UK Health Security Agency

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

Technical briefing 51

10 March 2023

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 6 March 2023 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. Whilst there are substantial numbers of genomes still being generated, the demographic composition of the cases sequenced is different from total cases in the population with a greater representation of older individuals. This may affect variant characterisation.

New data and analysis findings

Composition of the genomic data set

The profile of sequenced coronavirus (COVID-19) cases continues to be biased toward older people due to prioritisation of samples for polymerase chain reaction (PCR) testing and sequencing from hospitalised patients and care homes. Between 13 December 2022 and 6 March 2023, the median age of sequenced COVID-19 cases was 73 years old.

Sequence variant prevalence

From UK sequences collected from 20 February 2023 to 27 February 2023, 44% were classified as V-23JAN-01 (XBB.1.5), 23% V-22DEC-01 (CH.1.1), 13% V-22OCT-01 (BQ.1), 7% V-22OCT-02 (XBB), 1% VOC-22APR-04 (BA.5), and 1% V-22JUL-01 (BA.2.75). The remaining sequences (11%) were from lineages or variants representing less than 1% of the total samples, classed as other, or of insufficient quality to assign.

Horizon scanning

Since the last technical briefing there are 3 additional signals in monitoring; these are being monitored either due to concerning growth, mutation profiles or national and/or international interest: XBB.1.9.1, XBB.1.9.2 and XBB.1.16.

XBB.1.9.1 is rapidly increasing in proportion and is currently the only lineage with a significant growth advantage relative to XBB.1.5, though with small numbers identified.

XBB.1.9.2 is also increasing as a proportion of the samples in the UK, this lineage has acquired Spike R408S, F486P; ORF8:G8*; ORF1ab:G1819S, S5360P in addition to a synonymous SNP T28297C. XBB.1.16 is a lineage with 3 additional spike mutations (E180V, K478R, and S486P) found both in the UK and internationally. However, the number of total number of samples is still less than 100.

Growth rates

XBB.1.9.1 and XBB.1.5 are the most competitive of the signals in monitoring or designated variants, across all models.

Hospitalisation

Preliminary analysis of the risk of hospital admission following presentation to emergency care indicates there is no increase in risk of hospital admission for V-22DEC-01 (CH.1.1) compared to V-22OCT-01 (BQ.1) (odds ratio: 0.96, 95% confidence interval (CI) 0.83 to 1.12), nor V-23JAN-01 (XBB.1.5) compared to V-22OCT-01 (BQ.1) (odds ratio 0.8, 95% CI 0.63 to 1.03). This analysis was adjusted for age, vaccination status, sex, reinfection status, deprivation, region and specimen test week. Results may change as further data becomes available.

Vaccine effectiveness: V-23JAN-01 (XBB.1.5)

V-23JAN-01 (XBB.1.5) numbers are currently too small to allow for accurate estimates of vaccine effectiveness.

1. Surveillance overview

World Health Organization (WHO) nomenclature from 24 January 2022 is incorporated. Table 1 shows the current variants of concern (VOCs), variants (V-date-number), and signals in monitoring detected in the UK incorporating WHO designations with Phylogenetic Assignment of Named Global Outbreak Lineages (Pangolin lineages).

Table 1. 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	Delta (B.1.617.2 and sub-lineages) V-21APR-02	*XBB.1.9.1
Omicron (B.1.1.529) sub-lineage BA.2 and descendant lineages VOC-22JAN-01	Omicron XE Recombinant (BA.1 x BA.2) V-22APR-02	*XBB.1.9.2
Omicron (B.1.1.529) sub-lineage BA.4 VOC-22APR-03	Omicron BA.2.75 V-22JUL-01	*XBB.1.16
Omicron (B.1.1.529) sub-lineage BA.5 VOC-22APR-04	Omicron BA.4.6 V-22SEP-01	
	Omicron BQ.1 V-22OCT-01	
	Omicron XBB Recombinant (BJ.1 x BM.1.1.1) V-22OCT-02	
	Omicron CH.1.1 V-22DEC-01	
	Omicron XBB.1.5 Recombinant (XBB plus additional mutations) V-23JAN-01	

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

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. In the past 12 weeks, there have been no variants or signals detected in the Global Initiative on Sharing Avian Influenza Data (GISAID) that have not been detected in the UK.

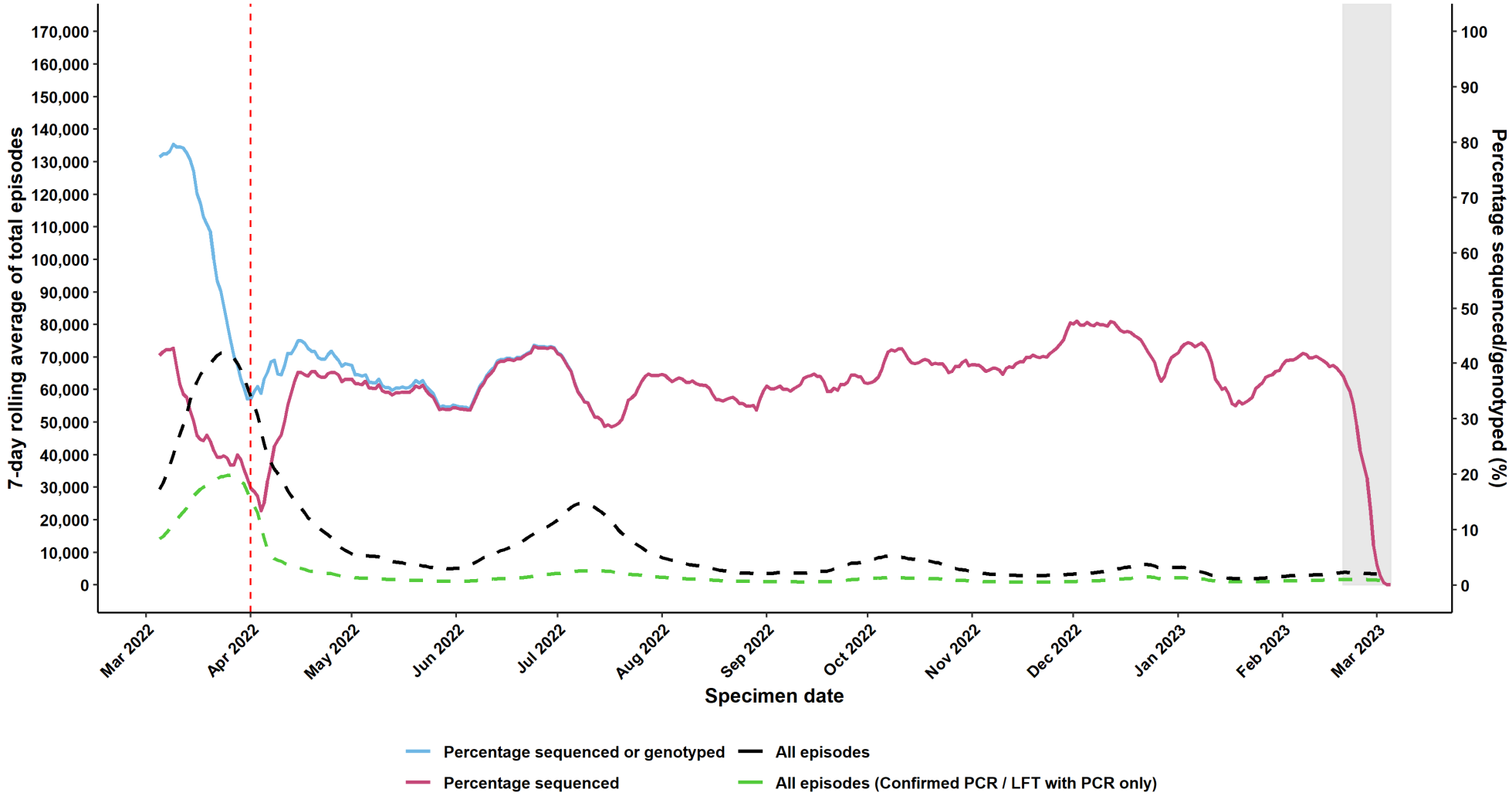
1.1 Sequencing coverage

Figure 1 shows the proportion of PCR-positive COVID-19 cases that have linked to a valid sequencing result (50% of the genome with sufficient read coverage) or genotyping PCR result over time. Figure 2 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 data set (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.

