



UK Health
Security
Agency

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

Technical briefing 34

14 January 2022

This report provides an update on previous [briefings](#) up to 31 December 2021

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Summary

This report has been published to share the detailed variant surveillance analyses which contribute to the variant risk assessments and designation of new 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.

[SARS-CoV-2 Routine variant data update](#) 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 10 January 2022 to allow time for analyses. In summary:

Genomic diversity

There is as yet little diversity within the Omicron BA.1 clade. Two acquired mutations in spike have been noted in the UK data set, A701V and R346K. The growth rate of Omicron with these mutations is not greater than the rest of the Omicron clade.

Omicron also contains the clade BA.2. This is being separately monitored and assessed from a technical perspective and is included in overall Omicron case counts.

Severity

There is no update on the overall severity analysis this week. A rise in admissions in children testing positive for coronavirus (COVID-19) has been noted and summary information is included on this. Analysis is underway to understand if this relates to Omicron and to characterise the admissions.

Symptoms

In NHS Test and Trace data, loss of smell or taste was reported less often by Omicron cases than Delta cases (53% of Omicron cases, 34% of Delta cases, aOR: 0.21, 95% CI: 0.20-0.21). Sore throat was reported more often by Omicron cases (13% of Omicron cases, 34% of Delta cases, aOR: 1.80, 95% CI: 1.80-1.90): note, however, that another recent study observed increase in sore throat also being reported amongst those who test negative for SARS-CoV-2 so this may be an incidental finding.

Vaccine effectiveness

In updated population data analysis, vaccine protection against mild disease has largely disappeared by 20 weeks after vaccination with a 2-dose primary course of vaccination. After a booster dose, protection initially increases to around 65 to 70% but drops to 45 to 50% from 10+ weeks. It is therefore likely that current vaccines offer limited long-term protection against infection or transmission. Protection against severe disease is much higher – after a booster dose vaccine effectiveness against hospitalisation is estimated at 92% and remains high at 83% 10+ weeks after the booster dose. This data will also appear in the weekly [COVID-19 vaccine surveillance report](#) published routinely on a Thursday.

SIREN study

In the SIREN study, a large cohort of healthcare workers are tested regularly by polymerase chain reaction (PCR) to detect asymptomatic infection in addition to normal testing practices for symptomatic infection. Updated analysis shows the additional incremental benefit from each vaccine exposure including for boosters, even in those who have had prior infection.

Updated risk assessment

An updated [risk assessment](#) for Omicron VOC-21NOV-01 (B.1.1.529) has been published.

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](#).

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 [GitHub](#).

[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.

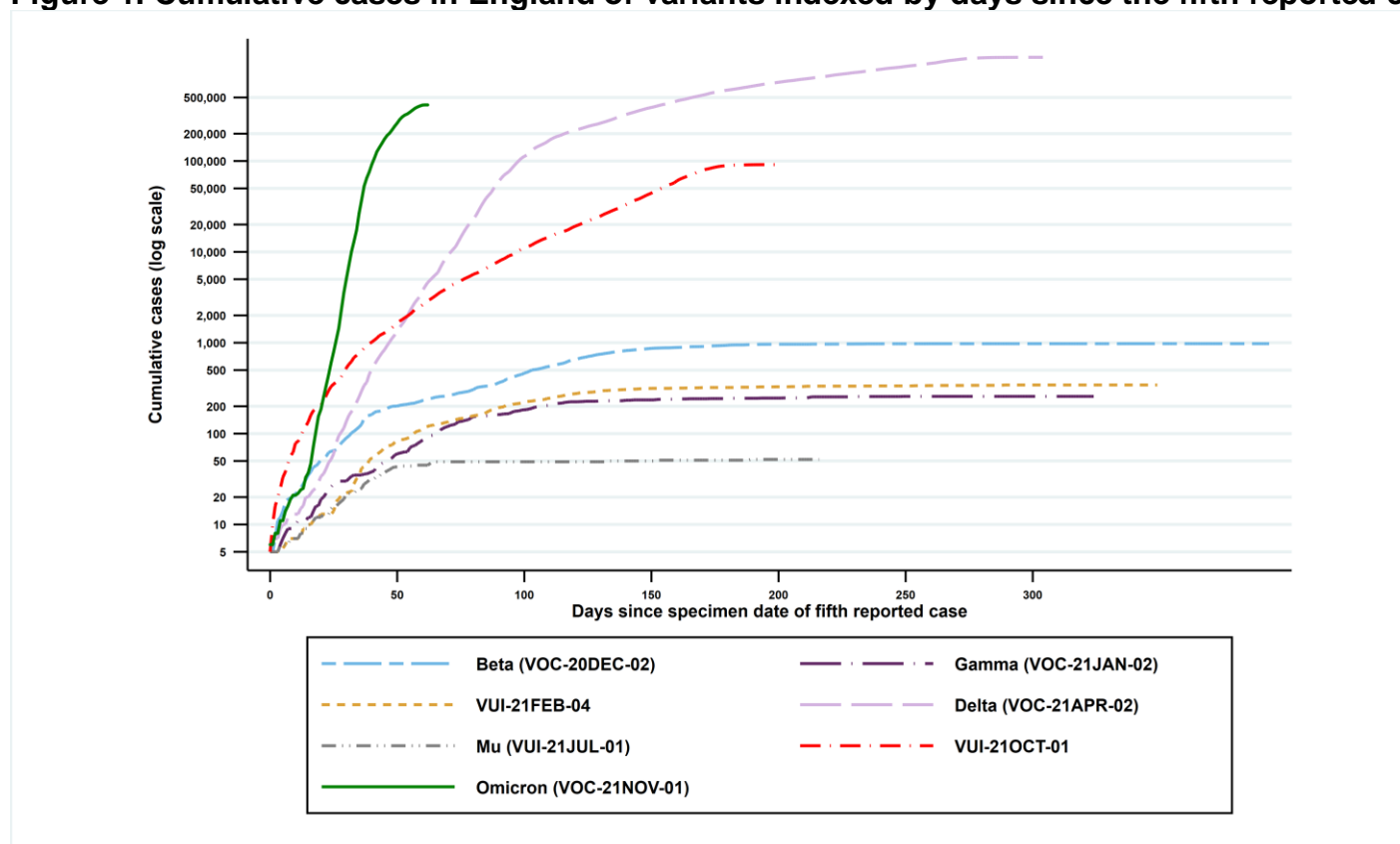
Part 1. Surveillance overview

1.1 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 9 January 2022



(Find accessible data used in this graph in [underlying data](#).)

1.2 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 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. The assay was further updated on 15 December 2021 to allow improved identification of Omicron variant, with the introduction of the Q493R mutation. 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 [Figure 2](#) and [Figure 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 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 Ct values ≤ 30) but the S-gene is not. SGTF patterns can be used to assess the spread of Omicron lineage BA.1. The number of COVID-19 cases with S-gene positive/SGTF by day, among those tested in TaqPath labs is shown in Figure 4. The Omicron lineage BA.2 does not contain the spike deletion and therefore is S-gene positive (SGTP). By 1 January 2022, BA.2 accounted for 5% of SGTP and this proportion is increasing. Therefore, SGTF is no longer sufficient to assess the spread of Omicron as a whole.

Figure 2. Variant prevalence for all England available genotyped cases from 1 February 2021 as of 10 January 2022
 (Find accessible data used in this graph in [underlying data.](#))

