UK Health Security Agency

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

Technical briefing 50

10 February 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 February 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.

Situational risk assessment

Growth advantage

XBB.1.5 and CH.1.1 (and associated sublineages) continue to show growth advantage in England in all models. It is likely that the growth of both CH.1.1. and XBB.1.5 are contributing to the current increase in COVID-19 incidence and that they will continue to increase overall transmission as they become more prevalent.

Severity

There has been no observed recent increase in the infection hospitalisation risk (IHR) however given expected lags the data will not yet reflect the recent growth of XBB.1.5. Although there is limited data, there is no evidence of increased severity for CH.1.1 compared to BQ.1 based on preliminary case control analysis of patients presenting to emergency care. There are insufficient sequenced cases of XBB.1.5 to make an assessment. Overall, there are no early warning signals of increasing severity (low confidence), but analyses will be iterated until there is sufficient data to confirm.

Vaccine effectiveness

Neutralisation data suggest that vaccine effectiveness (VE) may be further reduced for CH.1.1 and XBB.1.5 when compared to BQ.1. Analyses of incremental VE against hospitalisation have been run but sequenced hospitalised case numbers remain too low for robust estimates. Current central estimates for CH.1.1. are lower than for BQ.1 but have a high level of uncertainty; there is insufficient data to estimate VE against XBB.1.5.

Therapeutics

Genome and structural modelling-based assessments do not suggest any changes predicted to affect drug susceptibility in XBB.1.5 and CH.1.1, compared to BQ.1 and previously circulating Omicron lineages, for drugs in the NHS clinical policy.

This data is assessed by the UK Health Security Agency (UKHSA) therapeutics surveillance team and are not included in the briefing.

The Variant Technical Group has reviewed available data on mutational profiles which may be related to molnupiravir and UKHSA will undertake further analyses together with partners.

New data and analysis findings

Composition of the genomic data set

Analysis of the mean proportion of sequenced samples originating from different sample groups shows that from the week commencing 7 November 2022 to the week commencing 23 January 2023, 16.3% of samples were from the Office for National Statistics COVID-19 Infection Survey (ONS CIS), 0.9% from VIVALDI (care home study) and 2.9% from AVA (individuals tested because they may be eligible for therapeutics in the community).

Between 9 January 2023 and 5 February 2023, the median age of reported coronavirus (COVID-19) cases was 57 years old. However, during the same period the median age of sequenced COVID-19 cases was 76 years old.

Sequence variant prevalence

From UK sequences collected from 23 January 2023 to 30 January 2023, 37.5% were classified as V-22OCT-01 (BQ.1), 28.3% V-22DEC-01 (CH.1.1), 15.3% V-23JAN-01 (XBB.1.5), 5.5% V-22JUL-01 (BA.2.75), 4.4% VOC-22APR-04 (BA.5), 3.4% V-22OCT-02 (XBB), 1.9% VOC-22JAN-01 (BA.2) and 0.3% V-22SEP-01 (BA.4.6). The remaining sequences were classed as other, or of insufficient quality to assign.

Horizon scanning

Since the last technical briefing there are 4 additional signals in monitoring.

CH.1.1.1 and CH.1.1.2 are sub-lineages of the V-22DEC-01 variant which are increasing in proportional abundance, but currently do not have concerning additional mutations relative to the parent lineage.

XBF is a recombinant lineage that shares the mutation F486P found in XBB.1.5. This lineage has been observed in the UK at low proportions. In Australia, this lineage represents more than 15% of recent sequences uploaded to GISAID.

BQ.1.1.20 was flagged due to growth in Denmark, however in recent weeks this appears to be declining.

Growth rates

CH.1.1 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 for people with CH.1.1 (V-22DEC-01) compared to BQ.1 (V-22OCT-01) (odds ratio: 1.03, 95% confidence interval 0.84 to 1.26). 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.

The number of hospitalised cases with complete data is currently too small to be able to assess the severity of XBB.1.5.

An increase in infection hospitalisation risk was observed over the summer of 2022; however, the most recent estimates have shown signs of a plateau. The latest estimate will not yet reflect any changes in severity from the recent growth in XBB.1.5.

Vaccine effectiveness (CH.1.1 and BQ.1)

A preliminary analysis has been undertaken comparing vaccine effectiveness (VE) against hospitalisation for CH.1.1 and BQ.1 as compared to BA.5. Although the effectiveness point estimates are lower for CH.1.1 and BQ.1 the confidence intervals are wide and overlap the estimate for BA.5. Currently the numbers of cases in the analysis are too small to confidently assess differences in VE between CH.1.1, BQ.1 and BA.5.

Reports from Variant Technical Group members

Genotype to Phenotype (UK-G2P) Consortium

The UK-G2P Consortium reports pseudovirus neutralisation data showing that neutralisation titres for XBB.1.5 are similar to those of XBB (which have been previously characterised as the lowest of any contemporary variant tested). This has been tested using both bivalent vaccine and vaccine-breakthrough antisera and monoclonal antibodies. This is consistent with other published and pre-printed studies. Assessment of the cell entry route of XBB.1.5 suggests it is similar to XBB and other Omicron sublineages rather than like that of Delta or the ancestral spike.

Assessment of the impact of molnupiravir on viral genetic diversity

Molnupiravir acts by introducing mutations into the viral genome to impair viral replication. The specific mechanism results in a typical mutational profile. The Francis Crick Institute reported

analysis showing the presence of variants with this profile in countries which have deployed molnupiravir (Sanderson and others, 2023). The Variant Technical Group recommended that there should be further investigation of the effect of molnupiravir on viral genetic diversity, to understand the risks to the individual and public health. This should particularly include chronic infections including those in immunocompromised patients and should use existing surveillance and UK clinical trial data sets.

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	Delta (B.1.617.2 and sub-lineages) V-21APR-02	Delta and Omicron recombinant XBC
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	BQ.1.1
Omicron (B.1.1.529) sub-lineage BA.4 VOC-22APR-03	Omicron BA.2.75 V-22JUL-01	BN.1 (BA.2.75.5.1)
Omicron (B.1.1.529) sub-lineage BA.5 VOC-22APR-04	Omicron BA.4.6 V-22SEP-01	*CH.1.1.1
	Omicron BQ.1 V-22OCT-01	*CH.1.1.2
	Omicron XBB Recombinant (BJ.1 x BM.1.1.1) V-22OCT-02	*XBF (BA.5 x CJ.1)
	Omicron CH.1.1 V-22DEC-01	*BQ.1.1.20
	Omicron XBB.1.5 Recombinant (XBB plus additional mutations) V-23JAN-01	

* 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
	BA.2.12.1 V-22MAY-01	Variants originating from China given changes in epidemiology

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

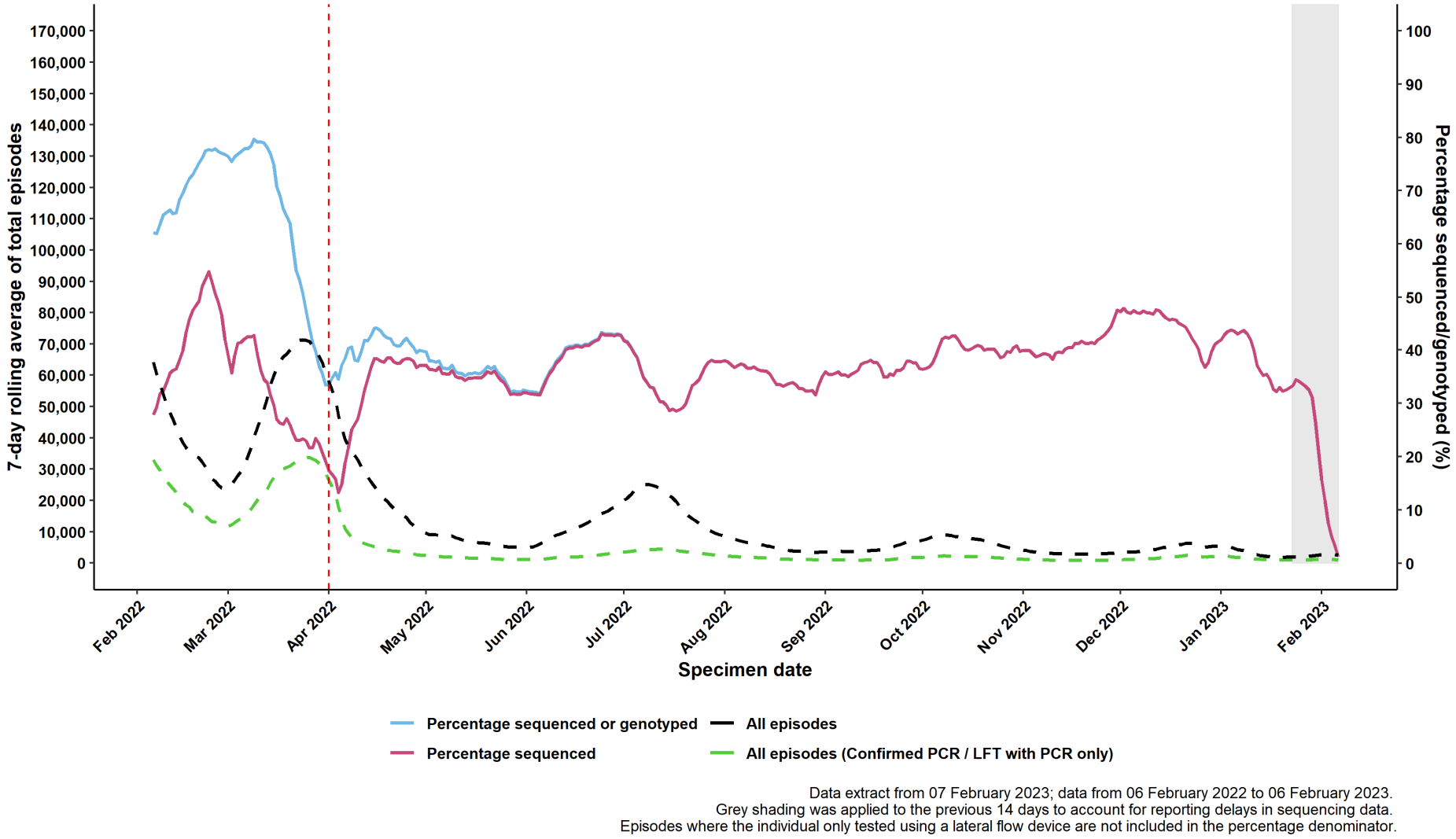
Figure 1 shows the proportion of PCR-positive COVID-19 cases that have linked to a valid sequencing result (50% of the genome with sufficient read coverage) or genotyping PCR result over time. Figure 2 shows the proportion of cases sequenced and genotyped amongst individuals who tested positive whilst 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.

