

SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 37

25 February 2022

This report provides an update on previous briefings up to 11 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 21 February 2022 to allow time for analyses.

Signals from horizon scanning

A putative Delta and Omicron recombinant has been identified in the UK, with likely parental lineages AY.4.2.2 and BA.1.1 and a breakpoint in non-structural protein 3 (nsp3). The presence of 34 genomes sampled between 7 January 2022 and 14 February 2022 suggest that this recombinant is able to transmit.

VUI-22JAN-01 (BA.2)

BA.2 does not usually contain 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 97.2% 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 20 February 2022 is 52.3% compared to 18.7% on 6 February 2022. There is geographical variation with the highest proportion of SGTP in London (63%) and the lowest in the North East region (33%). The proportion of BA.2 in sequenced data in the 7 days starting 13 February was 30.5%. 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. The growth rate estimated with data up to 21 February 2022 is 0.83 per week, compared to 1.03 using data up until 7 February 2022. Growth rates can be overestimates early in the emergence of a variant, and the growth advantage remains substantial.

Hospitalisation

Preliminary analysis finds no evidence of a greater risk of hospitalisation following infection with BA.2 compared to BA.1. These are early estimates which may change as data accrue.

Vaccine effectiveness

A test negative case control analysis continues to indicate no evidence of reduced vaccine effectiveness against symptomatic disease with BA.2 compared to BA.1. Two weeks after a booster dose vaccine effectiveness against symptomatic disease with the BA.2 variant was

67%. Further details of the BA.2 vaccine effectiveness analyses are available in the <u>weekly</u> <u>vaccine surveillance report.</u>

Reports from Variant Technical Group Members

Oxford University reported that in laboratory assessment, ACE2 binding was increased for the BA.2 receptor binding domain compared to the BA.1 receptor binding domain.

Imperial College London reported that in preliminary experiments hamsters infected with BA.2 showed mild disease, similar to those infected with BA.1. Hamsters previously infected with BA.1 were reinfected upon exposure by co-housing to Delta-infected animals but were not reinfected upon exposure to BA.2 infected animals.

Citations will be provided once available.

Updated risk assessment

An updated risk assessment for VUI-22JAN-01 (BA.2) has been published.

Omicron (B.1.1.529/ BA.1)

Severe Acute Respiratory Infection Watch surveillance system

Amongst patients admitted to an intensive care unit or high dependency unit (ICU/HDU) with SARS-CoV-2 and with a valid sequencing result, the proportion of cases which were Omicron increased from 12% in the week commencing 15 December 2021 to 100% in the week commencing 16 February 2022, although the overall number of critical care admissions has continued to decline. Using available data on sequenced cases linked to hospitalisation data, the risk of ICU/HDU admission from lower levels of care is significantly lower for Omicron than Delta cases.

Feedback survey

Take our short user <u>feedback survey</u>. Your feedback will help us decide which features to build and what improvements could be made.

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 polymerase chain reaction (PCR) test, including the categorisation of sequenced and genotyped variant results and a rules-based decision algorithm (RBDA) to identify variant and mutation (VAM) 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. (Find accessible data used in this graph in <u>underlying data</u>.)





1.2 Variant prevalence

The prevalence of different variants amongst sequenced episodes is presented in Figure 2. Of the sequenced episodes between 13 and 20 February 2022, 69.2% were Omicron BA.1 (VOC-21NOV-01), 30.5% 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 Cycle threshold (Ct) values <=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 37% in London to 67% in the North East (Figure 4).

Figure 2. Variant prevalence of available sequenced cases for England from 1 February 2021 as of 22 February 2022 (Find accessible data used in this graph in <u>underlying data</u>.)



Figure 3. Number of COVID-19 cases with SGTP/SGTF by day, among those tested in TaqPath labs as of 22 February 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 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 22

February 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>.)



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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 5. Prevalence of Pangolin lineages in UK with sequence data from 1 April 2021 to 22 February 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'. (Find accessible data used in this graph in <u>underlying data</u>)



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 31.</u>

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, S-gene target failure 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), although recently a small number of VUI-22JAN-01 (BA.2) sequences containing the deletion have been identified. As of 16 February 2022, there was a total of 20 VUI-22JAN-01 (BA.2) sequences in the UK genome data with the deletion detected, out of a total of 27,179 VUI-22JAN-01 (BA.2) sequences. This represents 0.07% of the VUI-22JAN-01 (BA.2) sequences. Eighteen of the sequences were from England. A graph showing the specimen dates of the sequences with 69/70 deletions increases as the total number of sequences available increases. There are no clear epidemiological links between these sequences, which are from 7 different regions of England. When analysed phylogenetically, these comprise one 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 6. Daily count of VUI-22JAN-01 containing S-gene 69/70 deletion, alongside the number of COG-UK VUI-22-JAN-01 sequences

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



Epidemiology of SGTP

The Omicron sub-lineage VUI-22JAN-01 (BA.2) rarely contains the spike deletion and therefore is S-gene target positive (SGTP). VUI-22JAN-01 (BA.2) has accounted for more than 95% of sequenced SGTP since 27 January 2022.

