 November 2022, 0.7% were BA.2 (VOC-22JAN-01), 0.1% BA.4 (VOC-22APR-03), 46.4% BA.5 (VOC-22APR-04), 9.0% BA.2.75 (V-22JUL-01), 2.5% BA.4.6 (V-22SEP-01), 38.3% BQ.1 (V-22OCT-01), 2.0% XBB (V-22OCT-02) and 0.9% were classified as other.

The prevalence of lineages amongst sequences by Pangolin designation is presented in Figure 7. This provides a greater resolution showing the breakdown of sub-lineages. Lineages are shown if there are more than or equal to 5,000 sequences since 2 May 2022 or if they are more than or equal to 1% of sequences within a single week over the last 6 weeks. Lineages that do not meet these criteria are combined with their parent lineage (for example, BA.2.4 is combined with BA.2). Figure 8 shows the prevalence of lineages within the ONS sequence data only.

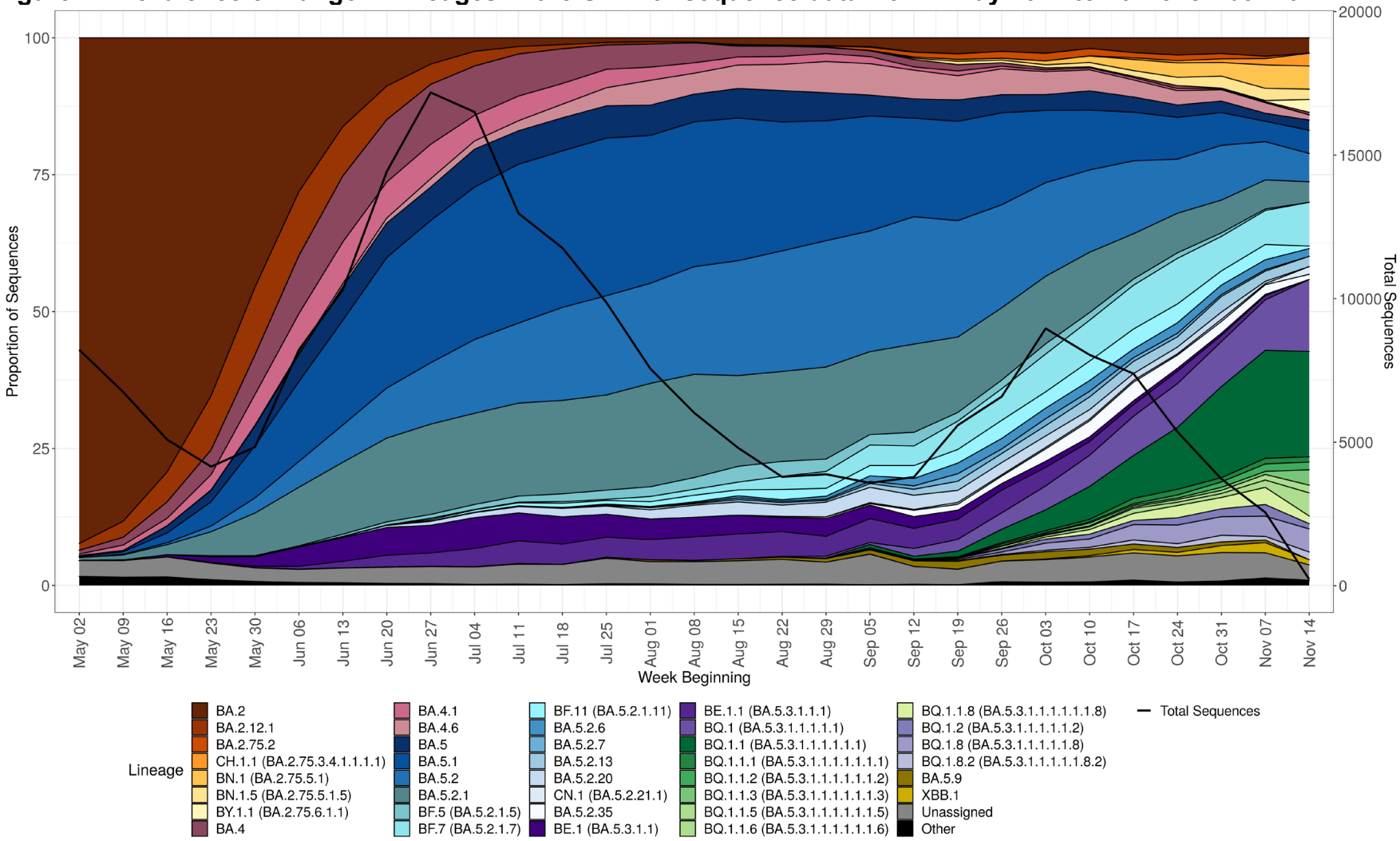
The lineages have been assigned using the accurate Ultrafast Sample placement on Existing tRee (UShER) mode and version 1.15 of the Pangolin data. The UShER mode identifies lineages based on their phylogenetic placement, rather than by specific mutation profiles. This allows sequences with reduced coverage to be assigned to lineages and easier separation of sub-lineages that are distinguished by a small number of mutations.

