

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

# Technical briefing 36

11 February 2022

This report provides an update on previous briefings up to 28 January 2022

# **Contents**

Summary	3
Published information on variants	5
Part 1. Surveillance overview	
1.1 VOC and VUI overview	
1.2 Variant prevalence	7
Part 2. Enhanced analysis of VUI-22JAN-01 (BA.2)	12
2.1 Genomic diversity	12
2.2 Epidemiology	14
2.3 International epidemiology	17
2.4 Epidemiology of SGTP	18
2.5 Growth rates	19
2.6 Serial Intervals	21
2.7 Reinfections	23
Part 3. Enhanced analyses of Omicron VOC-21NOV-01 (B.1.1.529)	26
3.1 Severity and hospitalisation	
Sources and acknowledgments	30
Data sources	30
Repository of human and machine-readable genomic case definitions	30
Acknowledgements	32
About the UK Health Security Agency	33

## **Summary**

This report has been published to share the detailed variant surveillance analyses which contribute to the variant risk assessments and designation of new variants of concern (VOC) and variants under investigation (VUI). 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 February 2022 to allow time for analyses. In summary:

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

As of 7 February 2022, 7,194 genomically confirmed cases of BA.2 have been identified in England. Sequencing data is complete up to 31 January, at which point 95.4% of sequences were BA.1, 4.1% were BA.2 and 0.5% were other lineages. BA.2 does not contain the spike gene deletion at position 69-70 and is S-gene target positive (SGTP) on polymerase chain reaction (PCR) diagnostic assays with targets in this area. SGTP is now a reasonable proxy for BA.2, accounting for 97% of sequenced SGTP cases with an increasing trend. The proportion of SGTP cases is now increasing. As of 6 February 2022, the overall proportion of SGTP cases in England is 18.7% compared to 5.1% on 24 January. There is geographical variation with the highest proportion in London (31%) and the lowest in the North-East region (3.9%).

#### Growth rate

BA.2 has an increased growth rate compared to BA.1 in all regions of England. Whilst growth rates can be overestimates early in the emergence of a variant, the apparent growth advantage is currently substantial.

#### Reinfections

Although a limited proportion of samples are sequenced, there is no detected sequence-confirmed BA.2 reinfection following a BA.1 infection at any interval to date in England.

#### Serial interval

Preliminary analysis from contact tracing data suggests that the average time from symptom onset of a primary case to symptom onset in their identified contacts (the mean serial interval) is around half a day shorter for BA.2 than BA.1, with a mean serial interval of 3.27 days compared to 3.72 days for BA.1. Both are shorter than the mean serial interval for Delta of 4.09 days. The serial interval suggests the time between primary and secondary infections is shorter, which could contribute to the increased growth rate of BA.2.

#### Neutralisation data and vaccine effectiveness

Oxford University reports neutralisation studies using monoclonal antibodies and some preliminary studies using sera suggest a small antigenic difference between BA.1 and BA.2, which is expected from the mutation profile. However, sera from individuals with recent booster

vaccinations neutralise both variants similarly. Neutralisation studies use recent vaccinee sera and it is unclear whether the difference between variants will increase as the responses wane. There is no detected change in vaccine effectiveness against symptomatic infection in England though international data are noted in the COVID-19 vaccine surveillance report.

#### Updated risk assessment

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

#### Omicron (B.1.1.529/ BA.1)

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

Since 29 December, among Intensive Care Unit/High Dependency Unit (ICU/HDU) cases linked to variant and mutations, Omicron (B.1.1.529/BA.1) has become the dominant strain, but weekly numbers of admissions are much lower than previous weeks. Small numbers overall preclude an accurate comparison of risk of ICU admission between variants at present.

#### 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>.

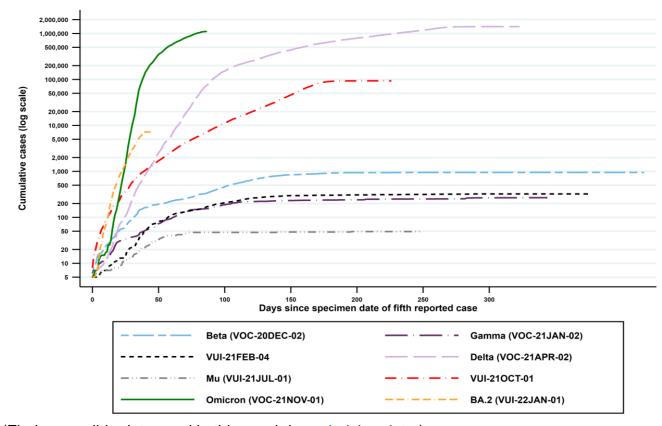
<u>Technical briefings</u> are published periodically. From technical briefing 15, briefings include variant diagnoses identified by whole-genome sequencing and a genotyping polymerase chain reaction (PCR) test, including the categorisation of sequenced and genotyped variant results and a rules-based 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.

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



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

### 1.2 Variant prevalence

The prevalence of different variants amongst sequenced cases is presented in <u>Figure 2</u>.

The 'Other' category in <u>Figure 2</u> 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), 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 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 69% in London to 96% in the North East (Figure 4).

