

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

Technical briefing 32

17 December 2021

This briefing provides an update on previous briefings up to 10 December 2021

Contents

Summary	3
Published information on variants	5
Part 1. Surveillance overview	6
1.1 Variants under surveillance	6
1.2 VOC and VUI overview	8
1.3 Variant prevalence	9
Part 2. Enhanced analysis on Omicron VOC-21NOV-01 (B.1.1.529)	14
2.1 Performance of diagnostic lateral flow devices	14
2.2 Omicron characterisation analyses	17
2.3 Interpretation of S gene target failure data	27
2.4 Epidemiology of confirmed Omicron, VOC-21NOV-01 (B.1.1.529) in England	28
2.5 Wastewater analysis	32
Sources and acknowledgments	35
Data sources	35
Repository of human and machine-readable genomic case definitions	35
Variant Technical Group	35
Acknowledgements	37
About the UK Health Security Agency	38

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 (VOCs) and variants under investigation (VUIs). This specialist technical briefing contains early data and analysis on emerging variants and findings have a high level of uncertainty.

A <u>separate report is published</u> covering surveillance data on all other VOCs and VUIs. In summary:

- there are 5 current VOCs and 7 VUIs (Table 1)
- unless stated otherwise, the technical briefing uses a data cut-off of 13 December to allow time for analyses – at the data cut off, there were 5,006 confirmed cases of Omicron VOC-21NOV-01 (B.1.1.529) (hereafter referred to as Omicron), identified through sequencing or genotyping in England; <u>S gene target failure (SGTF) data</u> are published daily and indicate that Omicron is already predominant in some regions of England, notably London
- Omicron has also been detected in 38 out of 2,437 wastewater samples collected between 26 November and 5 December 2021 from 477 sewage treatment works and sewerage network sites in England – the largest number of detections was in London, which aligns with clinical data trends
- genomes within Omicron (B.1.1.529) fall within 3 subclades. BA.1 makes up the
 majority of cases. Both BA.2 and BA.3 have been observed in South Africa and the
 United Kingdom (UK), but in very small numbers. BA.2 is does not have the deletion
 at S:69/70 (is S gene target positive) and BA.3 has the deletion (is S gene target
 negative)
- characterisation analyses on UK cases have been updated these remain preliminary estimates based on routine testing data
 - household transmission risk remains higher for Omicron than for Delta the adjusted odds ratio for household transmission from an Omicron index case was 2.9 (95%Cl 2.4-3.5, p <0.001) compared to Delta index cases
 - the secondary attack rate also remains higher for Omicron than for Delta using routine contact tracing data, the secondary attack rate in household contacts is estimated at 15.8% (95%Cl 14.3-17.5%) for confirmed Omicron cases compared to 10.3% (95%Cl 10.1-10.5%) for Delta, and in non-household contacts it is 8.7% (95%Cl 7.5-10.0%) for Omicron compared to 3.0% (95%Cl 2.8-3.2%) for Delta
 - the weekly rate of possible reinfections increased across the population in week 48 (ending 5 December) alongside increases in first infections – overall

- reinfection rates remain low but early analysis suggests the risk of reinfection with the Omicron variant may be about 3 times higher than the risk of reinfection with other variants
- new vaccine effectiveness data are currently being analysed and are not updated this week
- initial laboratory validation of lateral flow devices in use in England finds no change in performance when trialled on Omicron
- an updated <u>risk assessment</u> for Omicron VOC-21NOV-01 (B.1.1.529) has been published

All <u>risk assessments</u> are published separately online, except for Gamma, which was published within <u>Technical Briefing 7</u> and Alpha within <u>Technical Briefing 9</u>. As Delta is the dominant variant in the UK, epidemiological data in the weekly surveillance report is also relevant.

Sequencing coverage data has moved to the Variant Data Update.

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>. Data on variants not detailed here is published in the <u>Variant Data Update</u>. Variant risk assessments are available in prior technical briefings.

The UK Health Security Agency (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. The repository is accessible on <u>GitHub</u>.

World Health Organization (WHO) nomenclature from 31 May 2021 is incorporated. A table incorporating WHO and UK designations with Phylogenetic Assignment of Named Global Outbreak Lineages (Pangolin lineages) is provided below (Table 1). Following the table, variants are referred to using their WHO designation where this exists and the UK designation where it does not.

<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. Genotyping is used to identify variants Alpha, Beta, Delta, Gamma and Mu. Targets were updated in mid-May 2021 to prioritise accurate identification of Delta over Alpha.

Part 1. Surveillance overview

1.1 Variants under surveillance

Table 1 shows the current VOCs, VUIs, and variants in monitoring detected and not detected in the UK as of 14 December 2021.

Table 1a. Variants detected in the UK in the past 12 weeks

Variants of concern	Variants under Investigation	Variants in monitoring
Alpha (B.1.1.7) VOC-20DEC-01	VUI-21OCT-01 (AY.4.2)†	B.1.640
Beta (B.1.351) VOC-20DEC-02	VUI-21JUL-01 (B.1.621)	B.1.617.2 + E484K
Gamma (P.1) VOC-21JAN-02	VUI-21APR-01 (B.1.617.1)	BA.2
Delta (B.1.617.2 and sub-lineages) VOC-21APR-02		
Omicron (B.1.1.529) VOC-21NOV-01		

[†] AY.4.2 is a sub-lineage within Delta that has been assigned as a distinct VUI.

Table 1b. Variants detected in GISAID, but not in the UK, in the past 12 weeks

Variants of concern	Variants under Investigation	Variants in monitoring
	VUI-21APR-03 (B.1.617.3)	C.37*
	VUI-21JAN-01 (P.2)	B.1.526
	VUI-21FEB-04 (B.1.1.318)	B.1 with 214insQAS
	VUI-21FEB-03 (B.1.525)	B.1.629
		B.1.630, B.1.631/B.1.628
		P.1.8
		C.1.2
		B.1.1.7 + B.1.617.2 possible recombinant

D61	7 descendant (S:L5F, G75V, 14G, L452Q, E484K, P499R, 01T, H655Y, P681R)
B.1.	.427/B.1.429

^{*}Previously VUI-21JUN-01, de-escalated on 20 October 2021.

VOCs and VUIs are monitored weekly for observations within the last 12 weeks. If variants have not been detected in the UK within this period, they are moved to international status with continued monitoring. If a VOC or VUI has not been observed in the UK or international data sets within the preceding 12 weeks, it is designated as provisionally extinct, but monitoring remains in place.