Figure 7. Number and distribution of variants per week among sequenced SGTP specimens as of 22 February 2022 Find accessible data used in this graph in <u>underlying data</u>)

Specimen dates between 2021-11-01 and 2022-02-15. Data as of 2022-02-22.

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 22 February 2022, 31,904 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 1. Number of confirmed VUI-22JAN-01 (BA.2) cases, by region of residence as of 22 February 2022

Region	Total case number	Case proportion
East Midlands	2,931	9.2%
East of England	4,488	14.1%
London	7,527	23.6%
North East	569	1.8%
North West	2,282	7.2%
South East	6,660	20.9%
South West	3,340	10.5%
West Midlands	2,194	6.9%
Yorkshire and Humber	1,554	4.9%
Unknown region	359	1.1%
Total	31,904	-

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



Figure 9. Age-sex pyramid of VUI-22JAN-01 (BA.2) cases as of 22 February 2022

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



120 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. Sample inclusion criteria are: 1) a non-traveller as determined by matching each case against passenger locator forms and managed quarantine service test codes, and 2) collected from Pillar 2 testing. 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 16 February 2022 were included. The estimated and empirical proportion of genomes from the BA.2 lineage are shown in Figure 10. The median growth rate is +82.7% 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 11. Current logistic growth rates range from 54% to 100% per week.

Figure 10. Sample frequency of VUI-22JAN-01 (BA.2) relative to other Omicron over time Supplementary data is not available for this figure.



Figure 11. Sample frequency of VUI-22JAN-01 (BA.2) relative to other Omicron over time in regions of England sampled through Pillar 2 testing (Supplementary data is not available for this figure)



2.4 Secondary attack rates

This section is based on analysis from sequence confirmed cases with test dates from 1 January to 31 January 2022. Secondary attack rates are based on positive tests amongst contacts named to NHS Test and Trace by an original case identified with sequence confirmed VUI-22JAN-01 (BA.2) or other sequence confirmed Omicron, with date of symptom onset or positive test of the secondary case occurring 2 to 14 days after original exposure. These data will no longer be available after the reduction in community testing and routine contact tracing.

Only close contacts named by the original case to NHS Test and Trace are included, that is, household members, face-to-face contacts, 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 2 shows adjusted secondary attack rates for sequence confirmed cases of Omicron VOC-21NOV-01 (BA.1) and VUI-22JAN-01 (BA.2), split by the setting of the contact. Separate models were used for household and non-household settings, adjusting for 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 nonhousehold settings were higher amongst contacts of cases with VUI-22JAN-01 (BA.2) than VOC-21NOV-01 (BA.1) (Table 2).

Table 2. Secondary attack rates for contacts of cases with confirmed sequenced Omicron VOC-21NOV-01 and VUI-22JAN-01 (BA.2)

Variant	Setting	Number of exposing cases	Number of contacts	Adjusted* secondary attack rate (95% Confidence Interval)
Omicron VOC- 21NOV-01	Household	128,207	268,952	11.4% (11.2%-11.5%)
VUI-22JAN-01 (BA.2)	Household	5,520	12,121	14.3% (13.6%-14.9%)
Omicron VOC- 21NOV-01	Non- household	21,031	50,658	4.6% (4.5%-4.8%)
VUI-22JAN-01 (BA.2)	Non- household	852	2,081	6.1% (5.0%-7.2%)

(Case test dates 1 to 31 January 2022, variant data and contact tracing data as of 21 February 2022)

*Adjusted for 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.

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 higher following a BA.2 infection than following a BA.1 infection (hazard ratio 0.87, 95% CI: 0.75-1.00).

Although the central estimate indicates that the risk of severe outcomes for BA.2 may be lower than for BA.1, the variability of the data, as reflected by the confidence intervals, mean that it is not possible to conclude this with certainty. These results are preliminary, and it is possible that the estimates of the risk of hospitalisation may change as cases accrue.

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 1). A mutation is investigated further if it meets more than one of these criteria and is present in at least 10 sequences. Fifty 3 additional mutations have been observed in BA.1 sequences according to the criteria in Table 2 (Figure 6). The presence of Y145D/N, L452R and N211S may be artefactual. L452R may be due to low level contamination with Delta sequence. The mutation N211S is an alignment artifact caused by the deletion at this position in Spike. The deletion is also the reason that N211S appears to be such a high proportion, despite being a low number of total sequences, as the amino acid at position 211 cannot be called in most Omicron genomes therefore reducing the total number of sequences used to calculate the proportion.