Figure 2. Variant prevalence of available sequenced cases for England from 1 February 2021 as of 7 February 2022 (Find accessible data used in this graph in <u>underlying data</u>.)

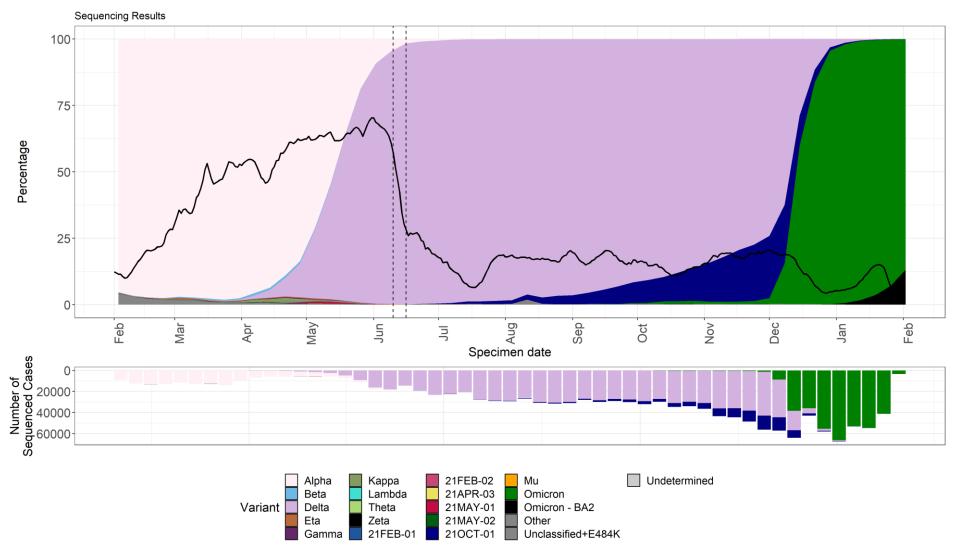
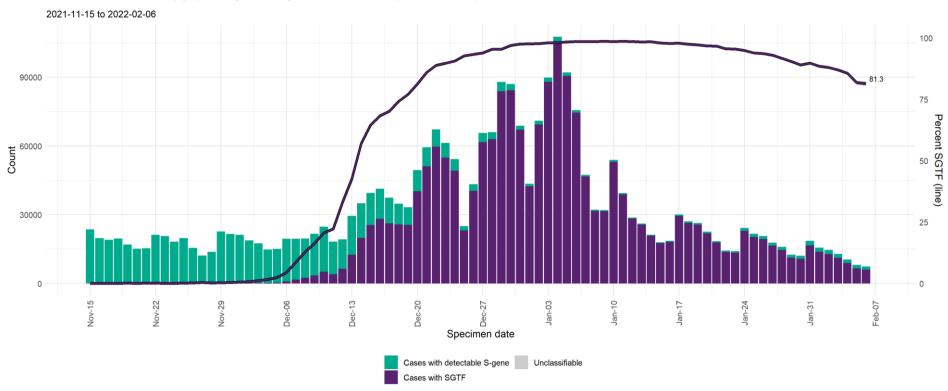


Figure 3. Number of COVID-19 cases with SGTP/SGTF by day, among those tested in TaqPath labs as of 8 February 2022 (Find accessible data used in this graph in <u>underlying data</u>.)

95% confidence intervals indicated by gray shading. Percentages for most recent 7 days shown. Data updated on 2022-02-08



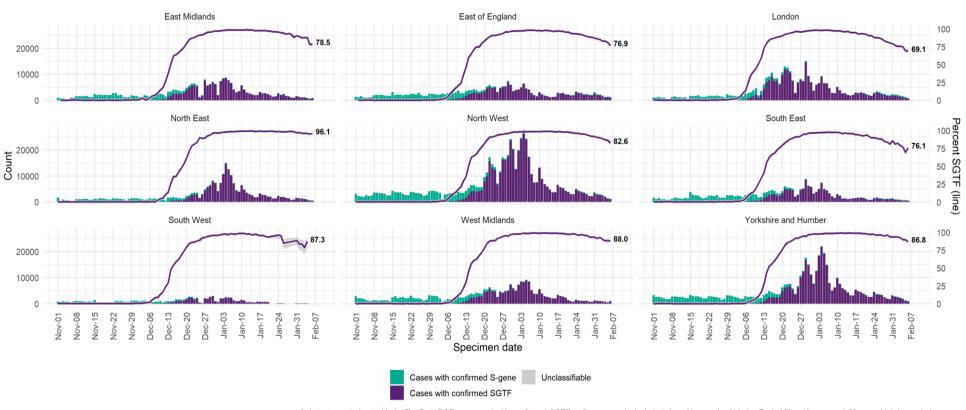
Only tests carried out with the TaqPath PCR assay and with confirmed SGTF or S gene results included, from Newcastle, Alderley Park, Milton Keynes and Glasgow Lighthouse Labs.

SGTF refers to non-detectable S gene and <=30 CT values for N and ORF1ab genes. Detectable S-gene refers to <=30 CT values for S, N, and ORF1ab genes.