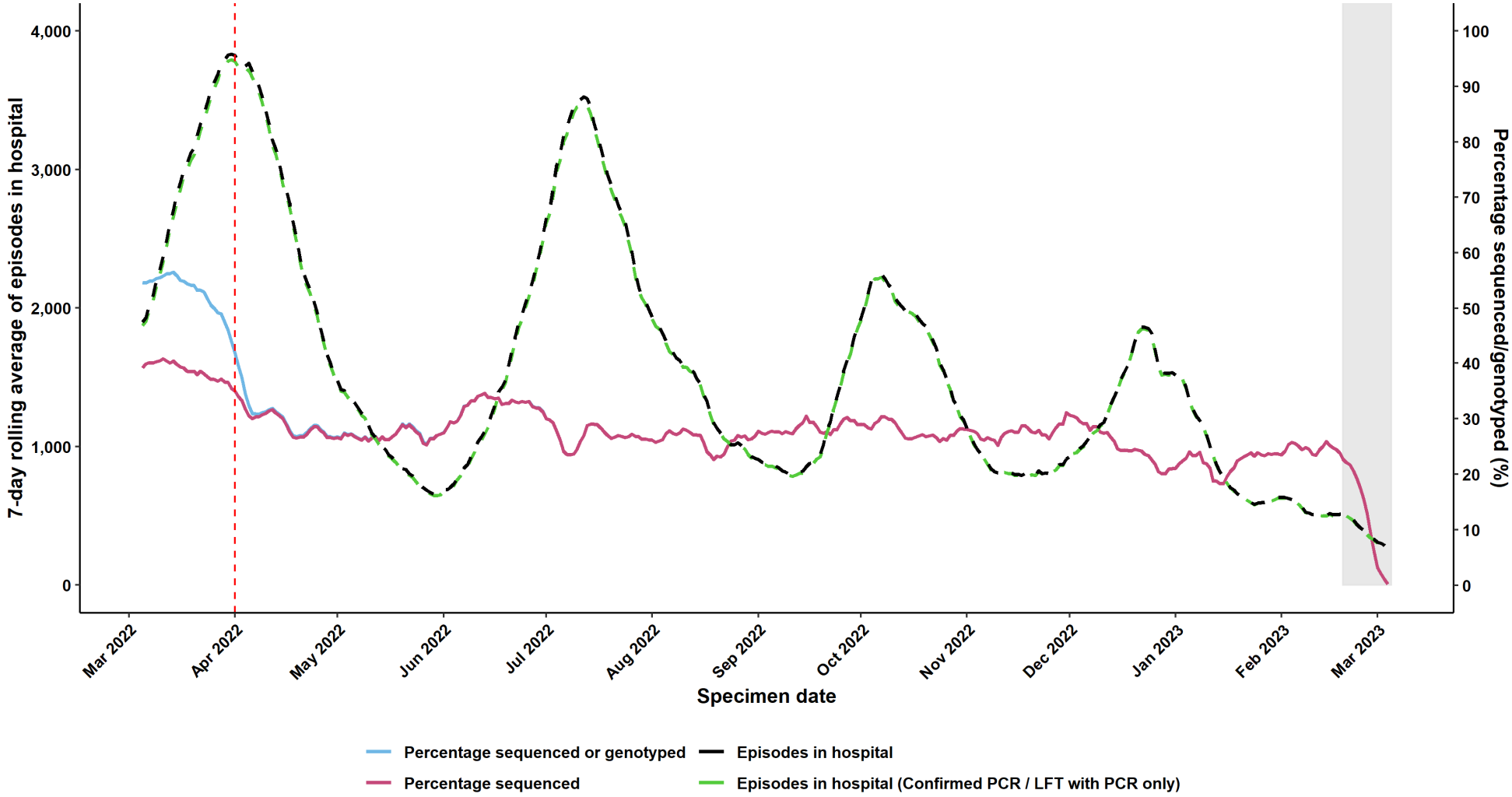
Currently, the sequencing strategy prioritises hospitalised cases, patients who are receiving specific antiviral therapy, and national core priority studies.

Figure 1. Coverage of sequenced cases with a valid result and genotyping over time (5 March 2022 to 5 March 2023)



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 valid result and genotyping for cases who test positive in hospital (5 March 2022 to 5 March 2023)



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.

Due to prioritisation of samples for PCR testing and sequencing from hospitalised patients and care homes, sequenced cases in England are significantly older than reported cases. Between 8 February 2023 and 7 March 2023, the median age of reported COVID-19 cases was 58 years old. However, during the same period, the median age of sequenced COVID-19 cases was 74 years old (Figures 3a and 3b).

Figure 3a. Age-sex distribution of all COVID-19 cases for the past 4 weeks in England (8 February 2023 to 7 March 2023)

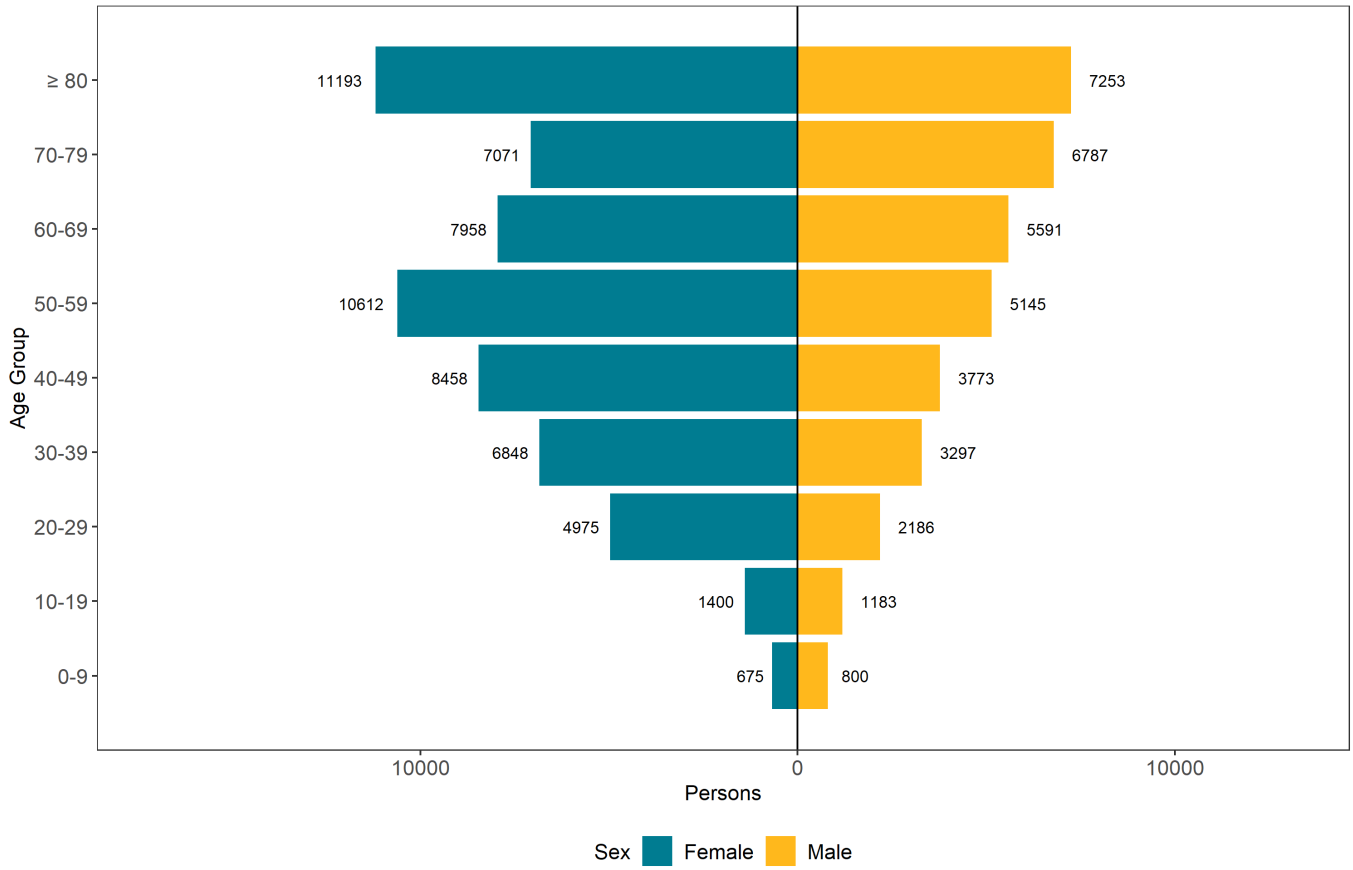
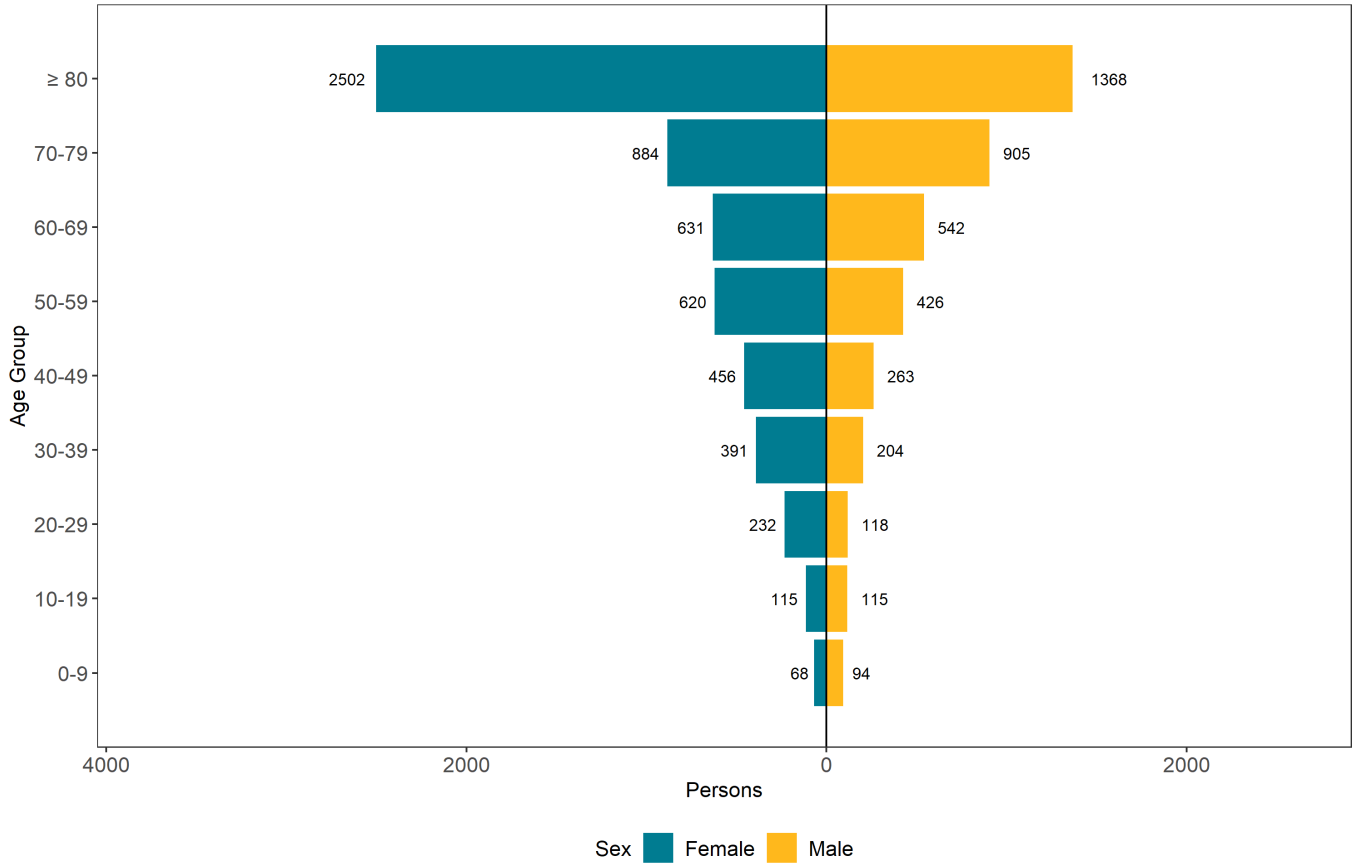


