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

Technical briefing 31

10 December 2021

This briefing provides an update on previous briefings up to 3 December 2021

Contents

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 separate report is published covering surveillance data on all other VOCs and VUIs. In summary:

- there are 5 current VOCs and 7 VUIs (Table 1)

- the technical briefing uses a data cut off of 6 December to allow time for analyses. Current national variant case numbers are published weekly. At the data cut off, there were 260 confirmed cases of Omicron VOC-21NOV-01 (B.1.1.529) (hereafter referred to as Omicron), identified through sequencing or genotyping in England. There are additional possible cases identified through S gene target failure (SGTF) and given the coverage of the different types of tests, the true number of cases is likely to be much higher. None of the cases of are known to have been hospitalised or died through routine data linkages

- the Omicron global phylogeny shows the presence of 2 clades, a large group (BA.1) with the typical Omicron mutations and a small outlying group (BA.2) with some shared mutations with Omicron and some differences, including an absence of the deletion at S:69/70 which gives the SGTF result. BA.2 has not yet been observed in the United Kingdom (UK) data set and currently comprises only a small number of sequences

- Omicron continues to grow rapidly in all regions of England as measured by confirmed cases and SGTF cases. S gene target failure data were published on 8 December 2021. Case ascertainment of Omicron has been enhanced through increased sequencing of SGTF cases. Use of the assay which produces S gene target failure has not changed. Genotyping has changed in interpretation but not in coverage. These changes may affect the analyses presented, which are preliminary estimates and will be iterated

- Omicron has also been detected in the wastewater in 5 samples collected between 26 and 28 November from 4 of the 477 sewage treatment works and sewerage network sites

- characterisation analyses on UK cases have commenced and report as follows:

o Studies of households and contacts find a higher risk of transmission to contacts from an Omicron index case, when compared to Delta index cases. Secondary attack rates may be influenced by improved ascertainment around Omicron cases. These studies have not adjusted for vaccination or prior infection status of the contacts, due to current data quality. This means that the findings are describing overall growth advantage, rather than pure transmissibility. The findings include:

- the risk of household transmission using routine testing data (adjusted odds ratio of transmission from an Omicron index case compared to a Delta index case 3.2 (95% CI 2.0-5.0))
- the risk of a close contact becoming a secondary case (adjusted odds ratio 2.09 (95% CI: 1.54-2.79))
- the household secondary attack rate using routine contact tracing data (Omicron, 21.6% (95% CI: 16.7%-27.4%), Delta 10.7% (95% CI: 10.5%-10.8%)

o The growth advantage is also visible in the community testing data. The proportion of cases with SGTF (now highly predictive of Omicron) continues to grow rapidly. The estimated growth rate of Omicron based on adjusted SGTF counts is 0.35 per day. If Omicron continues to grow at the present rate, Omicron case numbers are projected to reach parity with Delta cases in mid-December.

o There is currently no evidence of increased reinfection risk at the population level, but preliminary analyses indicate approximately three- to eight-fold increased risk of reinfection with the Omicron variant.

o The Variant Technical Group reviewed the available neutralisation data from published international and internal UK studies (UK Health Security Agency, University of Oxford). UK data will be published as soon as possible and cited here when available. Across 5 preliminary live virus studies (3 international and 2 UK), there was a 20- to 40-fold reduction in neutralising activity by Pfizer 2-dose vaccinee sera for Omicron compared to early pandemic viruses. There was at least 10 fold loss of activity when compared to Delta; in both UK studies this was over 20 fold. A greater reduction in activity was seen for AZ 2-dose sera, and for a high proportion of such sera, neutralising activity fell below the limit of quantification in the assay. An mRNA booster dose resulted in an increase in neutralising activity irrespective of primary vaccination type, including an increase in the proportion of samples that were above the limit of quantification. This is true regardless of which vaccine was used for the primary course. These data are from the early period after the booster and data are urgently required on the durability of neutralising activity

- o early estimates of vaccine effectiveness (VE) against symptomatic infection find a significantly lower VE for against Omicron infection compared to Delta infection. Nevertheless, a moderate to high vaccine effectiveness of 70 to 75% is seen in the early period after a booster dose. With previous variants, vaccine effectiveness against severe disease, including hospitalisation and death, has been higher than effectiveness against mild disease. It will be a few weeks before effectiveness against severe disease with Omicron can be estimated, however based on this experience, this is likely to be substantially higher than the estimates against symptomatic disease. The duration of restored protection after mRNA boosting is not known at this juncture

- initial laboratory validation of lateral flow devices in use by NHS Test and Trace has determined similar sensitivity to detect Omicron compared to Delta. Data will be shared in the next technical briefing

- an updated risk assessment for Omicron VOC-21NOV-01 (B.1.1.529) has been published

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

Sequencing coverage data have moved to the Variant Data Update.

Published information on variants

The collection page gives content on variants, including prior technical briefings. Definitions for variants of concern, variants under investigation, and signals in monitoring are detailed in Technical Briefing 8. Data on variants not detailed here are published in the Variant Data Update. 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 the 5 March 2021 containing the up-to-date genomic definitions for all VOCs and VUIs. The repository is accessible on GitHub.

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.

Technical briefings are published periodically. From technical briefing 15, briefings include variant diagnoses identified by whole-genome sequencing and a genotyping polymerase chain reaction (PCR) test, including the categorisation of sequenced and genotyped variant results and a rules-based decision algorithm (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 7 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)	
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
		C.37 descendant (S:L5F, G75V, D614G, L452Q, E484K, P499R, N501T, H655Y, P681R)
		C.36.3††

Variants of concern	Variants under Investigation	Variants in monitoring
		B.1.427/B.1.429
		B.1.620
		R.1
		BA.2

* Previously VUI-21JUN-01, de-escalated on 20 October 2021.
†† Previously VUI-21MAY-02, 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, Iota, 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 5 December 2021
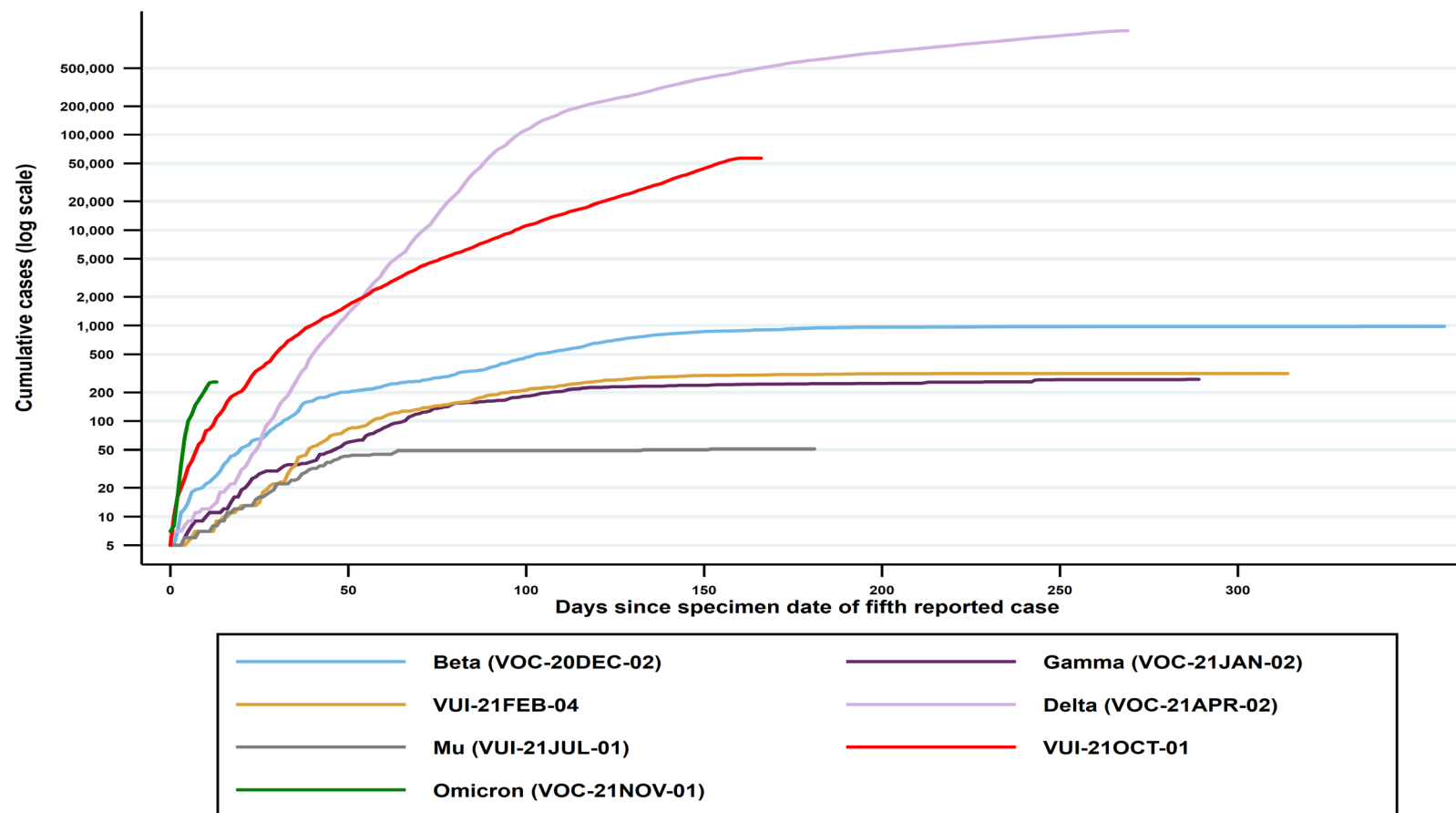
(Find accessible data used in this graph in underlying data.)

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 region in Figure 3 and by travel in Figure 4.

Genotyping provides probable variant results with a shorter turnaround time of 12 to 24 hours after initial confirmation of coronavirus (COVID-19) by polymerase chain reaction (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 to 4 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.

