

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

# Technical briefing 38

11 March 2022

This report provides an update on previous briefings up to 25 February 2022

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# **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.

<u>SARS-CoV-2 Routine variant data update</u> covers surveillance data and sequencing coverage data on all other VOCs and VUIs. Unless stated otherwise, this technical briefing uses a data cut-off of 7 March 2022 to allow time for analyses.

#### VUI-22JAN-01 (BA.2)

BA.2 rarely contains the spike gene deletion at position 69-70 and is S-gene target positive (SGTP) on diagnostic assays with targets in this area. SGTP is now a reasonable proxy for BA.2, which accounts for >99.3% of sequenced SGTP cases. The proportion of SGTP cases has increased: the overall proportion of SGTP amongst cases tested by the relevant assay in England on 6 March 2022 is 83.3% compared to 52.1% on 20 February 2022. There is geographical variation with the highest proportion of SGTP in London (87.5%) and the lowest in the North East region (73.5%). The proportion of BA.2 in sequenced data from 27 February to 6 March 2022 was 68.6%. This is compatible with the known lag in sequence data compared to test data.

#### Growth rate

BA.2 has demonstrated an increased growth rate compared to BA.1 in all regions of England. Since mid-February, the growth rate has settled at approximately 80% greater relative growth for BA.2 compared to BA.1. Estimated with data up to 1 March 2022 it was 79% per week compared to 103% using data up until 7 February 2022.

#### Secondary attack rates

Secondary attack rates amongst contacts exposed in household and non-household settings (adjusted for factors including vaccination status) are higher for BA.2 than other sequenced Omicron cases: 13.6% vs 10.7% in households and 5.3% vs 4.2% in non-household settings. This modest reduction since <u>Technical briefing 37</u>, reflecting the inclusion of cases testing positive during 1 to 14 February 2022, is not due to the new vaccination adjustment.

#### Hospitalisation

Preliminary analysis finds no evidence of a greater risk of hospitalisation following infection with BA.2 compared to BA.1.

#### Reinfections

A small number of potential BA.2 reinfections following a BA.1 primary infection have been detected. Further investigations are being undertaken to confirm and characterise these cases.

General reinfection surveillance data is published in the <u>coronavirus (COVID-19) vaccine</u> weekly surveillance reports.

#### Cycle threshold analysis

BA.2 have similar (but not identical) cycle threshold (Ct) values to BA.1 in pillar 2 (community) data, with a possible small increase in the proportion of cases classified as high viral load. Further investigations are ongoing.

#### Reports from Variant Technical Group Members

Genotype2Phenotype consortium funded by UK Research and Innovation conducted pseudovirus neutralisation tests with convalescent sera from infected, unvaccinated people. This unpublished study showed a large antigenic distance between Delta and Omicron variants.

Individuals infected with Delta made strong homologous responses but showed poor neutralisation of BA.1. Individuals infected with BA.1 showed strong neutralisation of BA.1, and lower but detectable neutralisation of BA.2.

Hamsters infected with Delta only or Omicron only at Imperial College London also showed large antigenic distances whereby despite robust homologous titres, there was no detectable cross neutralisation between Delta and Omicron variants. In addition, sera from hamsters infected with BA.1 had low neutralising activity against BA.2.

King's College London data also showed a much broader neutralisation pattern following 3 dose vaccination whereby BA.1 and BA.2 were effectively neutralised. Vaccination and infection showed a similar broader response.

## **Published information on variants**

The <u>collection page</u> gives content on variants, including prior <u>technical briefings</u>. Definitions for variants of concern, variants under investigation, and signals in monitoring are detailed in <u>technical briefing 8</u>.

The UKHSA, formerly Public Health England (PHE), has curated a repository from 5 March 2021 containing the up-to-date genomic definitions for all VOCs and VUIs. <u>The repository is accessible here</u>.

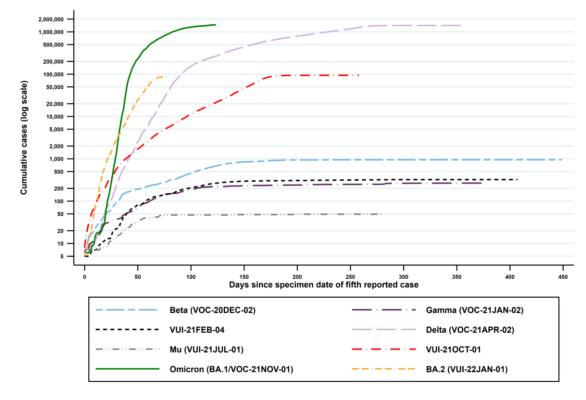
<u>Technical briefings</u> are published periodically. From technical briefing 15, briefings include variant diagnoses identified by whole-genome sequencing and a genotyping PCR test, including the categorisation of sequenced and genotyped variant results and a rules-based decision algorithm to identify variant and mutation profiles from genotype assay mutation profiles.

### Part 1. Surveillance overview

### 1.1 VOC and VUI overview

<u>Summary epidemiology for each variant and case numbers</u> are updated online. Figure 1 shows the cumulative number of cases per variant indexed by days since the first report.

Figure 1. Cumulative cases in England of variants indexed by days since the fifth reported case as of 6 March 2022



(Find accessible data used in this graph in underlying data.)

## 1.2 Variant prevalence

The prevalence of different variants amongst sequenced episodes is presented in Figure 2. Of the sequenced episodes from 27 February to 6 March 2022, 31.1% were Omicron BA.1 (VOC-21NOV-01), 68.6% were Omicron lineage BA.2 (VUI-22JAN-01), and 0.3% were other variants.

The 'Other' category in Figure 2 includes genomes where the quality is insufficient to determine variant status and genomes that do not meet the current definition for a VUI or VOC.

The Omicron genome (lineage BA.1) contains the spike deletion at position 69-70 which is associated with S-gene target failure (SGTF) in some widely used PCR tests. Such PCR tests evaluate the presence of 3 SARS-CoV-2 genes: Spike (S), nucleocapsid (N) and ORF1ab. SGTF is defined as a PCR test where the N and ORF1ab genes are detected (with Ct values less than or equal to 30) but the S-gene is not. SGTF patterns can be used to assess the spread of Omicron lineage BA.1. The Omicron lineage BA.2, VUI-22JAN-01, does not contain the spike gene deletion and is S-gene target positive (SGTP). The number of coronavirus (COVID-19) cases with SGTP/SGTF by day, among those tested in TaqPath labs is shown in Figure 3. There is significant variability across the country in SGTF varying from 12.5% in London to 26.5% in the North East (Figure 4).

London, the South West, and the South East are observing the highest proportions in BA.2 (Figure 5 and Table 1). Conversely, the North East is lagging behind the overall national trend. The South West has poor gene target coverage and estimates are therefore driven by more well sampled lower tier local authorities (LTLA). The uncertainty in the credible intervals reflect the intra-regional heterogeneity.

The probability of triple positivity was analysed in tests from labs that report results for all 3 gene targets on SARS-CoV-2. Triple positivity is used as a proxy for Omicron BA.2. The model is a Bayesian hierarchical logistic growth model fit to regional and LTLA-level data, accounting for geographic heterogeneity.

Figure 2. Variant prevalence of available sequenced cases for England from 1 February 2021 as of 8 March 2022 (Find accessible data used in this graph in <u>underlying data</u>. Dashed lines indicate period incorporating issue at a sequencing site. Grey line indicates proportion of cases sequenced.)