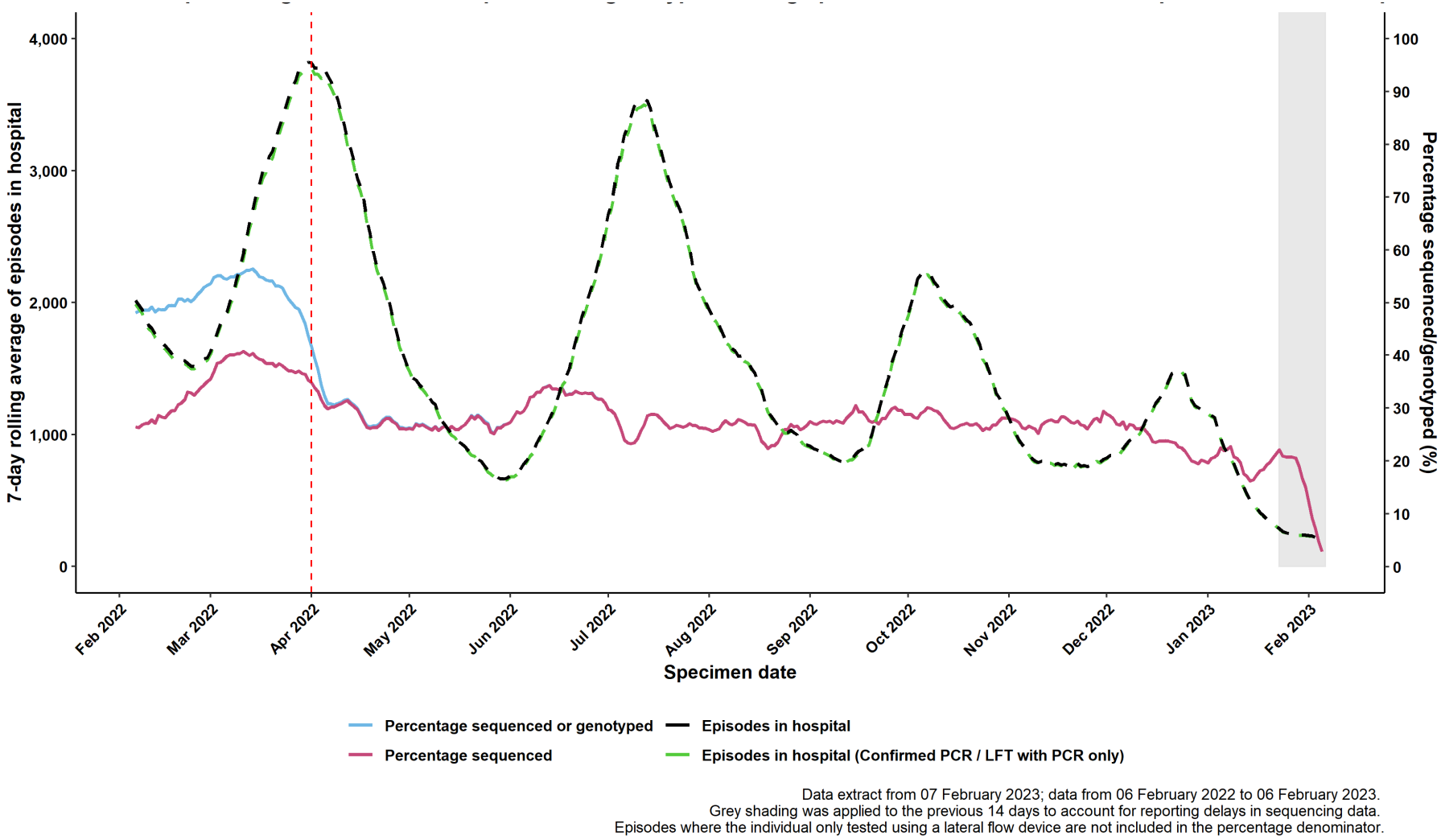
Figure 3 shows the proportion of sequenced samples that originate from different sample groups, assigned as ‘AVA’ (individuals tested because they may be eligible for therapeutics in the community), ‘VIVALDI’ (care homes study) and ‘ONS’ (Office for National Statistics COVID-19 Infection Survey) over 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 7 November 2022 to week commencing 23 January 2023), mean proportions were 16.3% ONS, 0.9% VIVALDI and 2.9% AVA.

Figure 1. Coverage of sequenced cases with a valid result and genotyping over time (6 February 2022 to 6 February 2023)



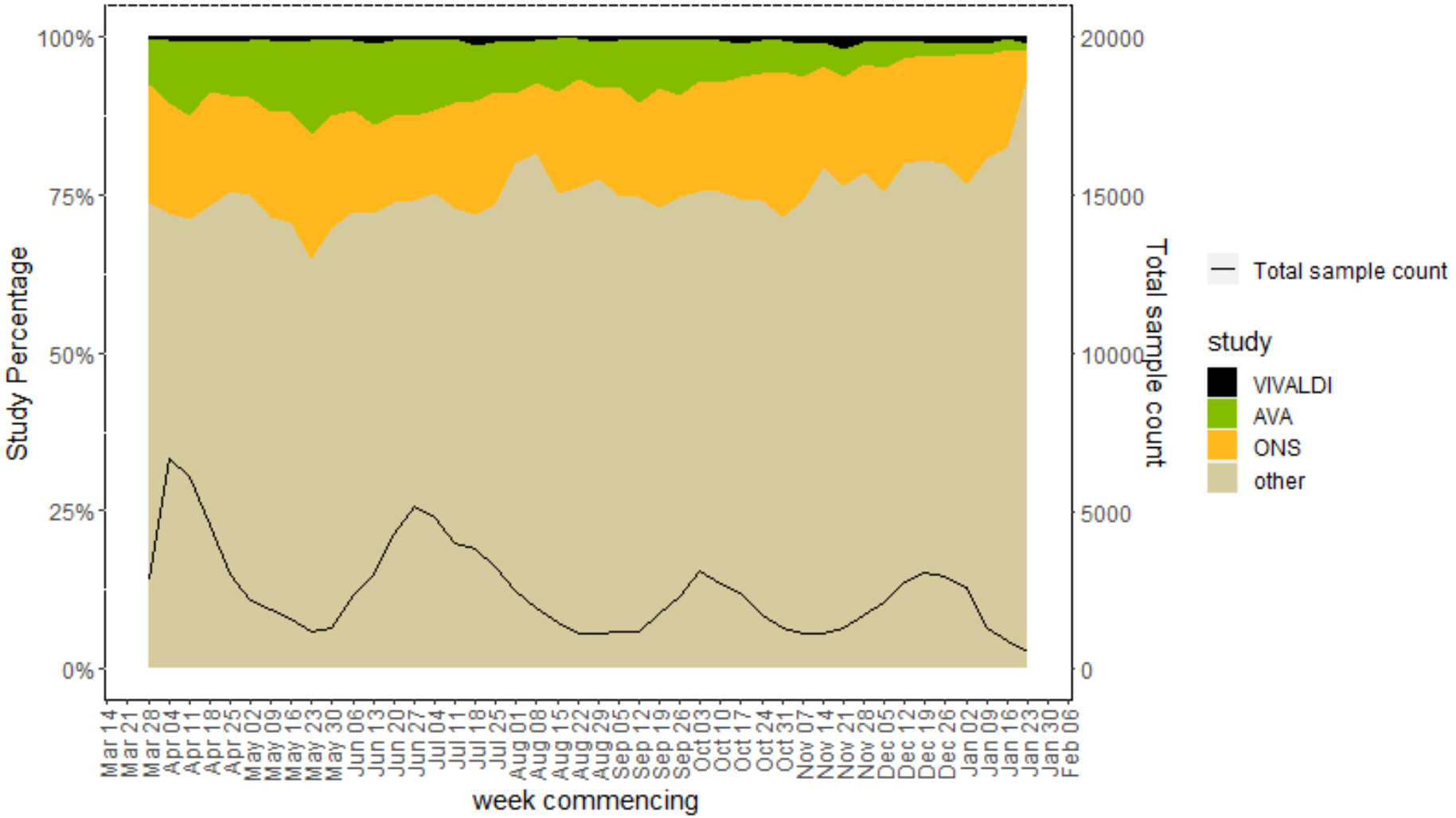
Cases where the individual only tested using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. (The data used in this graph can be found in the accompanying spreadsheet.)

