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

Technical briefing 49

11 January 2023

This report provides an update on previous briefings up to 25 November 2022
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 4 January 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

The current high UK incidence is composed primarily of BQ.1 and sub-lineages. This is consistent with the prediction in the situational risk assessment published on 28 October 2022.

Two variants show marked positive growth compared to BQ.1: CH.1.1, which is at moderate prevalence, and XBB.1.5, which is at low prevalence. Whilst the rapid growth of XBB.1.5 in the USA is noted, UK growth estimates are very early and have high uncertainty due to the small number of sequenced XBB.1.5 cases.

The growth advantage associated with XBB.1.5 is biologically plausible given the combination of immune escape properties and ACE-2 affinity that are expected based on available laboratory data.

CH.1.1 and XBB.1.5 are currently the variants most likely to predominate in the UK following BQ.1, unless further novel variants arise. It is plausible that XBB.1.5 will cause an increase in incidence after the current wave, however it is currently too early to confirm this trajectory.

New data and analysis findings

Composition of the genomic dataset

Between 12 December 2022 and 8 January 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.
Variant prevalence

Of all UK sequenced samples from 26 December 2022 to 1 January 2023, 51.3% BQ.1 (V-22OCT-01), 19.5% CH.1.1 (V-22DEC-01), 7.2% BA.5 (VOC-22APR-04), 4.9% BA.2.75 (V-22JUL-01), 4.5% XBB.1.5 (V-23JAN-01), 3.6% XBB (V-22OCT-02), 2.1% were BA.2 (VOC-22JAN-01), 0.12% BA.4.6 (V-22SEP-01), and 0.7% were classified as other.

New variant designations from horizon scanning

Since the last technical briefing CH.1.1 (BA.2.75.3.4.1.1.1.1) was designated as variant V-22DEC-01 on 19 December 2022 and XBB.1.5 was designated as variant V-23JAN-01 on 9 January 2023. The genomic definition for V-23JAN-01 is currently pending and will be published once available.

Growth rates

The small number of sequenced samples of XBB.1.5 limits confidence in current modelling predictions. CH.1.1 and XBB.1.5 are the most competitive of the signals in monitoring or designated variants. CH.1.1 has a 21.56% (95% credible interval (CrI): 19.25 to 23.97) relative growth rate advantage over BQ.1.1 and has reached a prevalence of 15.78% (95% CrI: 10.41 to 24.56). XBB.1.5 remains at low prevalence at 1.66% (95% CrI: 0.89 to 2.74) and has a 38.87% (95% CrI: 32.2 to 45.63) relative growth rate advantage based on an extremely limited sample size. Estimates for XBB.1.5 are very uncertain and likely to change due to low prevalence.

Hospitalisation (BQ.1)

Preliminary analysis of the risk of hospital admission following presentation to emergency care indicates that there is no increase in risk for people with BQ.1 (V-22OCT-01) compared to BA.5 (VOC-22APR-04) (odds ratio: 1.06, 95% confidence interval 0.97 to 1.17). This estimate has limited adjustment for confounding factors and more detailed analysis is continuing.

Vaccine effectiveness (BQ.1)

A preliminary analysis has been undertaken comparing vaccine effectiveness against hospitalisation for BQ.1 compared to BA.5, but numbers of sequences in the currently available data are too small to make a confident assessment.

Reports from Variant Technical Group members

The Genotype to Phenotype Consortium reports pseudovirus neutralisation data showing that neutralisation titres against XBB are the lowest of any contemporary variant tested, with vaccine and Omicron breakthrough sera. This is consistent with several other published studies. Live virus neutralisation also shows titres between 4 and 6 times lower against BQ1.1 or XBB than against Delta or Omicron BA.5 (sera from individuals with 4 doses of vaccine). Assessment of replication and cell fusion confirm that XBB is phenotypically similar to other Omicron variants rather than to Delta or earlier variants of concern (VOCs). (A full description of the data is included in section 3).
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