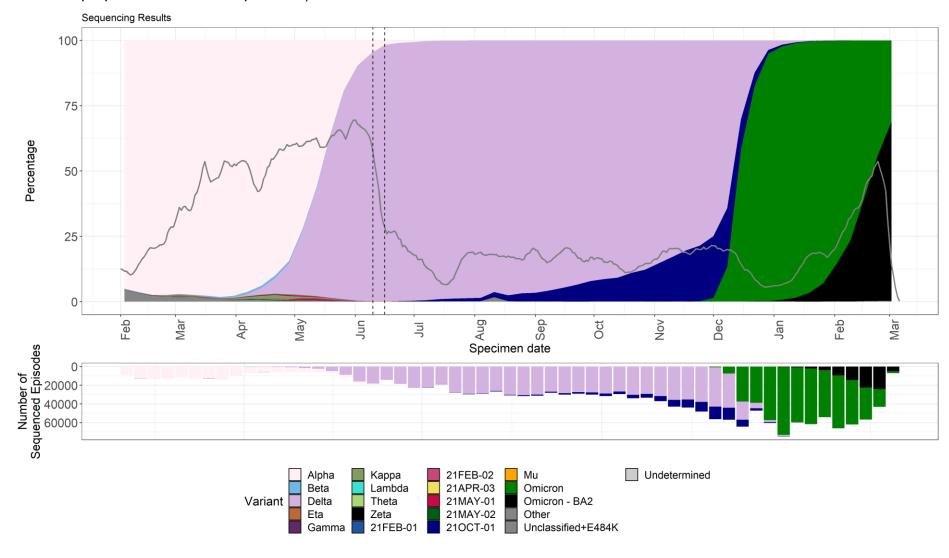
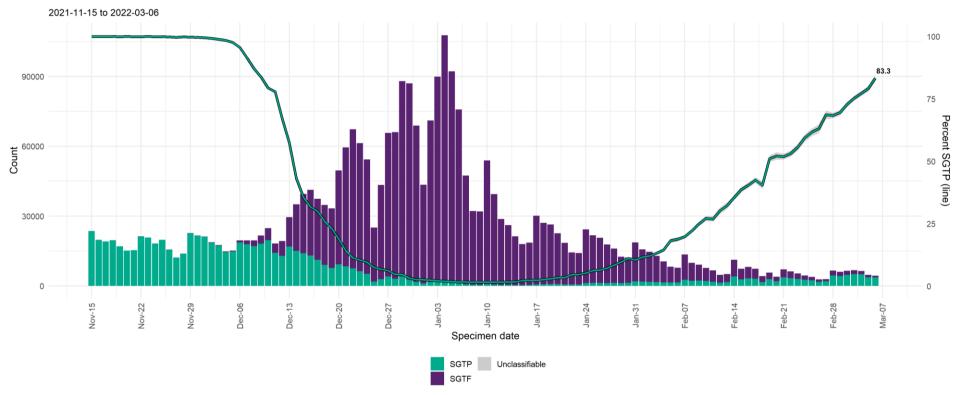


Figure 3. Number of COVID-19 cases with SGTP/SGTF by day, among those tested in TaqPath labs as of 8 March 2022 (95% confidence intervals indicated by grey shading. Percentage for most recent day shown)

(Find accessible data used in this graph in underlying data.)

95% confidence intervals indicated by gray shading. Percentages for most recent day shown. Data updated on 2022-03-08



SGTF (S gene target failure) has been proxy for VOC-21NOV-01 since December 2021. SGTP (S gene target positive) has been a reliable proxy for Omicron BA.2 since January 2022, and before this since April 2021 was a Delta proxy.

Local trends in these data may be affected by decisions to direct the processing of samples via a TaqPath laboratory.

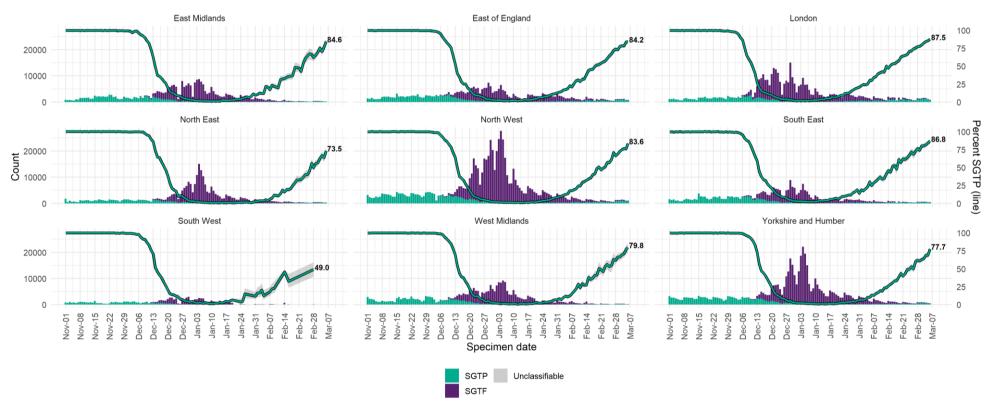
Only tests carried out with the TaqPath PCR assay and with SGTF or SGTP results included, from Newcastle, Alderley Park, Milton Keynes and Glasgow Lighthouse Labs.

SGTF refers to non-detectable S gene target and <=30 CT values for N and ORF1ab gene targets. SGTP refers to <=30 CT values for S, N, and ORF1ab gene targets.

Produced by Outbreak Surveillance Team. UKHSA.

Figure 4. Number of COVID-19 cases with SGTP/SGTF by day, among those tested in TaqPath labs by region of residence as of 8 March 2022 (95% confidence intervals indicated by grey shading. Percentage for most recent day shown) \* (Find accessible data used in this graph in <u>underlying data</u>.)





SGTF (S gene target failure) has been proxy for VOC-21NOV-01 since December 2021. SGTP (S gene target positive) has been a reliable proxy for Omicron BA.2 since January 2022, and before this since April 2021 was a Delta proxy.

Local trends in these data may be affected by decisions to direct the processing of samples via a TaqPath laboratory.

Only tests carried out with the TaqPath PCR assay and with SGTF or SGTP results included, from Newcastle, Alderley Park, Milton Keynes and Glasgow Lighthouse Laboratory.

SGTF refers to non-detectable S gene target and <=30 CT values for N and ORF1ab gene targets. SGTP refers to <=30 CT values for S, N, and ORF1ab gene targets.

Produced by Outbreak Surveillance Team, UKHSA.

<sup>\*</sup>Percentage of SGTP in the South West region likely to be underestimated due to geographic heterogeneity on the local authority level and lower testing coverage.

Figure 5. Plot showing the modelled percentage of PCR tests in each region of England that are probable BA.2 on 4 March 2022 Points are the median estimates from a Bayesian logistic growth model, with 95% credible intervals shown as lines. The model accounts for difference in the percentage of BA.2 compatible tests in local authorities within each region. The model uses positivity on all 3 gene targets as an indicator of BA.2 and SGTF as a proxy of BA.1. Supplementary data is not available for this figure.