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 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>.)

95% confidence intervals indicated by gray shading. Percentage for most recent day shown. 2021-11-01 to 2022-02-06. Data updated on 2022-02-08



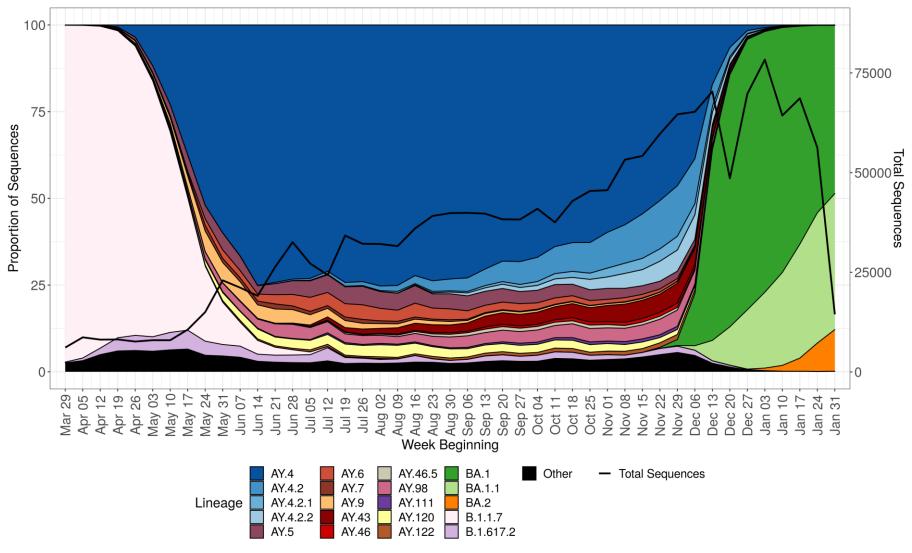
Only tests carried out with the TaqPath PCR assay and with confirmed SGTF or S gene results included, from Newcastle, Alderley Park, Milton Keynes and Glasgow Lighthouse Labs.

SGTF refers to non-detectable S gene and <=30 CT values for N and ORF1ab genes. Detectable S-gene refers to <=30 CT values for S, N, and ORF1ab genes.

Produced by Outbreak Surveillance Team, UKHSA.

Figure 5. Prevalence of Pangolin lineages in UK with sequence data from 1 April 2021 to 6 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)

An increase in the number of sequences of the Omicron sub-lineage BA.2 was noted from both the United Kingdom (UK) and Denmark in the week starting 3 January 2022. The spike profile of BA.2 contains 28 mutations and a deletion at 25-27. The comparison 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.

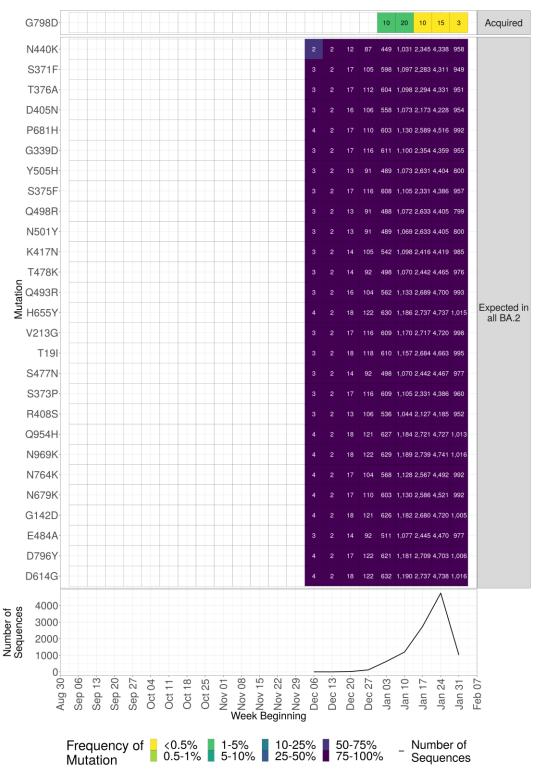
## 2.1 Genomic diversity

Spike mutations are monitored within BA.2 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. One mutation has been observed in BA.2 sequences that meet the required thresholds (Figure 6).

Table 1. Criteria used to assess emerging mutations

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

Figure 6. Proportion of sequences containing a given mutation within UK BA.2 sequences that meet more than one criterion and are present in at least 10 sequences Data shown is sequence data from 6 September 2021 to 6 February 2022.



Supplementary data is not available for this figure. The proportion of sequences is indicated by the colour and the number of genomes is shown within the tile. Proportion is calculated based on the total number of sequences where the amino acid can be called. Mutations expected to be in all BA.2 genomes are shown separately to those considered to have been acquired since initial emergence of the lineage. The total number of sequences per week is shown by the black line in the lower plot.