Figure 2. Variant prevalence for all England available genotyped cases from 1 February 2021 as of 6 December 2021
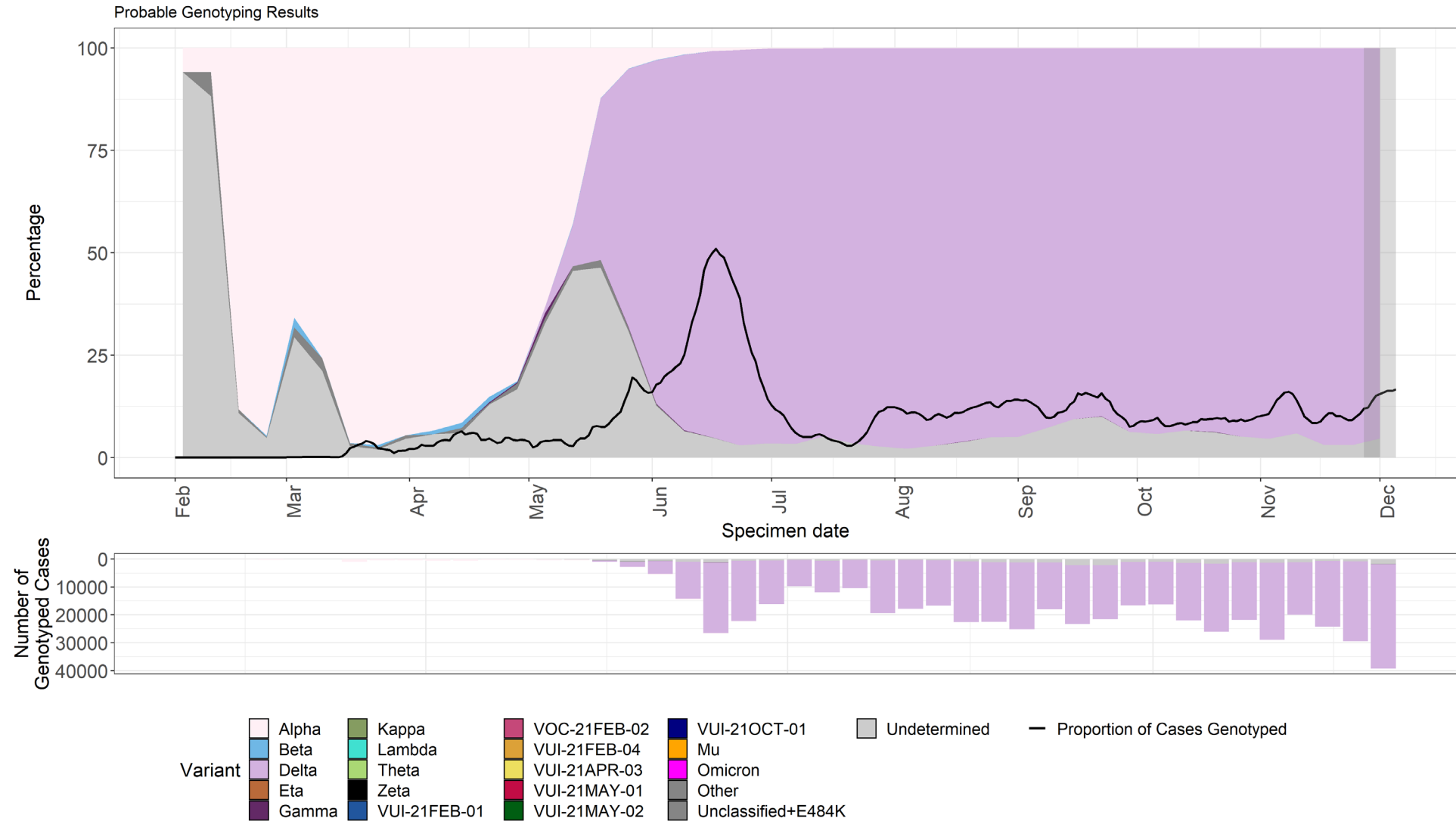(Find accessible data used in this graph in underlying data.)

Figure 3. Variant prevalence from 1 February 2021 as of 6 December 2021 by region for all sequenced cases in England (excluding 5,688 cases where the region or specimen date were unknown)

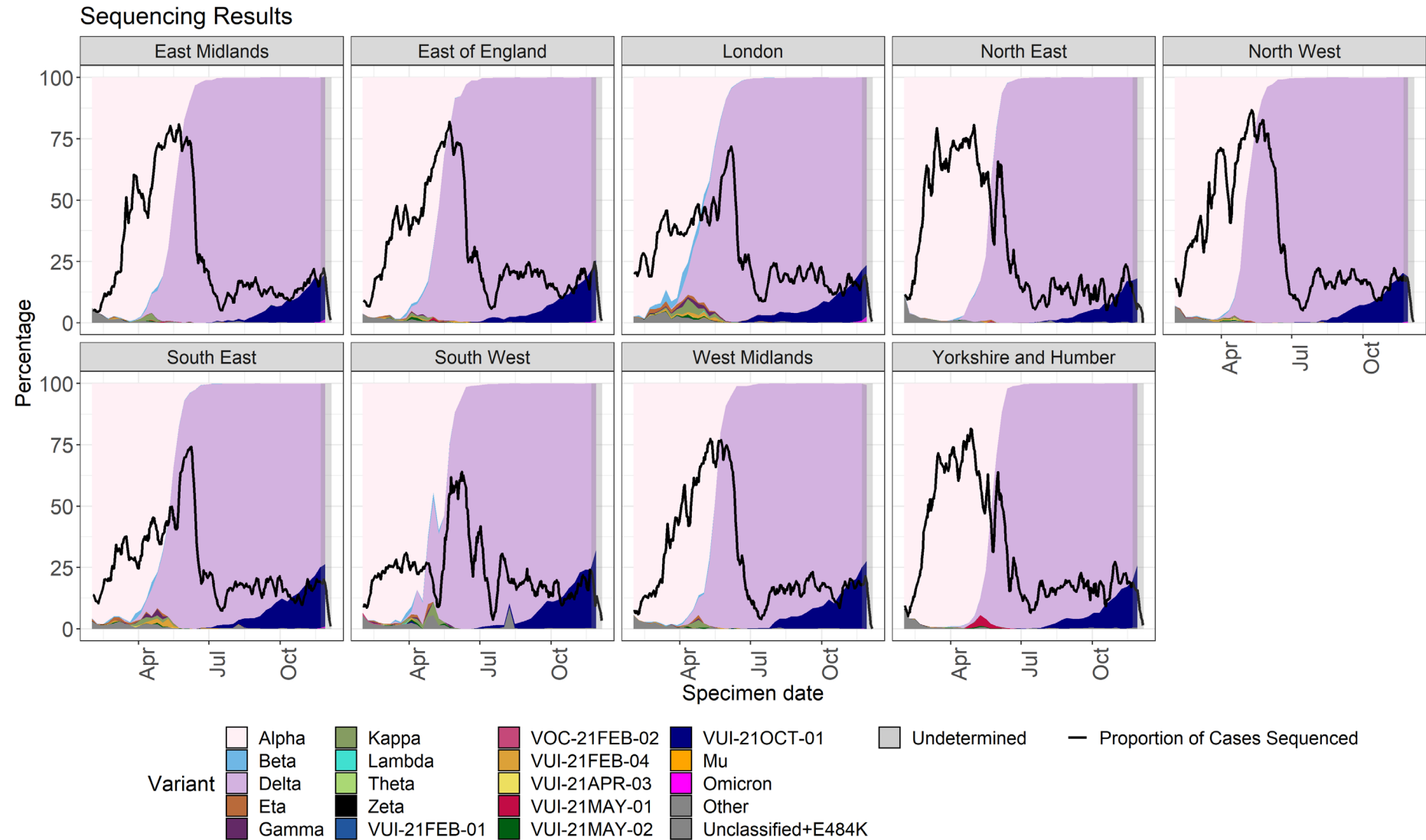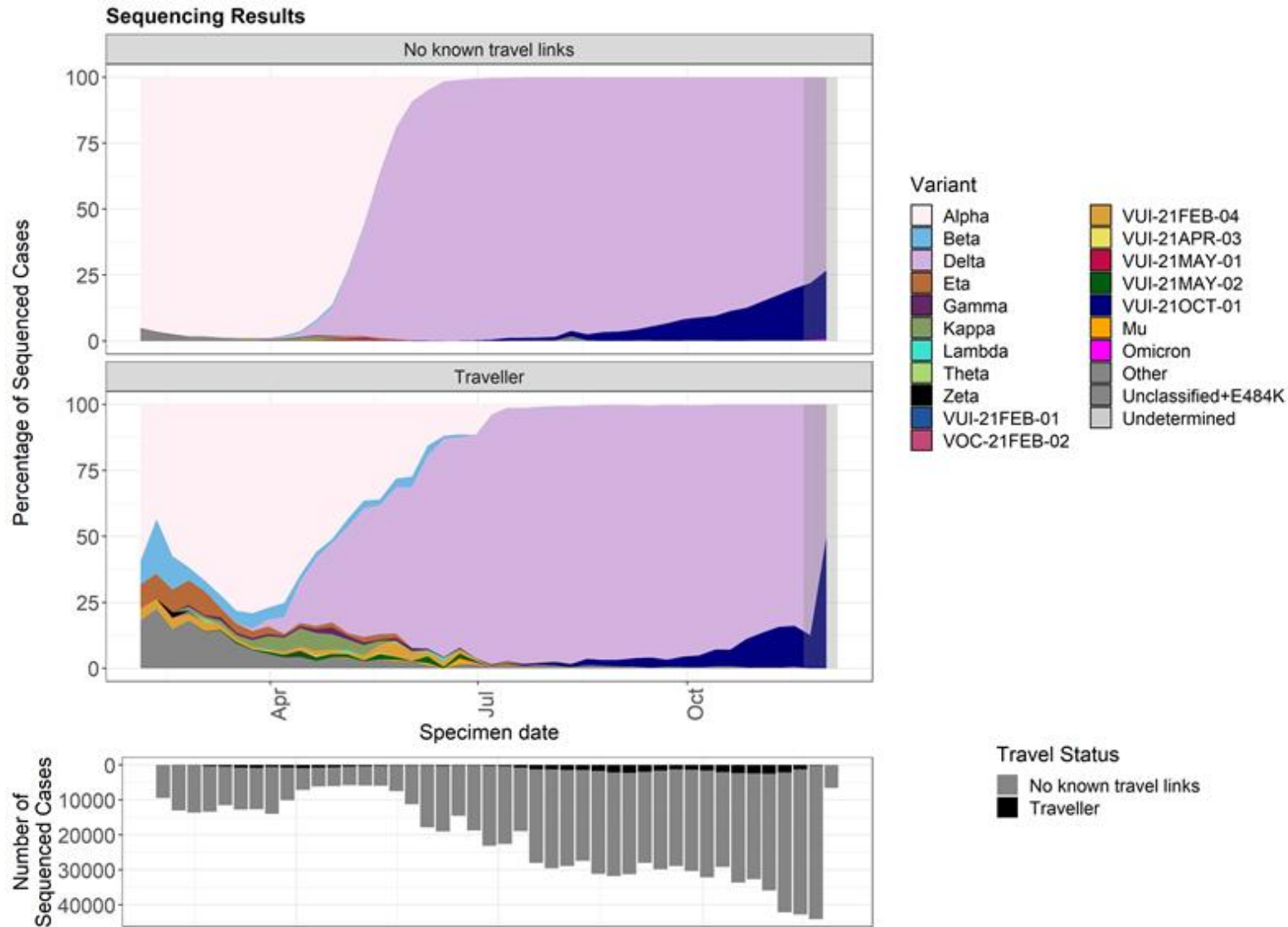(Find accessible data used in this graph in underlying data.)