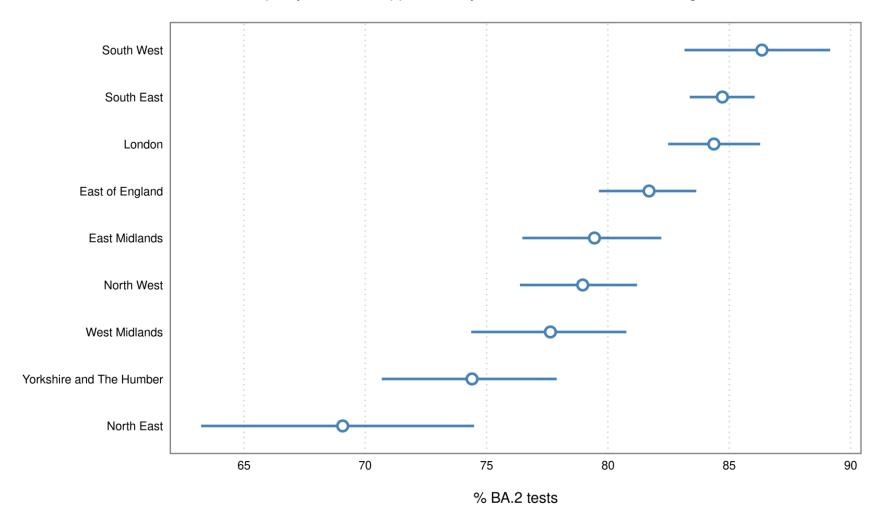


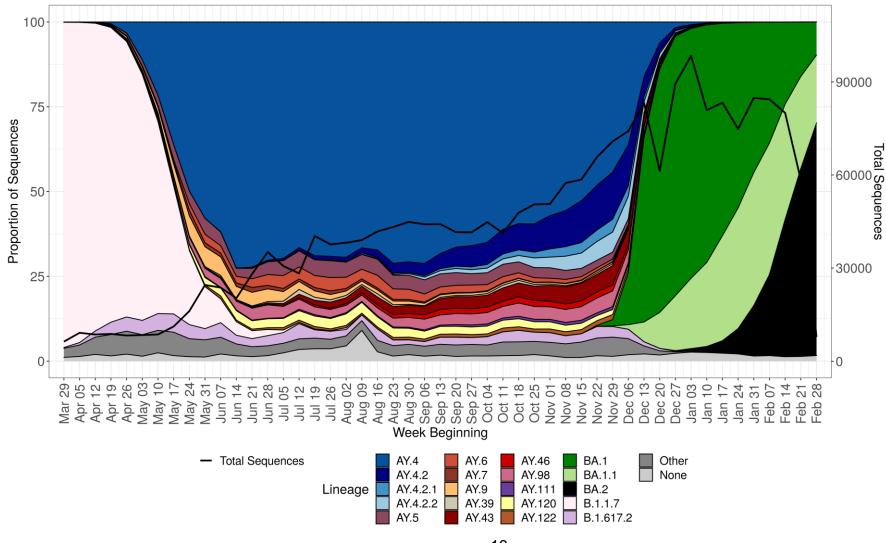
Table 1: Table showing the modelled percentage of PCR tests in each region of England that are probable BA.2 as of 4 March 2022

Region	% Triple Positive	Lower CI	Upper CI
South West	86.35	83.16	89.16
South East	84.72	83.37	86.05
London	84.37	82.48	86.27
East of England	81.7	79.63	83.64
East Midlands	79.45	76.48	82.2
North West	78.96	76.37	81.2
West Midlands	77.63	74.37	80.76
Yorkshire and The Humber	74.4	70.68	77.89
North East	69.07	63.24	74.49

Figure 6. Prevalence of Pangolin lineages in the United Kingdom (UK) with sequence data from 1 April 2021 to 6 March 2022

The total number of valid sequence results per week is shown by the black line. Only lineages with more than 5,000 sequences are shown. Smaller lineages are either merged with parent lineages (for example, AY.3.1 is included in AY.3) or are included in 'Other'. Sequences where Pangolin could not assign a lineage due to poor quality data are assigned 'None' in this plot.

(Find accessible data used in this graph in underlying data.)



# Part 2. Enhanced analysis of VUI-22JAN-01 (BA.2)

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

BA.2 was designated VUI-22JAN-01 (BA.2) by the UKHSA Variant Technical Group on 19 January 2022.

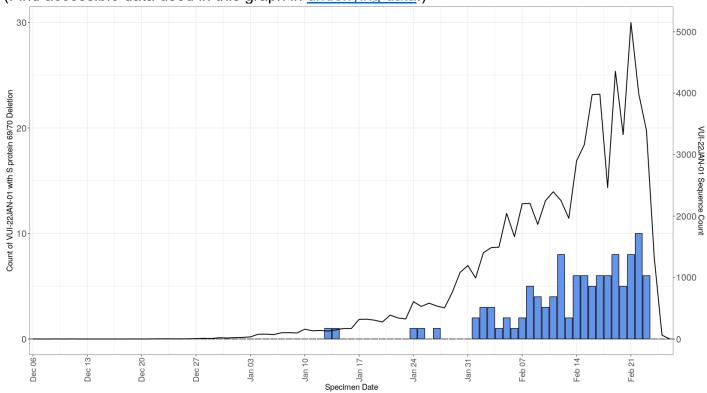
# 2.1 Genomic diversity

#### S-gene 69/70 deletion

Currently, SGTF is a suitable proxy for the VOC-21NOV-01 (BA.1) variant due to the deletion of amino acids at position 69 and 70 of the S protein for laboratories using the specific assays. The deletion is not present in VUI-22JAN-01 (BA.2) definition, although recently a small number of VUI-22JAN-01 (BA.2) sequences containing the deletion have been identified. As of 2 March 2022, a total of 123 VUI-22JAN-01 (BA.2) sequences were detected with the deletion in the UK genome data, out of a total of 93,937 confirmed or probable VUI-22JAN-01 (BA.2) sequences. This represents 0.13% of the VUI-22JAN-01 (BA.2) sequences. A graph of English sequences, where specimen date is available is shown in Figure 7. The frequency of detections of VUI-22JAN-01 (BA.2) sequences with 69/70 deletions increases as the total number of sequences available increases. When analysed phylogenetically, these comprise one main phylogenetic cluster and a number of individual sequences which do not cluster together. The correlation between the S-gene target results, deletion and Omicron lineages will be monitored.

Figure 7. Daily count of confirmed or probable English VUI-22JAN-01 containing S-gene 69/70 deletion that can be called (bar), alongside the number of England VUI-22-JAN-01 sequences (line), where specimen dates are available

(Find accessible data used in this graph in underlying data.)



### Diversity in Spike

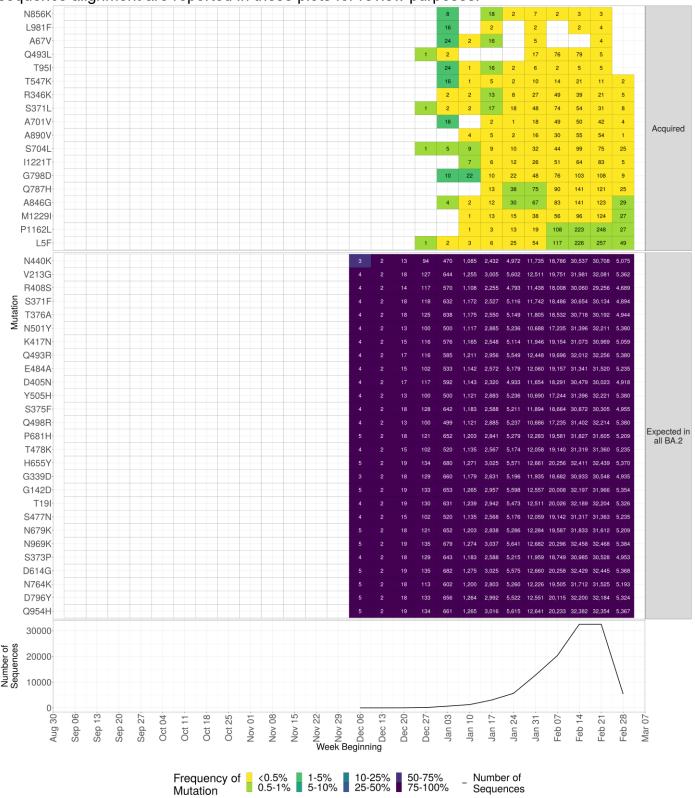
Spike mutations are monitored within BA.2 using 4 criteria (Table 2). A mutation is investigated further if it meets more than one of these criteria and is present in at least 10 sequences. Eighteen additional mutations have been observed in BA.2 sequences according to the criteria in Table 2 (Figure 8).