# 2.2 Epidemiology

As of 7 February 2022, 7,194 sequences of VUI-22JAN-01 (BA.2) have been identified in the UK. VUI-22JAN-01 (BA.2) accounts for an increasing proportion of SGTP tests. Caution is required when interpreting comparative analyses which use S-gene target results as the only determinant of Omicron and Delta. As VUI-22JAN-01 (BA.2) is designated by sequencing results 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 2. Number of confirmed VUI-22JAN-01 (BA.2) cases, by region of residence as of 7 February 2022

Region	Confirmed case number	Total case number	Case proportion
East Midlands	504	504	7.0%
East of England	836	836	11.6%
London	1,958	1,958	27.2%
North East	96	96	1.3%
North West	511	511	7.1%
South East	1,773	1,773	24.6%
South West	665	665	9.2%
West Midlands	350	350	4.9%
Yorkshire and Humber	340	340	4.7%
Unknown region	161	161	2.2%
Total	7,194	7,194	-

Figure 7. Confirmed VUI-22JAN-01 (BA.2) cases by specimen date and region of residence as of 7 February 2022 (Find accessible data used in this graph in <u>underlying data</u>.)

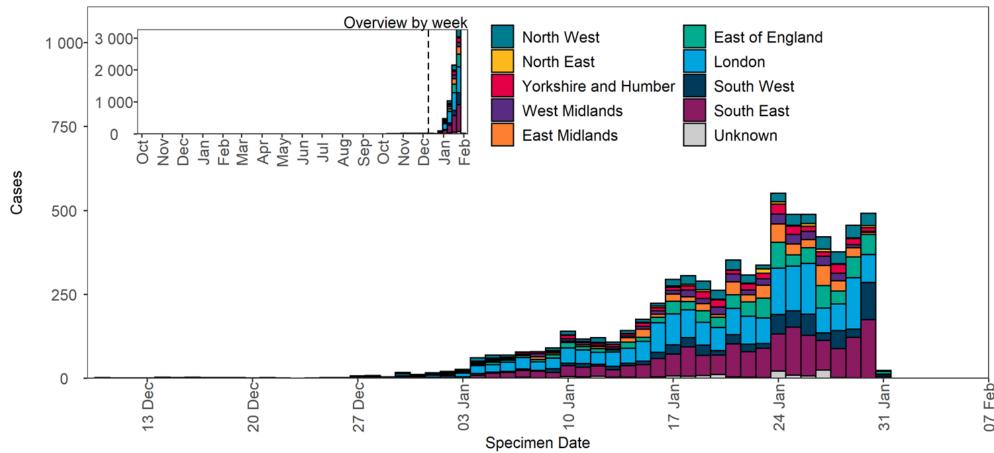
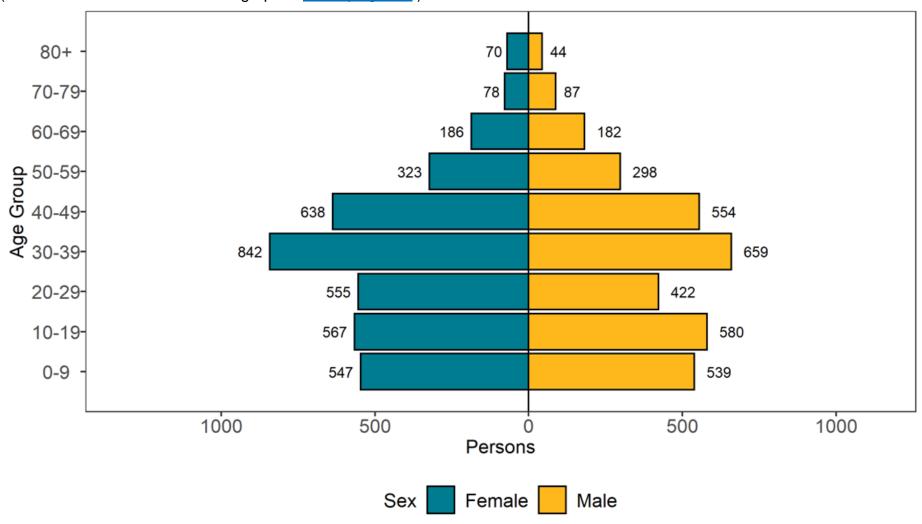


Figure 8. Age-sex pyramid of VUI-22JAN-01 (BA.2) cases as of 7 February 2022 (Find accessible data used in this graph in <u>underlying data</u>.)

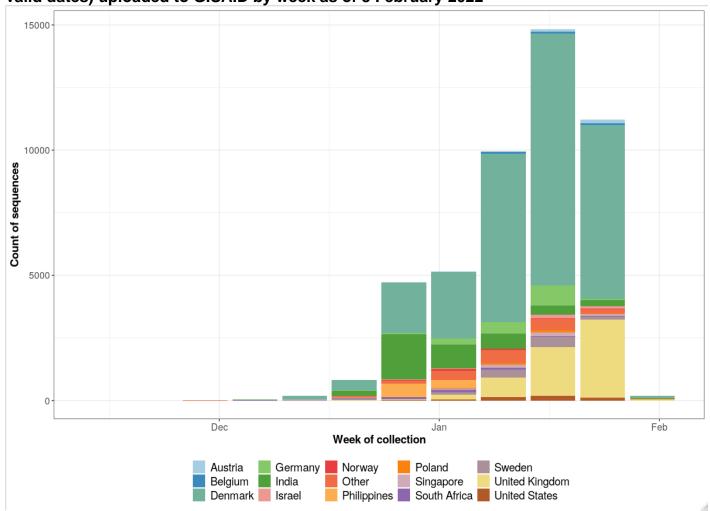


22 cases excluded where sex or age not reported

## 2.3 International epidemiology

As of 8 February 2022, 48,622 sequences on GISAID meet the VUI-22JAN-01 (BA.2) Pangolin definition from 67 countries including the UK. Figure 9 shows an increasing number of VUI-22JAN-01 (BA.2) sequences in recent weeks, many from Denmark. The most recent week will be affected by data lags.