Figure 6. Variant prevalence (UKHSA designated variant definitions only) of available sequenced cases for England from 1 February 2021 as of 21 November 2022



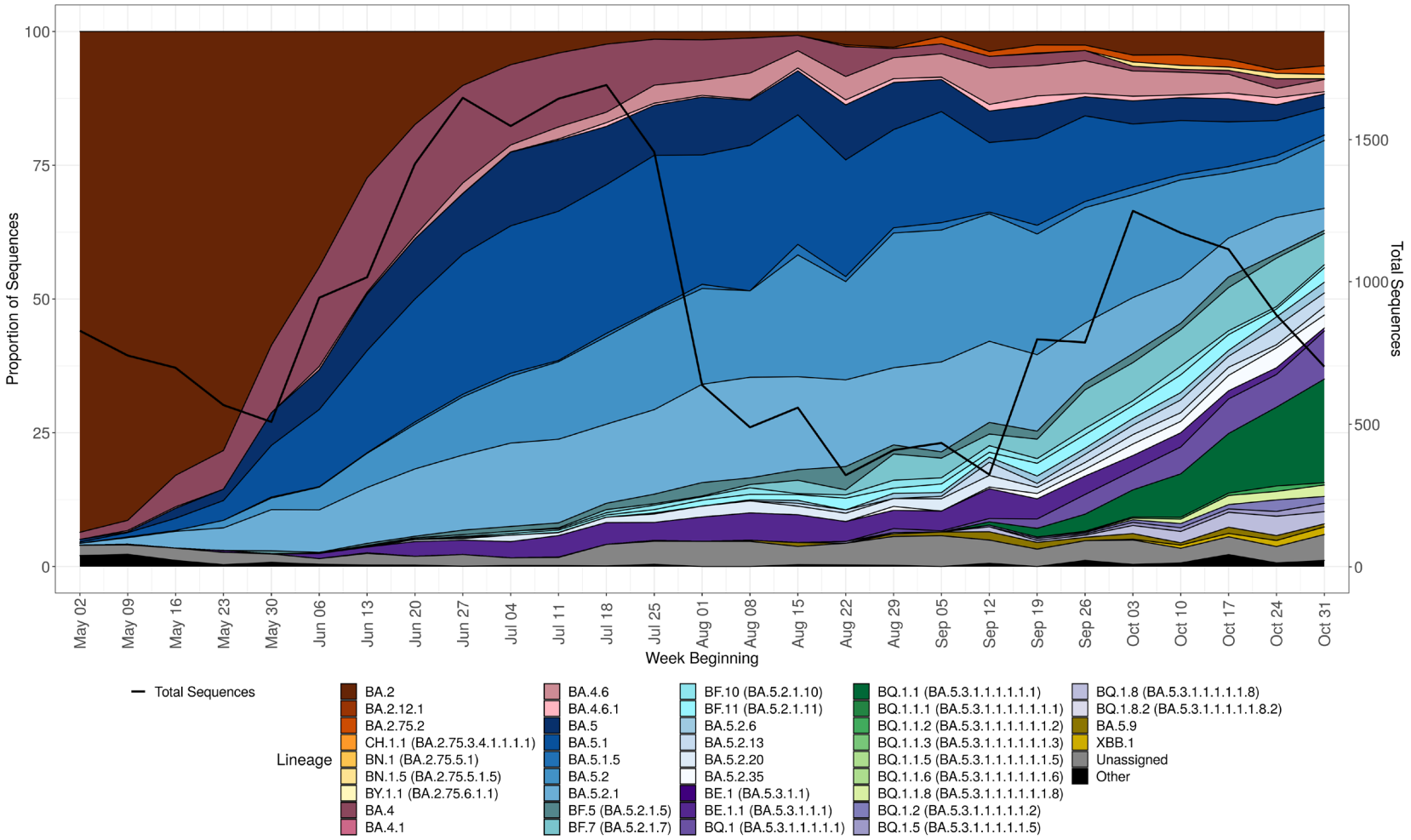
Find accessible data used in this graph in the accompanying spreadsheet. Dashed lines indicate period incorporating issue at a sequencing site. Grey line indicates proportion of cases sequenced. The first red dashed line denotes the start of England's 'Living with COVID-19' plan at the start of April 2022 and the second indicates the pause of asymptomatic testing for high-risk settings at the end of August 2022.