Table 2. Criteria used to assess emerging mutations

Criteria	Threshold
Cumulative count	Running total for the number of sequences containing mutation is at least 50
Proportion	1% of sequences classified as this variant contain this
	mutation within a single week
Difference in proportion	The difference in the proportion of sequences in 2
	consecutive weeks is at least 0.25%
Percentage change in	The percentage change between the number of sequences
the number of sequences	containing the mutation in 2 consecutive weeks is at least
·	5%

Figure 8. Spike mutations found in BA.2 genomes in the UK dataset relative to the Wuhan sequence NC\_045512.2 between 8 November 2021 and 6 March 2022

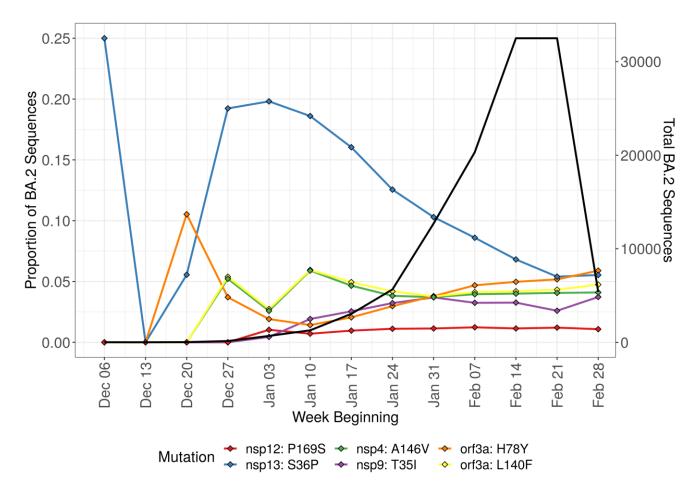
Supplementary data is not available for this figure. It should be noted all mutations in the sequence alignment are reported in these plots for review purposes.



Outside of Spike, there are 6 mutations that have increased in proportion of BA.2 sequences over time (Figure 9). One of these (nsp13: S36P) has been declining since December 2021.

Figure 9. Proportion of sequences containing mutations found in BA.2 genomes in the UK dataset relative to the Wuhan sequence NC\_045512.2 between 6 December 2021 and 6 March 2022

The total number of BA.2 mutations per week are indicated by the black line. Supplementary data is not available for this figure.

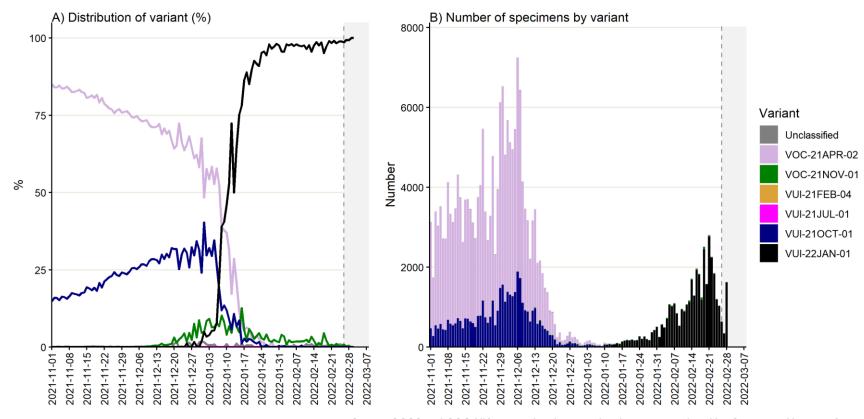


### **Epidemiology of SGTP**

The Omicron sub-lineage VUI-22JAN-01 (BA.2) rarely contains the spike deletion and therefore is SGTP. VUI-22JAN-01 (BA.2) has accounted for more than 95% of sequenced SGTP from 27 January to 8 March 2022.

Figure 10. Number and distribution of variants per week among sequenced SGTP specimens as of 8 March 2022 (Find accessible data used in this graph in underlying data.)

Specimen dates between 2021-11-01 and 2022-03-02. Data as of 2022-03-08. Specimen dates within last 11 days shaded in gray due to associated reporting delay; 10 days is median turn-around-time for sequencing.



Source: SGSS and COG-UK sequencing data, restricted to sequenced positive S-gene positive tests from Newcastle, Alderley Park, Glasgow, and Milton Keynes Lighthouse Laboratories. S gene +ve defined as positive SARS-CoV-2 test with CT values <=30 for S, N, and ORF1ab.

# 2.2 Epidemiology

As of 8 March 2022, 82,678 sequences of VUI-22JAN-01 (BA.2) have been identified in England. As VUI-22JAN-01 (BA.2) is designated by sequencing only, there is a known time lag of 11 days (interquartile range: 9 to 18) from obtaining a sample to reporting of VUI-22JAN-01 (BA.2) as the cause of infection. This will be reflected in case numbers presented.

Table 3. Number of confirmed VUI-22JAN-01 (BA.2) cases, by region of residence as of 8 March 2022

Region	Total case number	Case Proportion
East Midlands	7,386	8.9%
East of England	12,661	15.3%
London	17,862	21.6%
North East	1,586	1.9%
North West	5,645	6.8%
South East	16,508	20.0%
South West	10,008	12.1%
West Midlands	6,357	7.7%
Yorkshire and Humber	4,088	4.9%
Unknown region	577	0.7%
Total	82,678	-

Figure 11. Confirmed VUI-22JAN-01 (BA.2) cases by specimen date and region of residence as of 8 March 2022 (Find accessible data used in this graph in <u>underlying data</u>.)

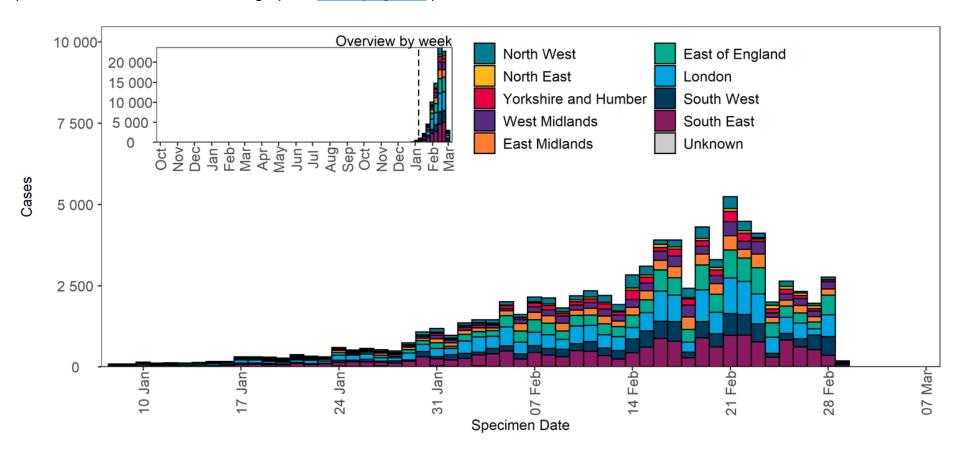
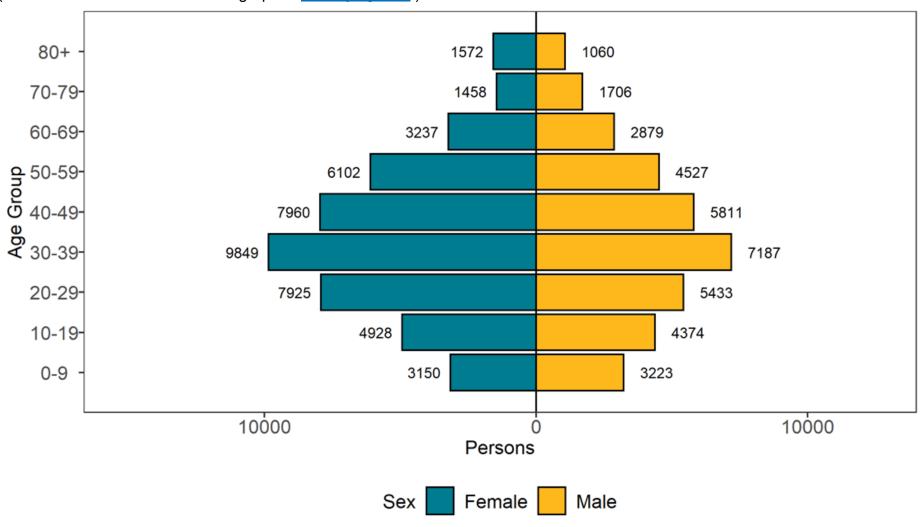