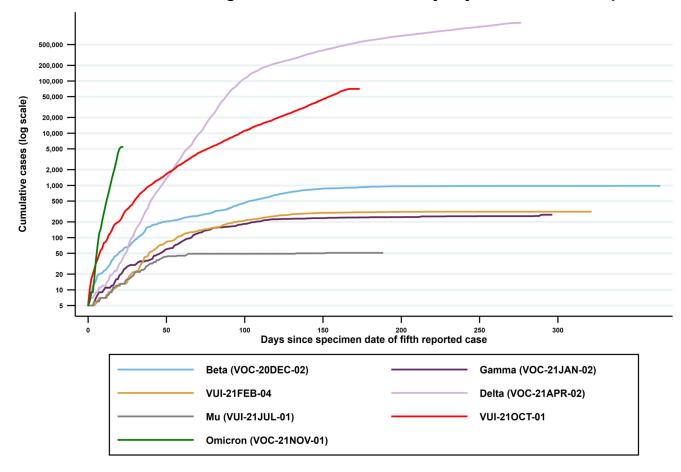
Zeta and Theta were de-escalated by WHO and are no longer WHO variants under monitoring. Kappa, lota, Eta and Epsilon were de-escalated by WHO and are now WHO variants under monitoring.

1.2 VOC and VUI overview

Summary epidemiology for each variant and case numbers 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 13 December 2021



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

1.3 Variant prevalence

The prevalence of different variants amongst genotyped cases is presented in Figure 2. The prevalence of different variants amongst sequenced cases is split by travel status in Figure 3.

Genotyping provides probable variant results with a shorter turnaround time of 12 to 24 hours after initial confirmation of coronavirus (COVID-19) by PCR. The initial panel of targets began trials in March 2021, using single nucleotide polymorphisms that included N501Y, E484K, K417N, and K417T. Results have been reported and used for public health action since 29 March 2021. On 11 May 2021, after rapid validation of targets to allow identification of Delta variant, P681R was introduced in the panel to replace N501Y. Genotyping results have now been fully integrated into the variant data reports and analyses. Changes in the use of genotyping over time should be considered when interpreting prevalence from genotyped data.

The 'Other' category in Figures 2 and 3 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 supplementary data for figures are available.

The number of COVID-19 cases with S gene positive/SGTF by day, among those tested in TaqPath labs is shown in Figure 4. COVID-19 cases with detectable S gene/SGTF and percentage with SGTF among those tested in TaqPath Labs by region is now published in the Omicron daily overview.

Figure 2. Variant prevalence for all England available genotyped cases from 1 February 2021 as of 12 December 2021 (Find accessible data used in this graph in <u>underlying data</u>.)

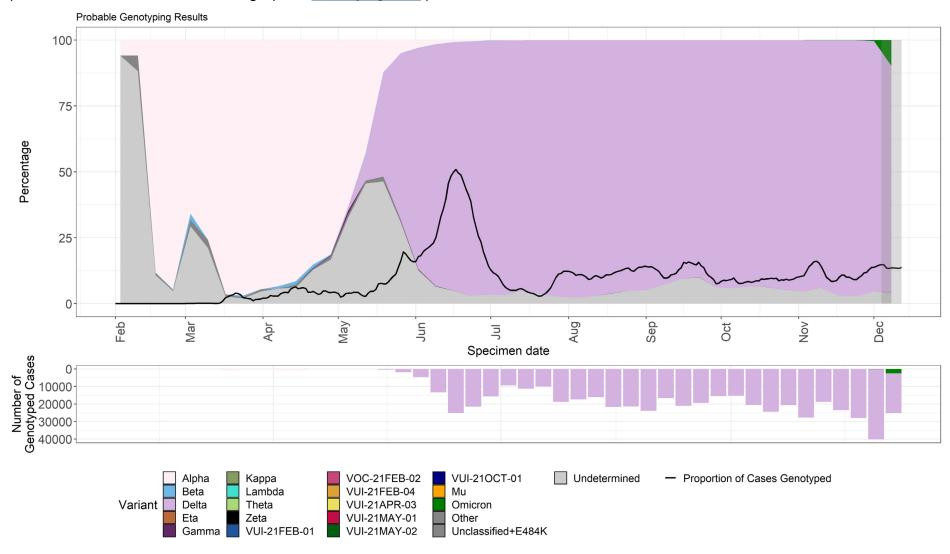


Figure 3. Prevalence of variants over time: all sequenced cases in England, split by travel status as of 12 December 2021 (excluding 694 cases where the travel status or specimen date were unknown)

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

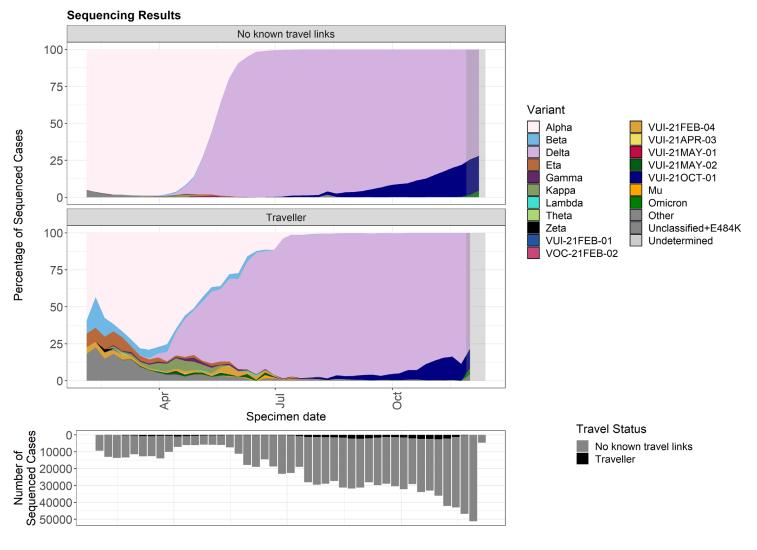
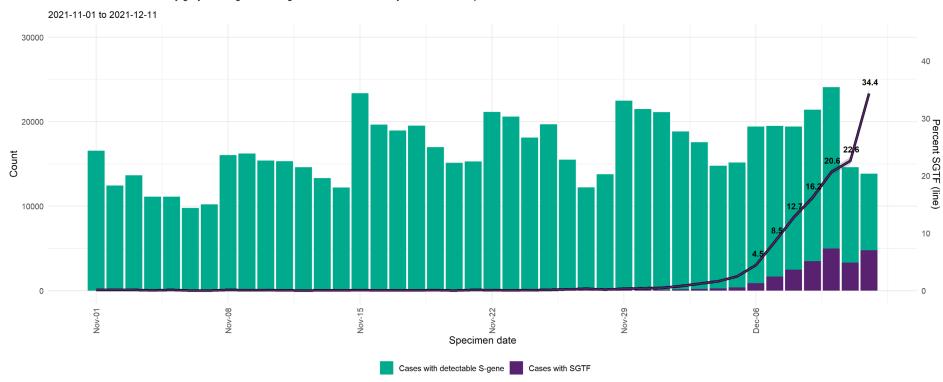


Figure 4. Number of COVID-19 cases with S gene positive/SGTF by day, among those tested in TaqPath labs as of 14 December 2021. (95% confidence intervals indicated by grey shading)

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

Number COVID19 cases with S gene +ve/SGTF and percentage SGTF by day, among those tested in TaqPath Labs 95% confidence intervals indicated by gray shading. Percentages for most recent 7 days shown. Data updated on 2021-12-14



A detectable S gene is a proxy for Delta since April 2021. SGTF was a surveillance proxy for VOC-20DEC-01 however has largely consisted of Delta since August 2021.