Figure 7. Prevalence of Pangolin lineages in the UK with sequence data from 2 May 2022 to 20 November 2022



The total number of valid sequence results per week is shown by the black line. The ‘Other’ category in this plot contains all lineages that do not meet the relevant criteria after combining smaller sub-lineages. ‘Unassigned’ are sequences that could not be assigned a lineage by Pangolin. Find accessible data used in this graph in the accompanying spreadsheet.

Figure 8. Prevalence of Pangolin lineages in the UK with ONS sequence data from 2 May 2022 to 6 November 2022



The total number of valid sequence results per week is shown by the black line. The ‘Other’ category in this plot contains all lineages that do not meet the relevant criteria after combining smaller sub-lineages. ‘Unassigned’ are sequences that could not be assigned a lineage by Pangolin. Find accessible data used in this graph in the accompanying spreadsheet.

Part 2. V-22OCT-02 (XBB recombinant)

XBB was first raised as a signal on 11 October 2022 through horizon scanning. This recombinant lineage is composed of 2 BA.2 parent lineages BJ.1 and BM.1.1.1, with an approximate break point between spike mutations G446S and N460K. This recombinant is characterised by the acquisition of E: T11A, Spike: V83A, H146Q, Q183E, F486S, F490S. Spike mutations inherited from BJ.1 are G339H, R346T, V445P, G446S and from BM.1.1.1 are N460K, F486V, F490S, and R493Q. XBB contains more receptor binding domain mutations at antigenic sites than any other widespread circulating variant and, according to Cao and others, is less well neutralised than either BQ.1.1 or BA.2.75.2.

As of 21 November 2022, 4,831 XBB samples have been uploaded to GISAID from 51 non-UK countries, across 6 continents. Currently, the country uploading the most samples is Singapore (1,329, 26%). A total of 345 UK samples have been sequenced so far.

2.1 Epidemiology

As of 21 November 2022, there were 152 cases with XBB in England.

In England, the first detected XBB case had a specimen date of 10 September 2022. Most cases (33) were London residents, with further cases resident in the North West (20), South East (19), East of England (18), South West (15), West Midlands (13), London (66), Yorkshire and the Humber (12), East Midlands (10) and North East (7) regions. A total of 53 cases have not been assigned a region. The majority of cases were aged 80 years or older.

Part 3. V-22OCT-01 (BQ.1)

BQ.1 (B.1.1.529.5.3.1.1.1.1.1) was first raised as a signal in monitoring on 12 September 2022 as part of horizon scanning. This BA.5 sub-lineage has acquired spike mutations L452R, N460K, and K444T. The affinity impact of N460K is reported to be significant (Saito and others, 2022; Cao and others, 2022). Additionally, the BQ.1.1 sub-lineage has acquired the spike mutation R346T, also seen in many of the current convergently evolving variants. This sub-lineage is captured as part of UKHSA's V-22OCT-01 lineage definition.

As of 21 November 2022, 33,206 BQ.1 (including its sub-lineages) samples have been uploaded to GISAID from 81 distinct non-UK countries, across 6 continents. A total of 9,285 BQ.1 UK samples have been sequenced so far.

Since 21 June 2022, 17,621 samples from BQ.1.1 and its sub-lineages have been uploaded to GISAID, spanning 70 non-UK countries and 6 continents. A total of 4,715 BQ.1.1 UK samples have been sequenced (lineage assigned by UShER).