Figure 3b. Age-sex distribution of sequenced COVID-19 cases for the past 4 weeks in England (8 February 2023 to 7 March 2023)



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

1.2 Variant prevalence

The prevalence of different UK Health Security Agency (UKHSA)-designated variants amongst sequenced cases in England is presented in Figure 4. UKHSA designated variants are those assigned for more comprehensive epidemiological studies and may incorporate multiple sub-lineages. If a sub-lineage of an existing variant is also declared as a variant, it will be removed from the prevalence of the parent lineage (for example, V-22OCT-01 does not form part of the prevalence of V-22APR-04 in Figure 4).

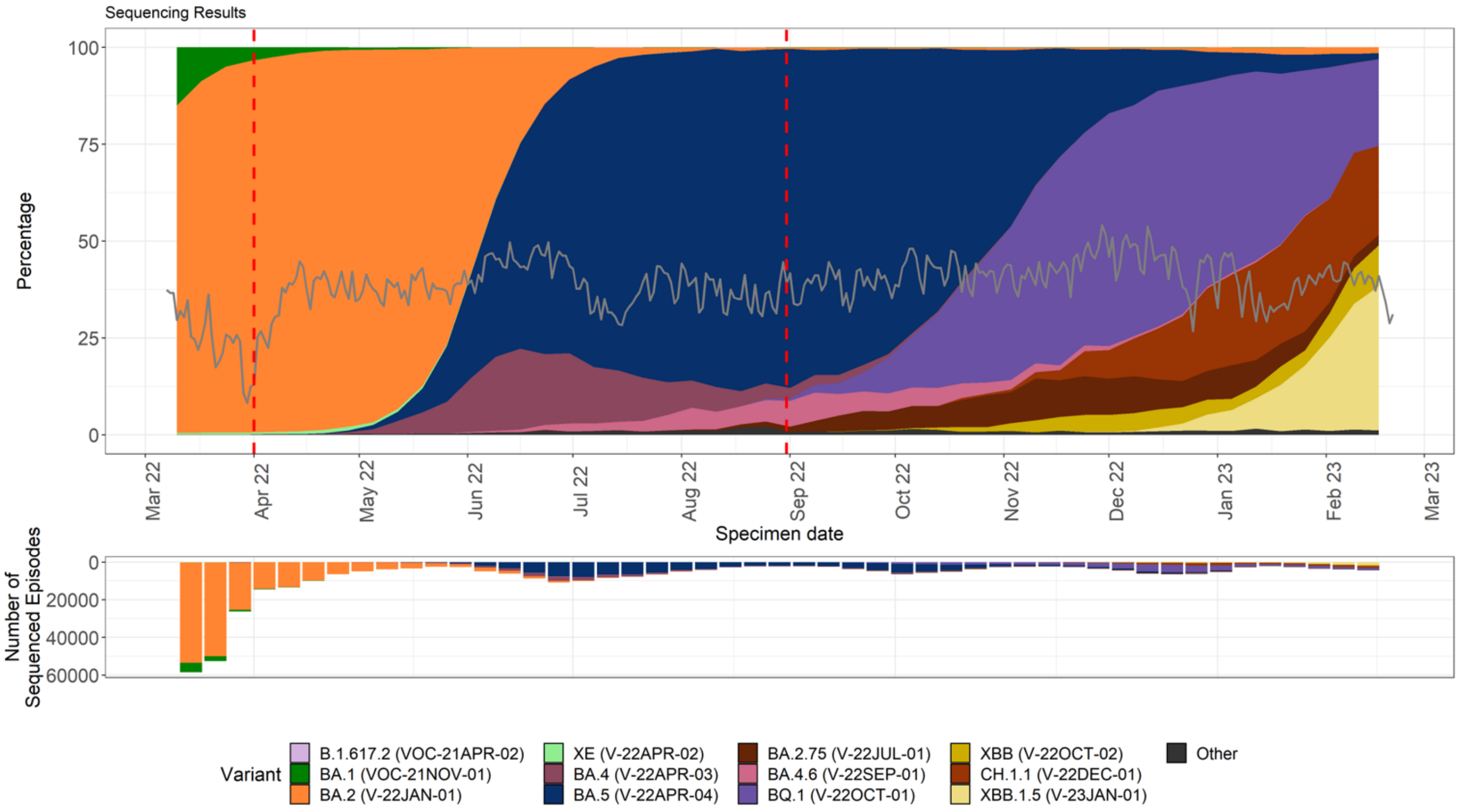
To account for sequencing delays, we report the proportion of variants from sequenced episodes between 20 February 2023 and 26 February 2023. Of those sequenced in this period, 40.6.% were classified as V-23JAN-01 (XBB.1.5), 25.8% as V-22DEC-01 (CH.1.1), 17.1% as V-22OCT-01 (BQ.1), 9.9% as V-22OCT-02 (XBB), 1.7% as V-22JUL-01 (BA.2.75), 1.5% as V-22JAN-01 (BA.2), 1.3% as V-22APR-04 (BA.5), and 2.1% as Other.

The prevalence of lineages amongst UK sequences by Pangolin designation is presented in Figure 5. 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 26 September 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 6 shows the prevalence of lineages within the ONS sequence data only.