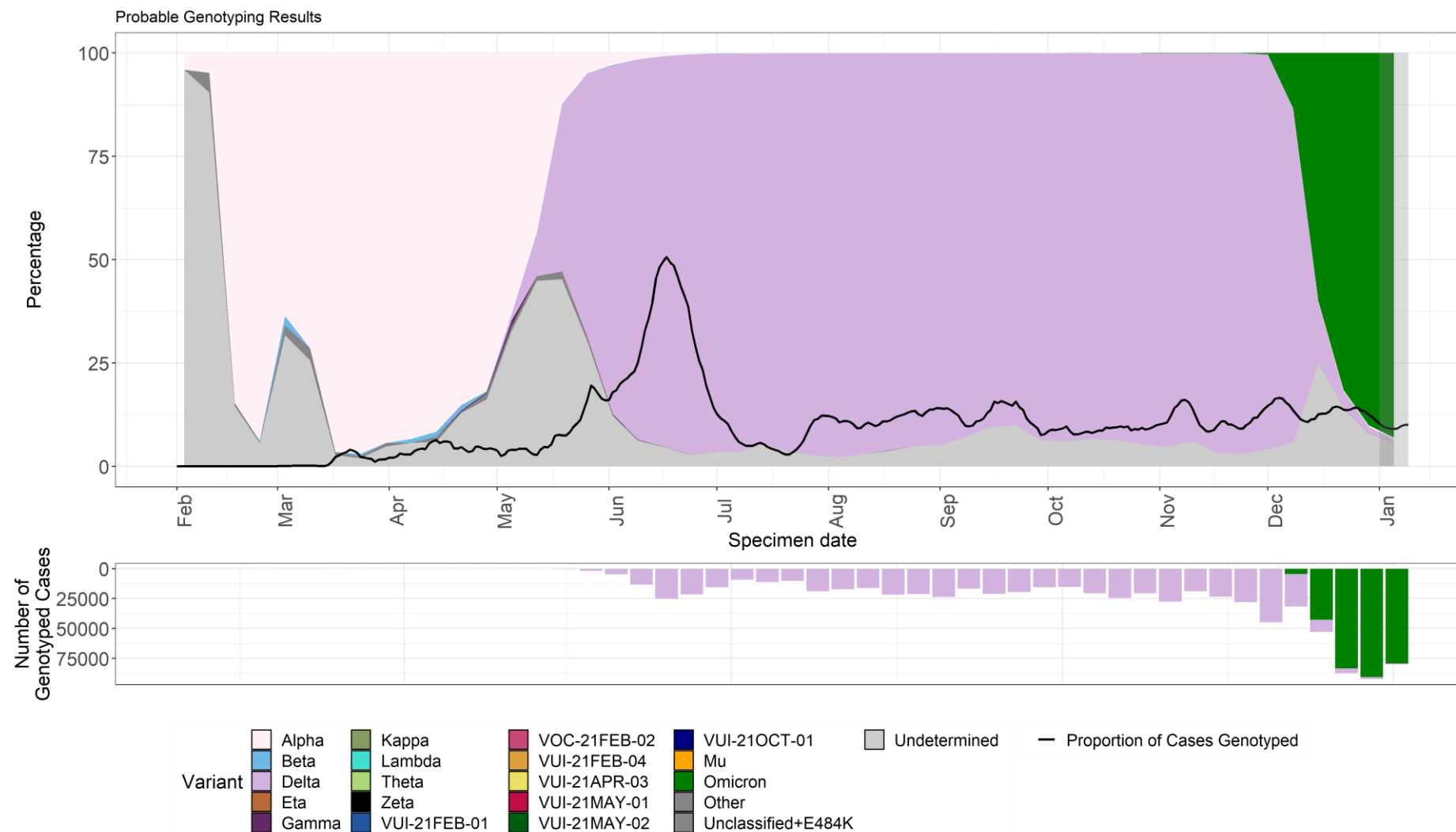


Figure 3. Prevalence of variants over time: all sequenced cases in England, split by travel status as of 10 January 2022 (excluding 1,001 cases where the travel status or specimen date were unknown)

(Find accessible data used in this graph in [underlying data](#).)

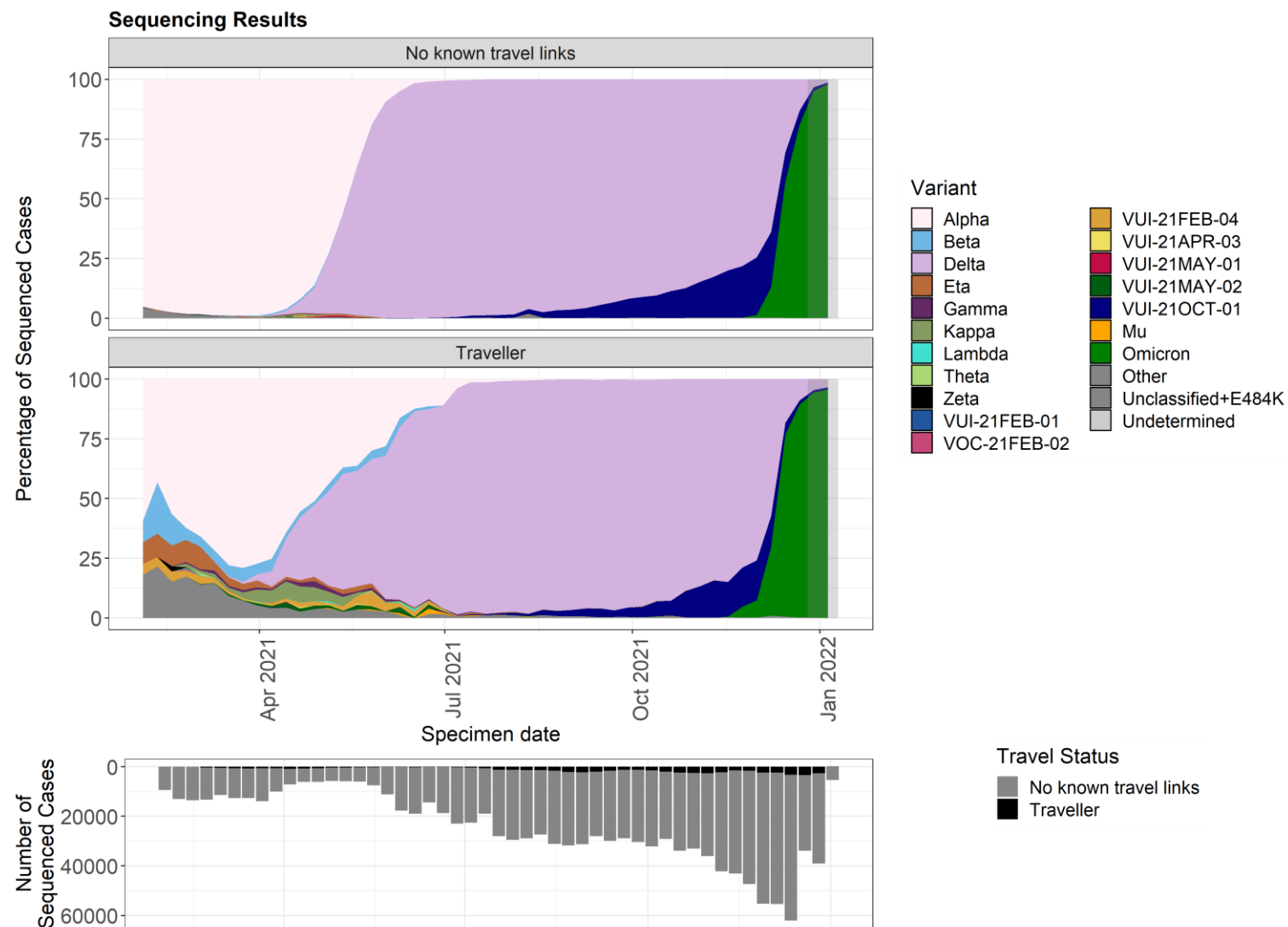
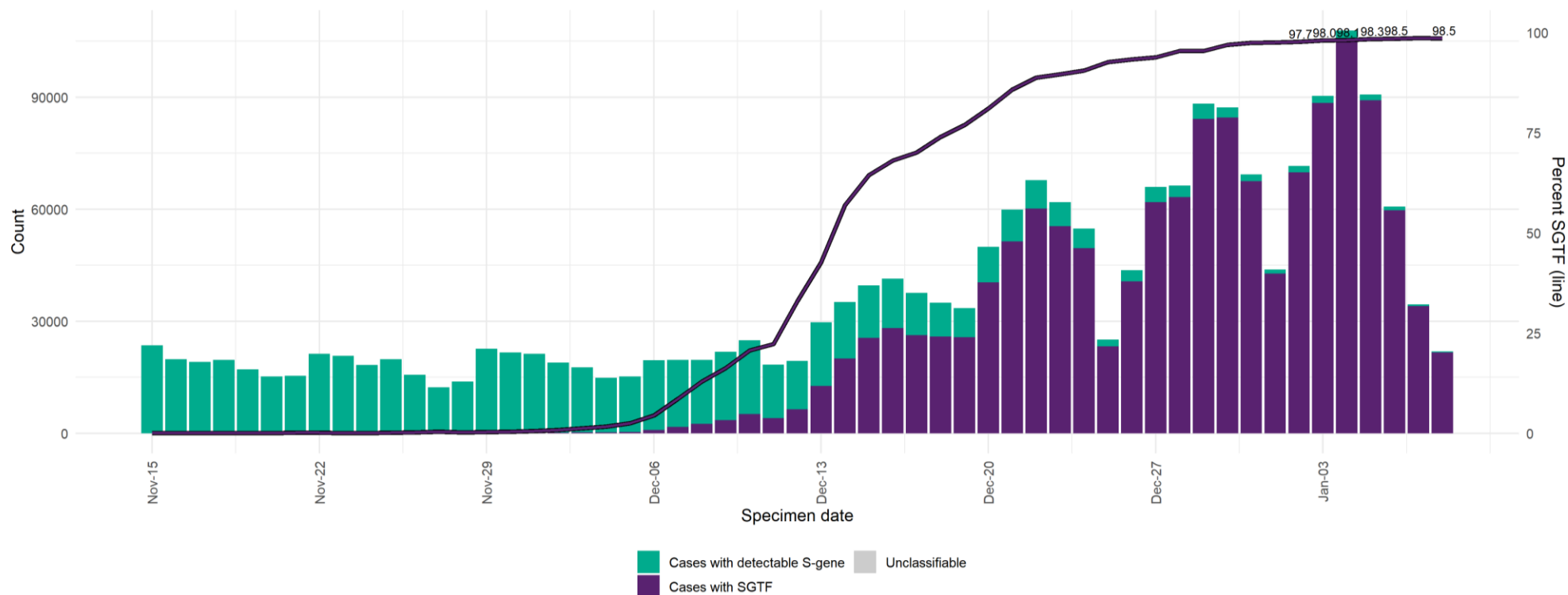