Figure 2. Coverage of sequencing with valid result and genotyping for cases who test positive in hospital (6 February 2022 to 6 February 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.)

Figure 3. Proportion of sequenced sample assigned to studies 'AVA' (community therapeutics), 'VIVALDI' (care home study) and 'ONS' (COVID-19 Infection Survey) from week commencing 28 March 2022 to 23 January 2023



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 in England are significantly older than reported cases. Between 9 January 2023 and 5 February 2023, the median age of reported COVID-19 cases was 57 years old. However, during the same period, the median age of sequenced COVID-19 cases was 76 years old (Figures 4a and 4b).

Figure 4a. Age-sex distribution of all COVID-19 cases for the past 4 weeks in England (9 January 2023 to 5 February 2023)

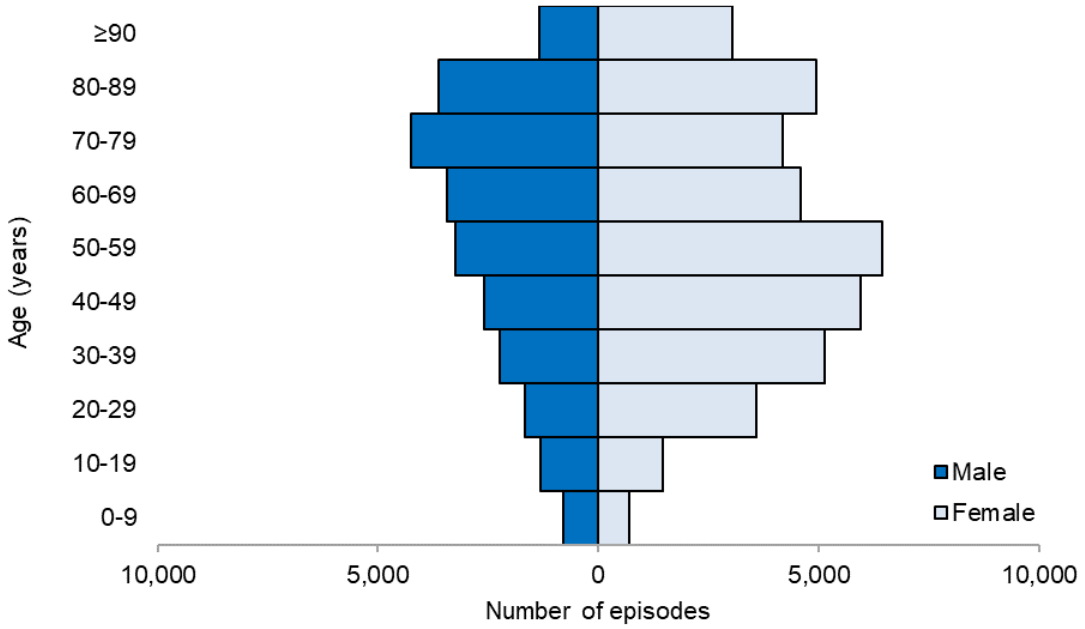
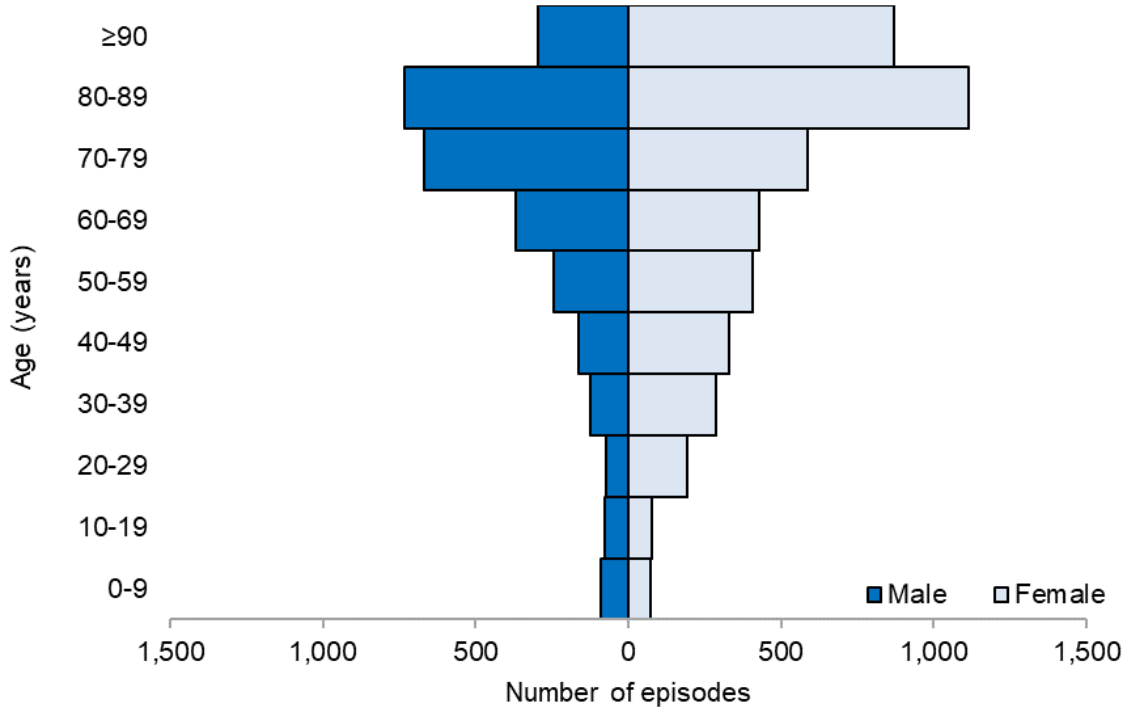


Figure 4b. Age-sex distribution of sequenced COVID-19 cases for the past 4 weeks in England (9 January 2023 to 5 February 2023)



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 in England is presented in Figure 5. UKHSA designated variants are those assigned for more comprehensive epidemiological studies and may incorporate multiple sub-lineages.

Of the sequenced cases in England from 23 January 2023 to 29 January 2023, 1.7% were BA.2 (VOC-22JAN-01), 4.1% BA.5 (VOC-22APR-04), 5.3% BA.2.75 (V-22JUL-01), 0.3% BA.4.6 (V-22SEP-01), 38.4% BQ.1 (V-22OCT-01), 3.3% XBB (V-22OCT-02), 29.7% CH.1.1 (V-22DEC-01), 16.0% XBB.1.5 and 1.3% were classified as other.

The prevalence of lineages amongst UK sequences by Pangolin designation is presented in Figure 6. 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 29 August 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 7 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.

In Figure 5 below, dashed lines indicate period incorporating issue at a sequencing site. 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 Figure 5 can be found in the accompanying spreadsheet.

Figure 5. Variant prevalence (UKHSA designated variant definitions only) of available sequenced cases for England from 7 February 2022 to 29 January 2023