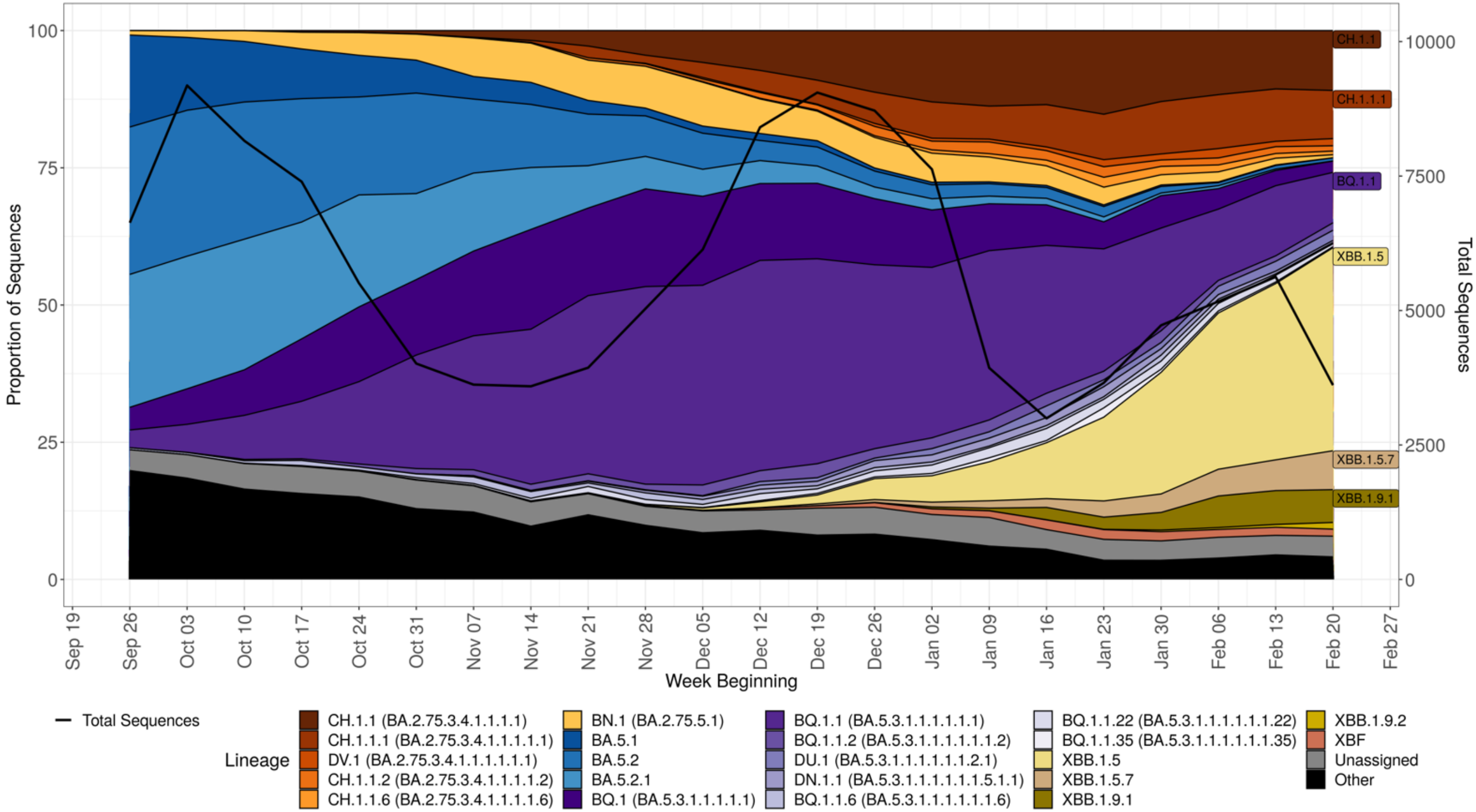
The lineages have been assigned using the accurate Ultrafast Sample placement on Existing tRee (UShER) mode and version 1.18.1.1 of the Pangolin data. The UShER mode identifies lineages based on their phylogenetic placement, rather than by specific mutation profiles. This allows sequences with reduced coverage to be assigned to lineages and easier separation of sub-lineages that are distinguished by a small number of mutations.

Figure 4. Variant prevalence (UKHSA designated variant definitions only) of available sequenced cases for England from 7 March 2022 to 26 February 2023



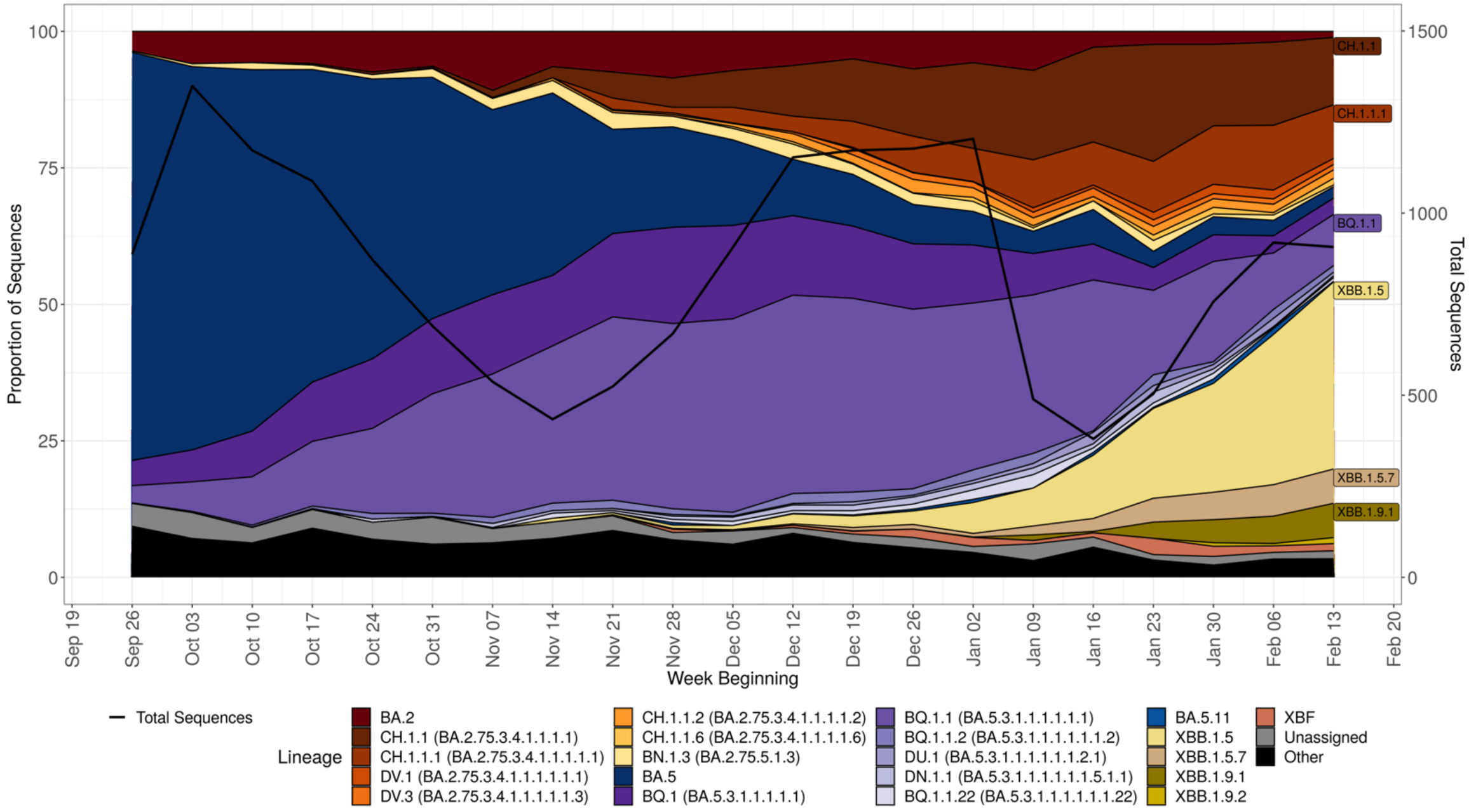
The grey line indicates proportion of cases sequenced. The first red dashed line denotes the start of England's 'Living with COVID' plan at the start of April 2022 and the second indicates the pause of asymptomatic testing for high-risk settings at the end of August 2022. The data used in this graph can be found in the accompanying spreadsheet.

Figure 5. Prevalence of Pangolin lineages in the UK with sequence data with a specimen date from 26 September 2022 to 26 February 2023, as of 6 March 2023



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. Lineages present in at least 3% of sequences in the most recent week are labelled to the right of the plot. The data used in this graph can be found in the accompanying spreadsheet.

Figure 6. Prevalence of Pangolin lineages in the UK in Office for National Statistics (ONS) COVID-19 Infection Survey (CIS) sequence data with a specimen date between 26 September 2022 to 19 February 2023



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. Lineages present in at least 3% of sequences in the most recent week are labelled to the right of the plot. The data used in this graph can be found in the accompanying spreadsheet.

2. 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 2). The multinomial model (MM) is fitted with the UShER assigned sequences described in section 1.2 using only samples from the Office for National Statistics COVID-19 Infection Survey (ONS CIS). Growth rates are estimated for each individual lineage and compared 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 24 February 2023, to model the relative growth rates of Omicron lineages. The model is fit at the upper tier local authority (UTLA) level to account for geographic heterogeneity in variant dynamics. Only ONS CIS samples were used in the model.