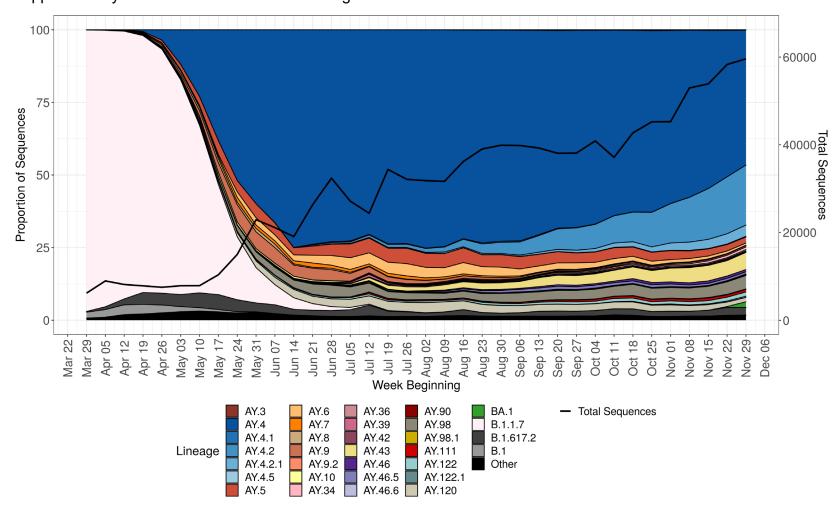
Local trends in these data may be affected by decisions to direct the processing of samples via a TaqPath laboratory.

Only tests carried out with the TaqPath PCR assay and with 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 within sequence data from 1 April 2021 to 12 December 2021 Supplementary data are not available for this figure.



The total number of valid sequence results per week is shown by the black line. Only lineages with more than 1000 sequences, and B.1.1.529 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 underlying data.)

Part 2. Enhanced analysis on Omicron VOC-21NOV-01 (B.1.1.529)

A new 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. This variant was designated VUI-21NOV-01 by the UKHSA Variant Technical Group and on review re-designated as VOC-21NOV-01 on 27 November 2021.

2.1 Performance of diagnostic lateral flow devices

UKHSA has performed an initial laboratory evaluation of the current lateral flow devices (LFDs) for COVID-19 in current use by NHS Test and Trace. Preliminary laboratory data assess these devices as detecting Omicron. Initial data from contrived samples indicate a comparable sensitivity to that observed for previous strains of SARS-CoV-2 including Delta, which has been the predominant strain in the UK from May to December 2021.

All LFDs eligible for DHSC procurement within the UK specifically detect the nucleocapsid protein of SARS-CoV-2 using a combination of 2 or more different antibodies, each targeting a distinct epitope. There is a significantly lower selective pressure for mutations on the nucleocapsid protein when compared to the spike. Omicron's nucleocapsid protein has a single unique mutational difference from other SARS-CoV-2 variants, a deletion at aa31-33, as such the general risk to LFD performance being impacted by Omicron was considered low.

To ensure that the sensitivity of the 5 tests that have been (or could rapidly be) deployed by NHS Test and Trace has not been significantly reduced by Omicron the following work is underway:

- routine and enhanced Real World Performance Monitoring of the LFDs deployed within NHS Test and Trace
- wet lab testing with contrived samples from sequence confirmed cultures of Omicron has been performed at Porton Down

Real World Performance Monitoring data from LFDs in Deployment

Real world data for Omicron are currently being processed and a separate technical report will be released when analysis has been completed.

Laboratory evaluation results

Laboratory evaluation has currently been performed on 5 tests which are:

- Acon Flow Flex 'self-test'
- Innova Biotime 'self-test and professional use test'
- Orient Gene 'self-test'
- SureScreen 'professional use test'
- SureScreen 'self-test'

The evaluation is performed using dilutions of cultured virus stock in Hanks Balanced Salt Solution (HBSS) plus mucin with 5 samples at each dilution. The dilutions provide 3 concentrations of virus in the following ranges, >1,000,000, >100,000, >10,000 viral copies per millilitre (ml). The Omicron variant was isolated from a primary clinical sample sourced in the UK and confirmed as being Omicron by sequencing.

In summary, the LFDs evaluated, all of which target the nucleocapsid protein, have detected the new Omicron variant that contains 4 amino acid changes from the original viral sequence. This does not affect their performance in the laboratory setting and we will monitor further variant changes as they arise as part of our ongoing evaluation programme.

Table 2: Laboratory testing results for the sensitivity of 5 lateral flow devices (in or near

deployment) for Omicron (contrived samples, sourced from UK patients Passage 2)

<u>deployment) for O</u>	deployment) for Omicron (contrived samples, sourced from UK patients Passage 2)						
LFD / Date	Variant	Dilution	Viral titre FFU/ml	Viral Copy number	Number of samples tested	Number of negative results	Number of positive results
Acon Flowflex	Omicron	1/80	1250	4,070,000	5	0	5
09/12/2021		1/800	125	280,000	5	0	5
		1/8,000	12.5	30,000	5	0	5
	Wild type	-	100	460,000	15	0	15
Innova Biotime	Omicron	1/80	1250	4,070,000	5	0	5
09/12/2021		1/800	125	280,000	5	0	5
		1/8,000	12.5	30,000	5	0	5
	Wild- type	-	100	290,000	15	1	14
Orientgene	Omicron	1/80	1250	4,070,000	5	0	5
09/12/2021		1/800	125	280,000	5	0	5
		1/8,000	12.5	30,000	5	0	5
	Wild- type	-	100	290,000	15	0	15
SureScreen Professional Test	Omicron	1/80	1250	4,070,000	5	0	5
09/12/2021		1/800	125	280,000	5	0	5
		1/8,000	12.5	30,000	5	0	5
	Wild- type	-	100	580,000	15	0	15
SureScreen Self Test	Live Omicron	1/80	1250	4,070,000	5	0	5
09/12/2021		1/800	125	280,000	5	0	5
		1/8,000	12.5	30,000	5	0	5
	Wild- type	-	100	560,000	15	0	15

2.2 Omicron characterisation analyses

Growth rate and advantage

The growth in frequency of adjusted SGTF which are likely to originate from Omicron cases in England is shown in Figure 6 and for each region in England in Figure 7.