Figure 12. Age-sex pyramid of VUI-22JAN-01 (BA.2) cases as of 8 March 2022 (Find accessible data used in this graph in underlying data.)



287 cases excluded where sex or age not reported

### 2.3 Growth rates

The growth rate is estimated by logistic regression of the number of genomes sampled with the BA.1 and BA.2 lineages on time of sample collection. Only Pillar 2 testing (community testing) samples are included. To adjust for geographic variation in case growth rates, BA.2 growth rates were estimated relative to a geographically matched sample of BA.1 genomes. A logistic growth rate of zero would indicate no difference in growth rates between BA.1 and BA.2.

Data sampled between 1 December 2021 and 1 March 2022 were included. The estimated and empirical proportion of genomes from the BA.2 lineage are shown in Figure 13. The median growth rate is +78.8% per week. The analysis was repeated on data from each region of England (all had at least 400 BA.2 genomes) and is shown in Figure 14. Current logistic growth rates are consistent across regions, ranging from 64% to 79% per week.

Figure 13. Sample frequency of VUI-22JAN-01 (BA.2) relative to Omicron (BA.1) over time Supplementary data is not available for this figure.

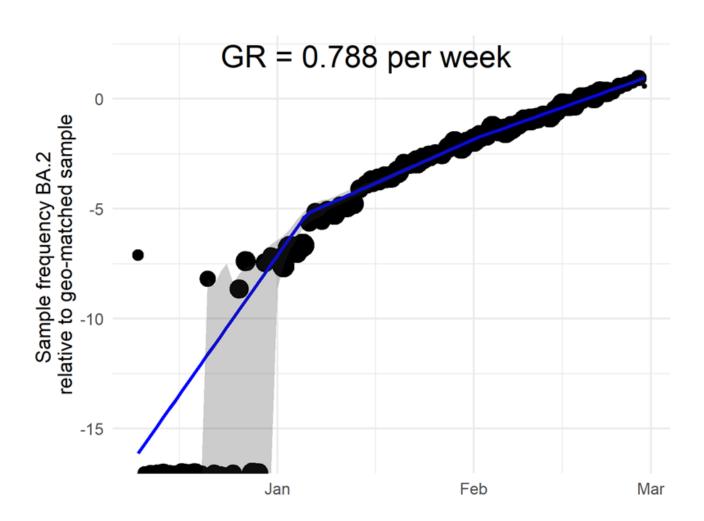
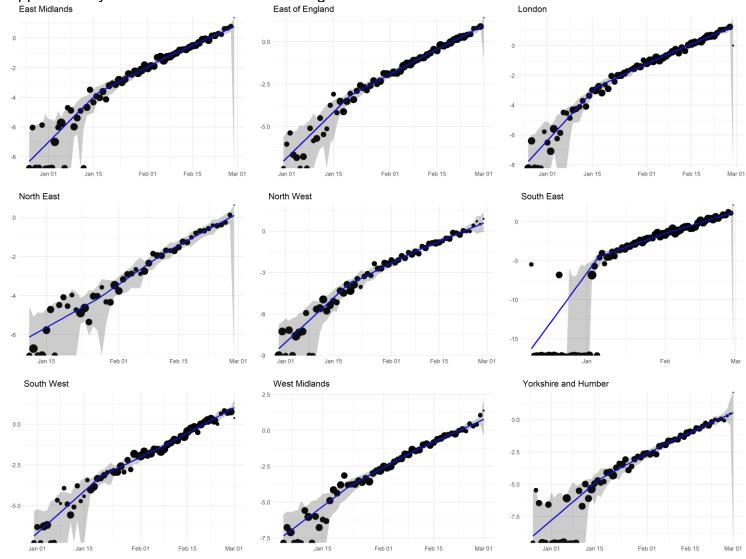


Figure 14. Sample frequency of VUI-22JAN-01 (BA.2) relative to Omicron (BA.1) over time in regions of England sampled through Pillar 2 testing

Supplementary data is not available for this figure.



## 2.4 Secondary attack rates

Only original cases with test dates in the period 1 January to 14 February 2022 are considered for this analysis. Secondary attack rates and odds ratios are based on positive tests amongst contacts named to NHS Test and Trace by an original case identified with sequenced confirmed BA.2 (VUI-22JAN-01) or other sequenced confirmed Omicron (VOC-21NOV-01, primarily BA.1) with date of symptom onset or positive test of the secondary case occurring 2 to 14 days after original exposure.

Only close contacts named by the original case to NHS Test and Trace are included, that is, household members, face-to-face contact, people within one metre of the case for one minute or longer, or people within 2 metres for 15 minutes. Contacts not named by the case but identified as part of contact tracing of international travellers on flights are excluded. The use of sequenced confirmed cases only may lead to bias: certain groups such as international travellers and those in hospital are more likely to be selected for sequencing and may not represent all community transmission.

Table 4 shows adjusted secondary attack rates split by the setting of the contact. Separate models were used for household and non-household settings, adjusting for vaccination status of the exposer and the contact (allowing for interaction with variant), age and sex of the exposer and the contact, the date (week) of positive test of the exposer and whether the contact completed contact tracing. Adjusted secondary attack rates in both household and non-household settings were higher amongst contacts of cases with BA.2 (VUI-22JAN-01) than other Omicron (VOC-21NOV-01, primarily BA.1) (Table 4). Secondary attack rates in household and non-household settings, and for both variants have reduced since <a href="Technical Briefing 37">Technical Briefing 37</a> (and this effect is not due to the new vaccination adjustment), suggesting an overall reduction in transmission detected by contact tracing in the first half of February.

Table 4. Secondary attack rates for contacts of cases with confirmed sequenced VUI-22JAN-01 and all other Omicron (VOC-21NOV-01)

(Case test dates 1 January to 14 February 2022, variant data as of 7 March 2022 and contact tracing data as of 8 March 2022)

		Number of exposing	Number of	Adjusted* secondary attack rate (95%
Variant	Setting	cases	contacts	Confidence Interval)
VOC-21NOV-01	Household	178,069	369,011	10.7% (10.6%-10.8%)
VUI-22JAN-01	Household	20,072	41,621	13.6% (13.2%-14.0%)
VOC-21NOV-01	Non-	30,325	74,343	4.2% (4.0%-4.3%)
	household			
VUI-22JAN-01	Non-	3,565	8,763	5.3% (4.7%-5.8%)
	household			

<sup>\*</sup>Adjusted for vaccination status of the exposer and the contact (allowing for interaction with variant), age and sex of the exposer and the contact, the date (week) of positive test of the exposer and whether the contact completed contact tracing.