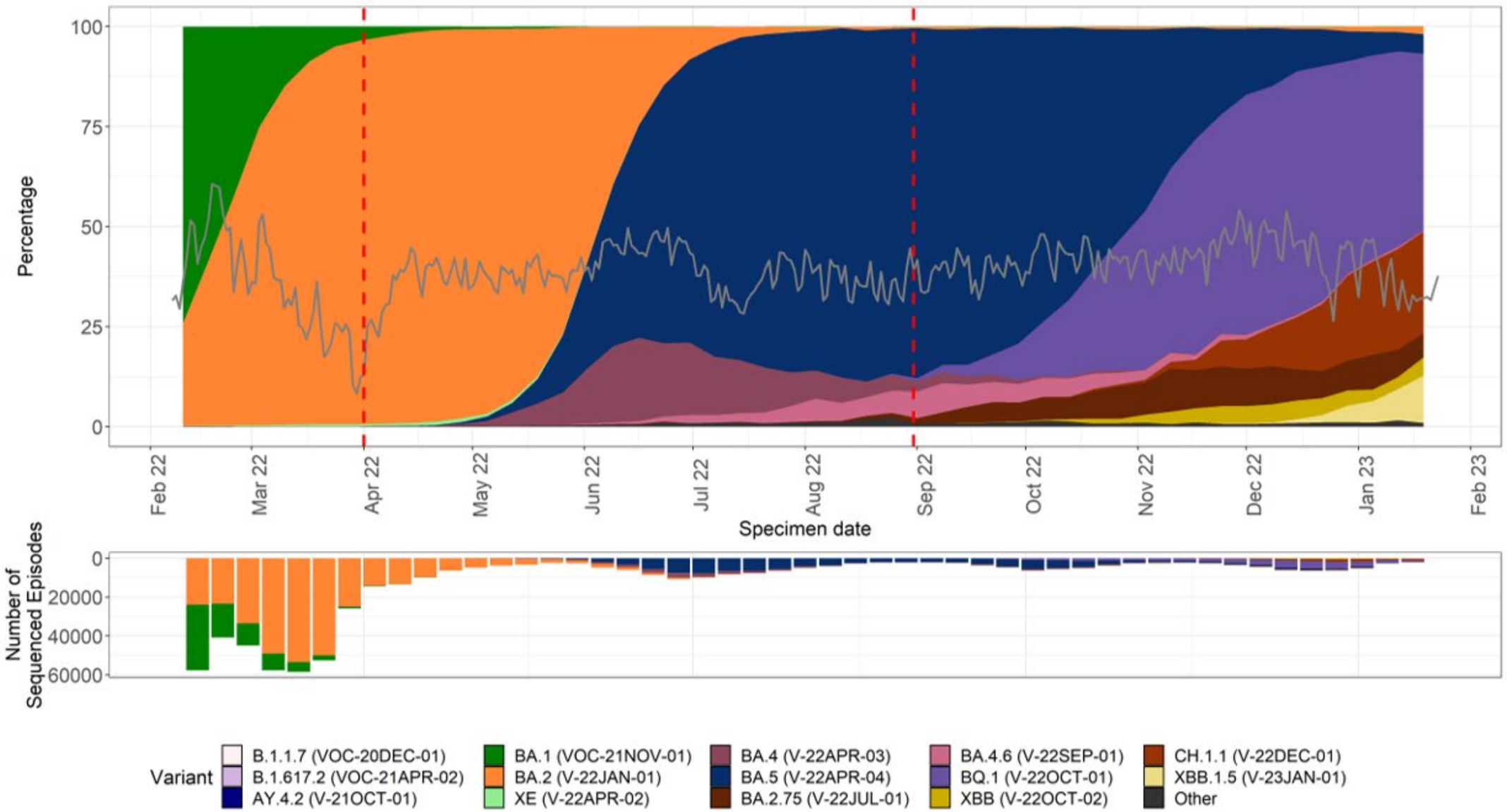
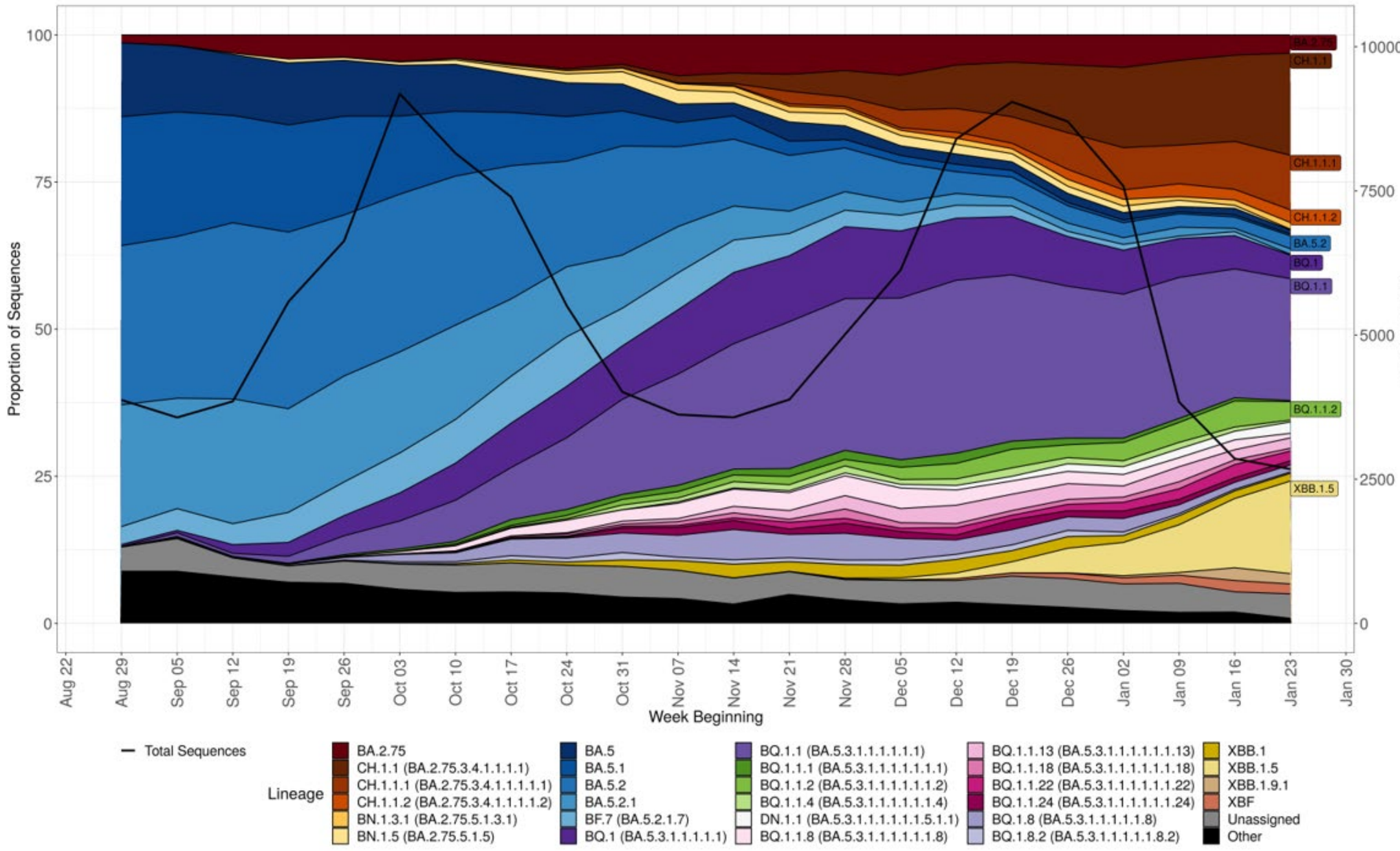
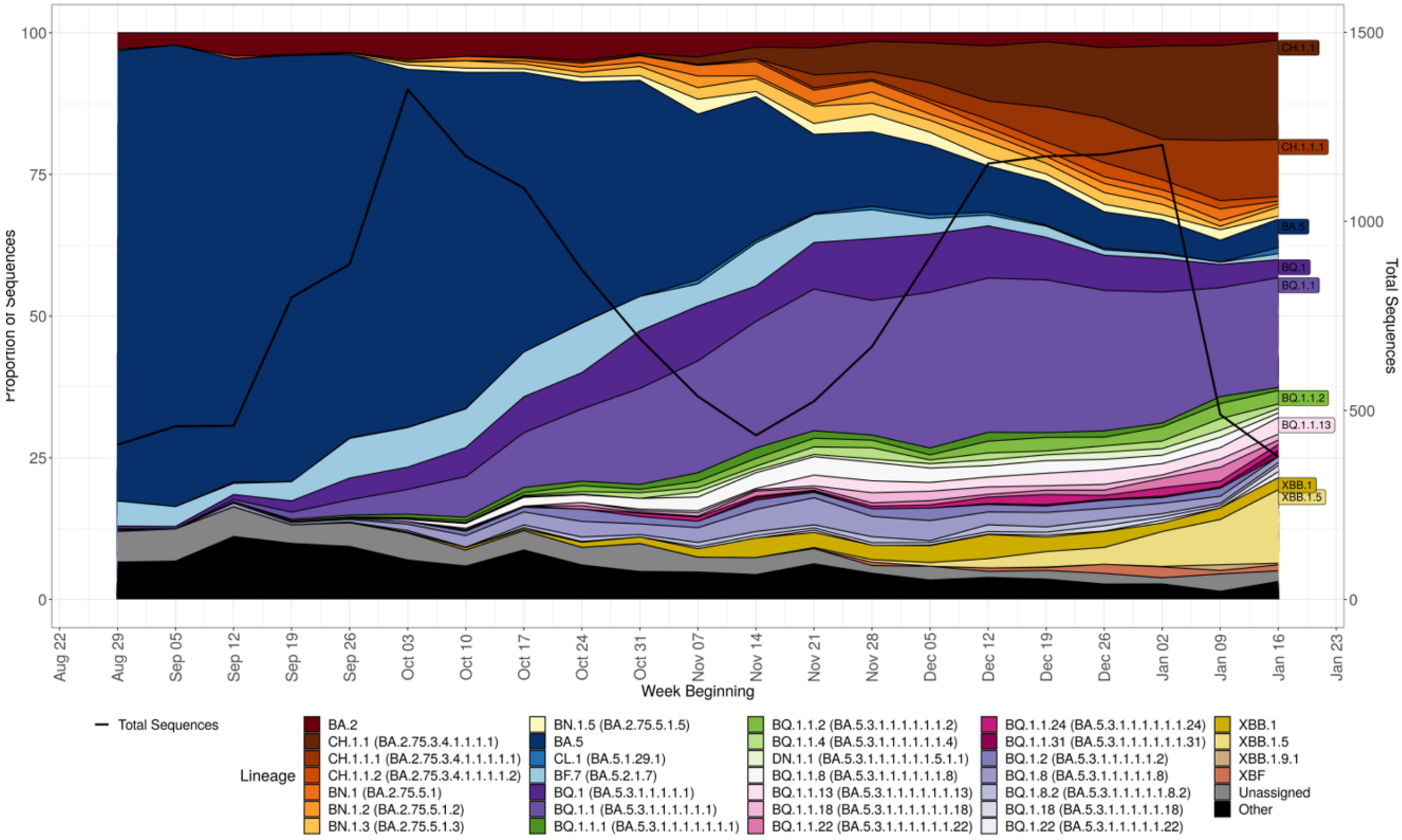