<table>
<thead>
<tr>
<th>Variants of concern</th>
<th>Designated variants (Vs)</th>
<th>Signals in monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omicron (B.1.1.529) sub-lineage BA.1 and descendant lineages VOC-21NOV-01</td>
<td>Delta (B.1.617.2 and sub-lineages) V-21APR-02</td>
<td>Delta and Omicron recombinant XBC</td>
</tr>
<tr>
<td>Omicron (B.1.1.529) sub-lineage BA.2 and descendant lineages VOC-22JAN-01</td>
<td>Omicron XE Recombinant (BA.1 x BA.2) V-22APR-02</td>
<td>BQ.1.1</td>
</tr>
<tr>
<td>Omicron (B.1.1.529) sub-lineage BA.4 VOC-22APR-03</td>
<td>Omicron BA.2.75 V-22JUL-01</td>
<td>BN.1 (BA.2.75.5.1)</td>
</tr>
<tr>
<td>Omicron (B.1.1.529) sub-lineage BA.5 VOC-22APR-04</td>
<td>Omicron BA.4.6 V-22SEP-01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Omicron BQ.1 V-22OCT-01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Omicron XBB Recombinant (BJ.1 x BM.1.1.1) V-22OCT-02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*Omicron CH.1.1 V-22DEC-01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*Omicron XBB.1.5 Recombinant (XBB + additional mutations) V-23JAN-01</td>
<td></td>
</tr>
</tbody>
</table>

* Newly escalated variants or signals in monitoring since the previous technical briefing.
Table 1b. Variants detected in GISAID, but not in the UK, in the past 12 weeks

<table>
<thead>
<tr>
<th>Variants of concern</th>
<th>Designated variants (Vs)</th>
<th>Signals in monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BA.2.12.1 V-22MAY-01</td>
<td>Variants originating from China given changes in epidemiology</td>
</tr>
</tbody>
</table>

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 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.

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 January 2022 to 5 January 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.)
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 sequencing from hospitalised patients and care homes, sequenced cases are significantly older than reported cases. Between 12 December 2022 and 8 January 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 3A and 3B).

Figure 3A. Age-sex distribution of all COVID-19 cases for the past 4 weeks (12 December 2022 to 8 January 2023)

Figure 3B. Age-sex distribution of sequenced COVID-19 cases for the past 4 weeks (12 December 2022 to 8 January 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 4. UKHSA designated variants are those assigned for more comprehensive epidemiological studies and may incorporate multiple sub-lineages.

Of the sequenced cases from 26 December 2022 to 1 January 2023, 1.5% were BA.2 (VOC-22JAN-01), 6.3% BA.5 (VOC-22APR-04), 10.3% BA.2.75 (V-22JUL-01), 0.2% BA.4.6 (V-22SEP-01), 50.9% BQ.1 (V-22OCT-01), 6.6% XBB (V-22OCT-02), 23.1% CH.1.1 (V-22DEC-01) and 1.1% were classified 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 1 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 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 1.15 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 4, 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 4 can be found in the accompanying spreadsheet.
Figure 4. Variant prevalence (UKHSA designated variant definitions only) of available sequenced cases for England from 1 February 2021 as of 6 January 2023
Table 2 shows the list of variant definitions and associated Pangolin lineage names.

**Table 2. List of variants and associated Pangolin lineage names**

<table>
<thead>
<tr>
<th>Variant</th>
<th>Associated Pangolin lineage</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-22JAN-01</td>
<td>BA.2</td>
</tr>
<tr>
<td>V-22APR-02</td>
<td>XE</td>
</tr>
<tr>
<td>V-22APR-03</td>
<td>BA.4</td>
</tr>
<tr>
<td>V-22APR-04</td>
<td>BA.5</td>
</tr>
<tr>
<td>V-22JUL-01</td>
<td>BA.2.75</td>
</tr>
<tr>
<td>V-22SEP-01</td>
<td>BA.4.6</td>
</tr>
<tr>
<td>V-22OCT-01</td>
<td>BQ.1</td>
</tr>
<tr>
<td>V-22OCT-02</td>
<td>XBB</td>
</tr>
<tr>
<td>V-22DEC-01</td>
<td>CH.1.1</td>
</tr>
</tbody>
</table>
Figure 5. Prevalence of Pangolin lineages in the UK with sequence data with a specimen date from 1 August 2022 to 1 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. The data used in this graph can be found in the accompanying spreadsheet.
Figure 6. Prevalence of Pangolin lineages in the UK in ONS CIS sequence data with a specimen date between 1 August 2022 to 1 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. 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 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 25 December 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. Unlike previous weeks, all sequenced cases were modelled. This was because there were too few ONS CIS samples of XBB.1.5 to model relative growth rates. These estimates must therefore be interpreted with caution, as the full dataset is confounded by care home and hospital sampling.