Secondary attack rates from NHS Test and Trace should generally be considered lower bounds due to the nature of contact tracing and testing. Data provided is for contacts of cases with test dates in the period until 1 January to 14 February 2022.

## 2.5 Hospitalisation

Preliminary analyses of sequenced cases have been undertaken to compare the risk of hospitalisation, as defined by admission as an inpatient, or presentation to emergency care that resulted in admission, transfer or death, following BA.2 compared to BA.1. This analysis adjusted for age, reinfection status, sex, ethnicity, local area deprivation and vaccination status. It also controlled for the effect of geography and specimen date. The risk of hospitalisation does not appear to be higher following a BA.2 infection than following a BA.1 infection (hazard ratio 0.91, 95% CI: 0.85-0.98).

The estimate for the risk of hospitalisation, and the confidence intervals around that estimate, are below one, indicating a slightly lower risk for BA.2 compared to BA.1. However, the reduction in risk if present is very small.

# 2.6 Update on the SARS-CoV-2 Immunity and Reinfection Evaluation in healthcare workers study

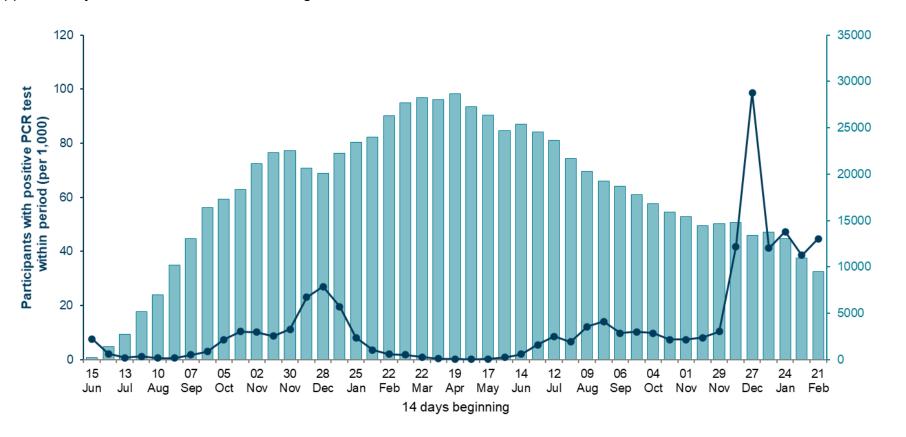
The SARS-CoV-2 Immunity and Reinfection Evaluation in healthcare workers (SIREN) study is a cohort of over 44,000 National Health Service healthcare workers, recruited from 135 hospital sites UK-wide. Participants under active follow-up undergo asymptomatic SARS-CoV-2 PCR testing every 2 weeks. This cohort had high seropositivity on recruitment (30% before the second wave) and is now highly vaccinated (more than 95%). The incidence of new infections and potential reinfections in SIREN is monitored. Figure 15 describes fortnightly trends in

primary PCR positivity and number of participants tested within the SIREN study from 15 June 2020 to 6 March 2022. Following a steep increase in PCR positivity in December 2021, the rate has decreased slightly since the peak at the end of December. However, the PCR positivity over the last 2 months remains higher than was seen before this peak.

Figure 16 shows the counts of reinfection over fortnightly time periods. Reinfections were defined as new PCR positive infections 90 days after a previous PCR positive date or 28 days after antibody positivity consistent with prior infection. Following a similar trend as the primary infections (Figure 15), the number of reinfections per fortnight has decreased slightly since the peak seen at the end of 2021, but the number remains higher than seen before this peak.

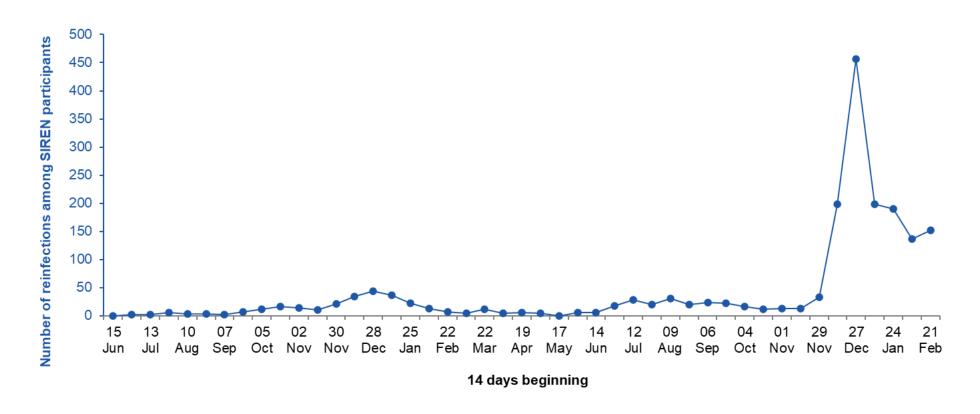
Figure 15. Fortnightly trends in primary PCR positivity and number of participants tested within the SIREN study from 15 June 2020 to 6 March 2022

Supplementary data is not available for this figure.



Note: Data is preliminary and undergoing review. Data at the latest timepoint may be affected by delayed reporting.

Figure 16. Number of reinfections in SIREN participants in the UK from 15 June 2020 to 6 March 2022 Supplementary data is not available for this figure.



Notes: Data is preliminary, and includes all possible reinfections flagged, but some may subsequently be excluded following clinical review. Data at the latest timepoint may be affected by delayed reporting.

### 2.7 Reinfections

An extract of 547,911 sequenced BA.1 and BA.2 specimens dated between 1 November 2021 and 21 February 2022 in England was used to look for recorded Omicron BA.1 and BA.2 SARS-CoV-2 infections, of which 527,066 individuals had a final unique identifier.

There were 487,415 individuals with BA.1 sequencing and 39,685 with BA.2 sequencing. Forty-three people recorded both a BA.1 and BA.2 sequence, 19 of whom had these samples taken within 5 days of each other, and 5 between 6 and 10 days apart. There were 18 people with BA.1 samples taken at least 25 days before a BA.2 sample. The sequences from these cases are being reviewed for confirmation. Age was known in 11 of these 18 cases and ranged from 6 to 93 years. In 12 cases where sex was known, 7 were female.

Details on overall reinfections are currently being published each fortnight in the <u>UKHSA National flu and COVID-19 surveillance reports</u> for episodes arising through January. Provisional data for week 2022-07 (to 20 February 2022) identified 21,768 reinfections accounting for 9.3% of all first or reinfection episodes that week.

## 2.8 Cycle threshold analysis

Cycle threshold (Ct) values are based on the number of cycles conducted before detecting the virus on a PCR test. The fewer cycles needed to detect the virus, the more virus there is in the sample (and therefore higher viral load).

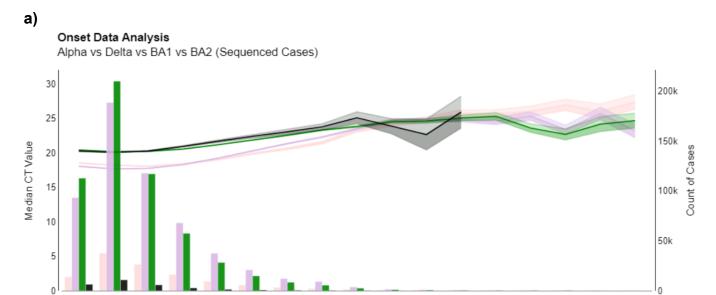
There have been changes in testing policy and practice over the analysis period (15 January to 5 March 2022), leading to a drop in PCR confirmatory testing and Taqpath coverage. This will primarily affect BA.2 and may bias the data.