Figure 6. Prevalence of Pangolin lineages in the UK with sequence data with a specimen date from 29 August 2022 to 29 January 2023, as of 7 February 2023



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 2% 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 7. 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 29 August 2022 to 22 January 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 2% 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 ONS CIS survey. This differs from previous versions of this report, where the MM was fitted to sequenced cases from the Sanger data set where pangoLEARN is used to assigned lineages. 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 26 January 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 8, with relative growth rates compared to BQ.1.1 lineages (Figure 9). Note that the multinomial model includes several emerging, competitive lineages. This means that a large relative growth rates relative to the presently dominant BQ.1.1 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 UTLA. The sampling range for both logistic regression and generalised additive models is from 9 November 2022 to 1 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 26 January 2023^

Lineage	English sequences used in the multinomial model (MM)	MM England estimated prevalence	MM estimate for the weekly growth rate relative to BQ.1.1 lineages	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)
BQ.1.1	3,889	29.35% (95% CrI: 27.18 to 31.72)	-	2,104	0.3%	-8.9%
CH.1.1	932	22.36% (95% CrI: 19.6 to 25.15)	16.29% (95% CrI: 14.19 to 18.52)	1,496	23.5%	4.9%
BQ.1*	1,265	4.82% (95% CrI: 4.19 to 5.43)	-5.95% (95% CrI: -7.02 to -5.01)	1,552	-7.1%	-13%
BN.1	713	3.89% (95% CrI: 3.34 to 4.56)	-2.81% (95% CrI: -3.97 to -1.53)	75	-8.4%	0.9%
BA.2.75†	483	0.59% (95% CrI: 0.47 to 0.73)	-13.35% (95%CrI: -14.71 to -11.94)	563	-1.5%	-8.8%
XBB**	500	3.63% (95% CrI: 2.95 to 4.42)	0.45% (95% CrI: -1.05 to 2.08)	772	0.1%	5%
XBB.1.5	296	17.88% (95% CrI: 14.69 to 21.45)	37.06% (95% CrI: 32.11 to 42.52)	297	51.3%	45.9%

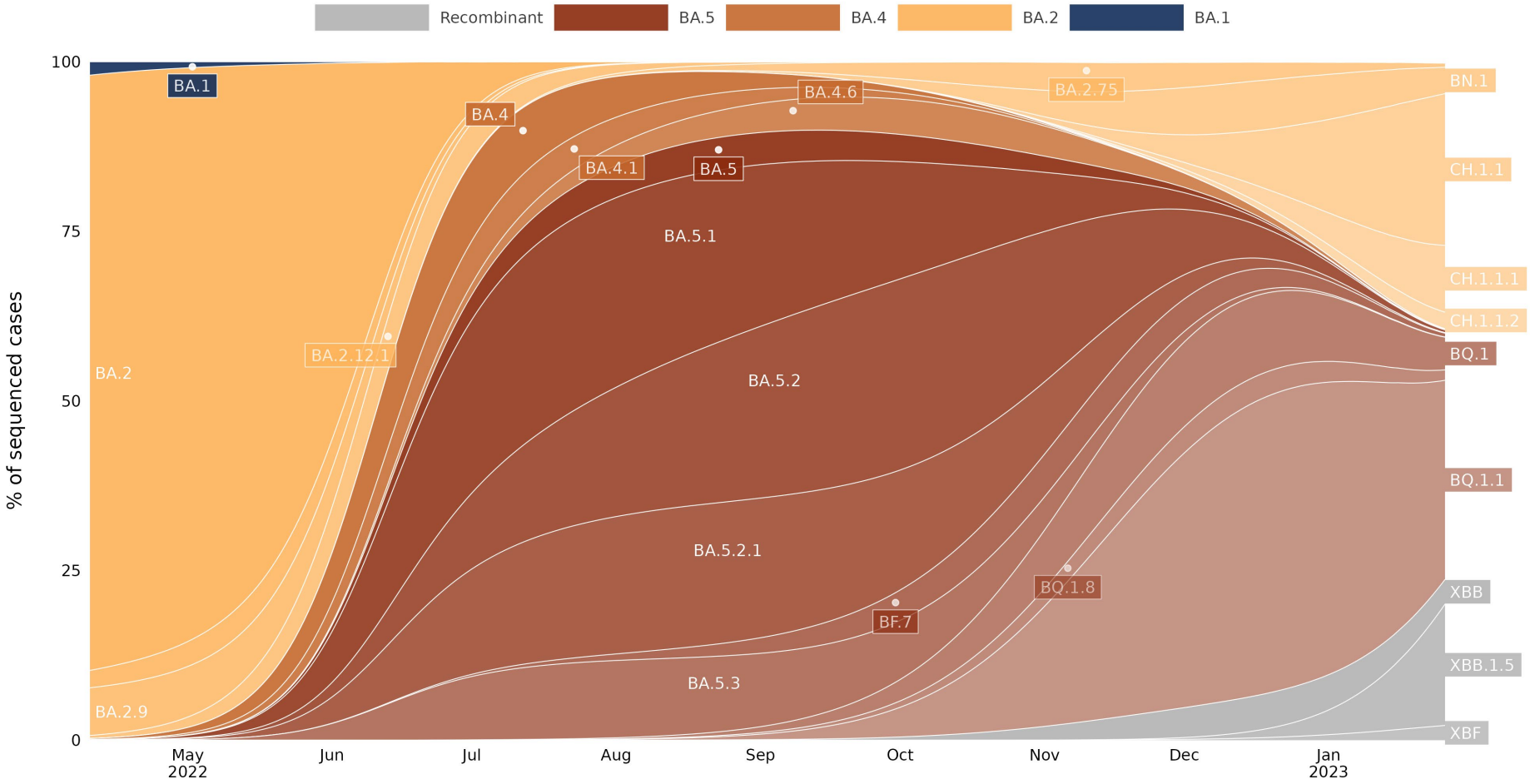
* BQ.1 excludes BQ.1.1 which was modelled separately.

† BA.2.75 excludes BN.1 and CH.1.1 lineages which were modelled separately.

** XBB excludes XBB.1.5 which was modelled separately.

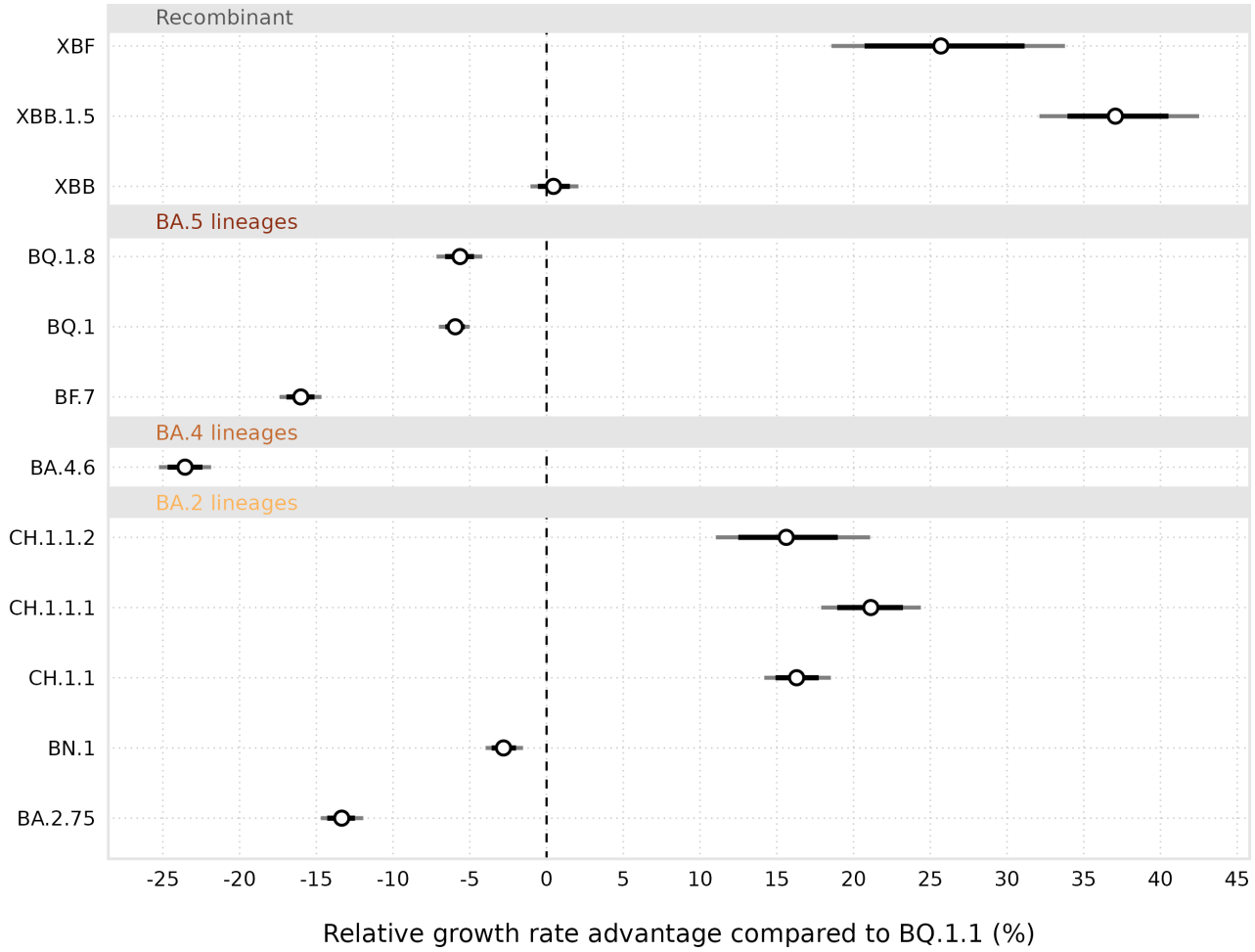
^ Sampling range for both logistic regression and generalised additive models is from 9 November 2022 to 1 February 2023.