Growth rates are computed relative to the number of S gene positive cases. Sample inclusion criteria are: 1) A non-traveller as determined by matching each case against passenger locator forms and managed quarantine service test codes 2) Collected from Pillar 2 testing and 3) Less than 30 cycle threshold (Ct) on targets other than the S-gene in order to reduce false positives in patients with low viral loads.

SGTF has variable specificity for detection of the Omicron variant because Delta cases will occasionally produce SGTF. Before Omicron was detected, the majority of SGTF originated from non-Omicron cases in the first half of November. The probability that an SGTF originates from an Omicron case over time was estimated using a generalised additive model applied to 112 SGTF cases paired with sequence data between 20 November and 5 December 2021. Among these 112 cases, 80 were Omicron. The true positive rate for using SGTF as a marker for Omicron increased from 20% on 20 November to >99% on 5 December 2021. Before estimating growth rates, SGTF counts were adjusted by redistributing cases from negative to positive in proportion to the true positive rate of SGTF for Omicron.

The growth rate is estimated by logistic regression of the number of SGTF on the time of sample collection. A growth rate of 0 would indicate parity with S gene positive cases. Confidence intervals were computed by parametric bootstrap.

Given the growth rate of Omicron, it remains likely that Omicron will reach parity with Delta (equal proportion of cases) in mid-December.

SGTF counts are adjusted in proportion to the probability that an SGTF case is from an Omicron case. Lines show a logistic regression fit to the data and shaded region a 95% confidence interval.

Figure 6. Sample frequency of log odds adjusted SGTF cases as compared to S gene positive cases

Supplementary data are not available for this figure. A linear increase, using log odds, is consistent with exponential growth.

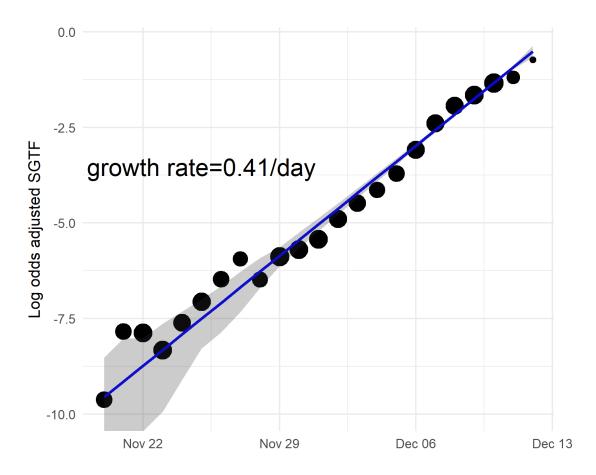
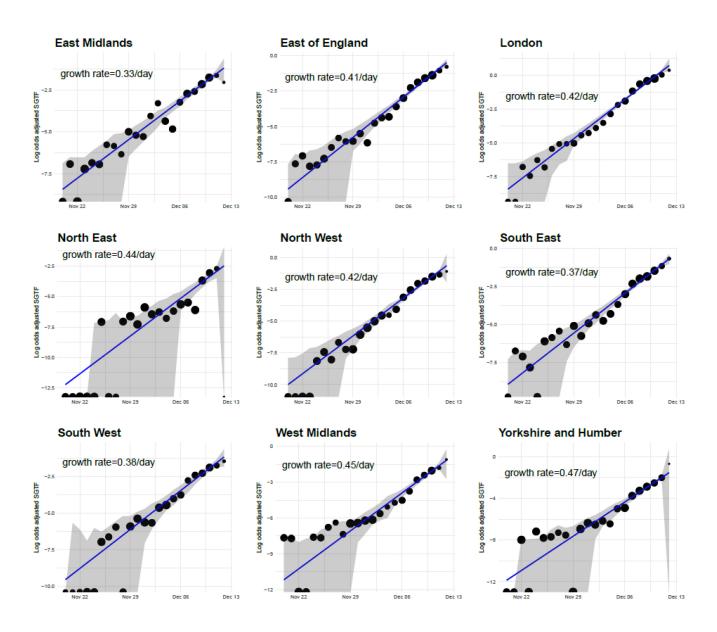


Figure 7. Sample frequency of log odds adjusted SGTF cases as compared to S gene positive cases for each region in England

Supplementary data are not available for this figure. A linear increase, using log odds, is consistent with exponential growth. Observed growth is consistent across regions.



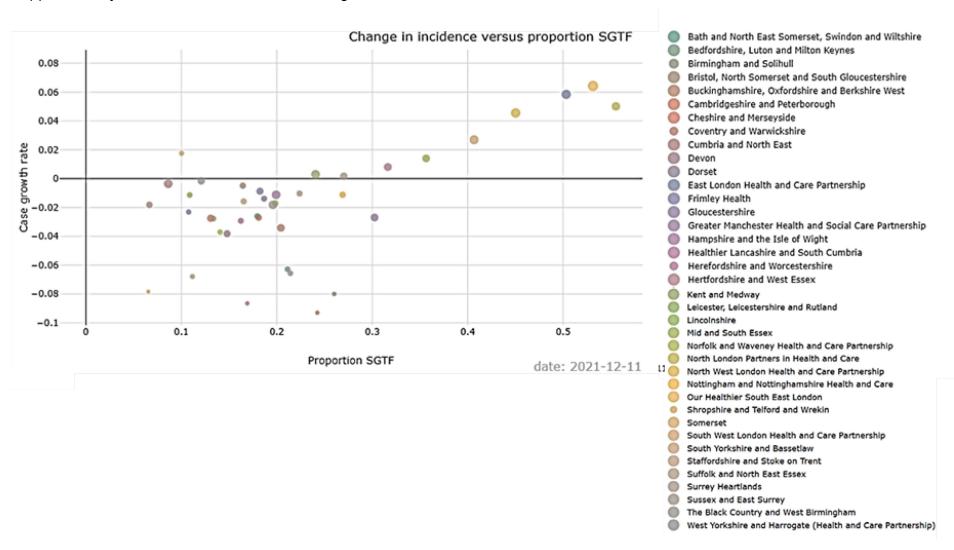
Growth rate and incidence

Incidence has increased rapidly in Sustainability and Transformation Partnerships (STPs) where the proportion of SGTF cases is highest, as shown in Figure 8.

Case growth rate was calculated as the daily change in number of diagnoses. The case growth rate across STPs is positively correlated with the proportion of SGTF.

Figure 8. Change in COVID-19 case growth rate versus proportion of SGTF across Sustainability and Transformation Partnerships as of 11 December 2021

Supplementary data are not available for this figure.