Figure 4. Number of COVID-19 cases with S-gene positive/SGTF by day, among those tested in TaqPath labs as of 10 January 2022 (95% confidence intervals indicated by grey shading. Percentages for most recent 7 days shown)

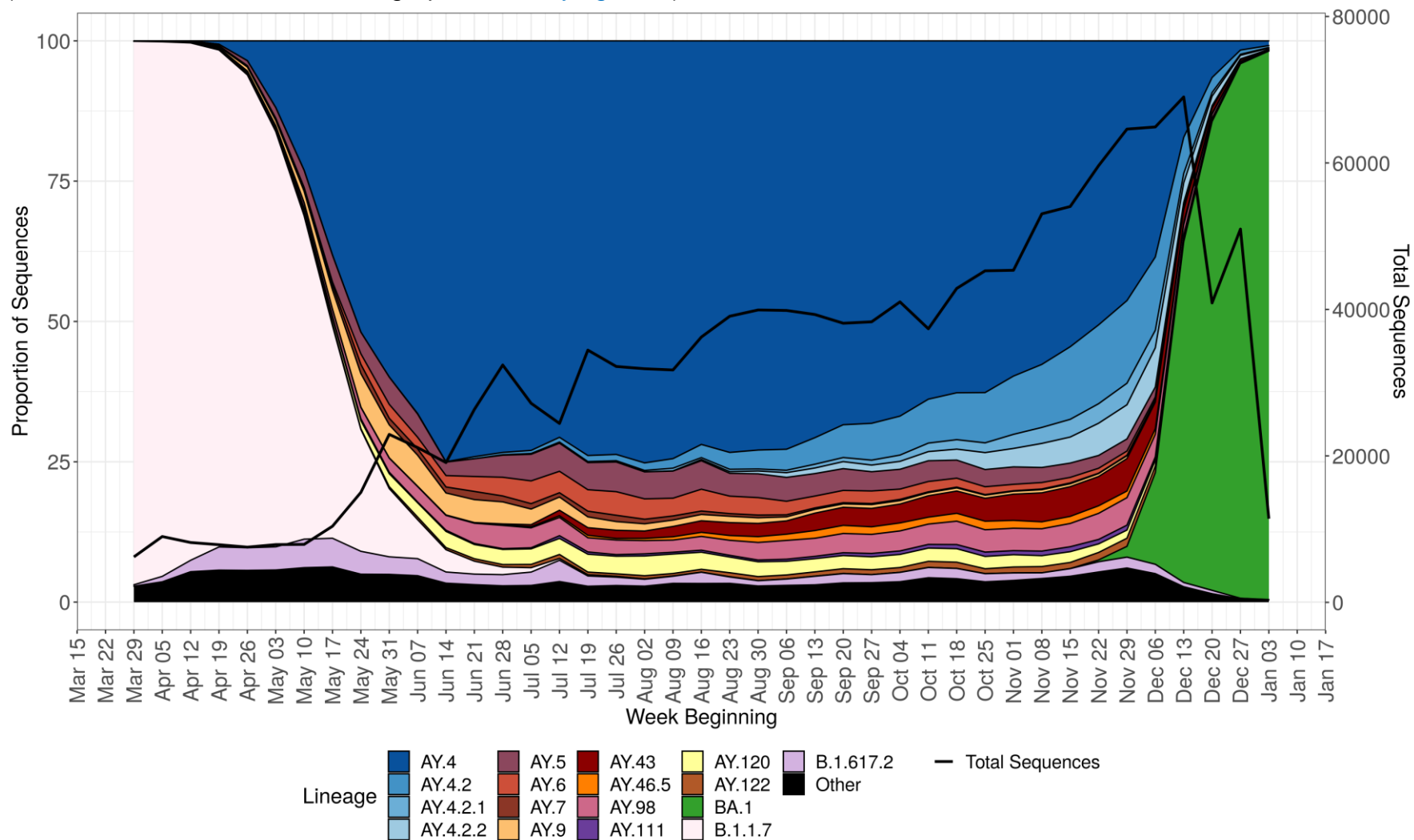
(Find accessible data used in this graph in [underlying data.](#))



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 in UK with sequence data from 1 April 2021 to 11 January 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 [underlying data](#).)



Part 2. Enhanced analyses of 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.

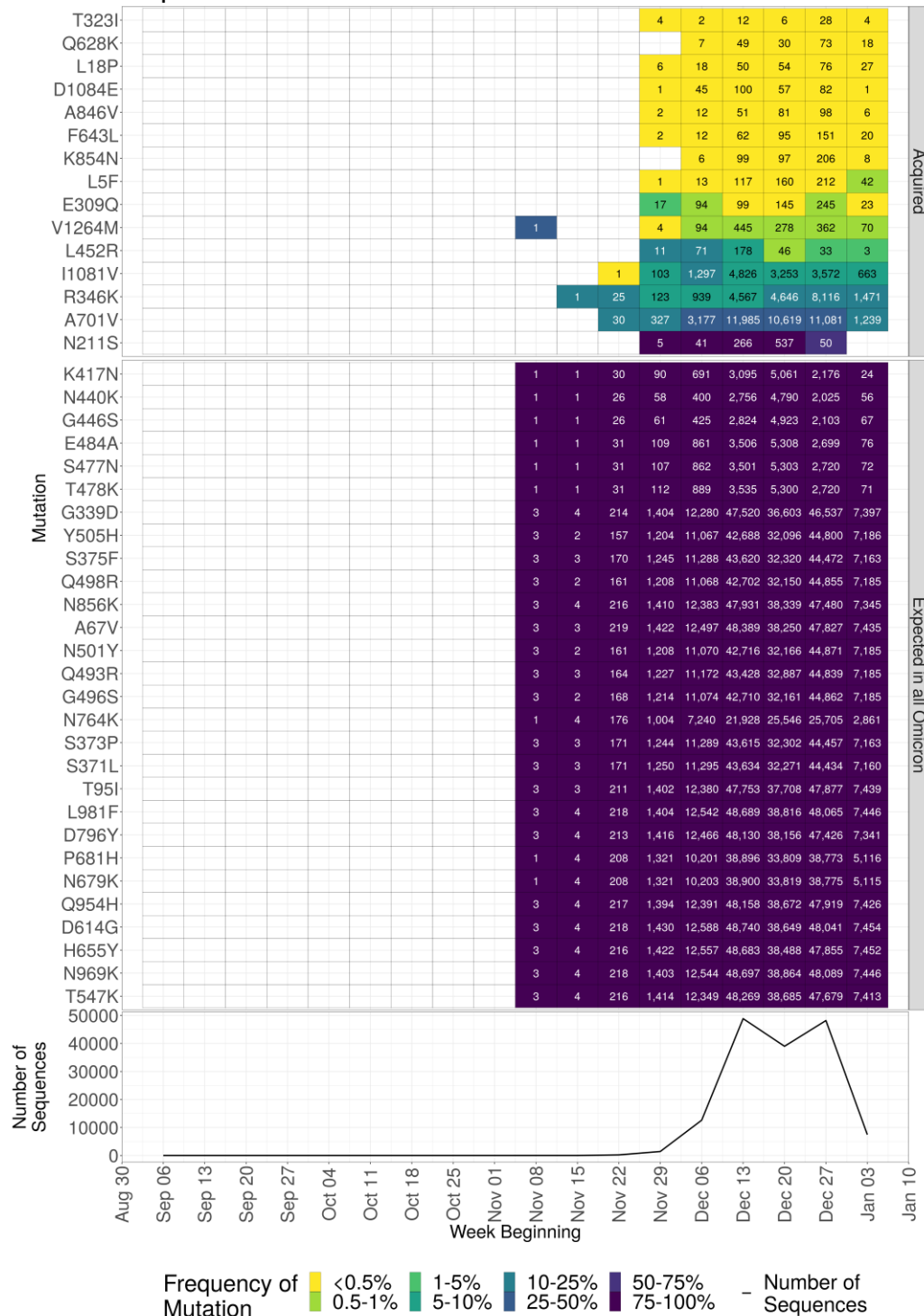
2.1 Genomic diversity

Spike mutations are monitored within BA.1 using 4 criteria (Table 1). A mutation is investigated further if it meets more than one of these criteria and is present in at least 10 sequences. Fifteen additional mutations have been observed in BA.1 sequences according to the criteria in Table 2 (Figure 6). However, L452R is observed in sequences that are suspected to have a low level of contamination. This Delta mutation is observed because amplicon 76 of the ARTIC V4 primers is not amplified in Omicron genomes due to mutations across the primer site. Therefore, the expected Omicron mutations are not observed in these sequences, and L452R is present in contaminating Delta reads. The mutation N211S is an alignment artifact caused by the deletion at this position in Spike. The deletion is also the reason that N211S appears to be such a high proportion, despite being a low number of total sequences, as the amino acid at position 211 cannot be called in most Omicron genomes therefore reducing the total number of sequences used to calculate the proportion.