The modelled percentage representation is shown in Figure 7, with relative growth rates compared to XBB.1.5 (Figure 8). Note that the multinomial model includes several emerging, competitive lineages. This means that a large relative growth rate relative to the most prevalent lineage XBB.1.5 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 ONS CIS testing in England. The sampling range for both logistic regression and generalised additive models is from 12 December 2022 to 27 February 2023.

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 2. Growth rate (GR) of variants and signals under monitoring as of 24 February 2023**

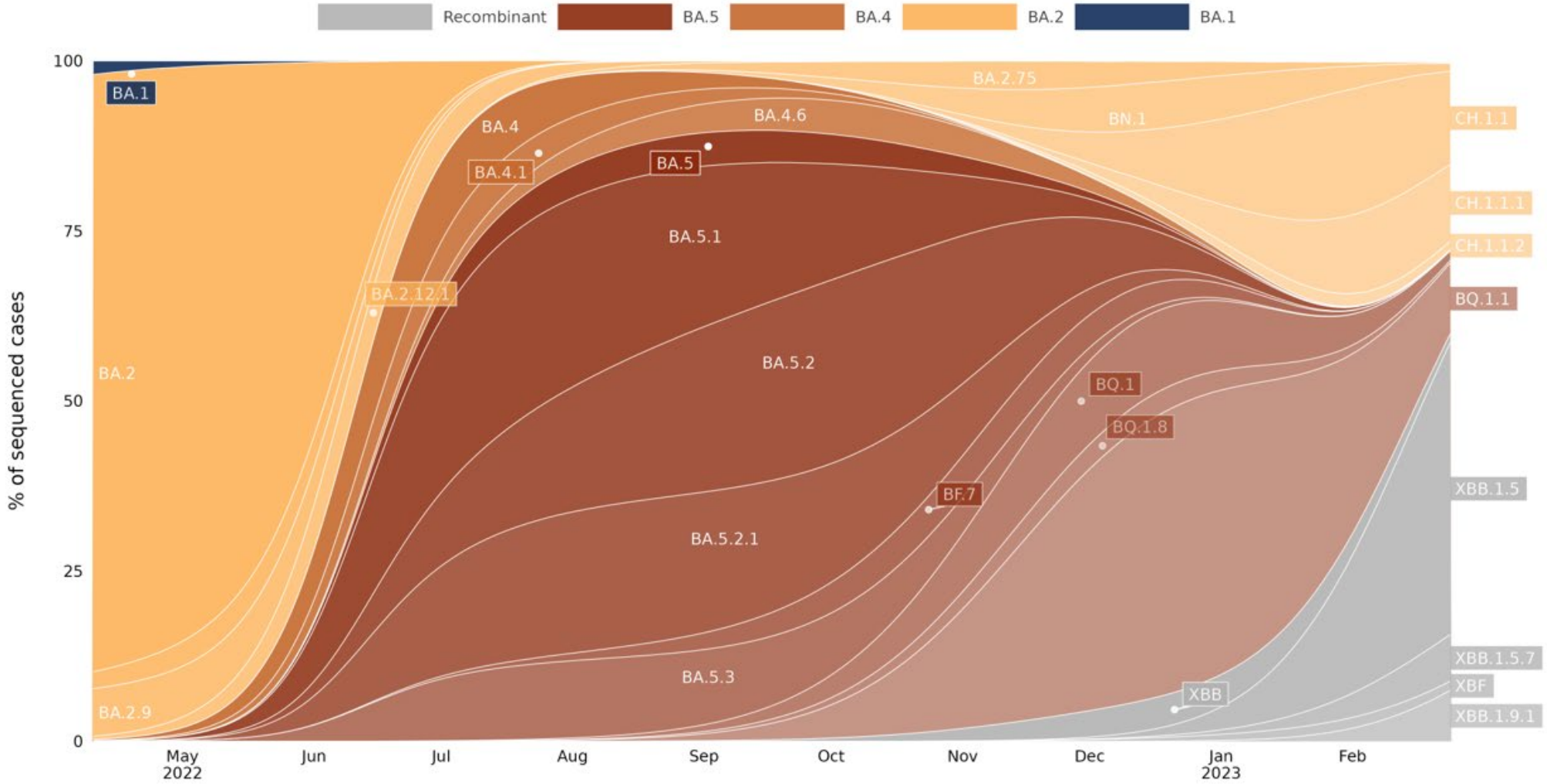
Lineage	English ONS sequences used in the multinomial model (MM)	MM England estimated prevalence	MM estimate for the weekly growth rate relative to XBB.1.5	UK ONS sequence counts used in the logistic regression and generalised additive model	Logistic regression GR (1/week)	Generalised additive model most recent GR (1/week)
XBB.1.9.1	171	7.49% (95% CrI: 5.54 to 9.66)	9.43% (95% CrI: 5.01 to 14.42)	188	44.7%	23.1%
V-23JAN-01(XBB.1.5)	1,181	42.88% (95% CrI: 39.75 to 46.02)	NA	1,178	38.2%	27.5%
XBB.1.5.7	233	6.85% (95% CrI: 5.44 to 8.44)	-1.38% (95% CrI: -4.1 to 1.44)	251	33.4%	22.9%
V-22DEC-01 (CH.1.1)	1,407	13.71% (95% CrI: 12.18 to 15.48)	-16.21% (95% CrI: -17.68 to -14.92)	2,301	5.9%	-11.3%
V-22OCT-01 (BQ.1)	1,385	1.39% (95% CrI: 1.18 to 1.61)	-30.05% (95% CrI: -31.8 to -28.36)	1,992	-9.3%	-18.2%
BQ.1.1	4,337	10.42% (95% CrI: 9.42 to 11.55)	-26.03% (95% CrI: -27.56 to -24.49)	4,316	-14.9%	-29.7%
BN.1	765	1.14% (95% CrI: 0.93 to 1.38)	-28.25% (95% CrI: -29.98 to -26.47)	761	-14.3%	-47.5%

* Logistic and generalised additive models include sublineages in estimates, whereas the MM separates some key sublineages out (please refer to Figure 7).

** Sampling range for both logistic regression and generalised additive models is from 12 December 2022 to 27 February 2023.

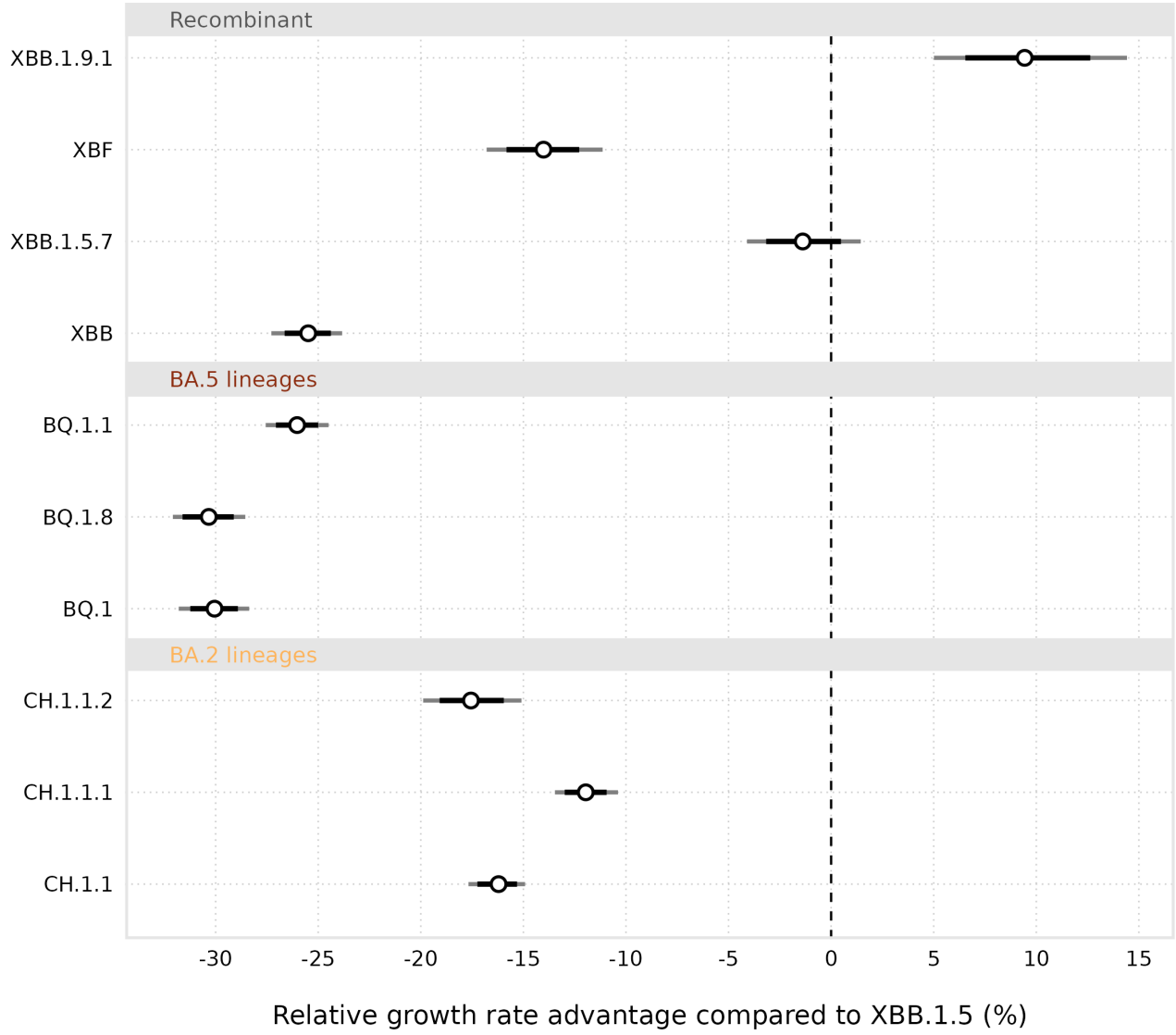
CrI = credible intervals.