Household transmission risk

A cohort analysis was performed to estimate the odds of household transmission for Omicron index cases (defined on sequencing, genotyping, or SGTF), compared with Delta index cases (defined as sequenced B.1.617.2). The analysis included 116,186 index cases (115,407 Delta, 777 Omicron) in residential households with a specimen date between 15 November and 6 December 2021. Household transmission was defined as an index (first) case followed by one or more laboratory confirmed SARS-CoV-2 cases at the same private dwelling within a 14-day period (minimum 7 days follow-up). Index cases with a minimum of one household contact were included in the analysis.

Overall, 18% (141) of Omicron index cases gave rise to a secondary household case, compared to 10% (11,593) of Delta index cases.

A multivariable logistic regression model found the adjusted odds ratio for household transmission from an Omicron index case was 2.9 (95%Cl 2.4-3.5, p <0.001) compared to Delta index cases.

These preliminary findings suggest that the Omicron variant has a transmission advantage compared to Delta. However, this analysis may be affected by increased ascertainment of Omicron cases. The analysis will be iterated to improve precision.

Table 3. Odds of household transmission for Omicron VOC-21NOV-01 (B.1.1.529) index cases compared to Delta

	Unadjusted Odds Ratio (95% CI)	P value	Adjusted Odds Ratio* (95%CI)	P value
Omicron household transmission	2.0 (1.7 - 2.4)	<0.001	2.9 (2.4 - 3.5)	<0.001

^{*}Adjusted for age, sex, ethnicity, index of multiple deprivation, type of residence, specimen date, number of household contacts, region and vaccination status of the index case

Secondary attack rates

This section is based on data for the period 15 November to 4 December 2021. 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 confirmed Omicron or confirmed Delta, with date of symptom onset or positive test of the secondary case occurring 2 to 7 days after original exposure. This shortened follow up period was used to expedite analysis on Omicron in the context of limited data so far.

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.

There are a number of limitations to this work. Enhanced identification and testing for contacts of cases with Omicron may be contributing to higher case ascertainment amongst those contacts and hence higher observed secondary attack rates. Low numbers of Omicron cases so far contribute to high uncertainty about secondary attack rate estimates: these should be interpreted with caution. Differences in demographics and activities of Omicron and Delta cases may also be contributing to different patterns of risk of onwards transmission to their contacts. A higher proportion (47.8%) of named close contacts of Omicron cases were outside of the household compared to Delta (19.8%), which is suggestive of differing contact patterns between these groups in the study period.

Table 4 shows the secondary attack rates split by type of contact. Table 5 shows odds ratios of a close contact becoming a case for Omicron compared to Delta index cases and adjusted for household or non-household exposure.

Secondary attack rates in households and non-household settings were higher for Omicron compared to Delta. The overall odds ratio, adjusted for household or non-household exposure, of a close contact becoming a case for confirmed Omicron compared to Delta index cases was 1.96 (95% CI: 1.77-2.16), see Table 5.

Table 4. Secondary attack rates for contacts of cases with Omicron VOC-21NOV-01 (B.1.1.529) and Delta

(Exposure dates 15 November to 4 December 2021, Delta cases as of 6 December 2021, Omicron cases as of 13 December 2021 and contact tracing data as of 14 December 2021).

Variant/variant definition	Household/non- household exposure	Count of exposing cases	Count of contacts	Secondary attack rate (95% CI)
Delta	Household	41,321	103,287	10.3% (10.1%-10.5%)
Delta	Non-household	9,328	25,546	3.0% (2.8%-3.2%)
Omicron Confirmed	Household	1,006	2,121	15.8% (14.3%-17.5%)
Omicron Confirmed	Non-household	557	1,940	8.7% (7.5%-10.0%)

Secondary attack rates from NHS Test and Trace should generally be considered lower bounds due to the nature of contact tracing and testing, and specifically so here because of the restricted (7 days) time period for follow up. Data provided are for the period until 4 December 2021 in order to allow some time for contacts to become cases, hence case counts are lower than other sources. Contacts are included in secondary attack rates if their date of exposure, onset, or test of exposing case if the contact is a household contact, is during the period of study. Cases are counted if they were the exposer of such a contact. This analysis will be repeated weekly until stable.

Table 5. Odds ratio of a close contact becoming a case for contacts of Omicron VOC-21NOV-01 (B.1.1.529) compared to Delta index cases and adjusted for household or non-household exposure

(Exposure dates 15 November to 4 December 2021, Delta cases as of 6 December 2021, Omicron cases as of 13 December 2021 and contact tracing data as of 14 December 2021).

	aOR (95% CI)
Omicron Confirmed	1.96 (1.77-2.16)

Reinfections

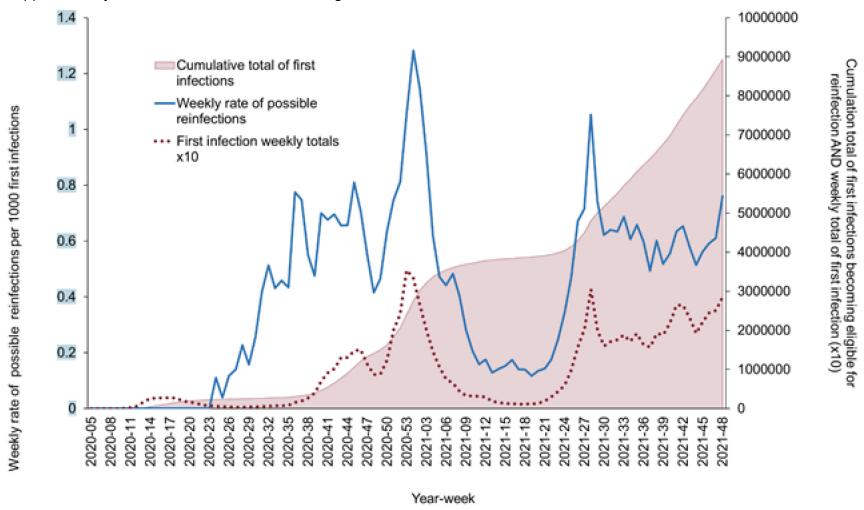
Cases of reinfection (at any interval) were identified amongst confirmed, highly probable and probable Omicron variant SARS-CoV-2 positive cases extracted on 13 December 2021, with a specimen date between 1 November and 11 December 2021. Of 5,153 individuals identified with an Omicron infection in this period, 305 (5.9%) were linked to a previous confirmed infection (by PCR or LFD testing) and had an interval from the previous test positive of >=90 days. These cases would therefore have been identified as a reinfection based on the diagnosis used in ongoing surveillance (an interval between 2 sequential positive SARS-CoV-2 test results of >=90 days). The age of cases ranged from 6 to 68 years (median 27 years) and the interval to reinfection from previous SARS-CoV-2 infection ranged from 90 to 541 days (median 335 days) with first episodes occurring both within periods of Alpha and Delta variant dominance or earlier. There were 4 individuals for whom the Omicron infection was their third episode of infection (>=90 days between each episode). There were 5 individuals with a possible reinfection between a 60-89-day interval after an earlier confirmed infection but in those with an interval of <90 days between episodes it can be difficult to distinguish reinfection from persistent viral detection.