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.1 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 9 January 2022. Nine sequences were excluded due to metadata issues. 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 Omicron 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.



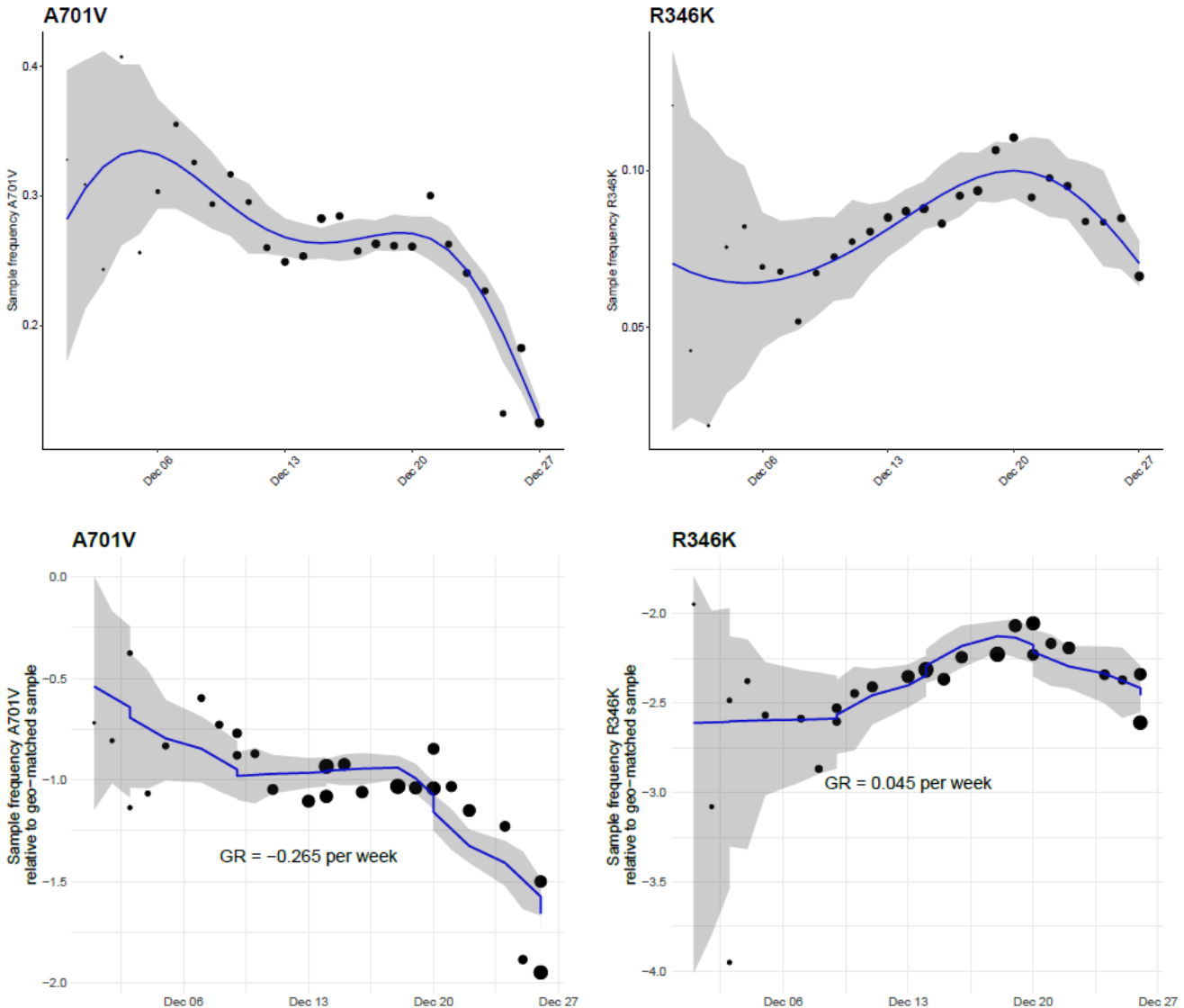
Growth rates for mutations occurring on Omicron

As Omicron the growth of variants with each mutation, relative to variants that do not have each mutation, is estimated. The growth rate is estimated by logistic regression of the number of variants with the mutation on the time of sample collection. Sample inclusion criteria are: a non-traveller as determined by matching each case against passenger locator forms and managed quarantine service test codes; collected from Pillar 2 testing. A growth rate of 0 would indicate parity with variants that do not have the mutation.

Data sampled up to 31 December 2021 were included, and the following Spike mutations were evaluated: E309K, R346K, A701V, D1048E, I1081V, V1264M. None of these mutations have increased significantly since the introduction of Omicron. The relative proportions through time and the growth rate of the 2 most frequent mutations R346K (n=5,415) and A701 (n=15,438), are displayed in Figure 7.

Figure 7. Sample frequency and growth rates for spike mutations A701V and R346K, as compared to Omicron sequences that do not have each mutation.

There is no supplementary data for this figure.



BA.2

This variant is a sub-lineage of Omicron (VOC-21NOV-01) that was designated by Pangolin on 6 December 2021. This sub-lineage does not have the spike gene deletion at 69-70 that causes SGTF. 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 the 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 Technical Briefing [31](#) (Figures 9 and 10).

Epidemiology

As of 10 January 2022, 53 sequences of BA.2 have been identified in the UK. BA.2 accounts for an increasing proportion of S-gene positive (SGTP) tests. Therefore, caution is required when

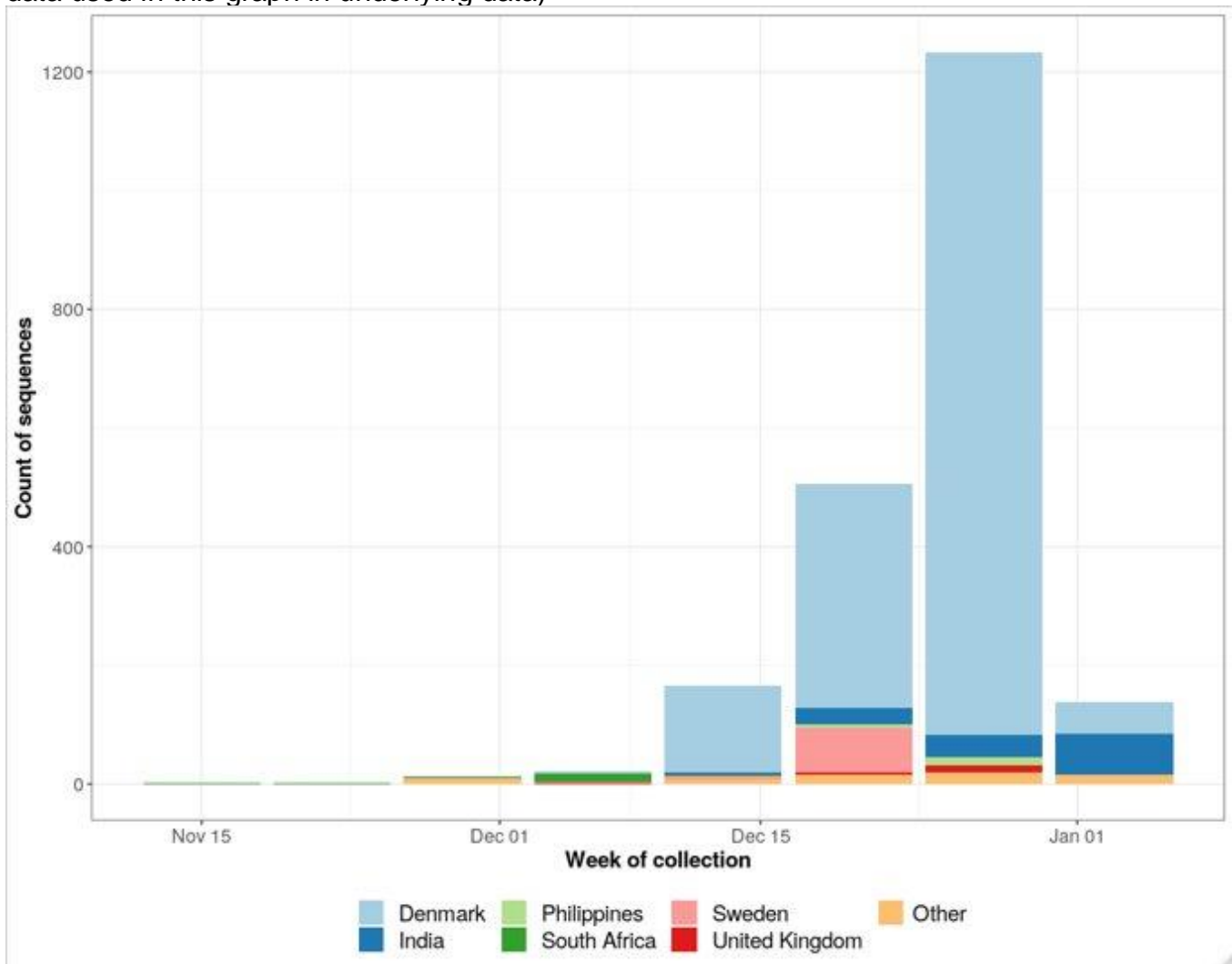
interpreting comparative analyses which use S-gene target results as the only determinant of Omicron and Delta.