Figure 7. Area plot showing the predicted representation of each lineage of the multinomial model of ONS sequenced cases in England, 4 April 2022 to 24 February 2023



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

Figure 8. Comparison of the estimated relative growth rates for emerging BA.5, BA.2 and recombinant lineages versus that for specifically XBB.1.5



The relative growth rates are taken from a multinomial model of ONS CIS sequenced cases in England, described above. Data for samples is from 4 April 2022 to 24 February 2023. Supplementary data is not available for this figure.

3. V-23JAN-01 (Omicron recombinant XBB.1.5)

XBB.1.5 was designated a variant (V-23JAN-01) on 9 January 2023; its genomic definition has previously been described in technical briefing 50. In total there are 62,836 XBB.1.5 sequences annotated in GISAID (excluding the UK). V-23JAN-01 (XBB.1.5) has been identified in 8,723 UK sequences.

3.1 Genomic diversity within V-23JAN-01 (XBB.1.5)

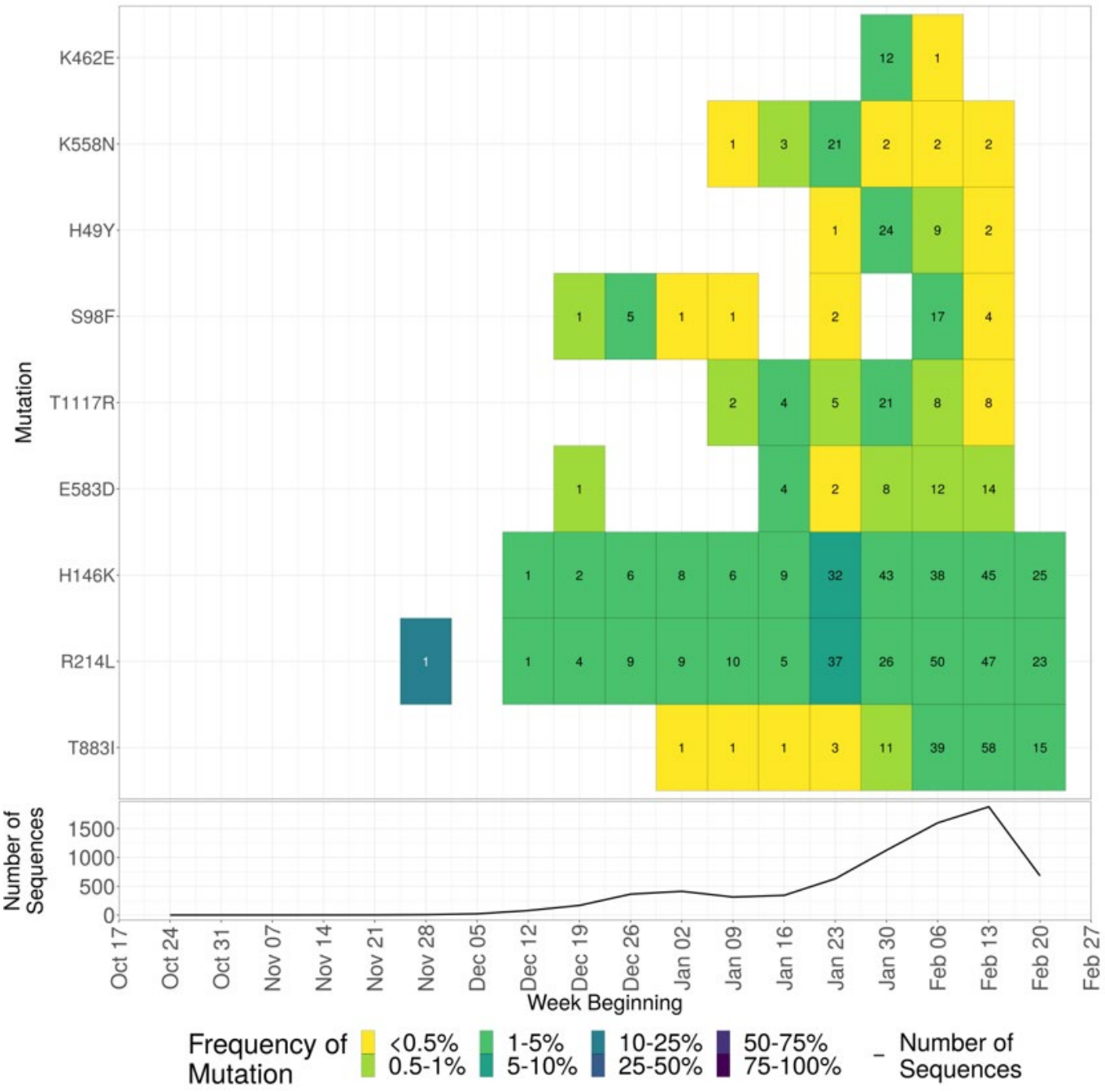
Spike mutations are monitored within V-23JAN-01 using 4 criteria (Table 3). A mutation is investigated further if it meets more than one of these criteria and is present in at least 10 sequences. Nine additional mutations have been observed in V-23JAN-01 sequences according to the criteria in Table 3 (Figure 9). The criteria for mutation monitoring are currently being reviewed and amended.

Table 3. 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%

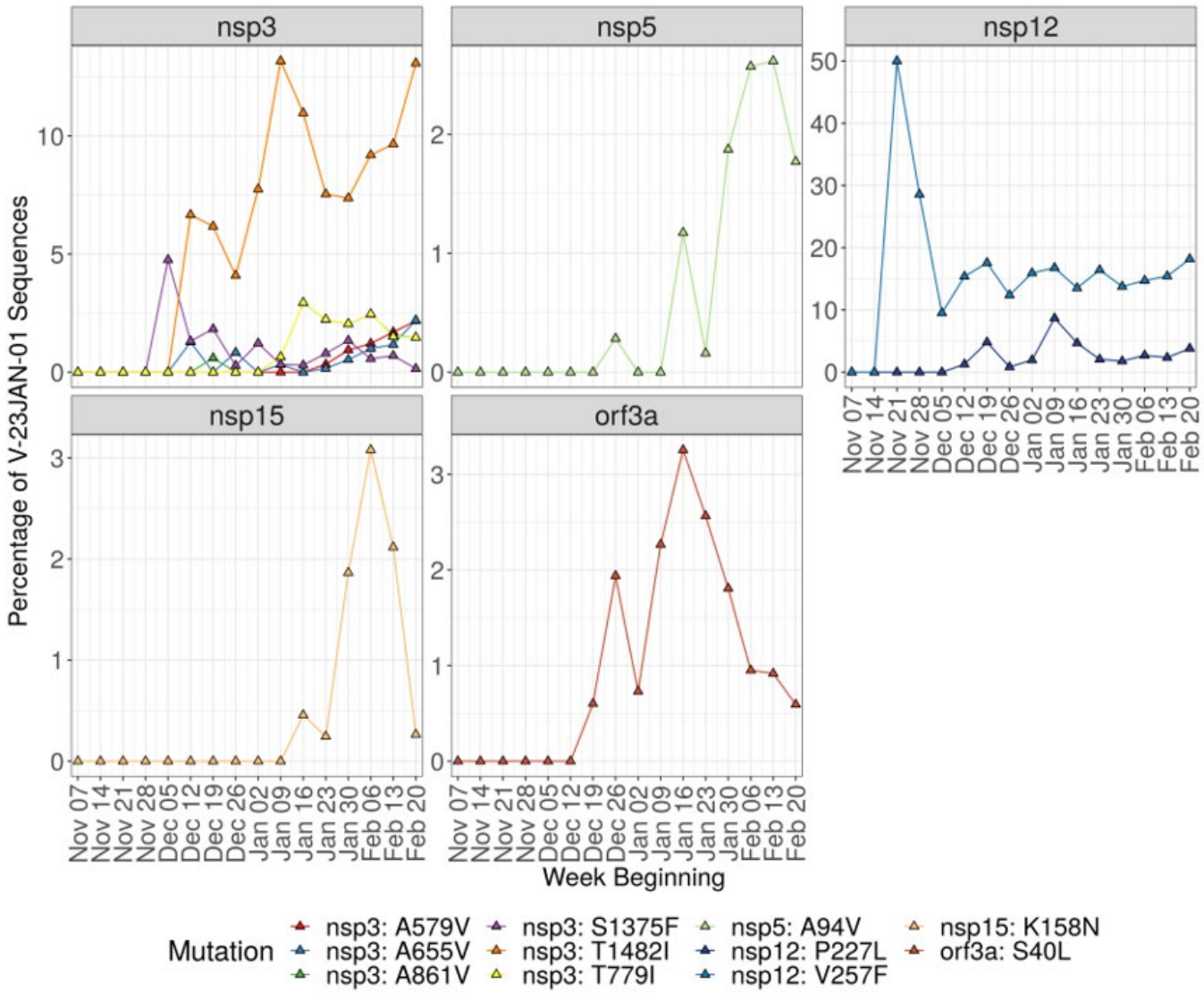
Mutations that are expected to be present in all V-23JAN01 sequences (T19I, V83A, G142D, H146Q, Q183E, V213E, G252V, G339H, R346T, L368I, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, V445P, G446S, N460K, S477N, T478K, E484A, F486P, F490S, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K) are not included in Figure 9, but are monitored, and any significant changes in the proportions of these mutations (for example a reversion) will be reported as required.