Figure 4. Prevalence of variants over time: all sequenced cases in England, split by travel status as of 6 December 2021(excluding 872 cases where the travel status or specimen date were unknown)

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

Figure 5. Prevalence of Pangolin lineages within sequence data from 1 April 2021 to 5 December 2021
Supplementary data are not available for this figure.
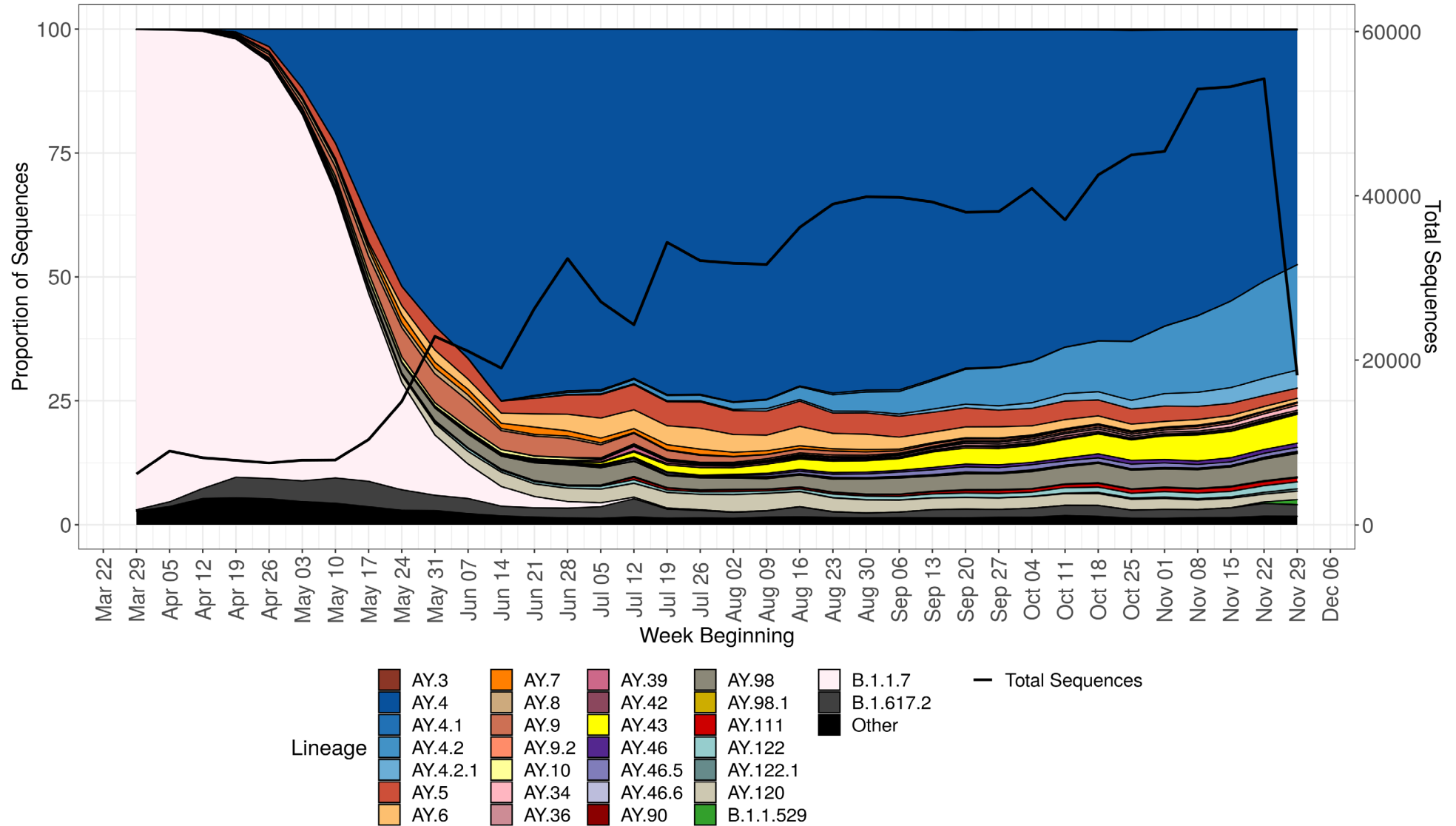
The total number of valid sequence results per week is shown by the black line. Only lineages with more than 1,000 sequences, and B.1.1.529 are shown. Smaller lineages are either merged with parent lineages (for example, AY.3.1 is included in AY.3) or are included in 'Other'. (Find accessible data used 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 and designated B.1.1.529 on 24 November. 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 Omicron characterisation analyses

Growth rate and advantage

The growth in frequency of adjusted SGTF which are likely to originate from Omicron cases is shown in Figure 6.

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 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.

Reproduction numbers were estimated using a renewal equation and assuming 1) the reproduction number of Delta is close to one; 2) generation times are gamma distributed with a mean of 5.2 days and a coefficient of variation equal to 2/3.

If Omicron continues to grow at the present rate, Omicron is projected to 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. The effective reproduction number is based on generation times of 5.2 days and a coefficient of variation of 2/3.

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.
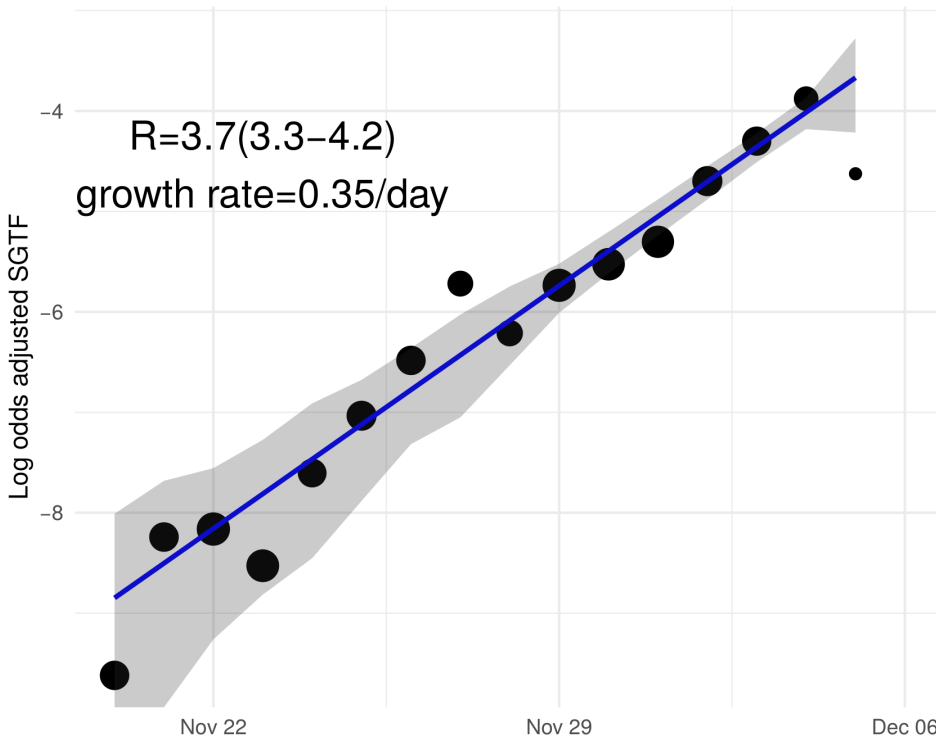
Household transmission risk

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 72,882 index cases (72,761 Delta, 121 Omicron) in residential households with a specimen date between 15 and 28 November 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.

Nineteen percent (23) of Omicron index cases gave rise to a secondary household case, compared to 8.3% (6,058) of Delta index cases.

A multivariable logistic regression model found the adjusted odds ratio for household transmission from an Omicron index case was 3.2 (95%CI 2.0-5.0, 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, but most household transmission in the analysis predate the start of enhanced contact tracing for Omicron. The analysis will be iterated to improve precision.

Table 2. 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	**2.6 (1.6 - 4.1)**	**<0.001**	**3.2 (2.0 - 5.0)**	**<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 1 November to 27 November 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 a variant, 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. Delta cases are identified using sequencing results only. Omicron cases are currently identified using all case definitions (Confirmed, Highly Probable, Probable, Possible) with analysis performed on successive combinations of these definitions.

- **Confirmed case:** Omicron by sequencing or genotyping.
- **Highly Probable case:** COVID-19 PCR positive, SGTF plus travel history from Republic of South Africa (RSA), Botswana, Namibia, Eswatini, Lesotho, Zimbabwe, Angola, Zambia, Malawi, Mozambique and Nigeria with specimen dates from 1 November as confirmed by case interview (cases that are confirmed as another strain are excluded *) Or COVID-19 PCR/LFD positive contact of a confirmed case
- **Probable case:** COVID-19 PCR positive S-gene unknown, plus travel history from RSA, Botswana, Namibia, Eswatini, Lesotho, Zimbabwe, Angola, Zambia, Malawi, Mozambique and Nigeria with specimen dates from 1 November (cases that are confirmed as another strain are excluded *)
- **Possible case:** COVID-19 PCR positive plus SGTF and specimen dates from 1 November 2021

* As of 29 November 2021, 3 genotyping results (in London) were originally called as Beta/Mu and reclassified to genotyped B.1.1.529.

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.

Enhanced isolation and follow-up 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.

Table 3 shows the secondary attack rates split by type of contact. Table 4 shows odds ratios of a close contact becoming a case for Omicron (successive combinations of definitions) compared to Delta index cases and adjusted for household/non-household exposure.

Secondary attack rates in households were higher for Omicron compared to Delta but the observed secondary attack rates were similar for non-household contacts. The overall odds ratio, adjusted for household/non-household exposure, of a close contact becoming a case for confirmed Omicron compared to Delta index cases was 2.09 (95% CI: 1.54-2.79).

Table 3. Secondary attack rates for contacts of cases with Omicron VOC-21NOV-01 (B.1.1.529) and Delta
(Exposure dates 1 November 2021 to 27 November 2021, Delta cases as of 29 November 2021, Omicron cases as of 6 December 2021 and contact tracing data as of 7 December 2021).