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%

Table 1. Criteria used to assess emerging mutations





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 not true, acquired mutations and are artefactual.

3.2 Severity and hospitalisation

Cases, hospitalisation, attendance and deaths by vaccination status are now presented in the <u>COVID-19 vaccine surveillance report</u>.

Severe Acute Respiratory Infection Watch surveillance system – Intensive Care Unit/High Dependency Unit admissions

UKHSA's Severe Acute Respiratory Infection (SARI)-Watch surveillance monitors hospitalisations and ICU/HDU admissions with laboratory confirmed SARS-CoV-2 in acute NHS Trusts in England. Patient level data on ICU/HDU admissions, linked to variants and mutations (VAM), is reported from 46 trusts (around one third of trusts). The weekly proportion of Delta versus Omicron ICU/HDU admissions from 24 November 2021 to 21 February 2022 are shown in Figure 13. A linkable sample was available for 23% of critical care admissions in this time period. Overall, 70% of admissions in this subset of VAM-linked critical care patients had Delta infection. However, towards the end of December 2021, Omicron infection was detected and became the dominant strain amongst ICU/HDU admissions from early January 2022, although the overall numbers of critical care admissions decreased. From cases where there was a valid sequencing result, those admitted to ICU that were Omicron increased from 12% in the week commencing 15 December 2021 to 100% in the week commencing 16 February 2022. Individuals admitted to ICU/HDU are often late in their course of infection and therefore lower yields from sequencing are expected.

The adjusted odds of admission to ICU/HDU from lower level of care was 59% lower among admitted patients with confirmed Omicron compared to confirmed Delta (Table 3). This result was found to be statistically significant. The result has also moved away from the null effect since the last report most likely due to higher volumes of sequenced cases in the latest update.

Further SARI-Watch data is also presented in the weekly combined <u>flu and COVID-19</u> <u>surveillance report.</u>





Notes to chart:

1. To ensure sequence-confirmed cases were closely related to the admission, only those with test 28 days before admission and 1 day post admission are included in the variant analysis

2. Delta was defined by VOC-21APR-02 or VUI-21OCT-01 from VAM list, or SGTF status (No) prior to 27 November if variant data unavailable in variant and mutations (VAM) list.

3. Omicron was defined by VOC-21NOV-01 (BA.1) or VUI-22JAN-01 (BA.2) in VAM list, or SGTF status (Yes)

4. Most unlinked records (924 of 985) did not have sequence data in VAM (coded as NULL). A small minority of unlinked records had sequence confirmation but were outside the testing window – see point 1

Table 3. Odds of ICU-HDU admission among hospitalised Omicron cases versus Delta cases, acute NHS trusts, England, data from 24 November 2021 to 20 February 2022

	Odds of admission to ICU/HDU OR= Odds Ratio CI= Confidence Interval									
	Number admitted to ICU/HDU	Total hospitalisations	Unadjusted OR	95%	% CI	P>z	Adjusted OR [†]	95%	o CI	P>z
Delta*	33	377	1.00				1.00			
Omicron*	17	610	0.30	0.16	0.54	<0.000	0.41	0.19	0.86	0.019

* sequenced linked cases/SGTF status if sequence data not available

+ adjusting for: age (<40y, 40 to 49, 50 to 64, \geq 65y), sex, vaccination status on admission (unvaccinated, D1 only, 2 Doses only, 3D+), levels of comorbidity (none reported, 1, 2 or \geq 3 conditions), ethnicity and hospital random effects

Part 4. Signals from horizon scanning

Putative recombinant of AY.4.2.2 and BA.1.1

On 14 February 2022, 34 similar UK sequences (linked to 32 cases) containing both Delta and Omicron-like mutations were detected. Analysis of these via 3SEQ (Lam HM and others, 2018) suggests a putative recombinant with parental lineages of AY.4.2.2 and BA.1.1, and a breakpoint in nsp3. Analysis of raw next generation sequencing data was performed to exclude contamination and coinfection, with no significant heterogeneous mix of bases noted. Specimen dates for the 32 cases are available (Figure 14) and are suggestive of successful transmission, although with small overall case numbers.

Figure 14. Daily count of recombinant (AY.4.2.2 and BA.1.1) cases

(Find accessible data used in this graph in <u>underlying data</u>)



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, the UKHSA Case and Incident Management System and the Severe Acute Respiratory Infection Watch surveillance.

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.

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About the UK Health Security Agency

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