Figure 9. Spike mutations found in V-23JAN-01 genomes in the UK data set relative to the Wuhan sequence NC_045512.2 between 24 October 2022 and 26 February 2023



Outside Spike there are 11 mutations that are present in at least 1% of V-23JAN-01 sequences for at least 3 consecutive weeks (Figure 10).

Figure 10. Mutations acquired by V-23JAN-01 outside Spike, shown as a proportion of total V-23JAN-01 sequences (7 November 2022 to 26 February 2023)



Mutations for each genome are called relative to reference Wuhan NC_045512.2 and acquired mutations are those additional to the ancestral V-23JAN-01 mutation set. Those that are considered additional, and that are present in at least 1% of V-23JAN-01 sequences for at least 3 consecutive weeks in the UK data set, are included in Figure 10 as a proportion of total V-23JAN-01 sequences.

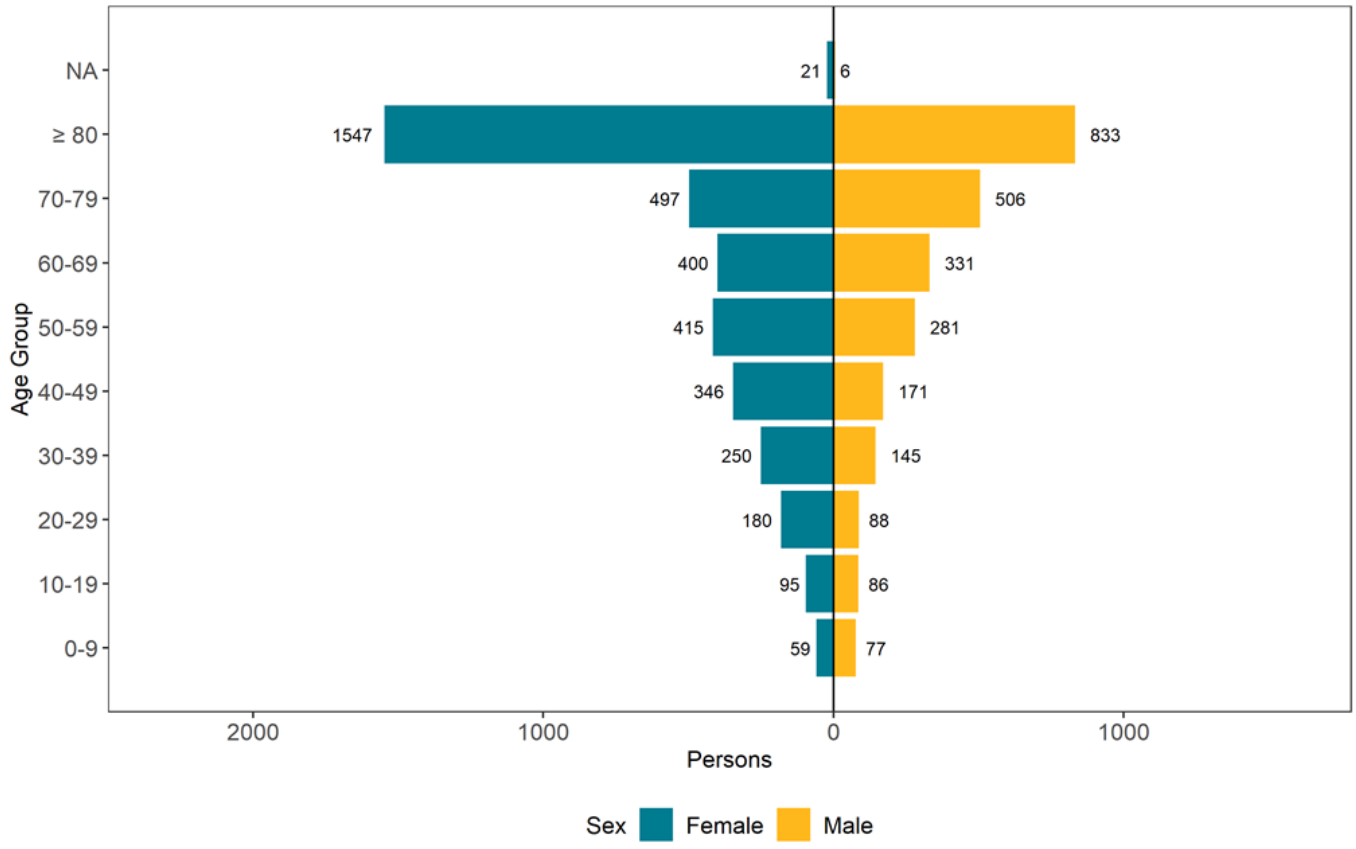
The data used in this graph can be found in the accompanying spreadsheet.

3.2 Epidemiology

As of 7 March 2023, 6,364 V-23JAN-01 (XBB.1.5) sequenced cases had been identified in England. There were 194 deaths among these cases.

The median age of cases was 72 years old. The majority of cases were female (3,810), with 2,524 male cases (Figure 11). Gender was unknown for 30 cases. There have been cases in each region of England with the most cases resident in the South East (964) and East of England (902). Care home residents comprised 30.2% (1,920 out of 6,364) of XBB.1.5 cases, a similar proportion to all sequenced cases.

Figure 11. Age-sex breakdown of V-23JAN-01 (XBB.1.5) cases as of 7 March 2023



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

4. Newly escalated signal: Omicron XBB.1.9.1

XBB.1.9.1 was first raised as a signal in monitoring on 8 February 2023 as part of horizon scanning, due to an increase in prevalence as a proportion of total UK sequences (currently 6%). Relative to the XBB, XBB.1.9.1 has acquired Spike mutations R408S and F486P, ORF1ab mutations G1819S and T4175I, and ORF8:G8*. The receptor binding domain (RBD) mutation F486P defines XBB.1.9.1 from the parent lineage XBB.1.9.

As of 4 March 2023, there are 1,229 XBB.1.9.1 UK sequences (England: 1,189, Wales: 34, Scotland: 5, Northern Ireland: 1).