3.1 Epidemiology

As of 21 November 2022, there were 630 cases with BQ.1 in England.

In England, the first detected BQ.1 case had a specimen date of 23 April 2022. Most cases (70) were North West residents, with further cases resident in the West Midlands (68), London (66), South East (66), Yorkshire and the Humber (64), East of England (63), East Midlands (61), North East (60) and South West (59) regions. A total of 53 cases have not been assigned a region.

Part 4. Variant modelling

Multiple models are used to estimate the growth advantage of emerging lineages relative to currently circulating lineages. By comparing outputs from multiple models, it is possible to balance strengths and weaknesses of both and provide a more robust perspective on a given lineage's growth. Here we describe lineages using a multinomial model and logistic regression and generalised additive models.

Variant growth rates were estimated using 3 models in comparison to different background reference data sets (Table 3). The multinomial model (MM) is fitted with the UShER assigned sequences described in section 1.2. This differs from previous versions of this report, where the MM was fitted to sequenced cases from the Sanger dataset where pangoLEARN is used to assigned lineages. Growth rates are estimated with respect to a given reference lineage. The logistic regression and generalised additive models are fitted with respect to a geographically

matched data set reflecting growth with respect to the mixture of lineages co-circulating with a given variant. All reported growth rates are in logistic units and reflect growth in frequency of a given variant, not growth in cases or numbers of samples.

Multinomial model

A Bayesian multinomial model was fit to English sequenced cases from 4 April 2022 to 9 November 2022, to model the relative growth rates of Omicron lineages. The model is fit at the regional level to account for geographic heterogeneity in variant dynamics. Only samples included as part of the ONS CIS were analysed. This represents a change to previous weeks when all sequenced cases were included.

The modelled percentage representation is shown in Figure 9, with relative growth rates compared to BA.5.2 lineages (Figure 10). Note that the multinomial model includes several emerging, competitive lineages. This means that a large relative growth rates relative to the presently dominant BA.5.2 must be considered in the context of other competing variants which may also be increasing in representation.

Logistic Regression and Generalised Additive Models

The growth rate is estimated by logistic regression of a variant or lineage of each sample unit on time of sample selection, relative to all other variants. Growth rates were based on sequences sampled through Pillar 1 testing and from Office for National Statistics (ONS) testing in England. To decorrelate Pillar 1 testing, the data was subsampled so that at most one sequence came from a given combination of hospital, day of sampling, and upper tier local authority (UTLA). The sampling range for both logistic regression and generalised additive models is from 24 August 2022 to 31 October 2022.

To characterise how growth rates change through time, a generalised additive model is also fitted which allows the growth rate to vary over time. To adjust for geographic variation in case growth rates and differences in sampling intensity, lineage growth rates were estimated relative to a geographically matched sample of genomes. A logistic growth rate of zero would indicate no difference in growth rates between a given lineage and other variants.

Table 3. Growth rate (GR) of variants and signals under monitoring as of 9 November 2022^