International epidemiology

As of 10 January 2022, 2,093 sequences on GISAID meet the Omicron BA.2 Pangolin definition from 22 countries including the UK (Figure 8). Figure 8 shows an increasing number of BA.2 sequences in recent weeks, many from Denmark. The most recent week will be affected by data lags.

Figure 8. Count of Omicron BA.2 classified sequences by week of collection uploaded to GISAID by week as of 10 January 2022

Countries with 10 or fewer sequences have been grouped together as 'Other'. (Find accessible data used in this graph in underlying data)



2.2 Severity and hospitalisation

Descriptive epidemiology of severe outcomes of Omicron in England

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

Analyses on the risk of hospitalisation were reported in [Technical Briefing 33](#). These analyses indicated that relative to Delta, the risk of hospitalisation following infection with Omicron is lower in adults. Studies to further investigate the severity of Omicron infection compared to Delta are underway.

Paediatric infections and admissions

Hospital admission data is reported by NHS England and Improvement and include people admitted to hospital who either tested positive for COVID-19 during their admission or in the previous 14 days before their admission.

The number of paediatric admissions with COVID-19 infection began to rise from 26 December 2021, from an average of 40 admissions per day to 120 per day, a 3-fold rise in 2 weeks. Further analysis by age group shows that the rise is most rapid among children under 5 years, and highest in infants aged under 1 year (Figure 9). This data is for all COVID-19 infections including all variants, but it should be noted that Omicron represented over 90% of sequenced samples in the UK from end November 2021 (Figure 5). The top 3 complaints on hospital attendance records for children under 5 remain consistent with respiratory infection.

A clinical case review of a small number of Omicron admissions in infants found those admitted were not severely unwell. The Royal College of Paediatrics and Child Health (RCPCH) has issued a [statement](#) to confirm that paediatricians are not reporting Omicron to be a more serious or severe disease in children and young people in the UK.

Figure 9. Rolling 7-day average number of children and young people admitted to hospital with COVID-19, 7 January 2021 to 9 January 2022



(Source: [NHS England and Improvement/GOV.UK Dashboard](#))

2.4 Symptom comparison of Omicron and Delta cases in England

This section contains an analysis exploring the difference in symptoms reported to NHS Test and Trace of sequenced or genotyped confirmed Omicron and Delta cases for the period 1 December to 28 December 2021.

Symptomatic cases represented 90.2% of all Omicron cases and 85.6% of all Delta cases who completed contact tracing. It should be noted that this data set is affected by testing behaviours and contact tracing engagement and should not be used to assess the asymptomatic fraction.

Analysis was based on 174,755 Omicron and 87,930 Delta cases reporting symptoms with onset in this period that had completed contract tracing and reported symptoms, and had provided data on their age, sex and region.

Confirmed cases were asked if they displayed any of the following symptoms: fever, cough, shortness of breath, fatigue, altered consciousness, muscle or joint pain, headache, loss of smell or taste, sore throat, runny nose, sneezing, rash, red or irritated eye, loss of appetite, nausea or vomiting, or diarrhoea. The median number of reported symptoms per case in this cohort was equal between variants (Median: 4.0, interquartile range (IQR): 2.0 – 6.0). Time taken between symptom onset and completing contact tracing was slightly longer for Omicron cases (Median: 3.84 days, IQR: 2.23-5.11) compared to Delta (Median: 3.1 days, IQR: 2.03-4.92) cases.

Odds ratio analysis compared the odds of a specific symptom being reported by an Omicron or a Delta case whilst adjusted odds ratio analysis compared the odds of a specific symptom being reported by an Omicron or a Delta case whilst adjusting for age group, sex, ethnicity, self-reported vaccination status (2 or more doses, one or no dose, or missing data), geographical region of residence, and the week in which symptoms began.

Figure 10 shows a forest plot of adjusted odds ratios of symptoms being reported by Omicron cases compared to Delta cases. Sore throat was more likely to be reported by cases with Omicron (53% of Omicron cases, 34% of Delta cases, odds ratio 1.8, 95% CI: 1.8-1.9). On the other hand, loss of smell and taste was found to be less common among Omicron compared to Delta cases (13% of Omicron cases, 34% of Delta cases, odds ratio 0.21, 95% CI: 0.20-0.21).

A [recent study led by Oxford University and the Office for National Statistics](#) studied symptoms reported by PCR-positive and PCR-negative individuals using data from the UK COVID-19 Infection Survey. As Omicron cases increased as a proportion of SARS-CoV-2 infections during December 2021, the study found increased reports of sore throat and a marked reduction in reporting of loss of smell and taste in PCR-positives. This study also found that sore throat became more commonly reported in symptomatic PCR-negative cases during this period,

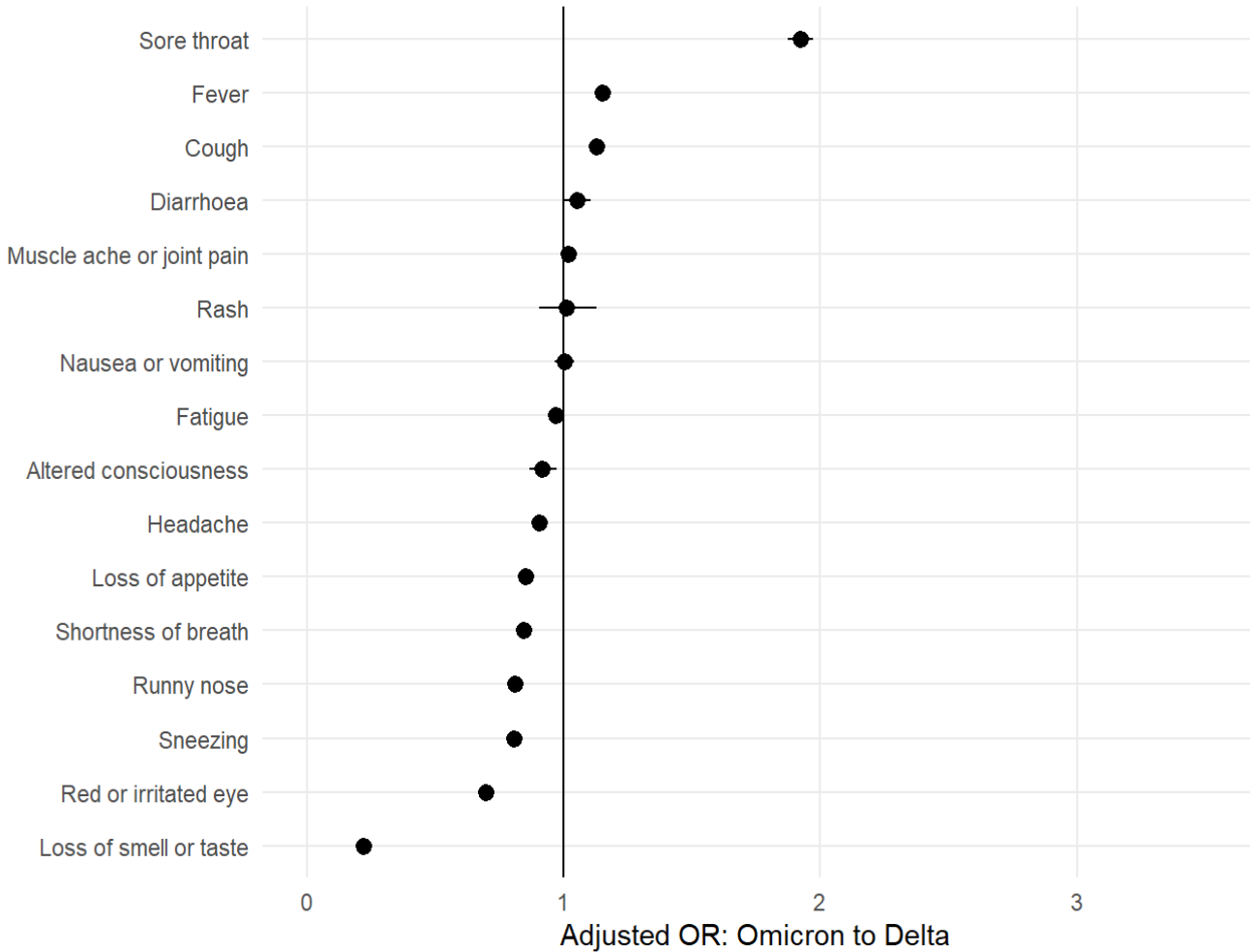
suggesting that sore throat may not be a specific predictor of SARS-CoV-2 infection with Omicron.