Variant/variant definition	Household/non-household exposure	Count of exposing cases	Count of contacts	Secondary attack rate (95% CI)
Delta	Household	60,364	147,057	10.7% (10.5%-10.8%)
Delta	Non-household	14,631	41,538	3.2% (3.1%-3.4%)
Omicron Confirmed	Household	107	227	21.6% (16.7%-27.4%)
Omicron Confirmed	Non-household	40	132	3.8% (1.6%-8.6%)
Omicron Confirmed or Highly Probable	Household	111	238	21.8% (17.1%-27.5%)
Omicron Confirmed or Highly Probable	Non-household	42	136	3.7% (1.6%-8.3%)
Omicron Confirmed, Highly Probable or Probable	Household	197	428	17.5% (14.2%-21.4%)

Variant/variant definition	Household/non-household exposure	Count of exposing cases	Count of contacts	Secondary attack rate (95% CI)
Omicron Confirmed, Highly Probable or Probable	Non-household	57	171	2.9% (1.3%-6.7%)
Omicron Confirmed, Highly Probable, Probable or Possible	Household	374	867	15.2% (13%-17.8%)
Omicron Confirmed, Highly Probable, Probable or Possible	Non-household	112	395	7.6% (5.4%-10.6%)

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 period until 27 November 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 exposure date or 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 exposer of such a contact. This analysis will be repeated weekly until stable.

Table 4. 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/non-household exposure
(Exposure dates 1 November 2021 to 27 November 2021, Delta cases as of 29 November 2021, Omicron cases as of 6 December 2021 and contact tracing data as of 7 December 2021)

Definition of Omicron (each compared to Delta)	aOR (95% CI)
Omicron Confirmed	2.09 (1.54-2.79)
Omicron Confirmed or Highly Probable	2.12 (1.58-2.80)
Omicron Confirmed, Highly Probable or Probable	1.67 (1.30-2.10)
Omicron Confirmed, Highly Probable, Probable or Possible	1.63 (1.38-1.93)

Vaccine effectiveness against symptomatic infection

A test negative case control design was used to estimate vaccine effectiveness against symptomatic COVID-19 with the Omicron variant compared to the Delta variant. Here vaccination rates in PCR positive cases are compared to vaccination rates in those who test negative. Individuals who reported symptoms and were tested in pillar 2 (community testing) between 27 November and 6 December 2021 were included in the analysis. Those who

reported recent foreign travel were excluded from the analysis due to differences in exposure risk and possible misclassification of vaccination status in this group.

Cases were defined as the Omicron variant or Delta variant based on whole genome sequencing or S-gene target status on PCR testing. The Omicron variant has been associated with a negative S-gene target result on PCR testing with the Taqpath assay whereas with the Delta variant the S-gene target is almost always positive. A priori, we considered that S-gene target failure would be used to define the Omicron variant when Omicron accounts for at least 80% of S-gene target failure cases. This meant that S-gene target status could be used from 27 November onwards.

Vaccine effectiveness was estimated by period after dose 2 and dose 3.

The final analysis included 56,439 Delta and 581 Omicron cases. Given the small numbers of Omicron cases in this first analysis, the Omicron estimates are subject to significant uncertainty with wide confidence intervals and will be refined in future analyses. Vaccine effectiveness against symptomatic disease by period after dose 2 and dose 3 is shown in Figure 7 for those who received a primary course of the AstraZeneca vaccine (Figure 7A) or Pfizer (Figure 7B), in both cases booster doses were Pfizer. In all periods, effectiveness was lower for Omicron compared to Delta; with the exception of those who had their second dose of Pfizer 2 to 9 weeks ago (which may reflect young adults who have recently received their second dose). From 2 weeks after a Pfizer booster dose, vaccine effectiveness increased to around 71% among those who received AstraZeneca as the primary course and around 76% among those who received Pfizer as the primary course.

These early estimates suggest that vaccine effectiveness against symptomatic disease with the Omicron variant is significantly lower than compared to the Delta variant. Nevertheless, moderate to high vaccine effectiveness of 70 to 75% is seen in the early period after a booster dose.

Figure 7: Vaccine effectiveness against symptomatic diseases by period after dose 1 and dose 2 for Delta (black squares) and Omicron (grey circles) for (A) recipients of 2 doses of AstraZeneca vaccine as the primary course and a Pfizer as a booster[1] and (B) recipients of 2 doses of Pfizer vaccine as the primary course and a Pfizer as a booster
Supplementary data are not available for this figure.
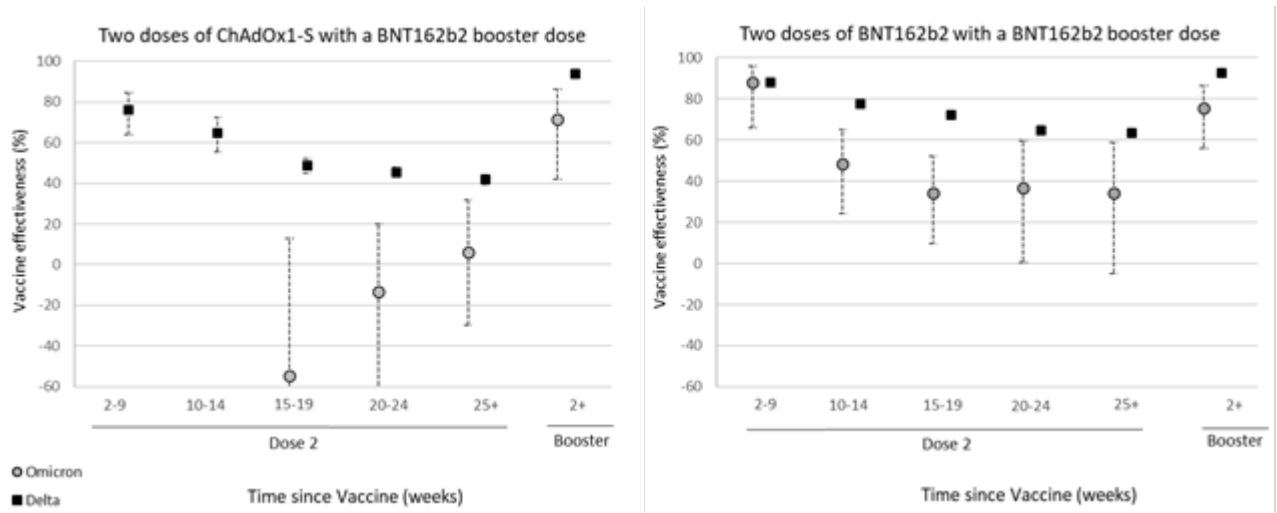
[1] The early observations for 2 doses of AstraZeneca are particularly likely to be unreliable as they are based on relative small numbers and are likely to reflect an older population and a population with more co-morbidities than those given the Pfizer vaccine, and this may explain the negative point estimates.

These results should be interpreted with caution due to the low numbers and the possible biases related to the populations with highest exposure to Omicron (including travellers and their close contacts) which cannot fully be accounted for.

With previous variants, vaccine effectiveness against severe disease, including hospitalisation and death, has been significantly higher than effectiveness against mild disease (that is those detected through community testing and included here). It will be a few weeks before effectiveness against severe disease with Omicron can be estimated, however based on this experience, this is likely to be substantially higher than the estimates against symptomatic disease. After the emergence of Delta in the UK, early estimates of vaccine effectiveness against mild infection after 2 doses of vaccine were substantially attenuated in comparison to alpha. Analysis of protection against hospitalisation however, showed no diminution of protection when comparing the 2 variants.

Reinfections

Cases of reinfection (at any interval) were identified amongst confirmed, highly probable and probable Omicron variant SARS-CoV-2 positive cases extracted on 6 December 2021 with a specimen date between 1 November and 3 December 2021. Of 329 individuals identified with an Omicron infection in this period, 17 (4.9%) were linked to a previous confirmed infection. Sixteen cases had an interval from the previous test positive of >=90 days and would therefore have been identified as a reinfection on the basis of the diagnosis used in ongoing surveillance

(an interval between 2 sequential positive SARS-CoV-2 test results of >=90 days) whereas one had an interval of 88 days between 2 positive episodes. The case ages ranged from 23 to 57 years (median 37 years) and the interval to reinfection from previous SARS-CoV-2 infection ranged from 88 to 541 days (median 314 days) with first episodes occurring both within periods of Alpha and Delta variant dominance.

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 earlier). Using this as a measure of current reinfection rates in the population there is currently no indication of an increase in overall reinfection rates, but this is being kept under ongoing review (Figure 8).

The relative risk of reinfection with the Omicron variant was estimated based on 361 Omicron cases and 85460 non-Omicron cases which could be linked to whole genome sequence data between November 20 and December 5, 2021 and extracted on 8 December. Among these, there were 25 possible Omicron reinfections and 336 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+), public health region, and collection pillar, the risk ratio of reinfection for Omicron is 5.2 (95%CI: 3.4 to 7.6). These estimates are preliminary. Higher rates of reinfection are observed in SGTF cases and SGTF cases have been prioritised for sequencing, which may increase the proportion of Omicron reinfections in our sample. Similar risk ratios are observed when only including provisional genotyping data, which should not be biased by sequence prioritisation, but small sample sizes prevent full statistical adjustment.

Figure 8: 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 47 2021)
Supplementary data are not available for this figure.
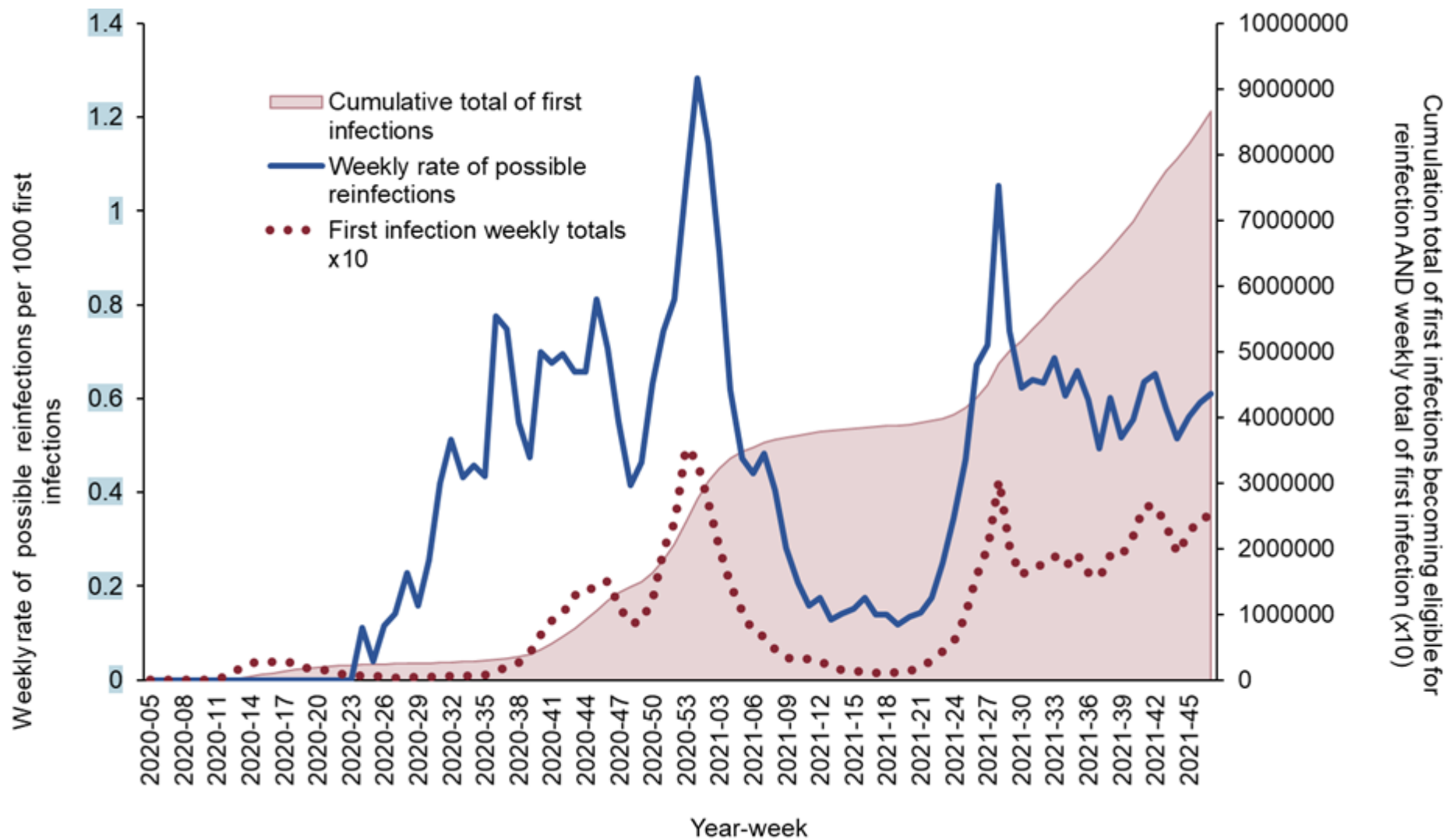
Genomic diversity within Omicron VOC-21NOV-01 (B.1.1.529)