Figure 8. Area plot showing the predicted representation of each lineage of the multinomial model of all sequenced cases in England



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

Figure 9. Comparison of the estimated relative growth rates for emerging BA.5, BA.4, BA.2 and recombinant lineages versus that for specifically BQ.1.1 lineages

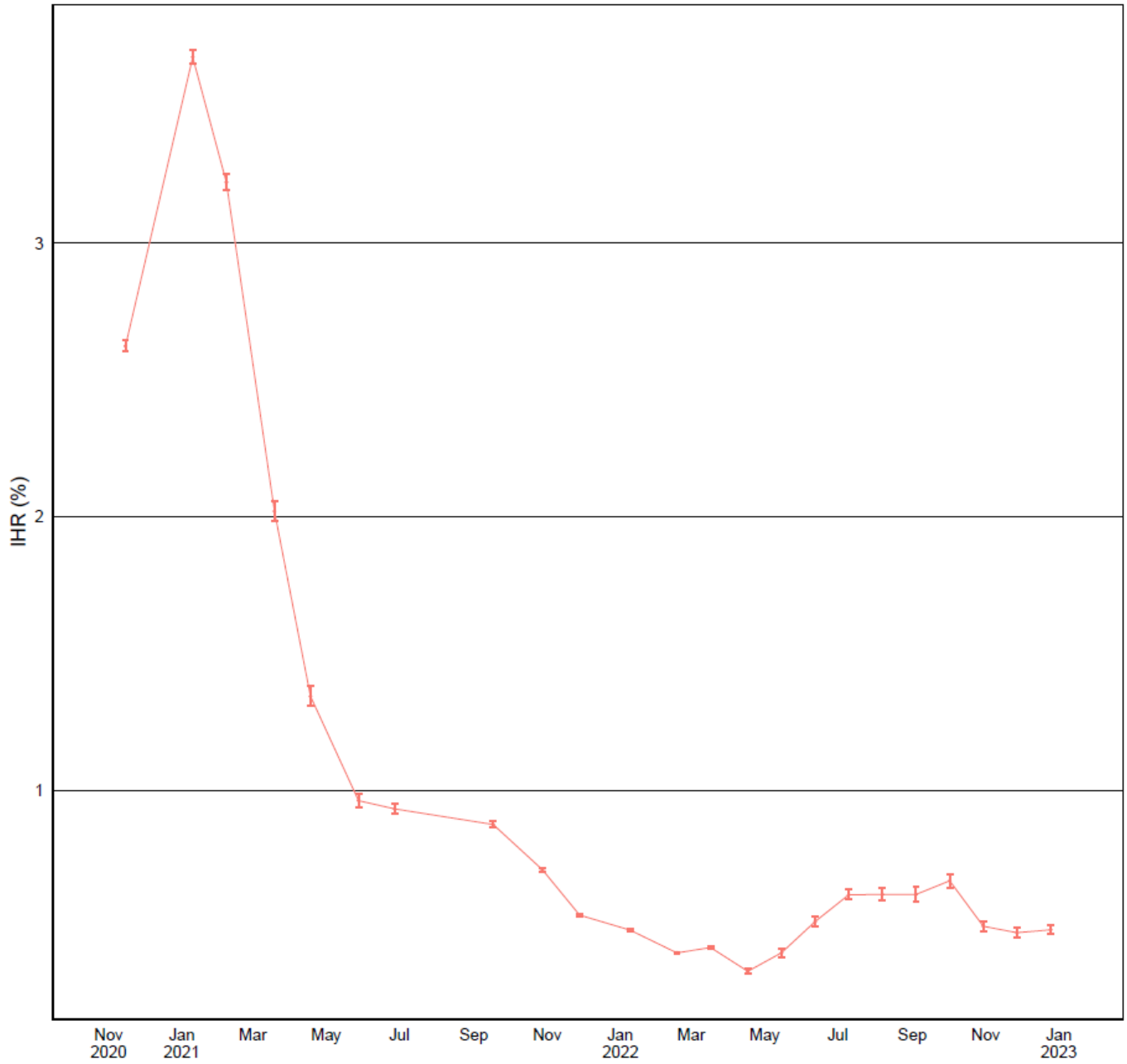


The relative growth rates are taken from a multinomial model of ONS CIS sequenced cases in England, described above. The latest sample date for tests 26 January 2023. Supplementary data is not available for this figure.

Infection hospitalisation risk

The real time infection hospitalisation risk shows the temporal risk of being hospitalised given an infection with SARS-CoV-2 (Figure 10). We observed an increase in the hospitalisation risk over the summer of 2022, and the most recent estimates have shown signs of a plateau. The latest estimate will not yet reflect any changes in severity from the recent growth in XBB.1.5.

Figure 10. Real time infection hospitalisation risk for all ages (with 95% confidence intervals) in England from October 2020 to January 2023



Supplementary data is not available for this figure.

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

XBB.1.5 contains 3 additional non-synonymous mutations when compared to XBB: Spike G252V (defining for XBB.1), S486P, and Orf8:G8*. Orf8:G8* is present in some XBB.1 samples but is not defining in its characterisation. In total there are 27,897 XBB.1.5 samples annotated in GISAID, with 21,128 samples uploaded by the USA (76%). XBB.1.5 has been identified in 2,157 UK samples through sequencing.

3.2 Genomic diversity within V-23JAN-01

Diversity in Spike

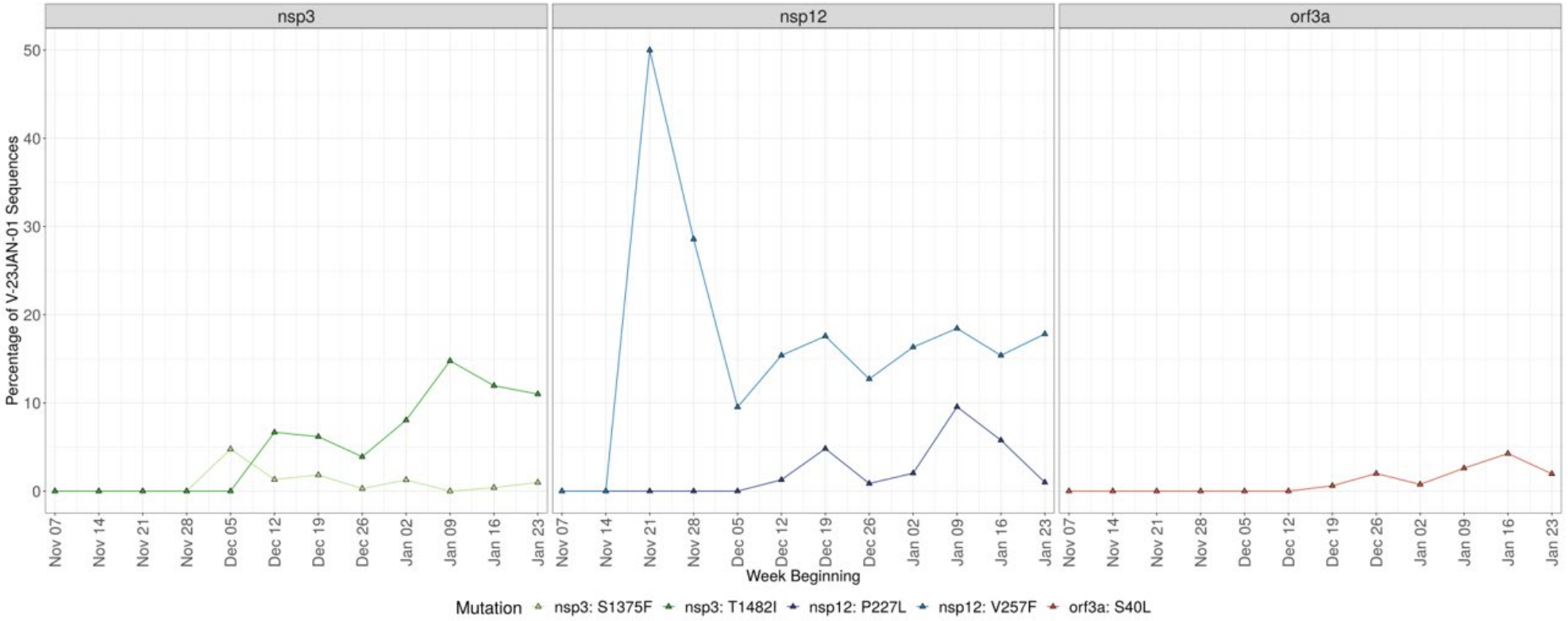
Spike mutations are monitored within V-23JAN-01 using 4 criteria (Table 3). A mutation is investigated further if it meets more than one of these criteria and is present in at least 10 sequences. No additional mutations have been observed in V-23JAN-01 sequences according to the criteria in Table 3. The criteria for mutation monitoring are currently being reviewed and amended. 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%

Outside Spike there are 5 mutations that are present in at least 1% of V-23JAN-01 sequences for at least 3 consecutive weeks (Figure 11).