Important limitations of this analysis are that:

- negative COVID-19 test results were not included in this data set, and therefore differences between symptoms in people testing negative and positive could not be compared; no conclusions can be drawn about the specificity of these symptoms as indicators of SARS-CoV-2 infection
- symptom data was collected at the time of contact tracing only (usually 3 to 4 days post symptom onset), and therefore additional symptoms presenting at a later timepoint are not captured
- any changes in testing behaviour during the month of December may also affect the results
- vaccination data used for adjustment is self-reported to NHS Test and Trace and does not include information on booster doses

Figure 10. Forest plot of adjusted* odds ratios of specific symptoms reported amongst Omicron vs Delta cases

Cases with symptom onset 1 December to 28 December 2021, transferred to NHS Test and Trace by 31 December 2021. Variant data as of 3 January 2022 and contact tracing data as of 11 January 2022.



* Odds ratios adjusted for age group, sex, ethnicity, self-reported vaccination status (2 or more doses, one or no dose, or missing data), geographical region of residence, and the week in which symptoms began

Note: Trends from crude analysis may differ from those in adjusted analysis due to differences in demographic and other characteristics between cases with each of the variants.

2.5 Vaccine effectiveness

A test negative case control design was used to estimate vaccine effectiveness (VE) 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 tested in Pillar 2 (community testing) between 27 November 2021 and 6 January 2022 were included in the analysis.

Cases were defined as the Omicron variant or Delta variant based on whole genome sequencing, genotyping 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. Vaccine effectiveness was estimated by period after dose 2 and dose 3. Results are presented for 18+ year olds.

Pillar 2 symptomatic confirmed cases were linked to the Emergency Care Data Set (ECDS) to identify admissions via emergency care 0 to 14 days after the positive test (excluding admissions due to injuries). Cox survival analysis was then used to estimate the risk of hospital admission by vaccination status. Due to small numbers all vaccine brands are considered together. Adjustments were made for age, gender, previous positive test, region, ethnicity, travel history, clinically extremely vulnerable status, risk group status and period. To estimate vaccine effectiveness against hospitalisation the odds ratios (OR) for symptomatic disease were multiplied by the hazards ratios (HR) for hospitalisation among symptomatic cases:

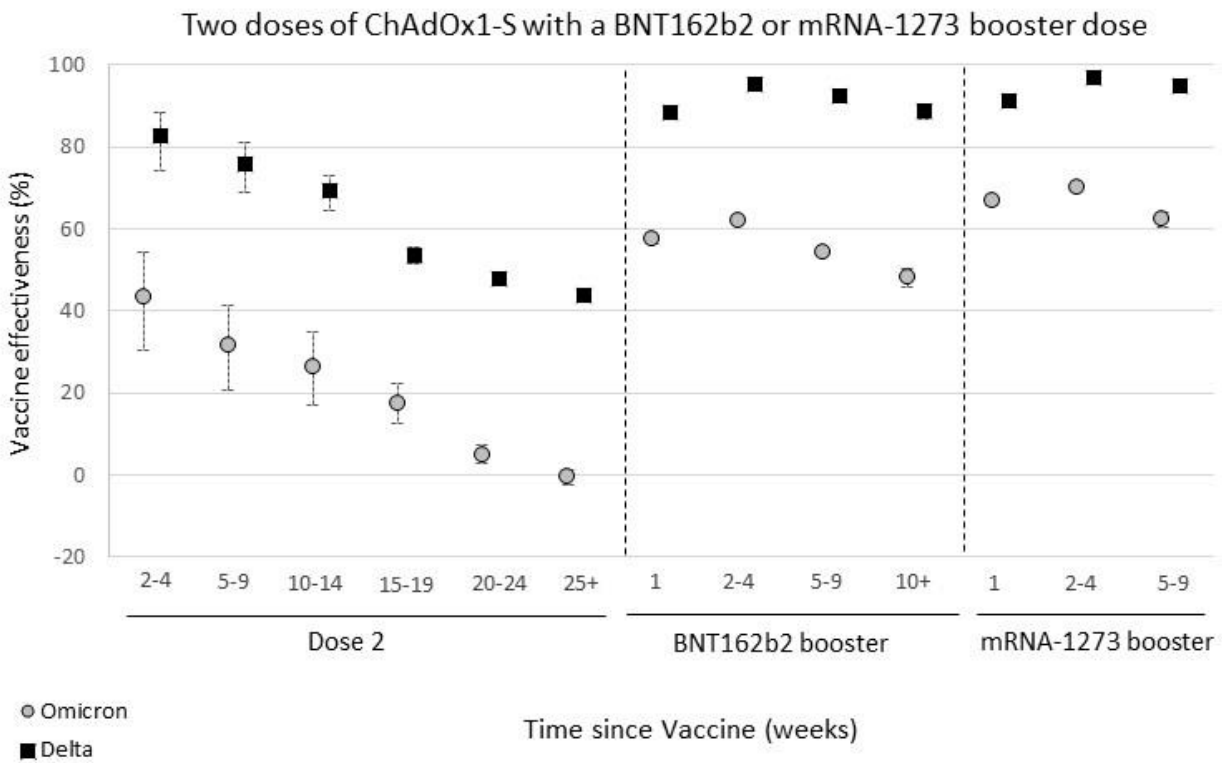
$$VE_{\text{hospitalisation}} = 1 - (OR_{\text{symptomatic disease}} \times HR_{\text{hospitalisation}})$$

The symptomatic disease test negative case control analysis included 236,023 Delta cases and 760,647 Omicron cases. Vaccine effectiveness against symptomatic disease by period after dose 2 and dose 3 is shown in Figure 11 for those who received a primary course of the AstraZeneca vaccine (Figure 11a), Pfizer (Figure 11b) or Moderna (Figure 11c). Effectiveness of booster doses of Pfizer and Moderna are shown. In all periods, effectiveness was lower for Omicron compared to Delta. Among those who had received 2 doses of AstraZeneca, effectiveness dropped from 45 to 50% to almost no effect against Omicron from 20 weeks after the second dose. Among those who had received 2 doses of Pfizer or Moderna effectiveness dropped from around 65 to 70% down to around 10% by 20 weeks after the 2nd dose. Two to 4 weeks after a booster dose vaccine effectiveness ranged from around 65 to 75%, dropping to 55 to 65% at 5 to 9 weeks and 45 to 50% from 10+ weeks after the booster.