The modelled percentage representation is shown in Figure 7, with relative growth rates compared to BQ.1.1 lineages (Figure 8). 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 upper tier local authority (UTLA). The sampling range for both logistic regression and generalised additive models is from 12 October 2022 to 3 January 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 3. Growth rate (GR) of variants and signals under monitoring as of 25 December 2022^  

<table>
<thead>
<tr>
<th>Lineage</th>
<th>English sequences used in the multinomial model (MM)</th>
<th>MM England estimated prevalence</th>
<th>MM estimate for the weekly growth rate relative to BQ.1.1 lineages</th>
<th>English sequences counts used in the logistic regression and generalised additive model</th>
<th>Logistic regression GR (1/week)</th>
<th>Generalised additive model most recent GR (1/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BQ.1.1</td>
<td>1,4711</td>
<td>51.67% (95% CrI: 38.09 to 64.31)</td>
<td>-</td>
<td>1,161</td>
<td>14%</td>
<td>-9%</td>
</tr>
<tr>
<td>CH.1.1</td>
<td>2,262</td>
<td>15.78% (95% CrI: 10.41 to 24.56)</td>
<td>21.56% (95% CrI: 19.25 to 23.97)</td>
<td>291</td>
<td>37%</td>
<td>12%</td>
</tr>
<tr>
<td>BQ.1*</td>
<td>5,963</td>
<td>10.46% (95% CrI: 6.71 to 16.06)</td>
<td>-8.85% (95% CrI: -10.09 to -7.42)</td>
<td>2,053</td>
<td>16%</td>
<td>-18%</td>
</tr>
<tr>
<td>BN.1</td>
<td>2,410</td>
<td>6.01% (95% CrI: 3.35 to 10.21)</td>
<td>-6.12% (95% CrI: -7.69 to -4.39)</td>
<td>71</td>
<td>3.6%</td>
<td>-55%</td>
</tr>
<tr>
<td>BA.2.75†</td>
<td>2,016</td>
<td>1.16% (95% CrI: 0.67 to 1.97)</td>
<td>-21.52% (95% CrI: -22.93 to -19.95)</td>
<td>1,153</td>
<td>13%</td>
<td>4%</td>
</tr>
<tr>
<td>XBB**</td>
<td>1,304</td>
<td>7.02% (95% CrI: 4.04 to 10.58)</td>
<td>4.52% (95% CrI: 2.57 to 6.57)</td>
<td>267</td>
<td>18%</td>
<td>0%</td>
</tr>
<tr>
<td>XBB.1.5</td>
<td>124</td>
<td>1.66% (95% CrI: 0.89 to 2.74)</td>
<td>38.87% (95% CrI: 32.2 to 45.63)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* BQ.1 excludes BQ.1.1 which was modelled separately.  
† BA.2.75 excludes BN.1 and CH.1.1 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 12 October 2022 to 3 January 2023.
Figure 7. 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 8. 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 all sequenced cases in England, described above. Note that using all sequenced cases may bias results and should be interpreted with caution. Supplementary data is not available for this figure.
3. V-22OCT-02 (XBB recombinant)

XBB was first flagged in horizon scanning on 11 October 2022. 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.

As of 9 January 2023, 28,127 XBB (V-22OCT-01) sequences have been uploaded to GISAID from 91 non-UK countries, across 6 continents. Currently, the country uploading the most samples is the USA (9,006, 30%). Sampling strategies for many countries remain unknown. A total of 2,394 UK XBB samples have been identified.

As of 9 January 2023, there were 1,520 cases with XBB (V-22OCT-01) in England. The first detected case in England had a specimen date of 10 September 2022.

3.1 Reports from Variant Technical Group members

The following data was submitted by the Genotype to Phenotype Consortium.

Pseudovirus (PV) neutralisation data on XBB from Kings College London and the Pirbright Institute show XBB has the lowest neutralisation titres of any contemporary variant tested, with vaccine and Omicron breakthrough antisera. Titres against XBB were between 5 to 10-fold lower than those against Omicron BA.4 or BA.5 Spike bearing PV. This is in line with several other published or pre-printed studies such as Yue and others, 2023.

Live virus neutralisation studies at the Francis Crick Institute detect neutralisation titres against XBB in sera from the Legacy study after a fourth vaccine boost but titres are between 4 and 6 times lower against BQ1.1 or XBB than against Delta or Omicron BA.5.