Figure 9. Count of VUI-22JAN-01 (BA.2) classified sequences by week of collection (with valid dates) uploaded to GISAID by week as of 8 February 2022



Countries with 200 or fewer sequences have been grouped together as 'Other'. Of the submitted sequences, 47,157 had valid collection dates. (Find accessible data used in this graph in <u>underlying data</u>.)

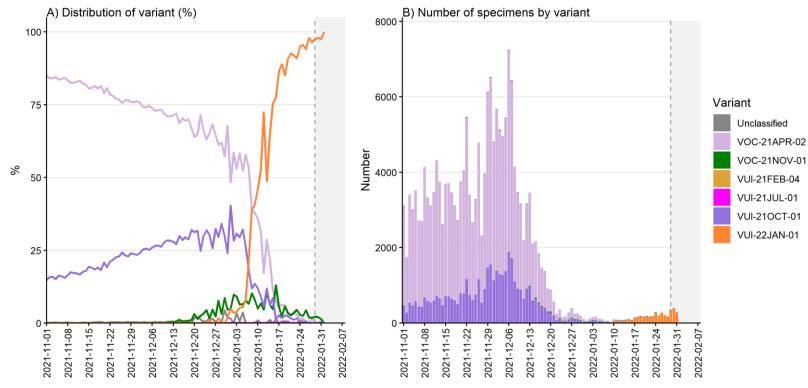
### 2.4 Epidemiology of SGTP

The Omicron sub-lineage VUI-22JAN-01 (BA.2) does not contain the spike deletion and therefore is S-gene target positive (SGTP). By 31 January 2022, VUI-22JAN-01 (BA.2) accounted for 97% of sequenced SGTP and this proportion is increasing, however, overall numbers remain low. Therefore, SGTF is no longer sufficient to assess the spread of Omicron as a whole.

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

Specimen dates between 2021-11-01 and 2022-02-01. Data as of 2022-02-08.

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.

#### 2.5 Growth rates

The growth rate is estimated by logistic regression of the number of genomes sampled with the BA.1 and VUI-22JAN-01 (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, VUI-22JAN-01 (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 VUI-22JAN-01 (BA.2).

Data sampled between 1 December 2021 and 1 February 2022 were included. The estimated and empirical proportion of genomes from the VUI-22JAN-01 (BA.2) lineage are shown in Figure 11. The median growth rate is +106% per week. The analysis was repeated on data from each region of England (all had at least 90 BA.2 genomes) and is shown in Figure 12. Current logistic growth rates range from 51% to 116% per week.

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

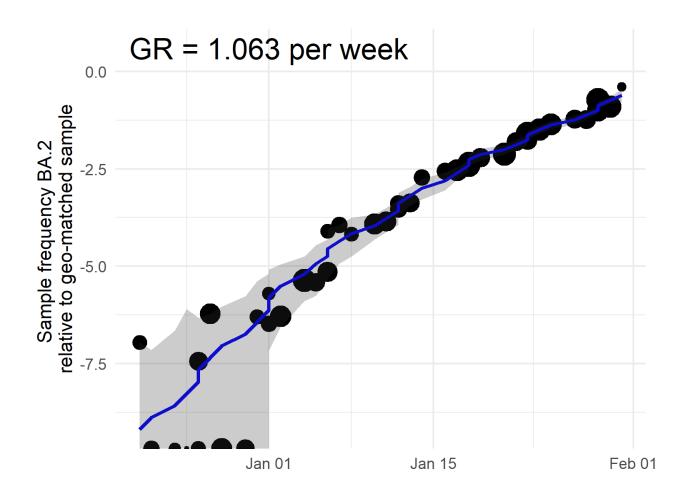
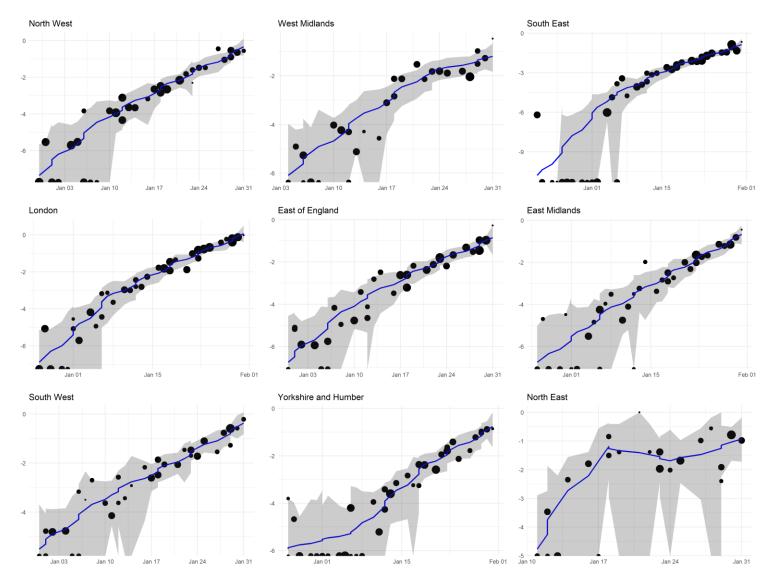