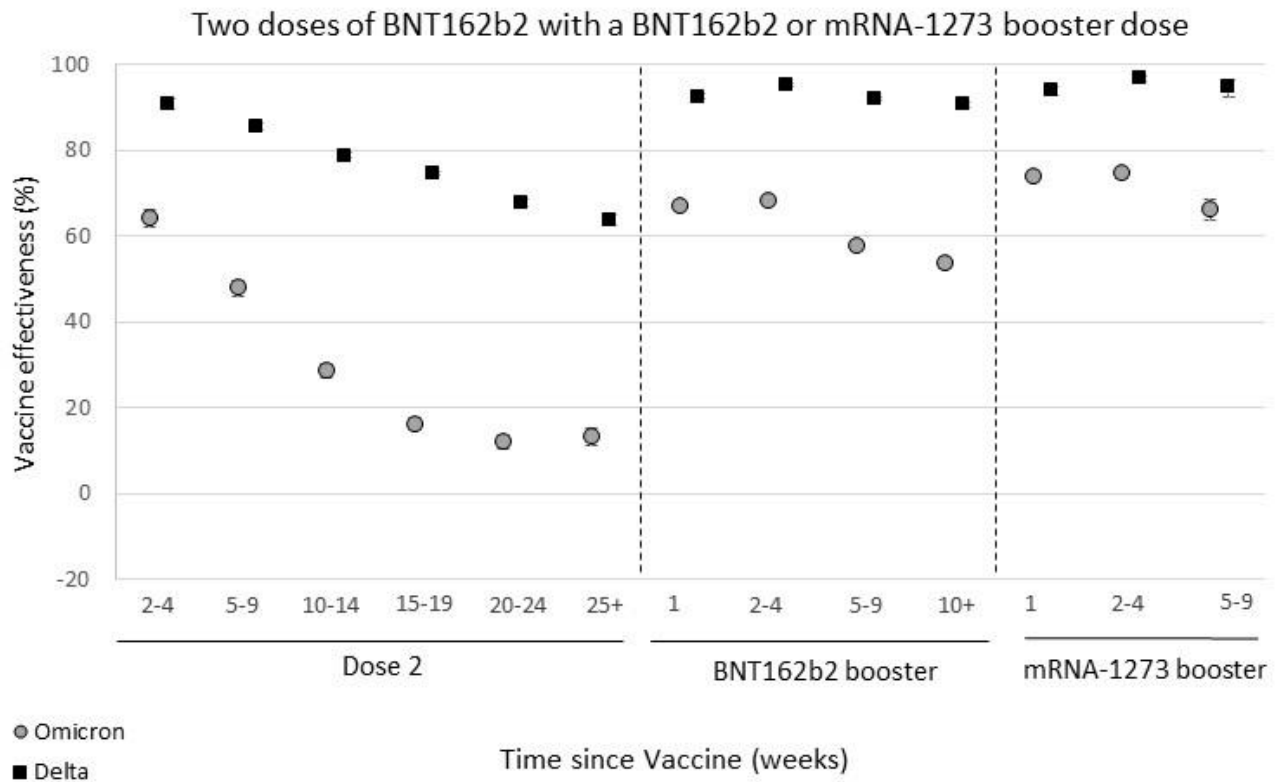
Figure 11. Vaccine effectiveness against symptomatic diseases by period after dose 1 and dose 2 for Delta (black squares) and Omicron (grey circles) for (a) recipients of 2 doses of AstraZeneca (ChAdOx1-S) vaccine as the primary course and Pfizer (BNT162b2) or Moderna (mRNA-1273) as a booster; (b) recipients of 2 doses of Pfizer vaccine as the primary course and Pfizer or Moderna as a booster, and (c) recipients of 2 doses of Moderna as a primary course (insufficient data for boosters after a Moderna primary course)

Supplementary data is not available for this figure.

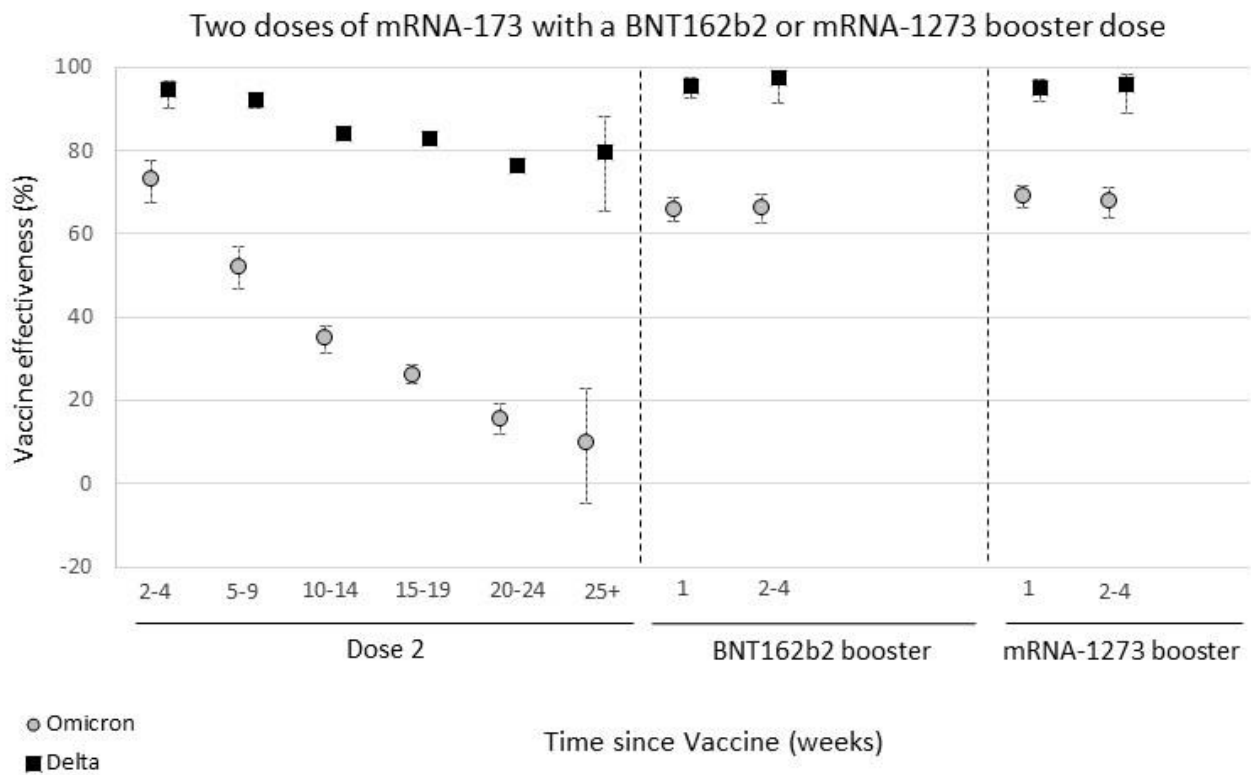
(a)



(b)



(c)



Results for hospitalisations are shown in Table 2. One dose of vaccine was associated with a 43% reduced risk of hospitalisation among symptomatic cases with the Omicron variant, 2 doses with a 55% reduction up to 24 weeks after the second dose and a 40% reduced risk 25 or more weeks after the second dose, and a third dose was associated with a 74% reduced risk of hospitalisation in the first 2 to 4 weeks after vaccination, dropping slightly to a 66% reduction by 10+ weeks after the booster dose. When combined with vaccine effectiveness against symptomatic disease this was equivalent to vaccine effectiveness against hospitalisation of 58% after one dose, 64% 2 to 24 weeks after 2 doses, 44% 25+ weeks after 2 doses, and 92% dropping to 83% 10+ weeks after a booster dose. Combining the periods for the third dose, overall vaccine effectiveness 2+ weeks after the booster was 89% (95% confidence interval 86 to 91%).

Table 2. Hazard ratios and vaccine effectiveness against hospitalisation (all vaccine brands combined). OR = odds ratio, HR = hazards ratio, VE = vaccine effectiveness

Dose	Interval after dose (weeks)	OR v symptomatic disease	HR vs hospitalisation	VE vs hospitalisation
1	4+	0.74 (0.72-0.76)	0.57 (0.38-0.85)	58% (37-72)
2	2 to 24	0.81 (0.8-0.82)	0.45 (0.36-0.56)	64% (54-71)
2	25+	0.94 (0.92-0.95)	0.6 (0.49-0.74)	44% (30-54)
3	2 to 4	0.32 (0.31-0.33)	0.26 (0.19-0.35)	92% (89-94)
3	5 to 9	0.42 (0.41-0.43)	0.29 (0.23-0.37)	88% (84-91)
3	10+	0.5 (0.49-0.51)	0.34 (0.26-0.44)	83% (78-87)

These estimates suggest that vaccine effectiveness against symptomatic disease with the Omicron variant is significantly lower than compared to the Delta variant and wane rapidly. Nevertheless, protection against hospitalisation is much greater, in particular after a booster dose, where vaccine effectiveness against hospitalisation is around 85 to 90%. Further data is needed to estimate the duration of protection against hospitalisation.