Omicron VOC-21NOV-01 (B.1.1.529) has been separated into 2 clades: BA.1 and BA.2. These clades share the majority of the mutations initially identified in B.1.1.529. Figure 9 shows the mutations across spike present in the 2 lineages (BA.1 = 793 sequences, BA.2 = 8 sequences). Sequence data that showed signs of contamination or were low quality were removed from this analysis (n=13). Figure 10 shows a maximum likelihood phylogeny for the 2 clades and highlights the distance between the 2 groups, despite the number of shared mutations.

Figure 9: Proportion of sequences within BA.1 and BA.2 containing mutations in Spike

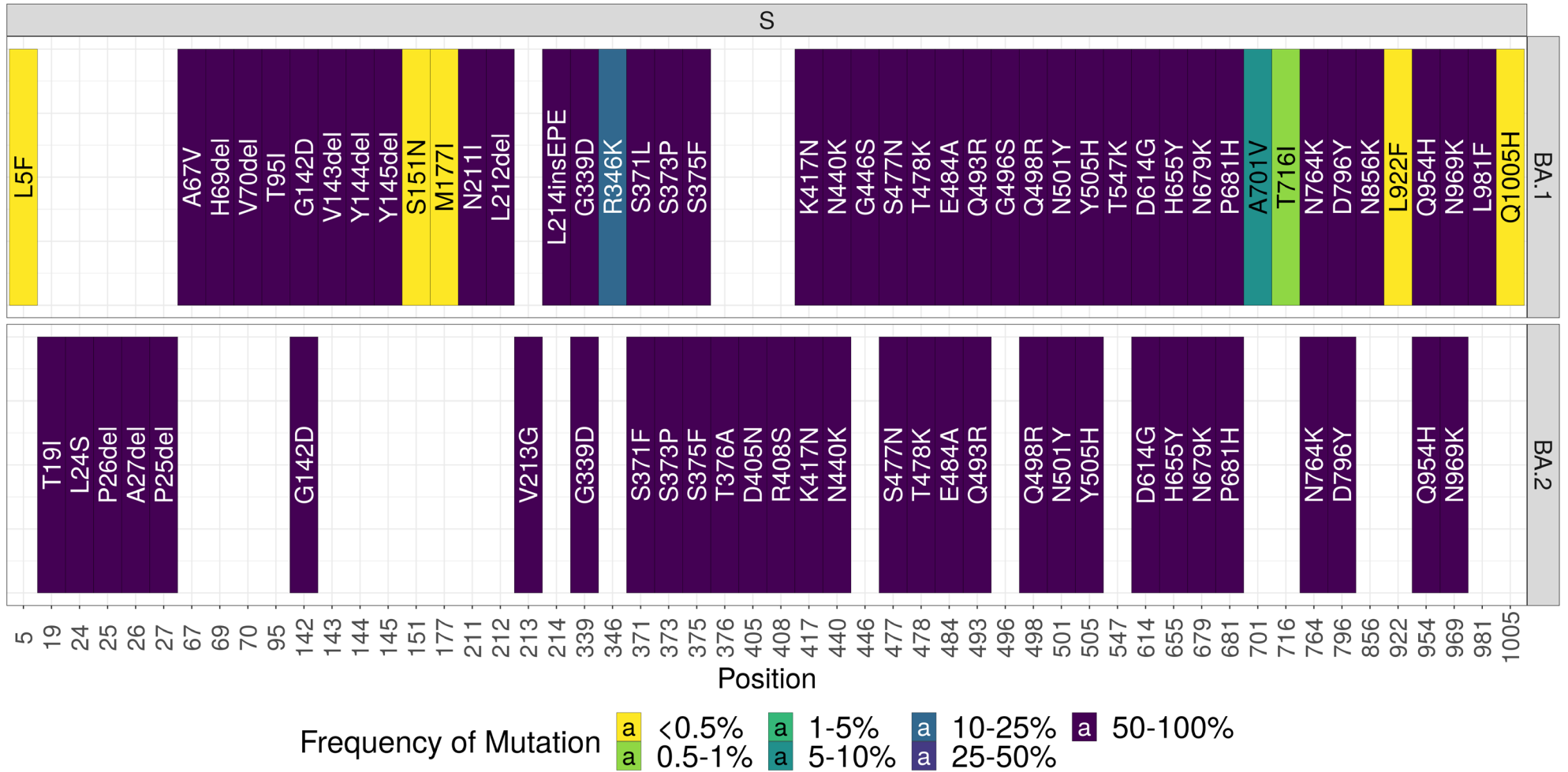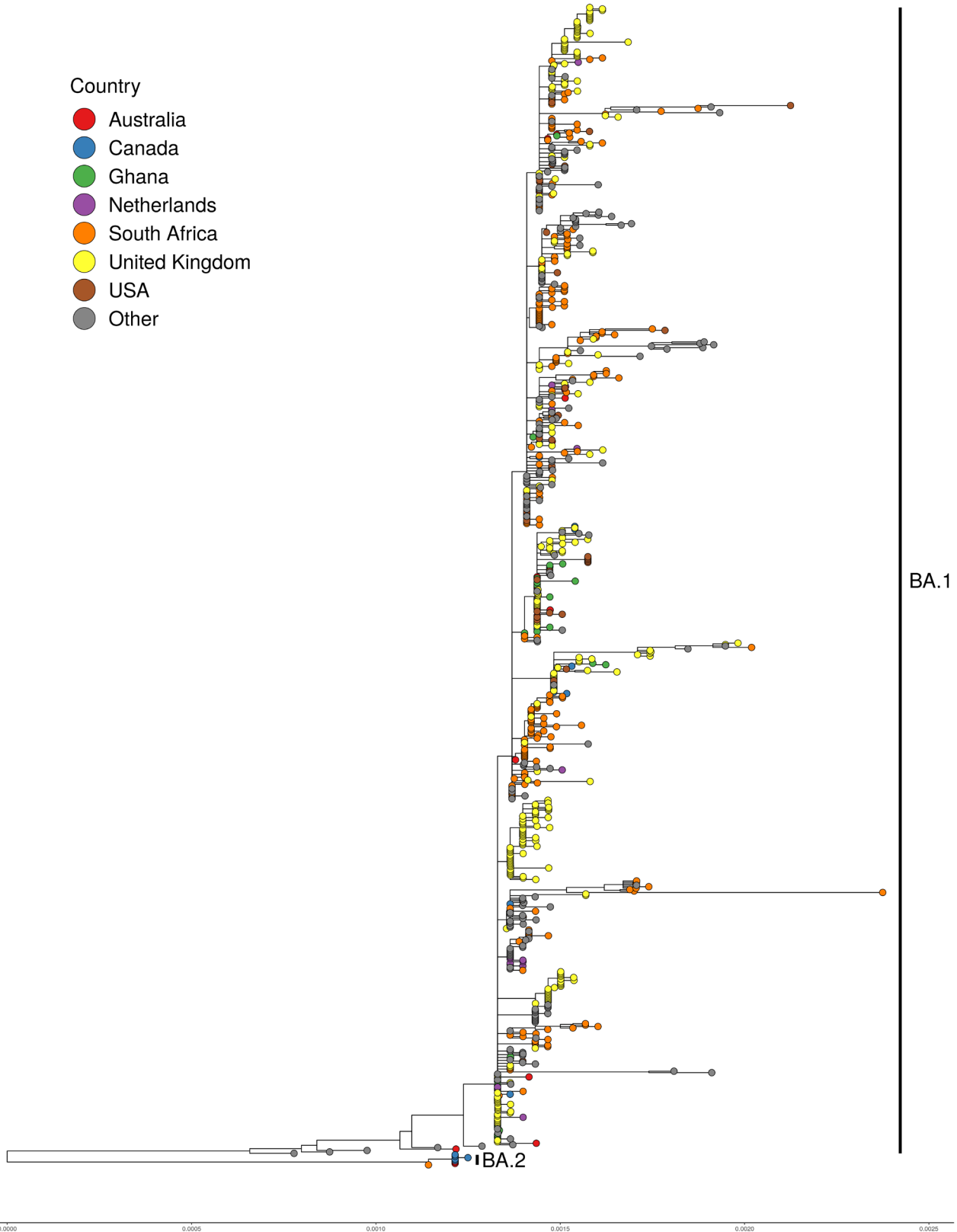Supplementary data are not available for this figure.

Figure 10: Maximum likelihood phylogeny for Omicron VOC-21Nov-01 (B.1.1.529) genomes (BA.1=793, BA.2=8) as of 7 December 2021

Country is indicated by tip colour. Only countries with > 20 sequences are shown, sequences from other countries are in grey. Supplementary data are not available for this figure.

2.2 Interpretation of S gene target failure data

Analyses in this report use S gene target failure data either alone or combination with genotyping and sequencing data. S gene target epidemiology was published on 8 December 2021.