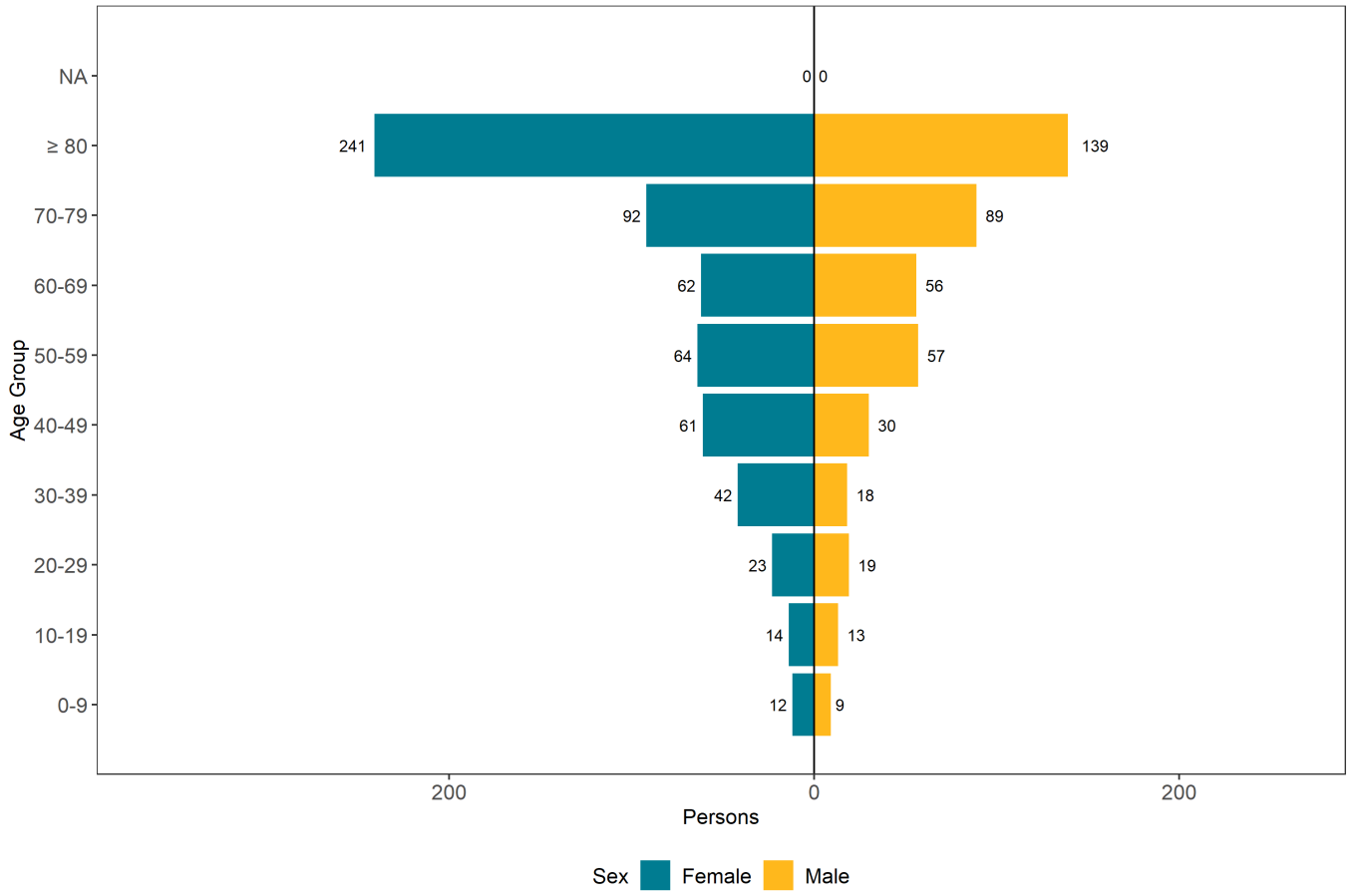
As of 4 March 2023, there are 1,317 XBB.1.9.1 non-UK sequences in the GISAID database. The earliest specimen date of XBB.1.9.1 in the GISAID database is 5 December 2022, in a sequence originating from Singapore. It has now been detected in 45 countries, including the UK. The top 3 countries submitting XBB.1.9.1 sequences to GISAID (excluding the UK) are Germany (349), the United States of America (124) and Austria (104).

4.1 Epidemiology

As of 7 March 2023, 1,168 XBB.1.9.1 sequenced cases had been identified in England. There were 39 deaths among these cases.

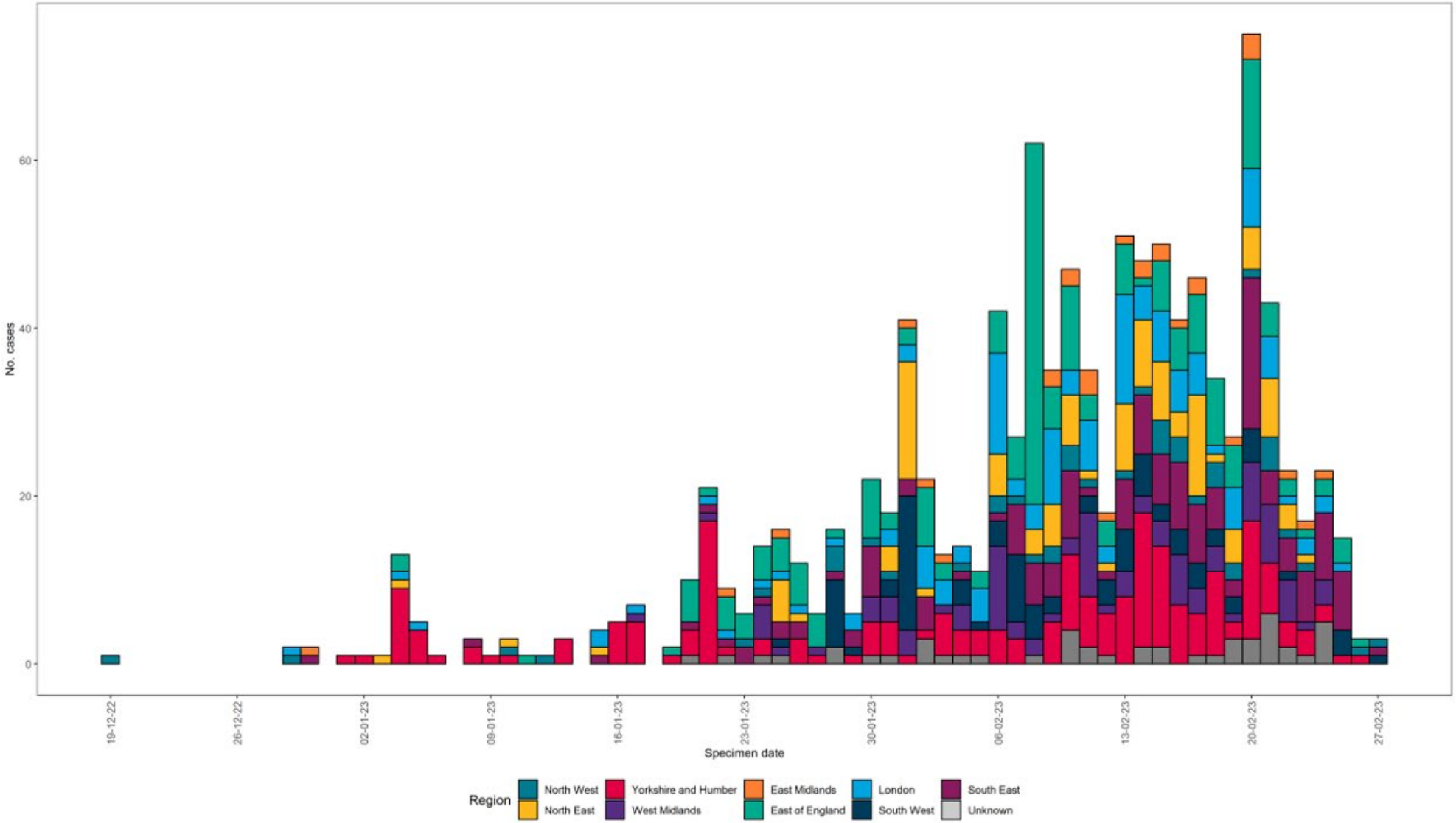
The median age of cases was 72 years old. The majority of cases were female (611), with 430 male cases (Figure 12). There have been cases in each region of England with the most cases resident in the Yorkshire and Humber (205) and East of England (195) (Figure 13). Care home residents comprised 25.3% (296 out of 1,168) of XBB.1.9.1 cases, a similar proportion to all sequenced cases.

Figure 12. Age-sex breakdown of XBB.1.9.1 cases as of 7 March 2023



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

Figure 13. Epicurve of XBB.1.9.1 cases by UKHSA region as of 7 March 2023



Supplementary data is not available for this figure.

5. Severity analysis

The relative severity of V-22DEC-01 (CH.1.1) and V-23JAN-01 (XBB.1.5) compared to V-22OCT-01 (BQ.1) was assessed in a case-control study of the risk of admission to hospital following presentation to emergency care among those testing positive on the day of presentation to hospital.

Preliminary analysis of this data on 757 V-22DEC-01 (CH.1.1) episodes, 502 V-23JAN-01 (XBB.1.5) and 2,129 V-22OCT-01 (BQ.1) episodes found that there was no increase in risk of hospital admission for V-22DEC-01 (CH.1.1) compared to V-22OCT-01 (BQ.1) (odds ratio: 0.96, 95% confidence interval 0.83 to 1.12) nor V-23JAN-01 (XBB.1.5) compared to V-22OCT-01 (BQ.1) (odds ratio 0.8, 95% confidence interval 0.63 to 1.03). This analysis was adjusted for age group (10-year age bands), vaccination status, sex, reinfection status, indices of multiple deprivation (IMD) quintile, NHS region and specimen test week. These results may change as further data becomes available.

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 variants of concern (VOCs) and variants under investigation (VUIs) up to 25 March 2022.

The collection page gives content on variants, including previous technical briefings. Technical briefings are published periodically.

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

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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