Reinfection rates are usually generated using the population of previous infections eligible to become a reinfection (that is with a previous positive test result >=90 days earlier). Using this as a measure of current reinfection rates in the population there is now the suggestion of an increase in overall reinfection rates, alongside an increase in first infections (Figure 9).

The relative risk of reinfection with the Omicron variant was estimated based on 2479 Omicron cases and 189,481 non-Omicron cases which could be linked to whole genome sequence data between 20 November and 10 December 2021 and extracted on 14 December. Among these, there were 188 possible Omicron reinfections and 2866 non-Omicron possible reinfections. Risk ratios were estimated using Poisson regression and a binomial outcome representing at least one PCR-positive test more than 90 days prior to the specimen date. After adjusting for age (0 to 18,19 to 40, 40+ years), public health region, and collection pillar, the risk ratio of reinfection for Omicron was 3.3 (95%CI: 2.8 to 3.8). These estimates are preliminary. Higher rates of reinfection were observed in SGTF cases and SGTF cases have been prioritised for sequencing, which may increase the proportion of Omicron reinfections in our sample.

Figure 9: The weekly rate of possible COVID-19 reinfections with cumulation of first infections becoming eligible for reinfection and weekly total of first infection* (England only to week 48 2021)

Supplementary data are not available for this figure.

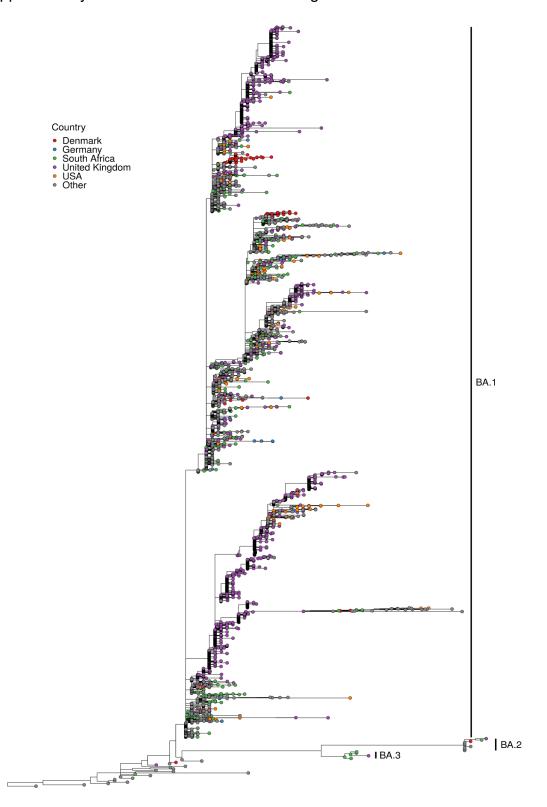


Genomic diversity within Omicron VOC-21NOV-01 (B.1.1.529)

Omicron VOC-21NOV-01 (B.1.1.529) has been separated into 3 clades: BA.1, BA.2, and BA.3. These clades share the majority of the mutations initially identified in B.1.1.529. Figure 10 shows a maximum likelihood phylogeny for UK and international Omicron genomes and highlights the distance between the 2 groups, despite the number of shared mutations. Given the likely diversity within the wider lineage, additional outlier genomes will be identified using a broader, ancestral definition for B.1.1.529. Changes in the proportion of samples in additional BA lineages will be monitored; however, due to the higher prevalence of BA.1, VOC-21NOV-01 will report only cases within this clade.

Figure 10. Maximum likelihood phylogeny for Omicron VOC-21Nov-01 (B.1.1.529) genomes (BA.1=5401, BA.2=10, BA.3=6, B.1.1.529=5) as of 14 December 2021 Country is indicated by tip colour. Only countries with > 100 sequences are shown, sequences from other countries are in grey. The BA.1 clade has been scaled to 0.1 for readability.

Supplementary data are not available for this figure



2.3 Interpretation of S gene target failure data

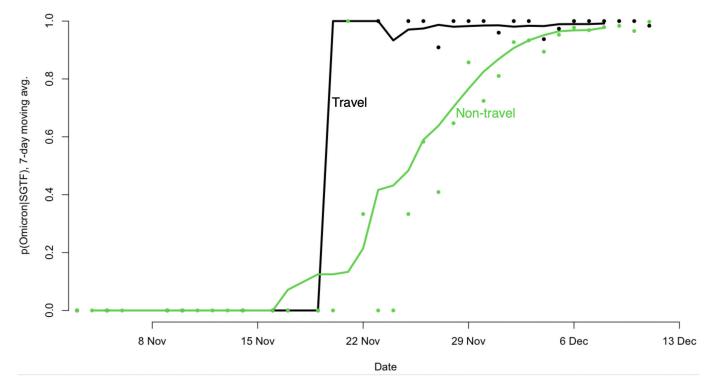
Correlation SGTF to Omicron and calculated PPV

Figure 11 shows the proportion of Omicron VOC-21NOV-01 (B1.1.529) sequences from all SGTF samples sequenced.

Figure 11. Proportion of sequences from the Wellcome Sanger Institute with SGTF that are Omicron VOC-21NOV-01 (B.1.1.529)

Black corresponds to tests with a history of recent travel, green to those with no travel history. Points are daily values, lines are 7-day moving averages. Final data point is 11 December 2021, when PPV for SGTF of Omicron is 99.8%.

Supplementary data are not available for this figure.



2.4 Epidemiology of confirmed Omicron, VOC-21NOV-01 (B.1.1.529) in England

Confirmed Omicron cases are those which have been identified by sequencing or genotyping. Additional cases are under investigation.

The Omicron genome also contains the spike deletion at position 69-70 which is associated with 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 Ct values <=30) but the S gene is not. SGTF patterns can be used to assess the spread of Omicron.