On the 6 December 2021, UKHSA estimated that around 1.6% of all COVID-19 positive cases with specimen dates on the 3 December, which could be assessed for their cycle threshold (Ct) values by gene, did not have a detectable S-Gene and so were highly likely to be the Omicron variant. Cycle threshold (Ct) values are based on the number of cycles conducted before detecting the virus on a PCR test. The fewer cycles needed to detect the virus, the more virus there is in the sample (and therefore higher viral load).
Therefore, the assumptions were that:

- this proportion was an unbiased estimate of the proportion of Omicron cases
- the lag between infections and specimen dates was 3 days
- there were 76,200 total infections on the 30 November, based on modelled daily incidence (including Delta infections) for 17 November 2021 (ONS Infection Survey)

These inputs are sufficient to estimate that on the 30 November there were 1,219 daily Omicron VOC-21NOV-01 (B.1.1.529) infections. By assuming a constant doubling time of 2.5 days, Figure 11 plots daily Omicron infections using this starting point. Using different assumptions for the starting number of infections, or lags in the process, only has small implications for the trajectory of the chart below. The path of modelled future infections is highly sensitive to the assumed doubling time over the modelled period. This trajectory does not account for possible changes in behaviour in response to high prevalence of the virus.

Figure 11. Plot of daily Omicron VOC-21NOV-01 (B.1.1.529) infections from 30 November with an assumption of doubling time of 2.5days
Supplementary data are not available for this figure.
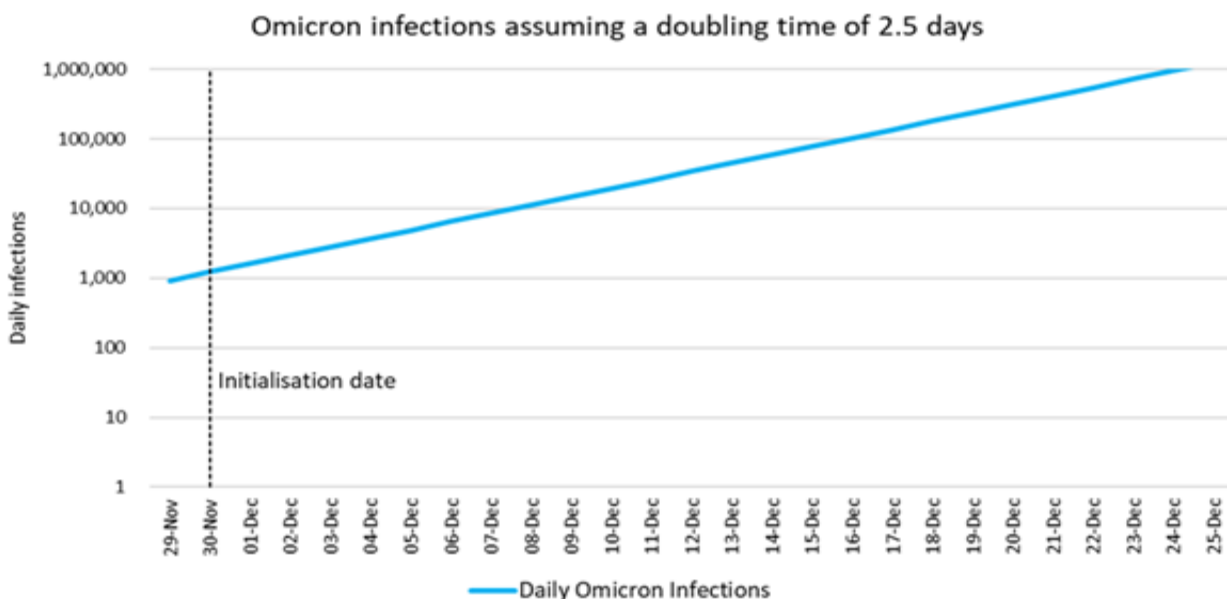
Figure 12 shows the proportion of Omicron VOC-21NOV-01 (B1.1.529) sequences from all SGTF samples sequenced. It is now highly predictive of Omicron (Figure 13). The positive predictive value of SGTF for Omicron in non-travellers in England is 95% on 5 December, the most recent date for which samples with sequence data are available.

Figure 12. 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 5 December 2021, when PPV for SGTF of Omicron is 95%.

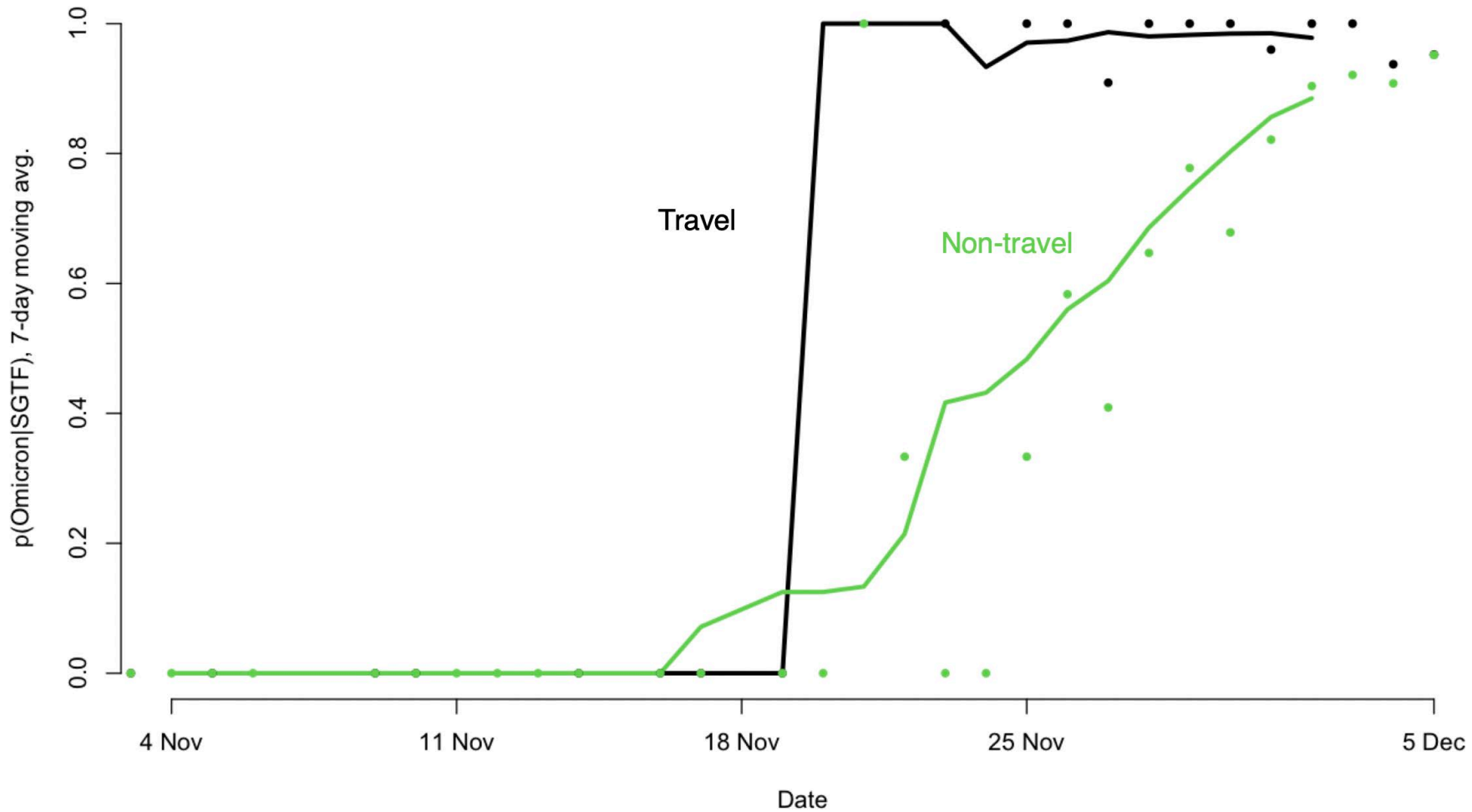Supplementary data are not available for this figure.

Figure 13. Number and distribution of variants per week among sequenced SGTF specimens as of 6 December 2021 (27 July 2021 to 29 November 2021)

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

Note this estimate is subject to bias, e.g. select sampling of suspected Omicron cases.
 Sample selection for sequencing occurs at plate level not sample level.
Among 11 SGTF samples with specimen dates in the week starting 2021-11-16 18% (n=2) were confirmed VOC-21NOV-1.
 Among 105 SGTF samples with specimen dates in the week starting 2021-11-23 74% (n=78) were confirmed VOC-21NOV-1.