Figure 17a shows the median Ct value by the number of days since symptom onset in cases that have been sequenced (full sequencing or reflex assay). Delta and Alpha are included for reference. So far, the median Ct values for BA.1 appear to be very similar to BA.2 from day 0 to 2 since symptom onset. After day 3 there is some indication of a small divergence, with BA.2 having slightly higher Ct values but there are too little data to be sure. This figure has approximately 30,000 sequenced BA.2 cases, a large enough sample to make inferences.

Figure 17b shows the same analysis but for PCR gene target data where the Ct values are less than or equal to 30 only. Data are shown for each variant since 15 January 2022 when the majority of cases in England were either BA.1 or BA.2. The Ct values SGTF (proxy BA.1) and SGTP (proxy BA.2) are currently very similar for the first 4 days since symptom onset, though there is some indication BA.2 may be lower for days 0 to 2.

Figure 17. a) Median Ct value for BA.1 vs BA.2 sequenced cases by the number of days since symptom onset and b) Median Ct value for BA.1 (SGTF) vs BA.2 (SGTP) by the number of days since symptom onset

(Find accessible data used in this graph in underlying data.)



8

Days

12

10

16

14

Delta Source: Data from SGSS Positive Tests data, UKHSA analysis Latest data: 2022-03-08

2

BA1

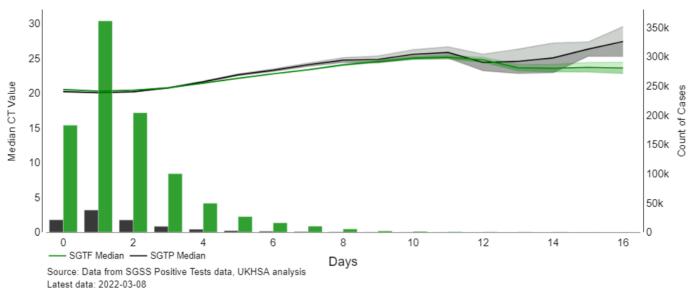
b) **Onset Data Analysis** 

0

SGTP vs SGTF since 15th January 2022 (Gene Target)

4

Alpha



A Gaussian mixture model is a probabilistic model for representing the subpopulations within an overall population. Figure 18 shows a gaussian mixture model for both BA.1 and BA.2 with 2 components (lowest and highest viral burden). The mixture probability density function (PDF) represents the probability distribution of the full data. The component PDF represents the probability distribution of each component (lowest and highest viral burden). Figure 18 shows similar distributions for both BA.1 and BA.2, with slight variation in the mean Ct values with BA.2 lower than BA.1 in both the highest viral burden and lowest viral burden group. There is also a difference in the proportion in both groups, BA.2 has a higher proportion within the highest viral burden category than BA.1 at 66% compared to 63% respectively (see Table 5).

Figure 18. Gaussian Mixture Models applied to sequenced BA.1 and BA.2 cases since 1 January 2022

Supplementary data is not available for this figure.



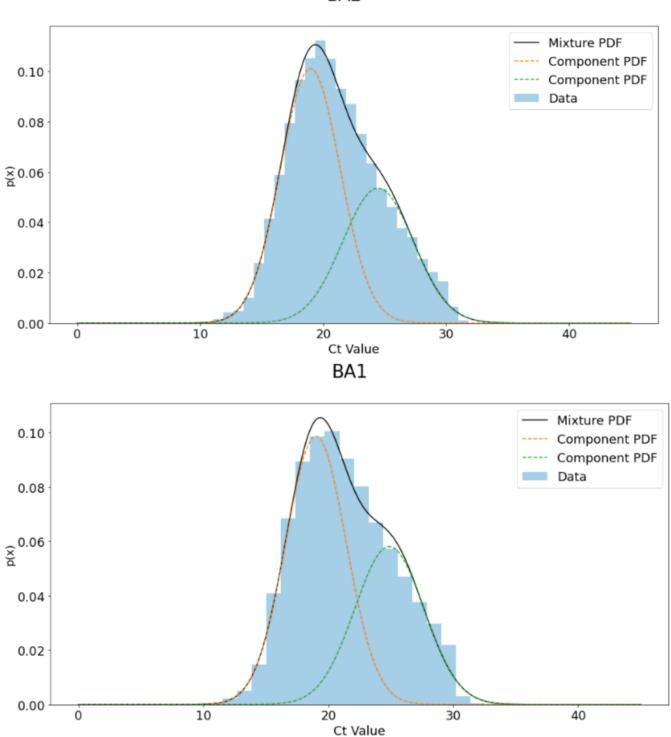


Table 5. Distribution of the Ct values for BA.2 and BA.1

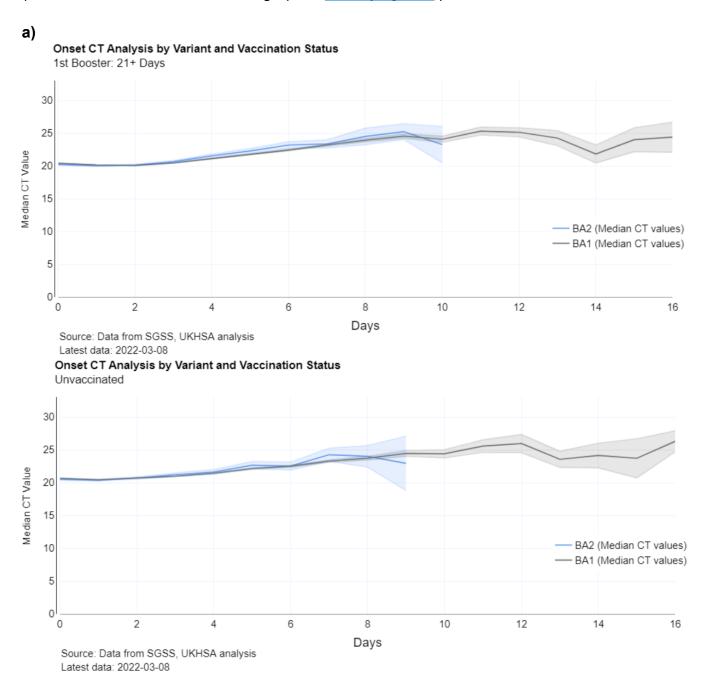
Class/sub-population	Mean Ct	Number	Standard deviation	Low 95% CI	High 95% CI	Percentage in class
Variant	BA.2					
Lowest viral burden	25.35	10,403	2.17	25.31	25.39	33.88
Highest viral burden	18.89	20,298	2.19	18.86	18.92	66.12
Variant	BA.1					
Lowest viral burden	25.52	183,258	2.18	25.51	25.53	37.21
Highest viral burden	18.93	309,203	2.17	18.92	18.93	62.79

Figures 19a and b show Ct values for BA.1 and BA.2 using sequenced results and SGTF and SGTP as proxy, by selected vaccination status and time since symptom onset.