Figure 11. Mutations acquired by V-23JAN-01 outside Spike, shown as a proportion of total V-23JAN-01 sequences (5 September 2022 to 29 January 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 11 as a proportion of total V-23JAN-01 sequences.

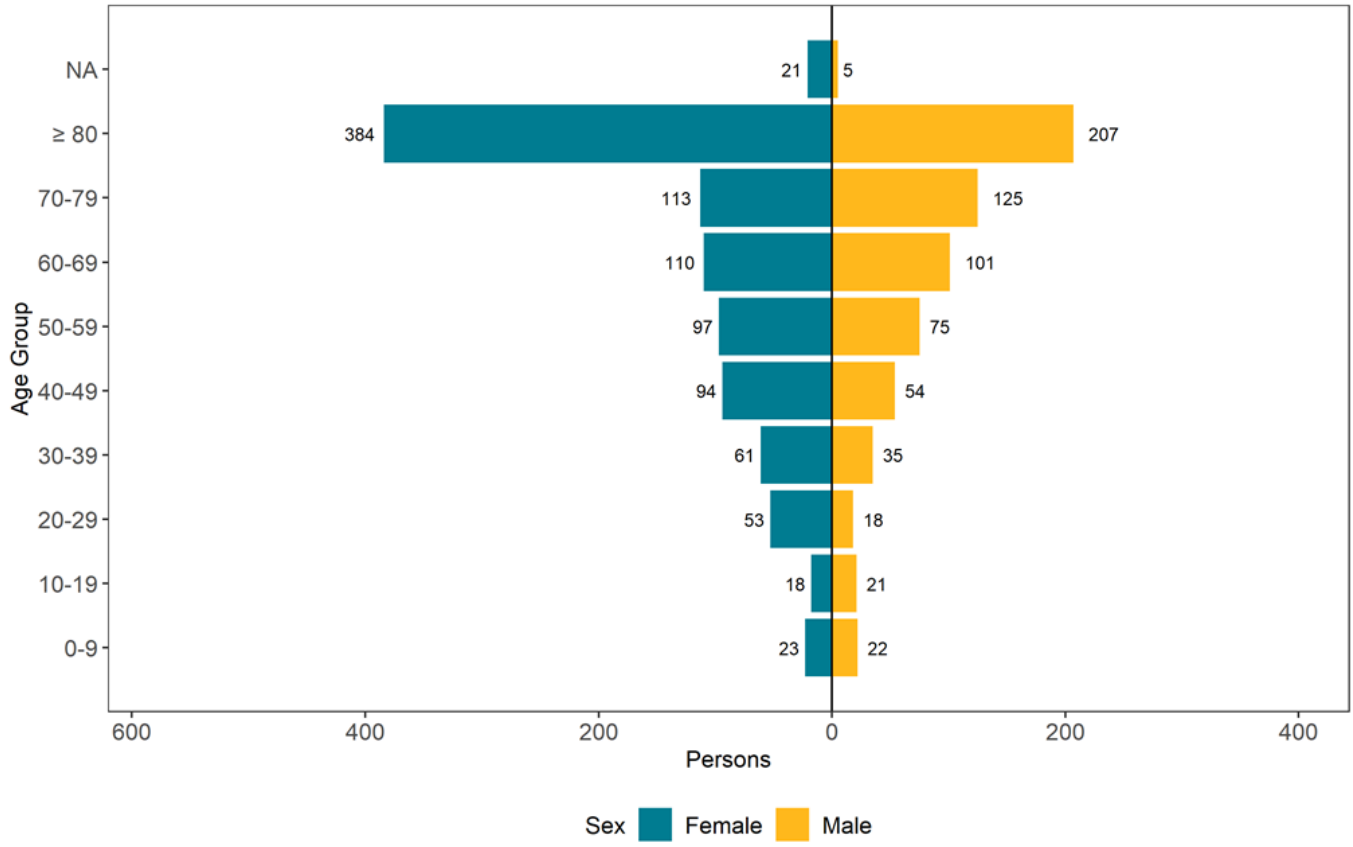
The data used in this graph can be found in the accompanying spreadsheet.

3.1 Epidemiology

As of 6 February 2023, 1,643 XBB.1.5 sequenced cases had been identified in England. There were 44 deaths among these cases.

The median age of cases was 70 years old. The majority of cases were female (974), with 663 male cases and 6 unknown cases (Figure 12). There have been cases in each region of England with the most cases resident in the North West (308) and East of England (244). Care home residents comprised 34% (468 out of 1,378) of XBB.1.5 cases, a similar proportion to all sequenced cases.

Figure 12. Age-sex breakdown of XBB.1.5 cases as of 6 February 2023



Supplementary data is not available for this figure.

4. Omicron CH.1.1 (V-22DEC-01)

CH.1.1 (B.1.1.529.2.75.3.4.1.1.1.1) was first raised as a signal in monitoring on 6 December 2022 as part of horizon scanning due to increases in growth rate. This BA.2.75 sub-lineage has acquired the defining spike mutation L452R in comparison to its parent lineage CH.1. As of 6 February 2023, there are 2,863 CH.1.1 samples in the GISAID database (including UK sequences), and 9,633 V-22DEC-01 UK classified sequences.

4.1 Epidemiology

As of 6 February 2023, 7,720 CH.1.1 sequenced cases had been identified in England. There were 281 deaths among these cases.

The median age of cases was 71 years old. The majority of cases were female (4,896), with 2,787 male cases and 37 unknown cases. Care home residents comprised 36% (2,477 out of 6,839) of CH.1.1 cases, a similar proportion to all sequenced cases.

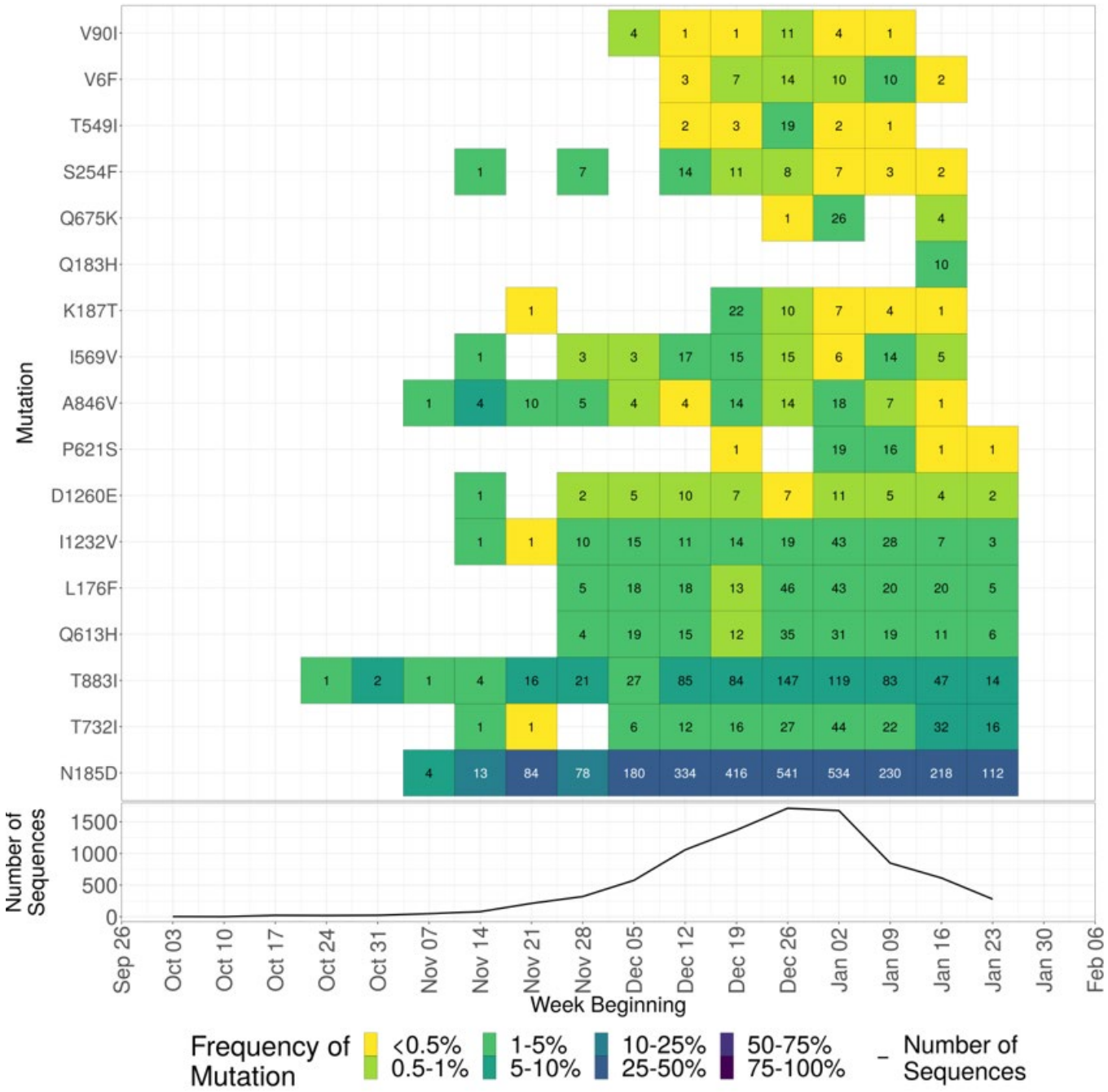
4.2 Genomic diversity within V-22DEC-01

Diversity in Spike

Spike mutations are monitored within V-22DEC-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. Seventeen additional mutations have been observed in V-22DEC-01 sequences according to the criteria in Table 3 (Figure 13). Many of these are reducing as a proportion of total sequences as the number of V-22DEC-01 sequences increase; the remainder are not increasing as a proportion of total sequences. The criteria for mutation monitoring are currently being reviewed and amended.