Replication assays in vitro at Imperial College London indicate that XBB and BQ1.1 remain attenuated in Calu-3 cells, but undergo rapid replication in primary culture of nasal epithelium (Figure 9). This phenotype is typical of all Omicron variants so far and different to that of Delta and earlier variants of concern (VOCs). We attribute this phenotype to a preference for cell entry through the endosomal route and have confirmed this using PV entry assays (Figure 10). This entry route has been associated with attenuation in vivo.

In addition, cell fusion data from the Pirbright Institute confirm that XBB, like all other Omicron variants, is less fusogenic than Delta and earlier VOCs (Figure 11).
Figure 9. Replication of Omicron variants in Calu3 or primary human nasal epithelial cell cultures

![Graph showing replication of Omicron variants in Calu3 and hNEC cultures](image)

Supplementary data is not available for this figure.

Figure 10. Cell entry pathway preference of SARS-CoV-2 Omicron variants in human Caco-2 cells

![Graph showing cell entry pathway preference](image)

Supplementary data is not available for this figure.
3.2 Genomic diversity within XBB

Diversity in Spike

Spike mutations are monitored within V-22OCT-02 using 4 criteria (Table 4). A mutation is investigated further if it meets more than one of these criteria and is present in at least 10 sequences. Seven additional mutations have been observed in V-22OCT-02 sequences according to the criteria in Table 4 (Figure 12). The criteria for mutation monitoring are currently being reviewed and amended.

Table 4. Criteria used to assess emerging mutations

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative count</td>
<td>Running total for the number of sequences containing mutation is at least 50</td>
</tr>
<tr>
<td>Proportion</td>
<td>1% of sequences classified as this variant contain this mutation within a single week</td>
</tr>
<tr>
<td>Difference in proportion</td>
<td>The difference in the proportion of sequences in 2 consecutive weeks is at least 0.25%</td>
</tr>
<tr>
<td>Percentage change in the number of sequences</td>
<td>The percentage change between the number of sequences containing the mutation in 2 consecutive weeks is at least 5%</td>
</tr>
</tbody>
</table>
The sequences included in the plot in Figure 12 are all V-22OCT-02 sequences; therefore, any XBB sub-lineages that meet the definition requirements will be included. Any defining mutations for these sub-lineages will not be excluded and so will appear in the plot if they meet the criteria described above. Mutations that are expected to be present in all V-22OCT-02 sequences (T191I, V83A, G142D, H146Q, Q183E, V213E, G339H, R346T, L368I, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440K, V445P, G446S, N460K, T478K, E484A, F486S, F490S, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K ) are not included in the plot, but are monitored, and any significant changes in the proportions of these mutations (for example a reversion) will be reported as required.

Figure 12. Spike mutations found in V-22OCT-02 genomes in the UK dataset relative to the Wuhan sequence NC_045512.2 between 5 September 2022 and 1 January 2023

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

NB: mutations expected to be in all V-22OCT-02 sequences are not included in this plot to increase readability.

Outside Spike, there are 23 mutations that are present in at least 1% of V-22OCT-02 sequences for at least 3 consecutive weeks (Figure 13). The premature stop codon, G8*, in orf8 found in XBB.1 and is expected to be present in all XBB.1.5 sequences. This mutation has been present in around 70% of V-22OCT-02 sequences for the last 4 weeks.
Figure 13. Mutations acquired by V-22OCT-02 outside Spike, shown as a proportion of total V-22OCT-02 sequences (1 September 2022 to 1 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-22OCT-02 mutation set. Those that are considered additional, and that are present in at least 1% of V-22OCT-02 sequences for at least 3 consecutive weeks in the UK dataset, are included in Figure 13 as a proportion of total V-22OCT-02 sequences. The plot includes all sequences designated as one of the XBB sub-lineages that meet the V-22OCT-02 definition (for example, XBB.1.5).

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

3.3 Newly designated variant: Omicron XBB.1.5 recombinant (V-23JAN-01)

XBB.1.5 contains 3 non-synonymous mutations 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 4,232 XBB.1.5 samples annotated in GISAID, with 3,870 samples uploaded by the USA (91%). XBB.1.5 has been identified in 161 UK samples through sequencing.