Table 6. Number of confirmed (sequencing) Omicron VOC-21NOV-01 (B.1.1.529) cases, by region of residence as of 12 December 2021

Region	Total case number	Confirmed (sequenced) case number	Provisional (genotyped) case number	% of sequences from England that are in this region
North West	116	61	55	3.1%
East Midlands	388	109	279	10.4%
East of England	371	170	201	10.0%
London	1,585	405	1,180	42.6%
North East	99	3	96	2.7%
South East	862	177	685	23.1%
South West	201	42	159	5.4%
Unknown region	15	5	10	0.4%
West Midlands	63	23	40	1.7%
Yorkshire and Humber	25	13	12	0.7%
Total	3,725	1,008	2,717	-

Figure 12. Cases of Omicron VOC-21NOV-01 (B1.1.529) in England by region as of 12 December 2021

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

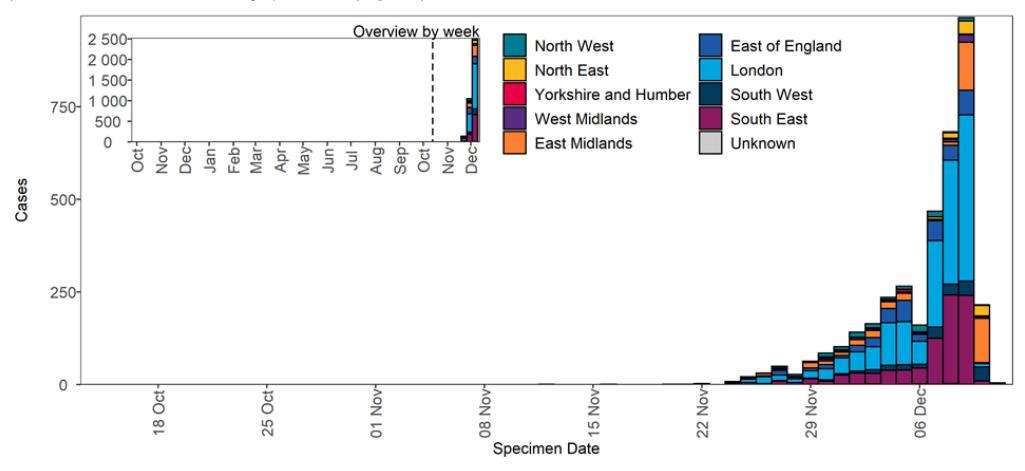


Figure 13. Cases of Omicron VOC-21NOV-01 (B1.1.529) in England by travel status as of 12 December 2021

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

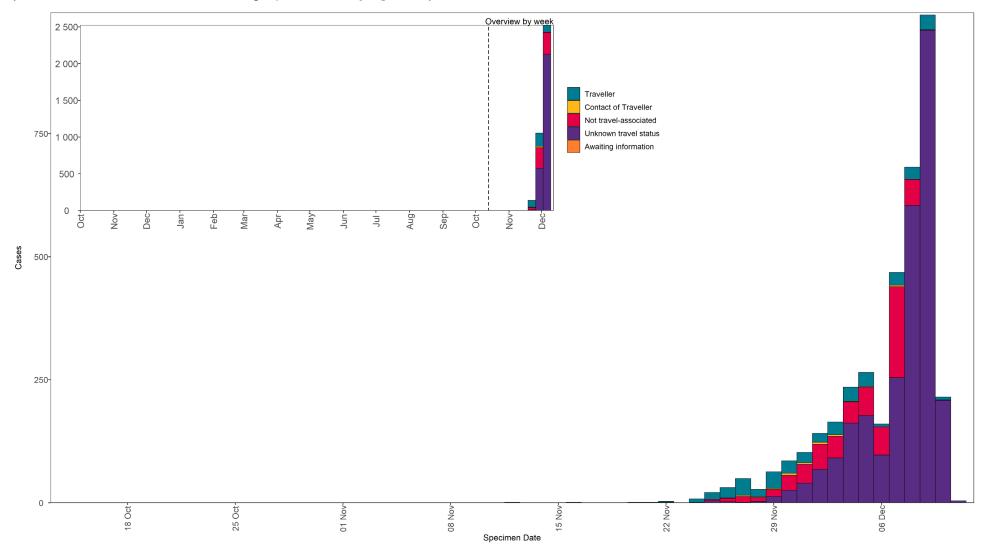
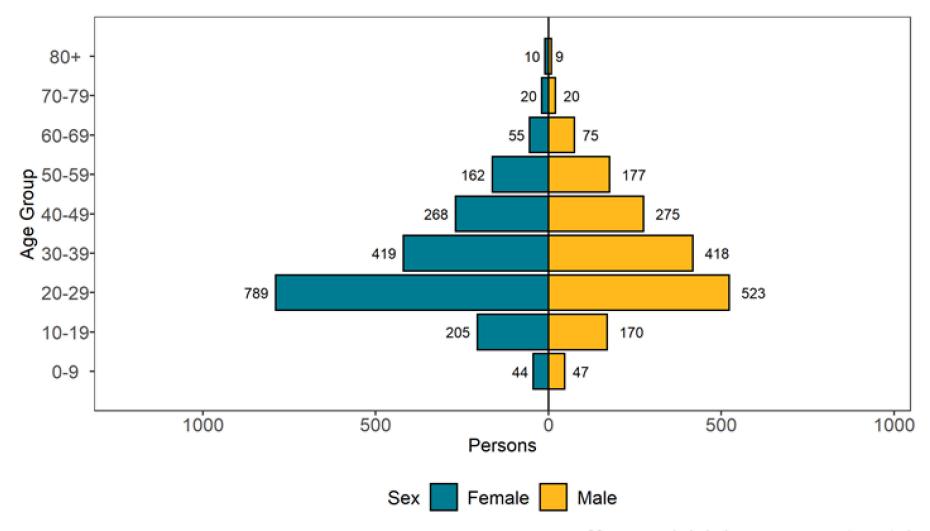


Figure 14. Cases of Omicron VOC-21NOV-01 (B1.1.529) in England by age and sex as of 12 December 2021

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



39 cases excluded where sex or age not reported

Severity outcomes

Hospital data are currently reported in the Omicron daily overview.

2.5 Wastewater analysis

Environmental monitoring of wastewater samples for the presence of SARS-CoV-2 variants is being undertaken across England and is in early stages of validation as a surveillance system. Wastewater is monitored for SARS-CoV-2 RNA at 477 sites including sewage treatment works (STW) and local sewer networks. Sampling is undertaken multiple times per week. This sampling framework is estimated to cover 70% of the English population. It is possible to look for mutations associated with variants in the wastewater, but detection of variants can be transient and the correlation between population prevalence and wastewater variant detection has not been established for Omicron. Wastewater monitoring remains under development and is currently considered as supplementary data in variant monitoring. Validation as an independent variant surveillance system is underway.

The definition of the detection of Omicron in wastewater has been revised. It remains based on the detection of a number of SNPs from the list in the official clinical definition and is noted below. Unless otherwise stated, no distinction is made between SNPs which can be used to define wastewater detections.