Number and distribution of variants per week among sequenced SGTF specimens
Specimen dates between 2021-07-27 and 2021-11-29. Data as of 2021-12-06. Weeks with latest 14 days of data shaded in gray due to associated reporting delay.
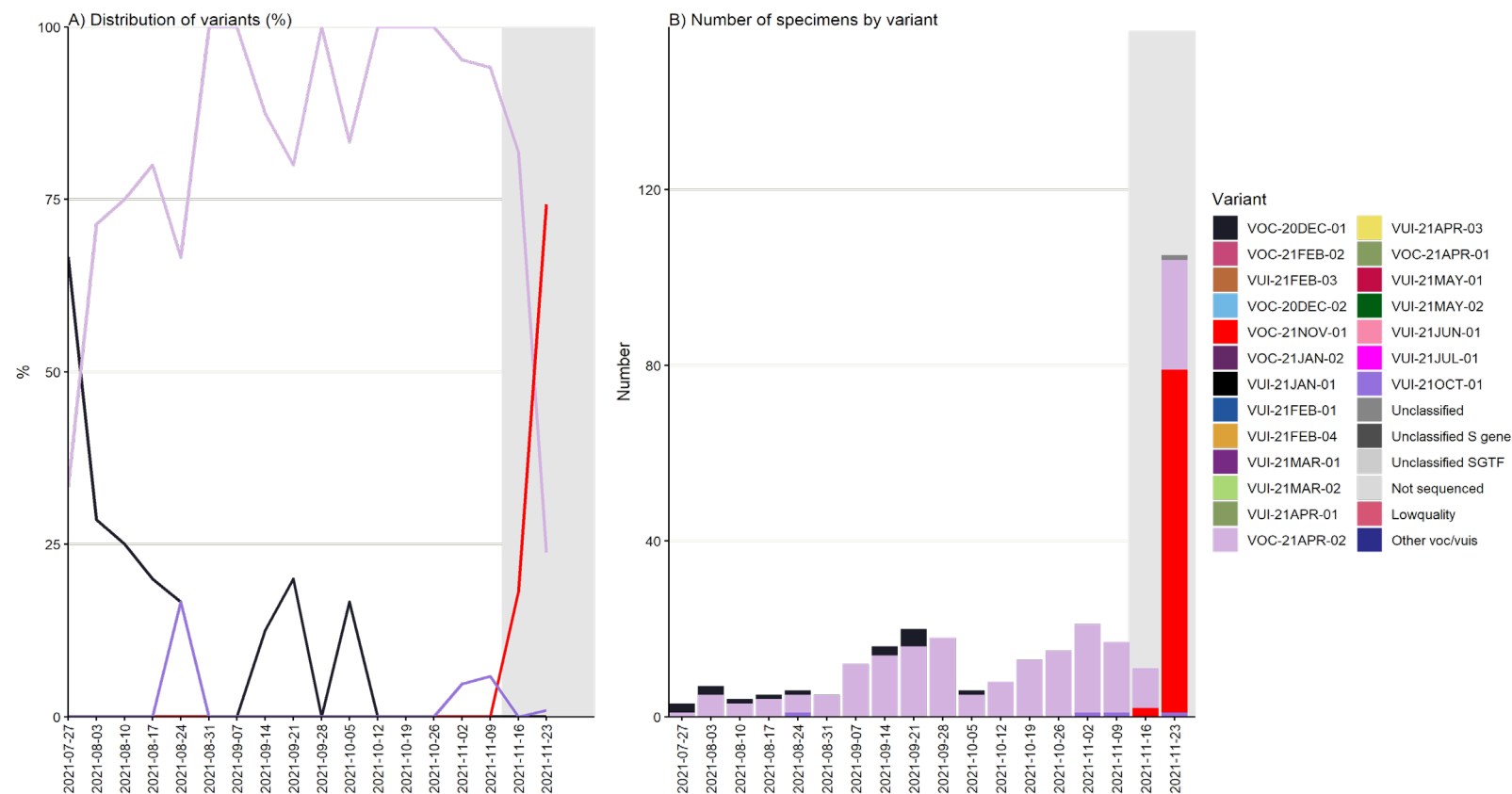
Source: SGSS and COG-UK sequencing data, restricted to sequenced positive S-gene positive tests from Newcastle, Alderley Park, Glasgow, and Milton Keynes Lighthouse Laboratories.
SGTF defined as positive SARS-CoV-2 test with non-detectable S gene target and CT values <=30 for N and ORF1ab.

Cycle threshold analysis

Figure 14 shows the Ct values in 10 day moving averages in cases, by PCR target gene. S gene target failure (SGTF) is a proxy for Omicron in (red), and all 3 PCR gene targets (S+) are a proxy for Delta (in green). Overall incidence per 100,000 population is also shown (dotted black line).

Increasing incidence of COVID-19 has been associated with declining Ct values at a population level, and infectivity and disease severity at an individual level.[1]

Nationally, the Ct values for cases with SGTF (proxy Omicron) decrease rapidly from the 30 November, from 30 to 23 on 6 December (Figure 14). In comparison, Ct values in S+ cases (proxy Delta) remain low, at around 20. In previous waves, declining CT values, suggests more individuals with acute infection and may be explained by rapid exponential growth of cases caused by the Omicron variant. Comparative analyses will be undertaken to better understand viral loads in Omicron cases.

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[1] Ct threshold values, a proxy for viral load in community SARS-CoV-2 cases, demonstrate wide variation across populations and over time | eLife (elifesciences.org) Understanding cycle threshold (Ct) in SARS-CoV-2 RT-PCR (publishing.service.gov.uk)

Figure 14. Cycle Threshold (Ct) values (10 day moving averages) in cases by PCR target gene (SGTF and S+) in England as of 7 December 2021
Supplementary data are not available for this figure.

England AVERAGE DAILY CT ANALYSIS - Positive test results
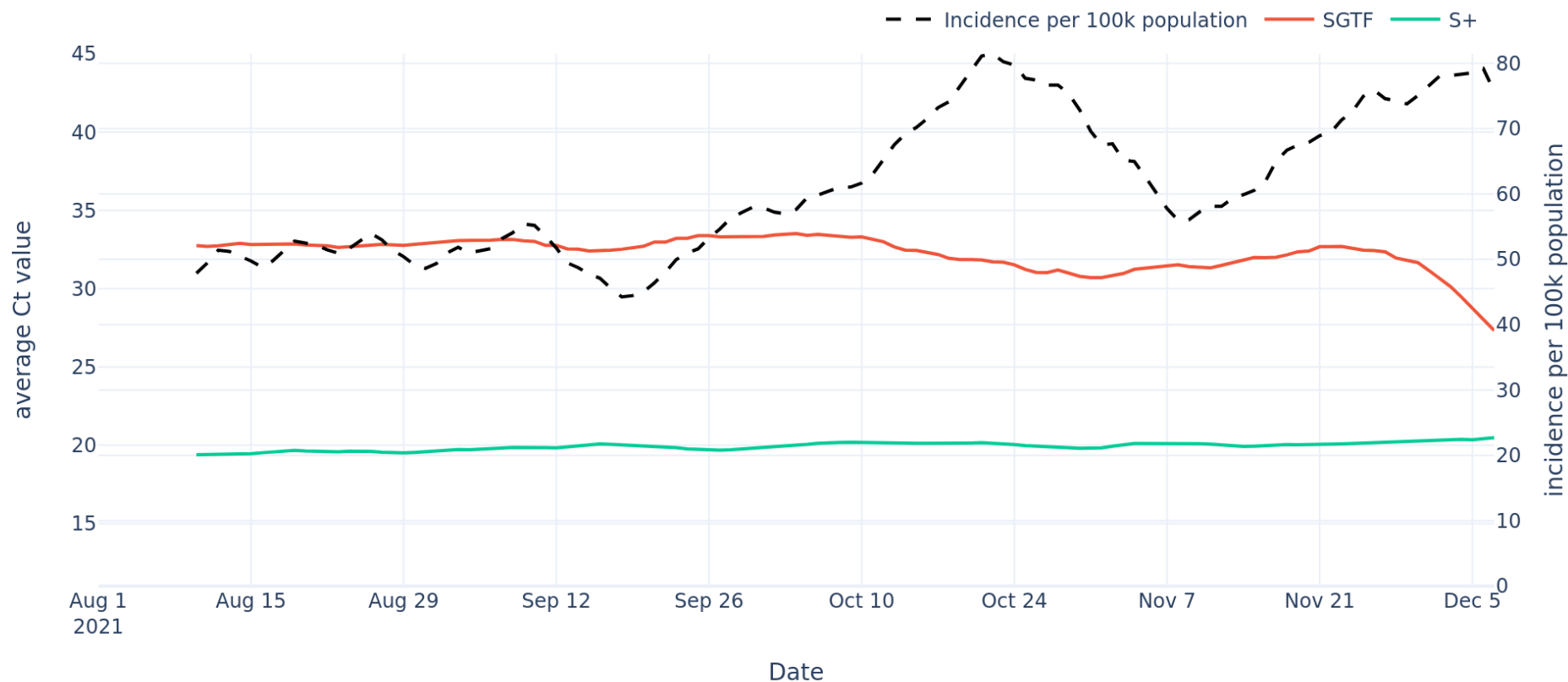
Source: Npex

2.3 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 5. Number of confirmed (sequencing) Omicron VOC-21Nov-01 (B.1.1.529) cases, by region of residence as of 6 December 2021

Region	Confirmed case number	Provisional case number	Total case number	Case proportion
East Midlands	19	6	25	9.6%
East of England	26	6	32	12.3%
London	49	57	106	40.8%
North East	0	4	4	1.5%
North West	7	8	15	5.8%
South East	26	28	54	20.8%
South West	0	12	12	4.6%
West Midlands	2	6	8	3.1%
Yorkshire and Humber	0	0	0	0.0%
Unknown region	2	2	4	1.5%
Total	131	129	260	-

Figure 15. Cases of Omicron VOC-21NOV-01 (B1.1.529) in England by region as of 6 December 2021
(Find accessible data used in this graph in underlying data)
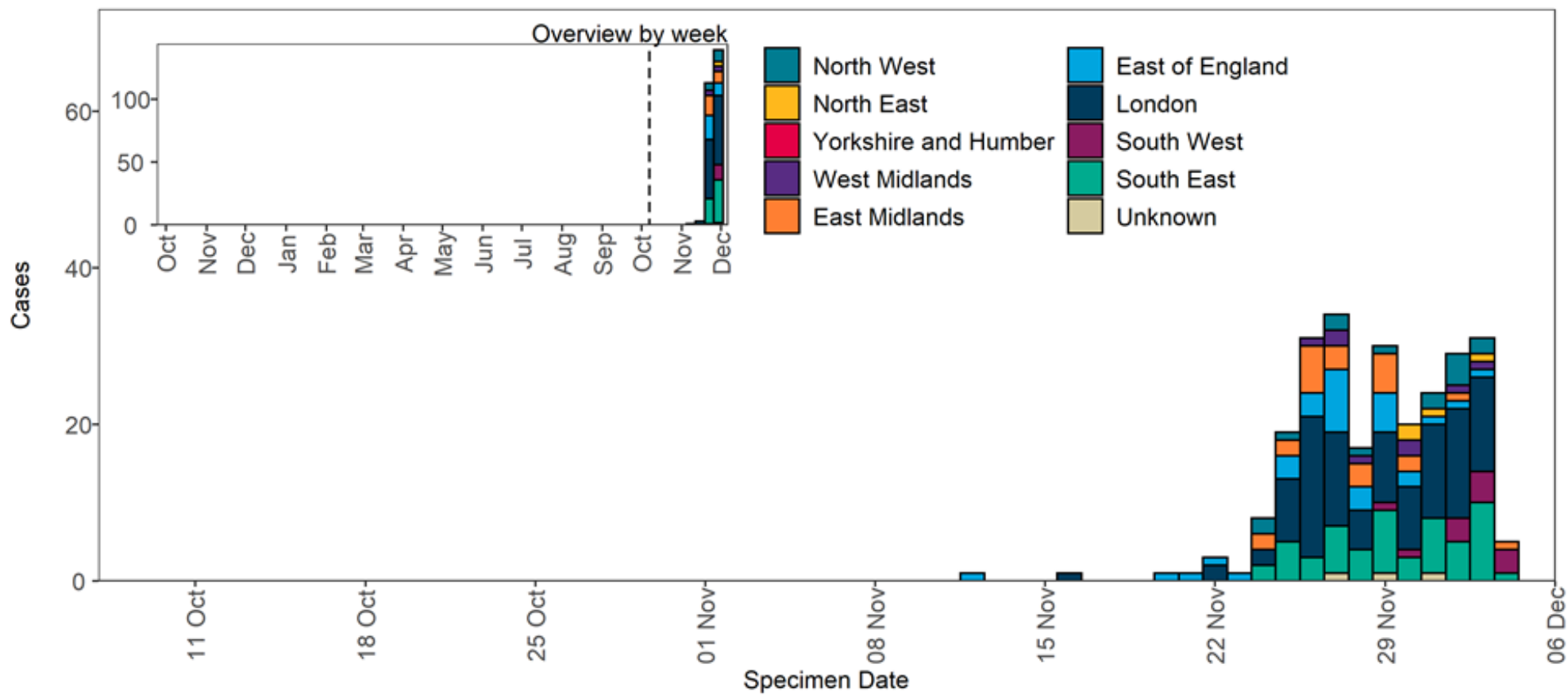
Figure 16. Cases of Omicron VOC-21NOV-01 (B1.1.529) in England by travel status as of 6 December 2021