In England, the first detected case had a specimen date of 21 November 2022; as of 5 January 2023, 136 XBB.1.5 sequences had been identified. One hundred and thirty-two sequences could be linked to demographic data for 129 individuals.

The median age of cases was 59 years old (interquartile range, 43 to 71). Most cases were female (80), with 47 male cases and 2 unknown cases. There have been cases in each region of England with the most cases resident in the North West (35) and London (27).
4. 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.
5. Severity analysis

The relative severity of BQ.1 (V-22OCT-01) compared to BA.5 (VOC-22APR-04) was assessed in a case-control study of the risk of admission to hospital following presentation to emergency care. Preliminary analysis of this data on 2,585 BQ.1 (V-22OCT-01) episodes and 8,112 BA.5 (VOC-22APR-04) episodes found that there was no increase in risk for BQ.1 (V-22OCT-01) compared to BA.5 (VOC-22APR-04) (odds ratio: 1.06, 95% confidence interval 0.97 to 1.17). This analysis was minimally adjusted for age and time since vaccination. The analysis was also stratified by week of specimen. These results may change as additional factors are included in the analysis.
6. Vaccine effectiveness

A test-negative case control study design was used to estimate vaccine effectiveness against hospitalisation with BQ.1 in England. Cases were identified from hospital (pillar 1) testing data and secondary uses service (SUS) hospital discharge data from the period from 5 September 2022 to 11 December 2022 and classified as BA.5 (VOC-22APR-04) or BQ.1 (V-22OCT-01) based on sequencing information.

Logistic regression was used to estimate the vaccination status of BQ.1 cases as compared to BA.5 control cases. Previous positivity, testing pillar, health and social care worker status, clinical risk status, age, gender, and week of test were adjusted for. Vaccine effectiveness was estimated for those who had received a bivalent booster vaccine as part of the autumn programme, as well as at least 2 previous doses at least 6 months previously, relative to those who were not boosted in the autumn but had at least 2 previous doses at least 6 months previously. All vaccine manufacturers were combined in the analysis.

The effectiveness of the bivalent booster against hospitalisation with BQ.1 in this analysis was 50.3% (95% confidence interval (CI): 34.9 to 62.0%) as compared to 64.0% (95% CI: 53.4 to 72.2%) with BA.5, at 2 or more weeks after receiving the booster.

Although the effectiveness point estimate is lower for BQ.1 the confidence interval is still fairly wide and overlaps the estimate for BA.5. Currently the number of BQ.1 cases in the analysis is too small to confidently assess differences in vaccine effectiveness between the 2 variants.
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.

Authors of this report

UKHSA Genomics Public Health Analysis Team
UKHSA COVID-19 Vaccines and Epidemiology Team
UKHSA Surveillance Team
UKHSA Data, Analytics and Surveillance
UKHSA Infectious Disease Modelling Team
Contributions from the Variant Technical Group

Variant Technical Group members

Chair
Meera Chand (UKHSA)

Genomics and bioinformatics

Andrew Rambaut (University of Edinburgh)
Thomas Peacock (UKHSA / Imperial College London)
Matt Holden (Public Health Scotland)
Nicholas Loman (UKHSA / University of Birmingham)
Richard Myers (UKHSA)
Ewan Harrison (Sanger Institute)

Virology and immunology

Bassam Hallis (UKHSA)
Gavin Screaton (University of Oxford)
Lance Turtle (University of Liverpool)
Maria Zambon (UKHSA)
Ravi Gupta (University of Cambridge)
Susanna Dunachie (University of Oxford)
Epidemiology and modelling

Chris Williams (Public Health Wales)
Daniela de Angelis (University of Cambridge)
Derek Smith (University of Cambridge)
Erik Volz (UKHSA / Imperial College London)
Fergus Cumming (UKHSA)
Jamie Lopez-Bernal (UKHSA)
John Edmunds (London School of Hygiene and Tropical Medicine)
Julia Gog (Scientific Pandemic Influenza Group on Modelling / University of Cambridge)
Maria Rossi (Public Health Scotland)
Neil Ferguson (Imperial College London)
Sarah Walker (University of Oxford)
Simon Thelwall (UKHSA)
Susan Hopkins (UKHSA)
Thomas Finnie (UKHSA)
Thomas Ward (UKHSA)

International epidemiology

Chris Lewis (Foreign, Commonwealth and Development Office)

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