Confirmed - ≥ 16 of 22 variant defining SNPs detected, ≥ 9 of 20 unique SNPs detected and co-occurrence detected on at least 7 or If ≥ 16 signature SNPs and ≥ 9 unique SNPs are present without co-occurrence, or co-presence of the following SNPs on amplicon 121 with co-occurrence, 22882, 22898, 22992, 23013, 23040, 23048 and 23055

Possible $- \ge 10$ of 22 variant defining SNPs detected and ≥ 6 of 20 unique SNPs detected OR If < 10 signature SNPs and ≥ 6 unique SNPs are detected, but ≥ 9 SNPs are not covered possible presence can be assigned if those not covered are present across 2 dates from the same site, but in the same sequencing run

Not detected – < 7 of 22 variant defining SNPs detected unless co-presence of the following SNPs on amplicon 121, 22882, 22898, 22992, 23013, 23040, 23048 and 23055

Applying the above definition, wastewater samples collected from sites across England up to 5 December 2021 have been analysed. Between 26 November and 5 December there were Confirmed and Possible detections of Omicron in 38 wastewater samples amongst 2,437 sequenced (Figure 15). Amongst Regional totals, the highest number of wastewater Omicron detections have been in London, the South East and the North West, which aligns with clinical trends.

32

Figure 15. Confirmed and possible detections of Omicron VOC-21NOV-01 (B.1.1.529) in wastewater samples collected in England weeks commencing 22 and 29 November 2021

Supplementary data not available.

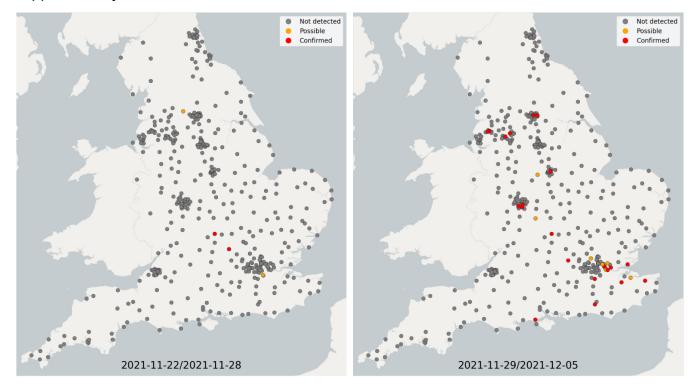


Table 7. Regional totals of wastewater samples sequenced and reported Omicron VOC-21NOV-01 (B.1.1.529) detections

Region	Week commencing 22 November			Week com	mencing 29 N	lovember
	Sequenced samples	Confirmed Omicron	Possible Omicron	Sequenced samples	Confirmed Omicron	Possible Omicron
East Midlands	89	2	0	94	3	1
East of England	88	0	0	85	2	0
London	144	0	1	179	5	4
North East	67	0	0	103	0	0
North West	228	0	0	228	5	0
South East	86	1	0	77	5	1
South West	161	0	0	173	0	0
West Midlands	98	0	0	110	3	1
Yorkshire and The Humber	192	0	1	235	3	0
England	1,153	3	2	1,284	26	7

Wastewater samples will continue to be sequenced and results reported as they become available. The data, including those presented here, are generated by non-accredited laboratories; they should be considered experimental and subject to change as methods are further developed. Monthly publication of these data on gov.uk as Experimental Statistics will commence in 2022.

Sources and acknowledgments

Data sources

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

Repository of human and machine-readable genomic case definitions

Genomic definitions for all VOCs and VUIs 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 VOCs and VUIs are also detailed on first description in prior technical <u>briefings</u>.

Variant Technical Group

Authors of this report

UKHSA Genomics Cell

UKHSA Outbreak Surveillance Team

UKHSA Epidemiology Cell

UKHSA Contact Tracing Data Team

UKHSA Environmental Monitoring for Health Protection Team

Contributions from the Variant Technical Group Members

Variant Technical Group members and contributors

Meera Chand (chair)	UKHSA
Genomics and bioinformatics	
Andrew Rambaut	University of Edinburgh
Nicholas Loman	UKHSA/University of Birmingham

Dichard Myore	UKHSA
Richard Myers	
Jeffrey Barrett	Wellcome Sanger Institute
Matt Holden	Public Health Scotland
Natalie Groves	UKHSA
Eileen Gallagher	UKHSA
Nicholas Ellaby	UKHSA
Virology and Immunology	
Wendy Barclay	Imperial College London
Gavin Screaton	University of Oxford
Maria Zambon	UKHSA
Paul Kellam	Imperial College London
Kevin Brown	UKHSA
Susanna Dunachie	University of Oxford
Lance Turtle	University of Liverpool
Ravi Gupta	University of Cambridge
Bassam Hallis	UKHSA
Tim Wyatt	Northern Ireland Public Health Agency
Thomas Peacock	Imperial College London
Epidemiology and modelling	
Susan Hopkins	UKHSA
Jamie Lopez-Bernal	UKHSA
Nick Andrews	UKHSA
Simon Thelwall	UKHSA
Meaghan Kall	UKHSA
Thomas Finnie	UKHSA
Richard Elson	UKHSA
Charlotte Anderson	UKHSA
Charlie Turner	UKHSA
Erik Volz	Imperial College London
John Edmunds	London School of Hygiene and Tropical Medicine
Neil Ferguson	Imperial College London

Daniela de Angelis	University of Cambridge
Maria Rossi	Public Health Scotland
Chris Williams	Public Health Wales
Anna Seale	UKHSA/University of Warwick
International epidemiology	
Katherine Russell	UKHSA
Chris Lewis	Foreign, Commonwealth and Development Office
Leena Inamdar	UKHSA

The UK Health Security Agency Variant Technical Group includes members and contributors from the following organisations: UKHSA, Public Health Wales, Public Health Scotland, Public Health Agency Northern Ireland, the Department of Health and Social Care, Imperial College London, London School of Hygiene and Tropical Medicine, University of Birmingham, University of Cambridge (including the MRC Biostatistics Unit), University of Edinburgh, University of Liverpool, the Wellcome Sanger Institute, Genotype to Phenotype Consortium, SPI-M.

Acknowledgements

The authors are grateful to those teams and groups providing data for these analyses including: the Lighthouse Laboratories, NHS, COG-UK, the Wellcome Sanger Institute, Health Protection Data Science teams, the University of Oxford, and the Genotype to Phenotype Consortium.

About the UK Health Security Agency

The <u>UK Health Security Agency</u> is an executive agency, sponsored by the <u>Department of</u> Health and Social Care.

© Crown copyright 2021 Version 1.0

Published: December 2021

Publishing reference: GOV-10717

OGL

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit <u>OGL</u>. Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.



UKHSA supports the UN Sustainable Development Goals