Mutations that are expected to be present in all V-22DEC-01 sequences (T19I, G142D, K147E, W152R, F157L, I210V, V213G, G257S, G339H, R346T, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, K444T, G446S, L452R, N460K, S477N, T478K, E484A, F486S, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K) are not included in Figure 13, but are monitored, and any significant changes in the proportions of these mutations (for example a reversion) will be reported as required.

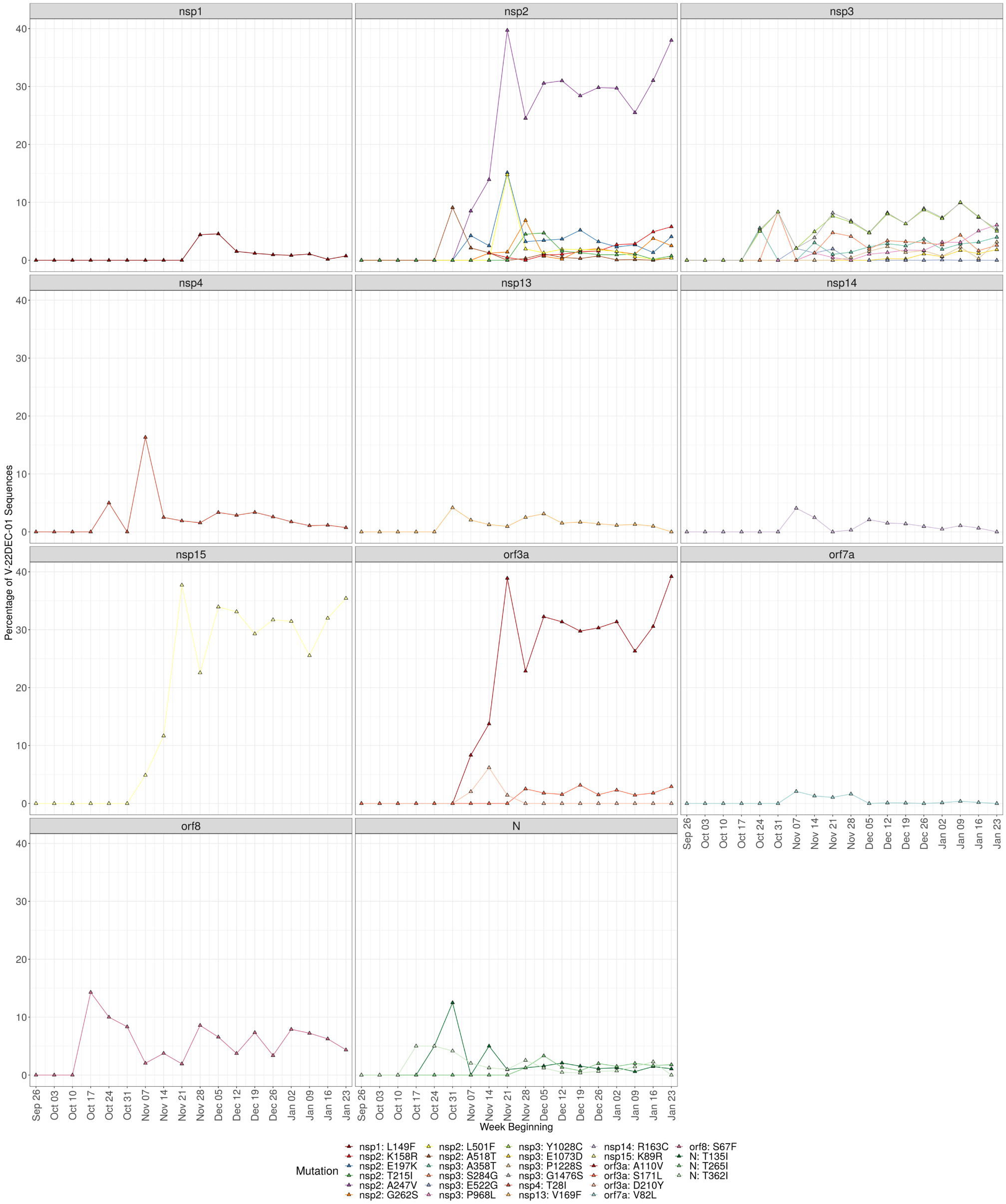
Figure 13. Spike mutations found in V-22DEC-01 genomes in the UK data set relative to the Wuhan sequence NC_045512.2 between 26 September 2022 and 29 January 2023



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

Outside Spike, there are 28 mutations that are present in at least 1% of V-22DEC-01 sequences for at least 3 consecutive weeks (Figure 14).

Figure 14. Mutations acquired by V-22DEC-01 outside Spike, shown as a proportion of total V-22DEC-01 sequences (26 September 2022 to 29 January 2023)



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

Mutations for each genome are called relative to reference Wuhan NC_045512.2 and acquired mutations are those additional to the ancestral V-22DEC-01 mutation set. Those that are considered additional, and that are present in at least 1% of V-22DEC-01 sequences for at least 3 consecutive weeks in the UK data set, are included in Figure 14 as a proportion of total V-22DEC-01 sequences.

5. Severity analysis

The relative severity of CH.1.1 (V-22DEC-01) compared to BQ.1 (V-22OCT-01) 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 512 CH.1.1 episodes and 1,776 BQ.1 episodes found that there was no increase in risk of hospital admission for CH.1.1 compared to BQ.1 (odds ratio: 1.03, 95% confidence interval 0.84 to 1.26). 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.

The number of hospitalised cases with complete data is currently too small to be able to assess the severity of XBB.1.5.

6. Vaccine effectiveness

A test-negative case control study design was used to estimate vaccine effectiveness (VE) against hospitalisation with CH.1.1, BQ.1 and BA.5 in England. Cases were identified from hospital (pillar 1) testing data and secondary uses service (SUS) hospital discharge data from the period from 13 October 2022 to 8 January 2023 and classified as BA.5 (VOC-22APR-04), BQ.1 (V-22OCT-01) or CH.1.1 (V-22DEC-01) based on sequencing information. VE was estimated for hospitalisations with a respiratory code in any diagnosis field and for all hospitalisations regardless of the diagnosis coding. VE was estimated for those with at least a 2 day stay.

Logistic regression was used to estimate VE. Previous positivity, health and social care worker status, clinical risk status, age, gender, and week of test were adjusted for. VE was estimated for those who had received a vaccine in the 12 weeks prior to testing (majority had received a bivalent booster vaccine as part of the autumn programme) as well as at least 2 previous doses. VE was estimated relative to those who were not boosted in the autumn but had at least 2 previous doses at least 6 months previously. This is referred to as the incremental vaccine effectiveness as it provides a measure of protection on top of the baseline protection from 2 or more previous doses (given at least 6 months previously), in contrast to absolute vaccine effectiveness where the comparison is to unvaccinated individuals. All vaccine manufacturers were combined in the analysis.

The incremental vaccine effectiveness against hospitalisation (any diagnosis code) with CH.1.1 was 34.8%% (95% confidence interval (CI): 14.9 to 50.0%) as compared to 47.2% (95% CI: 40.7 to 53.0%) with BQ.1 and 51.3% (95% CI: 43.4 to 58.1%) with BA.5. VE estimates using hospitalisations restricted to those with a respiratory diagnosis code were very similar (Table 4).

Although the effectiveness point estimates are lower for CH.1.1 and BQ.1 the confidence intervals are still fairly wide and overlaps the estimate for BA.5. Currently the numbers of cases in the analysis are too small to confidently assess differences in VE between CH.1.1, BQ.1 and BA.5.

Table 4. Vaccine effectiveness against hospitalisation with CH.1.1, BQ.1 and BA.5

Variant	2 days stay with a respiratory diagnosis code			2 days stay with any diagnosis code		
	Controls	Cases	VE (95% CI)	Controls	Cases	VE (95% CI)
CH.1.1	16,829	66	34.3 (-0.3 to 57.0)	83,970	169	34.8 (14.9 to 50.0)
BQ.1	16,829	342	43.4 (32.7 to 52.5)	83,970	749	47.2 (40.7 to 53.0)
BA.5	16,829	166	56.8 (46.1 to 65.3)	83,970	371	51.3 (43.4 to 58.1)

VE = vaccine effectiveness
CI = confidence intervals.

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.

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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About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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