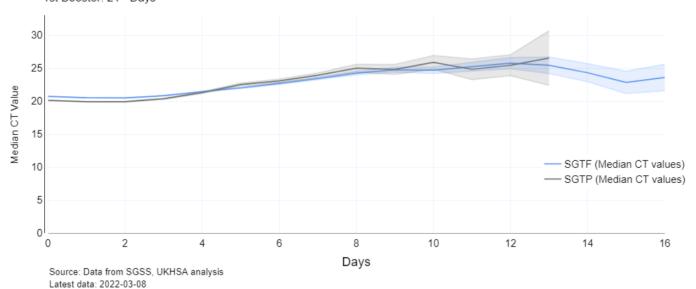
In Figure 19b, the trends look similar in these categories for the overall picture – whereby BA.1 and BA.2 have very similar Ct values for the first 5 days since symptom onset. There may be a very small difference in Ct values in those with a booster from day 0 to 2, and in those who are unvaccinated on day 0, with BA.2 slightly lower. Beyond day 5 there is too little data to be conclusive if there is a difference or not. Overall, there is no evidence of a substantial difference in Ct values between BA.1 and BA.2 by vaccination status. For sequenced cases, the trends look very similar to the comparison using S-gene data, and again show no evidence of a substantial difference in Ct values by vaccination status.

Figure 19. a) Median Ct value for BA.1 vs BA.2 sequenced cases by the number of days since symptom onset for selected vaccination status and b) Median Ct value for BA.1 vs BA.2 SGTP/SGTF cases by the number of days since symptom onset for selected vaccination status

(Find accessible data used in this graph in underlying data.)

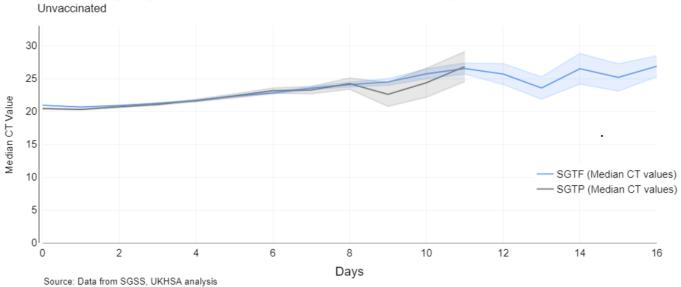


# b) Onset CT Analysis by Vaccination Status and S+ vs SGTF since 15th January 2022 1st Booster: 21+ Days



#### Onset CT Analysis by Vaccination Status and S+ vs SGTF since 15th January 2022

Latest data: 2022-03-08



# Part 3. Enhanced analyses of Omicron VOC-21NOV-01 (BA.1)

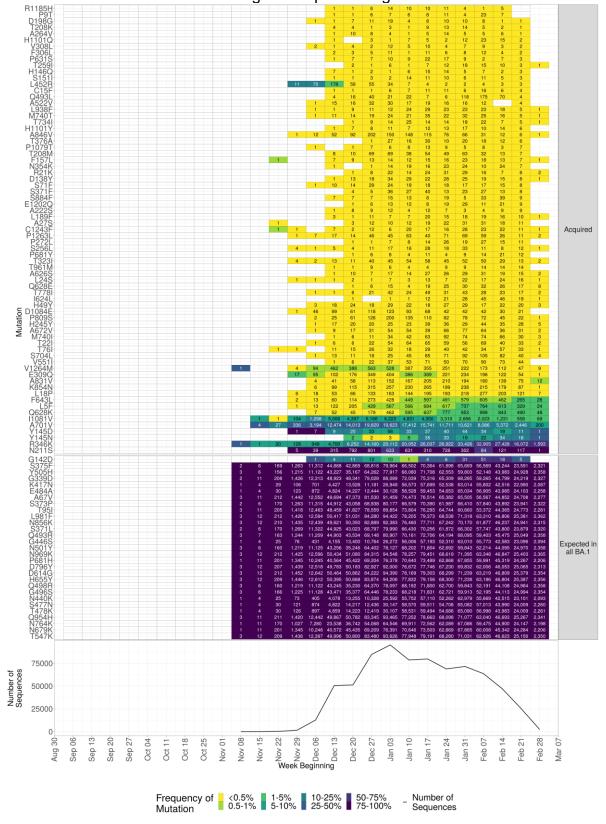
This variant was detected on GISAID on 23 November 2021 and designated B.1.1.529 on 24 November 2021. It was designated VUI-21NOV-01 by the UKHSA Variant Technical Group and on review re-designated as VOC-21NOV-01 on 27 November 2021.

# 3.1 Genomic diversity within Omicron VOC-21NOV-01 (BA.1)

Spike mutations are monitored within BA.1 using 4 criteria (Table 2). Seventy-one additional mutations have been observed in BA.1 sequences according to the criteria in Table 2 (Figure 20). The presence of Y145D/N, L452R and N211S may be artefactual. L452R may be due to low level contamination with Delta sequence. The mutations at position 211 and 145 are an alignment artefact caused by the deletions at these positions in Spike. These deletions also reduce the number of sequences where the positions can be called therefore artificially increasing the proportion of sequences where these mutations are present.

Figure 20. Spike mutations found in BA.1 genomes in the UK dataset relative to the Wuhan sequence NC\_045512.2 between 8 November 2021 and 6 March 2022

Supplementary data is not available. It should be noted all mutations in the sequence alignment are reported in these plots for review purposes. Those reported here at positions 145 and 211 arise due to base deletions affecting the sequence alignment and are artefactual.



# Sources and acknowledgments

#### Data sources

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

# Repository of human and machine-readable genomic case definitions

Genomic definitions for all VOC and VUI are provided in order to facilitate standardised VOC and VUI calling across sequencing sites and bioinformatics pipelines and are the same definitions used internally at UKHSA. Definition files are provided in YAML format so are compatible with a range of computational platforms. The repository will be regularly updated. The genomic and biological profiles of VOC and VUI are also detailed on first description in prior technical briefings.

## Authors of this report

**UKHSA Genomics Cell** 

**UKHSA Outbreak Surveillance Team** 

**UKHSA Epidemiology Cell** 

**UKHSA Immunisations Team** 

**UKHSA Surveillance Team** 

**UKHSA Contact Tracing Data Team** 

UKHSA Environmental Monitoring for Health Protection Team

**UKHSA Public Health Incident Directors** 

UKHSA Data, Analytics and Surveillance

**UKHSA Public Health Science** 

Contributions from the Variant Technical Group

# Variant Technical Group members

Person	Institution		
Meera Chand (chair)	UKHSA		
Genomics and bioinformatics			
Andrew Rambaut	University of Edinburgh		
Jeffrey Barrett	Wellcome Sanger Institute		
Matt Holden	Public Health Scotland		
Nicholas Loman	UKHSA/University of Birmingham		
Richard Myers	UKHSA		
Virology and Immunology			
Bassam Hallis	UKHSA		
Gavin Screaton	University of Oxford		
Kevin Brown	UKHSA		
Lance Turtle	University of Liverpool		
Maria Zambon	UKHSA		
Paul Kellam	Imperial College London		
Ravi Gupta	University of Cambridge		
Susanna Dunachie	University of Oxford		
Tim Wyatt	Northern Ireland Public Health Agency		
Thushan da Silva	University of Sheffield		
Wendy Barclay	Imperial College London		
Emma Thomson	University of Glasgow/London School of Hygiene and Tropical Medicine		
Epidemiology and modelling			
Anna Seale	UKHSA/University of Warwick		
Charlotte Anderson	UKHSA		
Chris Williams	Public Health Wales		
Daniela de Angelis	University of Cambridge		
Erik Volz	Imperial College London		
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		

Person	Institution
Neil Ferguson	Imperial College London
Richard Elson	UKHSA
Simon Thelwall	UKHSA
Susan Hopkins	UKHSA
Thomas Finnie	UKHSA
Thomas Ward	UKHSA
International epidemiology	
Chris Lewis	Foreign, Commonwealth and Development Office
Katherine Russell	UKHSA
Leena Inamdar	UKHSA

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