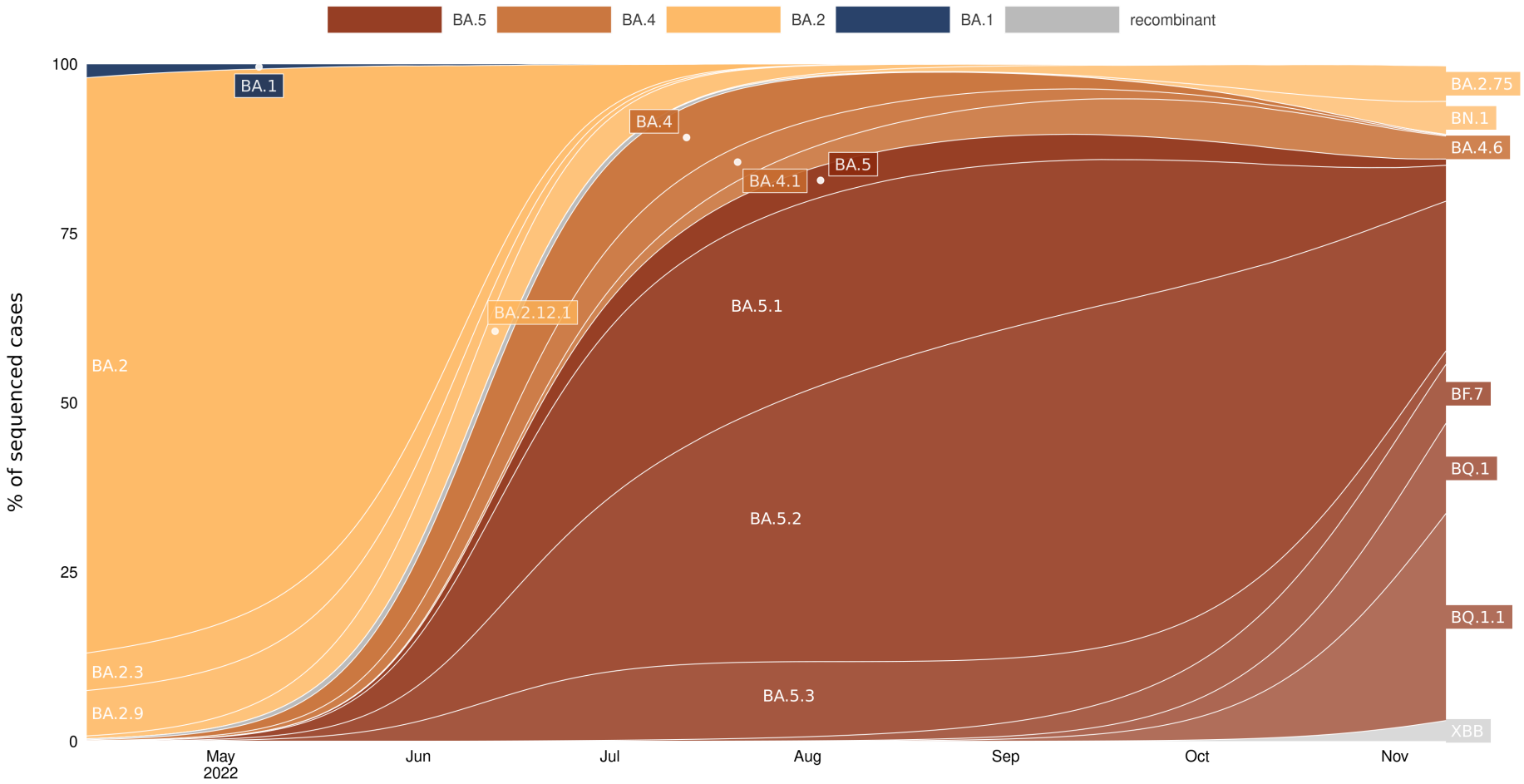
Lineage	English ONS sequences used in the multinomial model (MM)	MM England estimated prevalence	MM estimate for the weekly growth relative to BA.5.2	English sequences counts used in the logistic regression and generalised additive model	Logistic regression GR (1/week)	Generalised additive model most recent GR (1/week)
BQ.1.1	848	30.56% (95% CrI: 26.75 to 34.78)	48.54% (95% CrI: 43.31 to 54.05)	496	41%	24%
BQ.1*	487	13.31% (95% CrI: 11.07 to 15.89)	38.6% (95% CrI: 33.92 to 44.04)	960	35.1%	15.4%
BN.1	162	4.89% (95% CrI: 3.67 to 6.5)	44.66% (95% CrI: 37.8 to 52.33)	31	-	-
BA.2.75†	336	5.23% (95% CrI: 4.18 to 6.54)	22.48% (95% CrI: 19.12 to 26.01)	515	19.3%	15.7%
BA.4.6	705	3.39% (95% CrI: 2.73 to 4.13)	4.35% (95% CrI: 3.11 to 5.71)	750	-1.7%	-11.8%
XBB	79	3.06% (95% CrI: 2.1 to 4.26)	56.94% (95% CrI: 46.93 to 67.17)	81	-	-

* BQ.1 excludes BQ.1.1 which was modelled separately.

† BA.2.75 excludes BN.1 which was modelled separately.