(Find accessible data used in this graph in underlying data.)
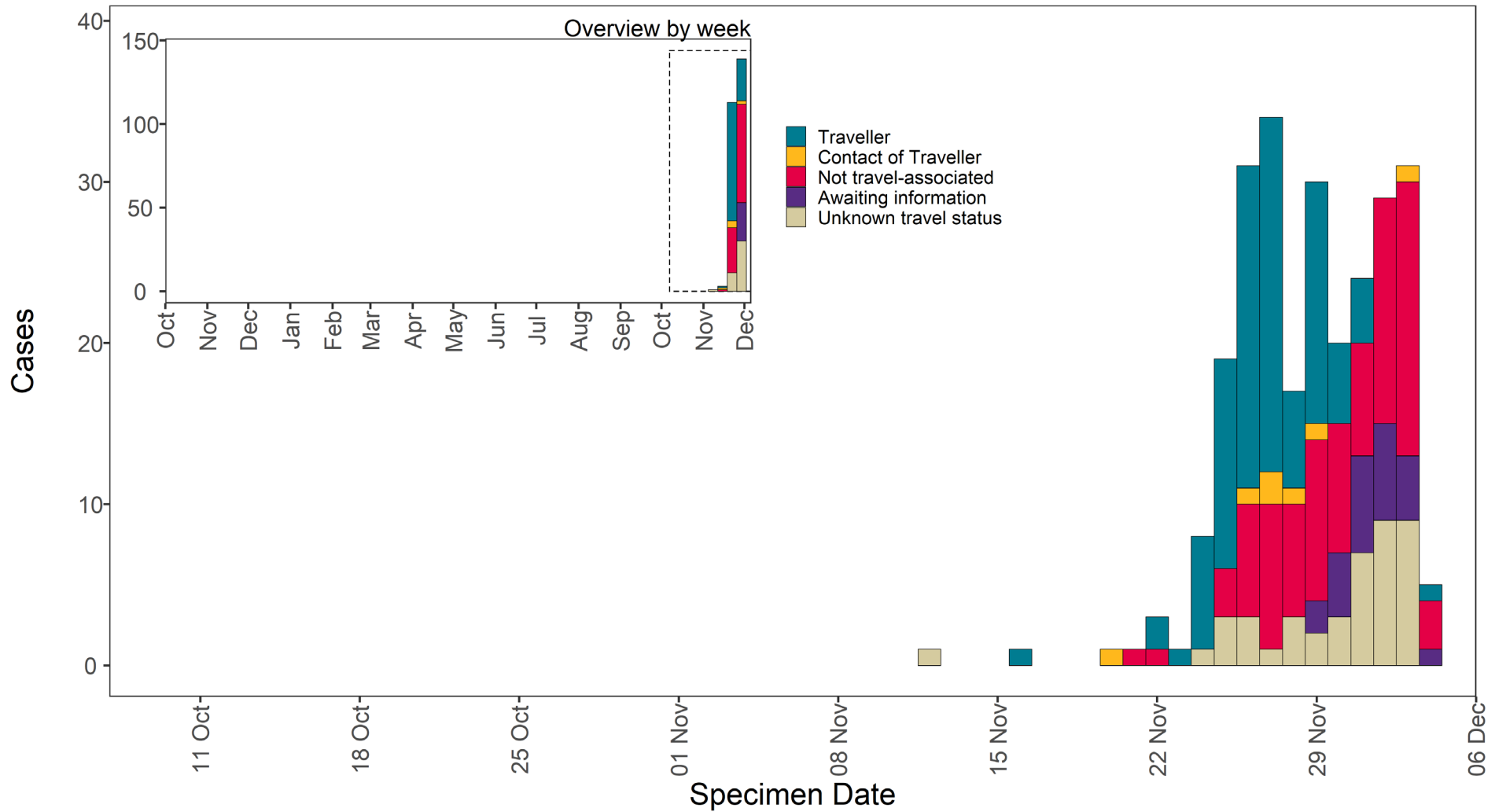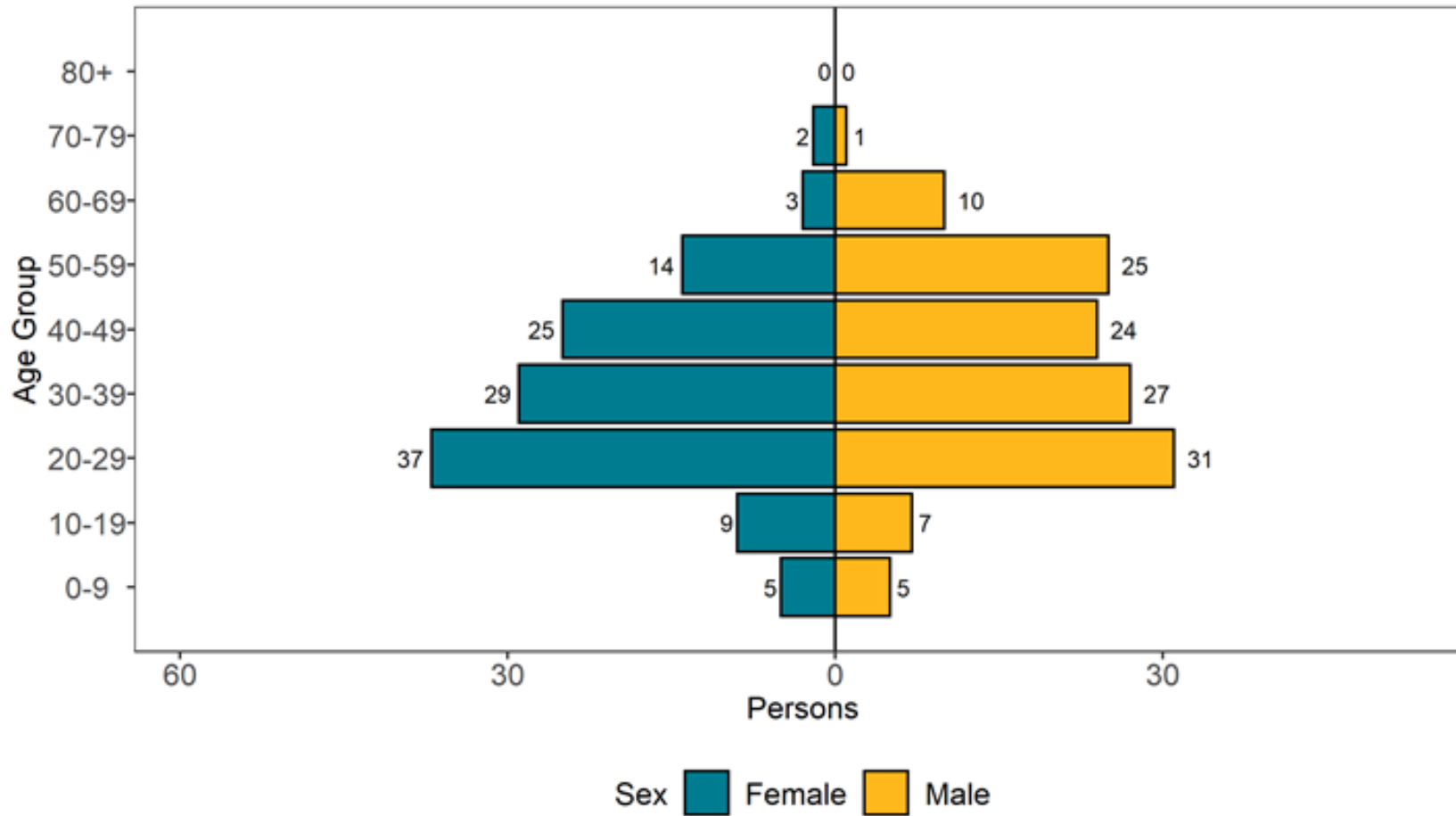
Figure 17. Cases of Omicron VOC-21NOV-01 (B1.1.529) in England by age and sex as of 6 December 2021
(Find accessible data used in this graph in underlying data)

6 cases excluded where sex or age not reported

Severity outcomes

To date, there are no cases of Omicron which are reported as having been hospitalised or died through routine reporting. As a result, it is not possible to compare the risk of hospitalisation or death with other variants. However, it should be noted that most of the cases have a specimen date that is very recent and that there is a lag between onset of infection and hospitalisation and death. Future updates will assess severe outcomes from Omicron cases against Delta cases from the same time period.

Information on attendance to emergency care is derived from the Emergency Care Data Set (ECDS) and Secondary Uses Service (SUS), provided by NHS Digital. These data only show whether a case has attended emergency care at an NHS hospital and was subsequently admitted as an inpatient. The data do not include cases who were directly admitted without first presenting to emergency care.

ECDS and SUS reporting is lagged, where NHS trusts routinely provide monthly data by the 21st of the following month. However, some trusts report daily data, and the linkage between COVID-19 cases and ECDS data are updated twice-weekly.

2.4 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 over 450 sites including sewage treatment works (STW) and local sewer networks. Sampling is undertaken multiple times per week. This sampling framework is estimated to cover approximately 70% of the English population. It is possible to look for mutations from 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. Wastewater is currently considered as supplementary data in variant monitoring and is unvalidated as an independent variant surveillance system.

Applying the definition described in Technical briefing 30 (3 December 2021), wastewater samples collected from sites across England up to 28 November have been analysed. There were Confirmed and Possible detections of Omicron in 5 samples collected between 26 and 28 November from 4 STW amongst 477 STW and sewerage network sites. Where there were known instances of transmission at the time of sampling, it has been reflected in the wastewater. Wastewater samples will continue to be sequenced and results reported to public health teams. Additional 71 STW have been identified to increase regional population coverage and to supplement TaqPath Laboratory coverage and are in the process of being bought online.

2.5 Validation of lateral flow devices

UKHSA have performed an initial laboratory validation of the current lateral flow devices for COVID-19 in current use by NHS Test and Trace. Preliminary data assess these devices as effective at detecting Omicron as Delta.

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 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.

Variant Technical Group

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Acknowledgements

About the UK Health Security Agency

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

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