Figure 12. Sample frequency of VUI-22JAN-01 (BA.2) relative to other Omicron over time in regions of England sampled through Pillar 2 testing

Supplementary data is not available for this figure.



#### 2.6 Serial intervals

Contact tracing data for non-household contacts was classified as SGTP or SGTF by linking contact tracing records to PCR testing data. Restricting records to only include exposer-exposee pairs where the exposee specimen date occurred after 10 January 2022, SGTP can be assumed to be BA.2 and SGTF can be assumed to be BA.1. Restricting data to this time period reduces the impact of the change to testing policy introduced on 6 January 2022. The mean serial interval for BA.2 is around half a day shorter than BA.1 in the contact-tracing data, 3.27 days (95% confidence interval (CI): 3.09, 3.46) for BA.2 compared to 3.72 (95% CI: 3.62, 3.80) for BA.1. Similarly, BA.2 has a shorter median serial interval than BA.1, 2.68 days (95% CI: 2.50, 2.87) for BA.2 compared to 3.27 days (95% CI: 3.17, 3.36) for BA.1. Both variants have similar tail densities in their serial interval distributions. For BA.2, 95% of serial intervals are expected to occur between 7.56 and 8.40 days after primary symptom onset. For BA.1, this occurs between 8.21 and 8.57 days after primary symptom onset. These are based on 368 BA.2 observations and 1,473 BA.1 observations. Figures 13 and 14 show the density functions and cumulative density functions, respectively.

This analysis only considers non-household contacts, so will be longer than serial intervals including household contacts. These serial intervals are overestimated due to the nature of the contact tracing data, which does not detect negative serial intervals. The model is only fit using serial intervals between 1 and 12 days in duration. This is due to the values outside of this range being potentially unreliable. The fast-changing dynamics, with high community incidence, may affect the serial interval distributions.

Figure 13. Fitted serial interval distributions, density function

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

BA.2 and BA.1 serial interval distributions

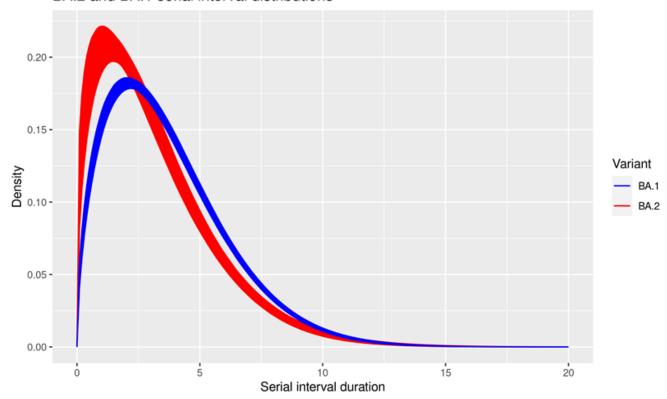
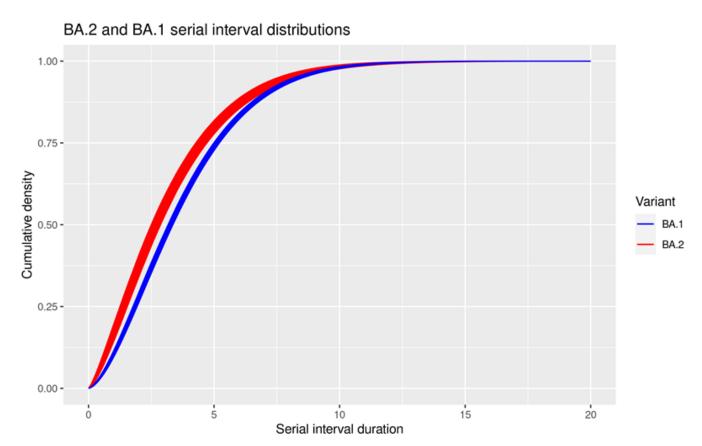


Figure 14. Fitted serial interval distributions, cumulative density function (Find accessible data used in this graph in <u>underlying data</u>.)



#### 2.7 Reinfections

All of 307,754 sequenced BA.1 and BA.2 specimens dated between 1 November 2021 and 29 January 2022 with person-based details available in England were linked to all positive SARS-CoV-2 test results (based on Lateral Flow Devices and PCR) since the beginning of the pandemic. Cases with more than one episode of infection (at any interval) as of 29 January 2022 were identified.