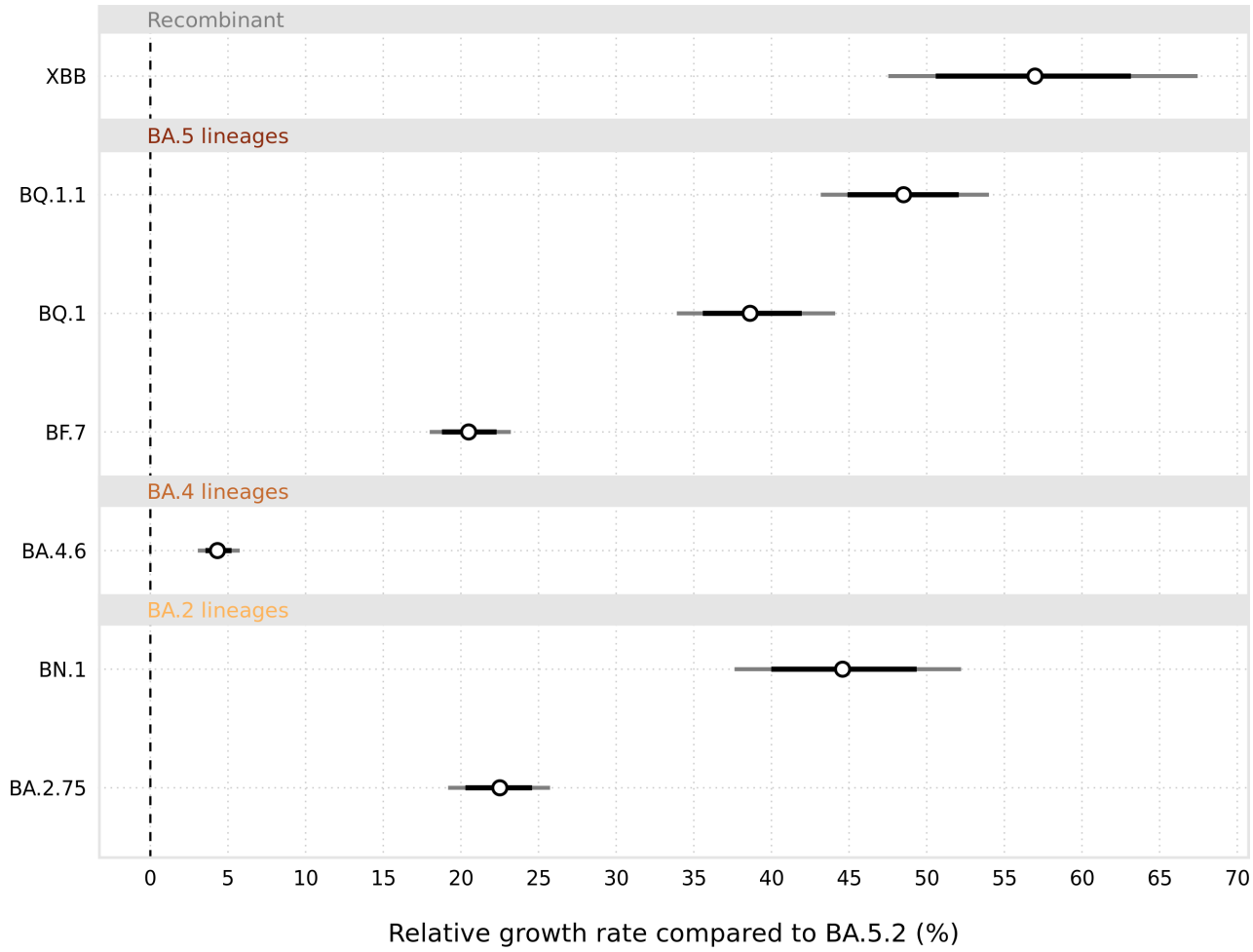
^ Sampling range for both logistic regression and generalised additive models is from 24 August 2022 to 31 October 2022.

Figure 9. Area plot showing the predicted representation of each lineage of the multinomial model of sequenced ONS CIS samples



This figure shows the predicted representation of different lineages from the multinomial model. Supplementary data is not available for this figure.

Figure 10. Comparison of the estimated relative growth rates for emerging BA.5, BA.4, BA.2 and recombinant lineages versus that for specifically BA.5.2 lineages



The relative growth rates are taken from a multinomial model of sequenced ONS CIS cases in England, described above. Supplementary data is not available for this figure.

Sources and acknowledgments

Data sources

Data used in this investigation is derived from the COG-UK and UKHSA genomic programme data set, ONS COVID-19 Infection Survey, the UKHSA Second Generation Surveillance System, the Secondary Uses Service data set, Emergency Care Data Set, the UKHSA Case and Incident Management System and GISAID.

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