Possible reinfection is defined as an interval between 2 sequential positive SARS-CoV-2 test results of more than or equal to 90 days. Of 3,581 individuals with BA.2 sequencing, 274 (7.7%) cases of possible reinfection were identified. These had an interval between infection episodes of 91 to 664 days with a median interval of 358 days. Details on overall reinfections are being published weekly in the <a href="UKHSA National flu and COVID-19 surveillance reports">UKHSA National flu and COVID-19 surveillance reports</a> for episodes arising through January. Provisional data for week 2022-03 (to 23 January 2022) identified 61,200 reinfections accounting for 9.6% of all first or reinfection episodes that week.

Infections at any interval prior to the BA.2 infection identified 28 (0.8%) at an interval of 28 to 59 days and 41 (1.2%) at 60 to 89 days. Information on the timing of first infection was indicative of a first infection with Delta for 14 cases. A further 37 had S-gene target data available and were SGTP at the earlier infection occurring on or after 1 November 2021 with low cycle threshold values, consistent with an earlier infection with Delta. Where information was available in 51 of 69 cases, none were consistent with a BA.1 followed by BA.2 infection.

The overall age distribution of possible reinfections tends to closely follow those of first infections as reinfections are driven by the force of infection within the population (See Figure 15 for Omicron BA.1). The age distribution of episodes of reinfection with BA.2 are shown in Figure Y, alongside first episodes of BA.2 infection.

Whilst the percentage of sequenced cases is currently low (less than 10% across all age groups), this analysis, in line with the population-based data on reinfections, is consistent with what we would expect based on Omicron BA.1 and population-based reinfection data.

Figure 15. The age profile of first episodes of infection (90+ day interval between sequential positive test results with Omicron BA.1 (1 November to 30 December 2021)

Supplementary data is not available for this figure.

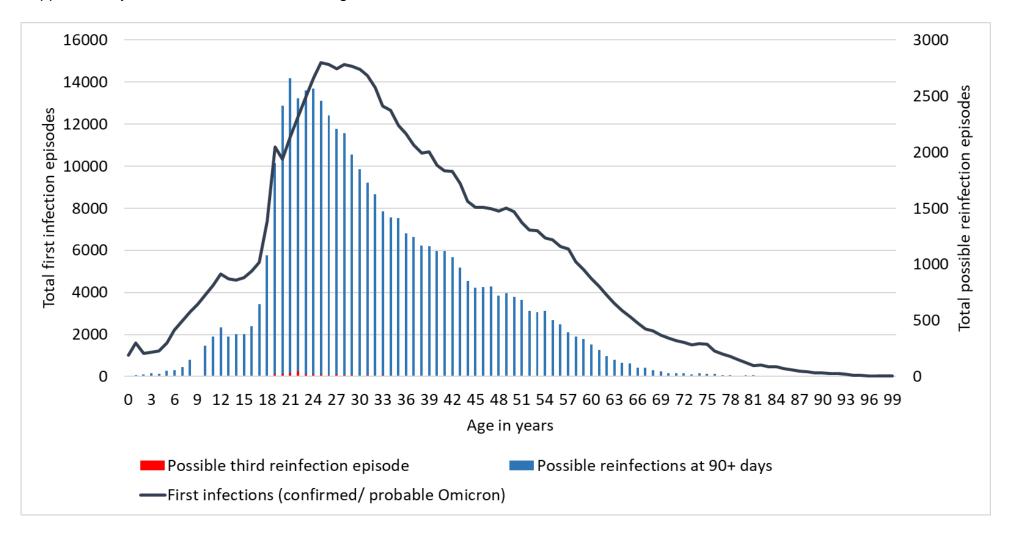
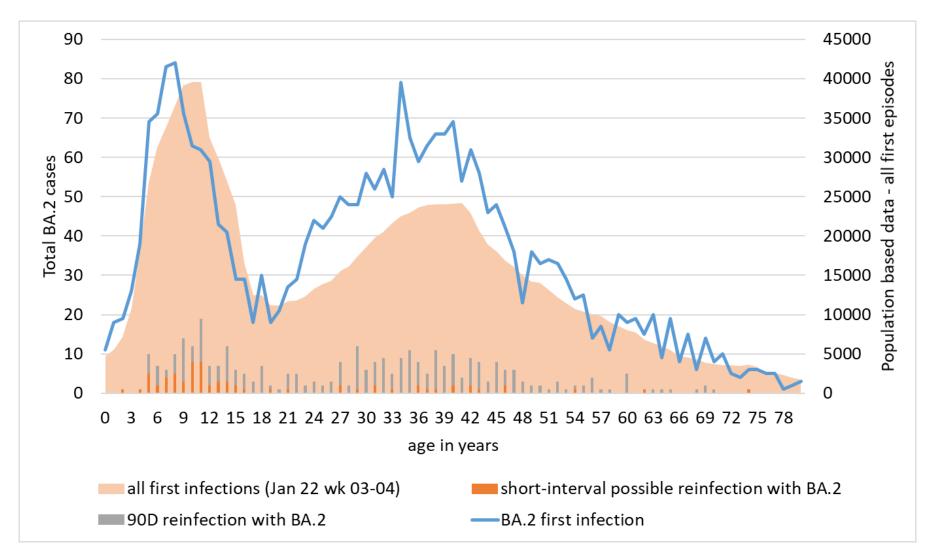


Figure 16. The age profile of first episodes of SARS-CoV-2 infection (weeks 2022-03 and -04) with Omicron BA.2 first episodes and possible reinfection episodes from 1 November 2021

Supplementary data is not available for this figure.



# Part 3. Enhanced analyses of Omicron VOC-21NOV-01 (B.1.1.529/BA.1)

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

### 3.1 Severity and hospitalisation

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

Analyses of the comparative risk of hospitalisation or death between Omicron or Delta found that after adjustment for confounding factors risk of hospital attendance among cases with Omicron was reduced compared to Delta (Hazard Ratio: 0.56, 95% CI: 0.54-0.58). The risk of death was approximately 60% lower among Omicron cases compared to Delta (Hazard Ratio: 0.31, 95% CI: 0.26-0.37). The relative risk of hospital admission varied by age, with similar risk of hospital admission among children aged under 10 years old, and approximately 75% reduction in the risk of hospital admission among those 60 to 69 years old (HR: 0.25, 95% CI: 0.21-0.30).

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

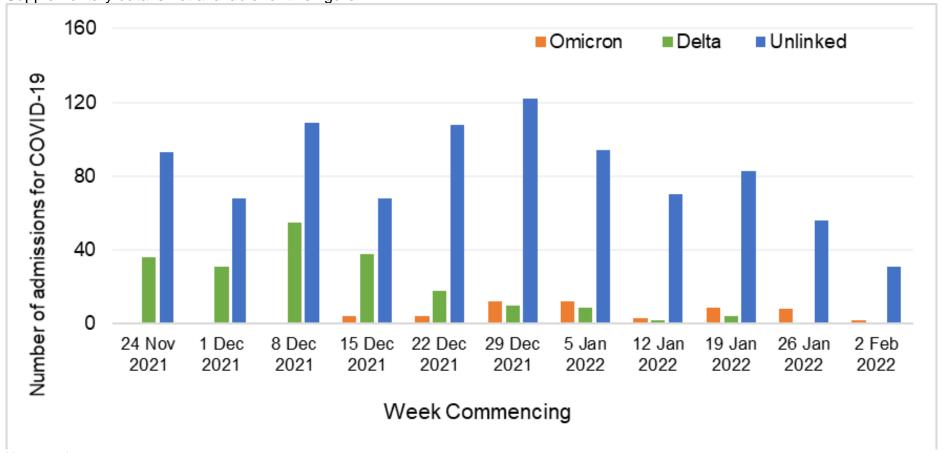
Severe Acute Respiratory Infection (SARI)-Watch monitors hospitalisations and ICU/HDU admissions with laboratory confirmed SARS-CoV-2 in acute NHS Trusts in England. Patient level data on ICU/HDU admissions, linked to variants and mutations (VAM), is reported from 45 trusts (around one third of trusts). The weekly proportion of Delta versus Omicron ICU/HDU admissions from 24 November 2021 to 7 February 2022 are shown in Figure 17. A linkable sample was available for 22% of critical care admissions in this time period. Overall, 79% 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 in 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 10% in the week commencing 15 December 2021 to 100% in the week commencing 2 February 2022. Individuals admitted to ICU/HDU are often late in their course of infection and therefore lower yields from sequencing is expected.

Adjusted odds of admission to ICU/HDU from lower level of care was 49% lower among admitted patients with confirmed Omicron compared to confirmed Delta (Table 3) but this finding was non-significant.

Figure 17. Distribution of sequence confirmed variants (or SGTF status) among ICU-HDU admission for COVID-19 in acute NHS trusts in England as of 2 February 2022

Supplementary data is not available for this figure.



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 (859 of 902) 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

Odds of admission to ICU/HDU  OR= Odds Ratio CI= Confidence Interval										
	Number admitted to ICU/HDU	Total hospitalisations	Unadjusted OR	959	% CI	P>z	Adjusted OR <sup>†</sup>	95%	S CI	P>z
Delta*	31	361	1.00				1.00			
Omicron*	13	439	0.32	0.17	0.63	0.001	0.51	0.22	1.15	0.103

<sup>\*</sup> sequenced linked cases/SGTF status if sequence data not available

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

<sup>+</sup>adjusting for: age (<40y, 40 to 49, 50 to 64, ≥65y), sex, vaccination status on admission (unvaccinated, D1 only, 2 Doses only, 3D+), levels of comorbidity (1, 2 or ≥3 conditions), ethnicity and hospital random effects

# 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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UKHSA Severe Acute Respiratory Infection Watch

**UKHSA Contact Tracing Data Team** 

UKHSA Environmental Monitoring for Health Protection Team

**UKHSA Public Health Incident Directors** 

UKHSA Data, Analytics and Surveillance

Contributions from the Variant Technical Group

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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			
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Tim Wyatt	Northern Ireland Public Health Agency			
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Wendy Barclay	Imperial College London			
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