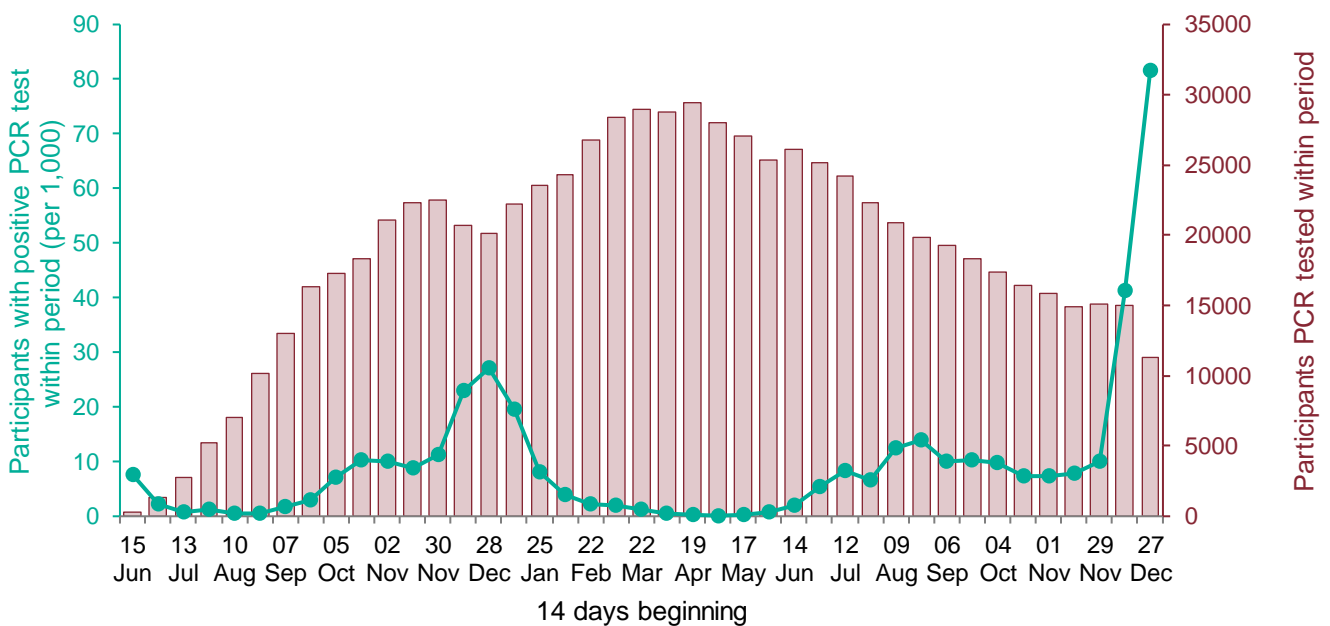
2.6 Update on the SARS-CoV-2 Immunity and Reinfection Evaluation in healthcare workers (SIREN) study

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

Figure 12 describes fortnightly trends in primary PCR positivity and number of participants tested within the SIREN study from 15 June 2020 to 9 January 2022. Since mid-December 2021, there has been a steep increase in the PCR positivity, which continues to increase over the last 2 time periods.

Figure 12. Fortnightly trends in primary PCR positivity and number of participants tested within the SIREN study from 15 June 2020 to 9 January 2022

Supplementary data is not available for this figure.

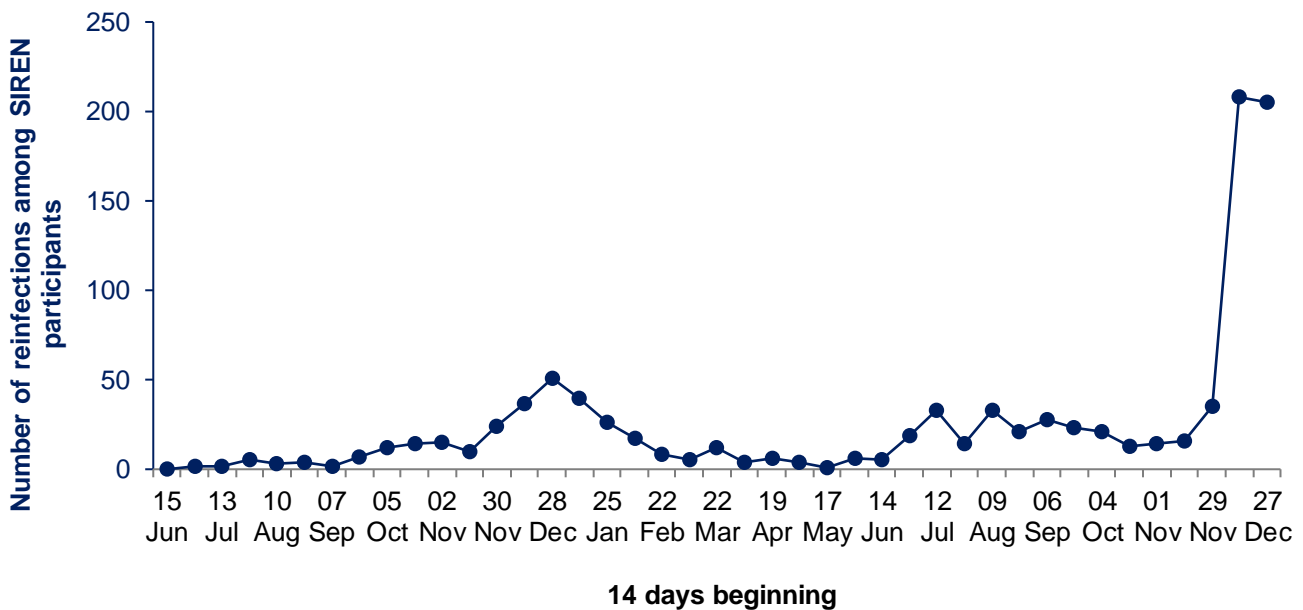


Notes: Data is preliminary and undergoing review. Data at the latest timepoint may be affected by delayed reporting.

Figure 13 shows the counts of reinfection over fortnightly time periods. Reinfections were defined as new PCR positive infections 90 days after a previous PCR positive date or 28 days after antibody positivity consistent with prior infection. The number of reinfections has also rapidly increased over a similar time period as the primary infections (Figure 12), since mid-December 2021 to date.

Figure 13. Number of reinfections in SIREN participants in the UK from 15 June 2020 to 9 January 2022

Supplementary data is not available for this figure.



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

We have conducted a rapid preliminary assessment of protection from Omicron infections (including symptomatic and asymptomatic infections) provided by COVID-19 vaccination and prior SARS-CoV-2 infection in the SIREN cohort between 1 December 2020 and 4 January 2022. We restricted our analysis to 18,464 participants remaining under active follow-up during this period. Participants were categorised by vaccination and prior infection status on 30 November 2021. End of follow-up for individual participants was either event date or date of last negative PCR test up to 4 January 2022. The outcome of interest was a PCR positive primary infection or reinfection (symptomatic and asymptomatic). Reinfections were defined as new PCR positive infections 90 days after a previous PCR positive date or 28 days after antibody positivity consistent with prior infection. Incidence Rate Ratios (IRR) were estimated using a Poisson regression model. These are preliminary estimates and do not account for other factors, including time since vaccination and variable baseline hazards (such as incidence of infections) during this period. It would be anticipated that after accounting for the non-constant

hazards the VE estimates for dose 3 would be slightly higher than those presented from this constant hazards analysis.

By 30 November 2021 11,084 (60%) participants had no previous SARS-CoV-2 infection and 6,974 (40%) participants had prior infection, and most had received 3 doses of COVID-19 vaccine, primarily the BNT162b2 mRNA vaccine.

The results show the increased protective effect of a booster dose of the COVID-19 vaccine, even in those with prior infection, against symptomatic and asymptomatic Omicron infections compared to uninfected unvaccinated participants, who experienced the highest infection risk (table 3). There is an additional incremental benefit from each vaccine exposure, even in those who have had prior infection (confirmed through antibody or detection through asymptomatic and symptomatic testing). This is an early unadjusted output with uncertainty in the estimates which will be iterated and refined in future analyses.

Table 3. Incidence of Omicron infections in the SIREN cohort between 1 December 2021 and 4 January 2022 by vaccination and prior infection status on 30 November 2021 (n=18,464)

Status	Number of participants	Number of days of follow up	Number of infections	Crude incidence rate (per 10,000 person days)	Vaccine Effectiveness (%) (100 x1-IRR)	95% CI
No previous infection and vaccine status on 30 November 2021						
Unvaccinated	87	1,935	21	108.5	Ref	Ref
Vaccinated 2 dose	1,156	24,801	182	73.4	32%	-6%-57%
Vaccinated 3 dose	9,841	225,126	937	41.6	62%	41%-75%
Prior infection and vaccine status on 30 November 2021						
Unvaccinated	255	5,750	35	60.9	44%	4%-67%
Vaccinated 2 dose	1,333	28,255	123	43.5	60%	36%-75%
Vaccinated 3 dose	5,386	121,762	377	31.0	71%	56%-82%

Notes: IRR Incidence Rate Ratios. IRR are not adjusted.

2.7 Reinfections

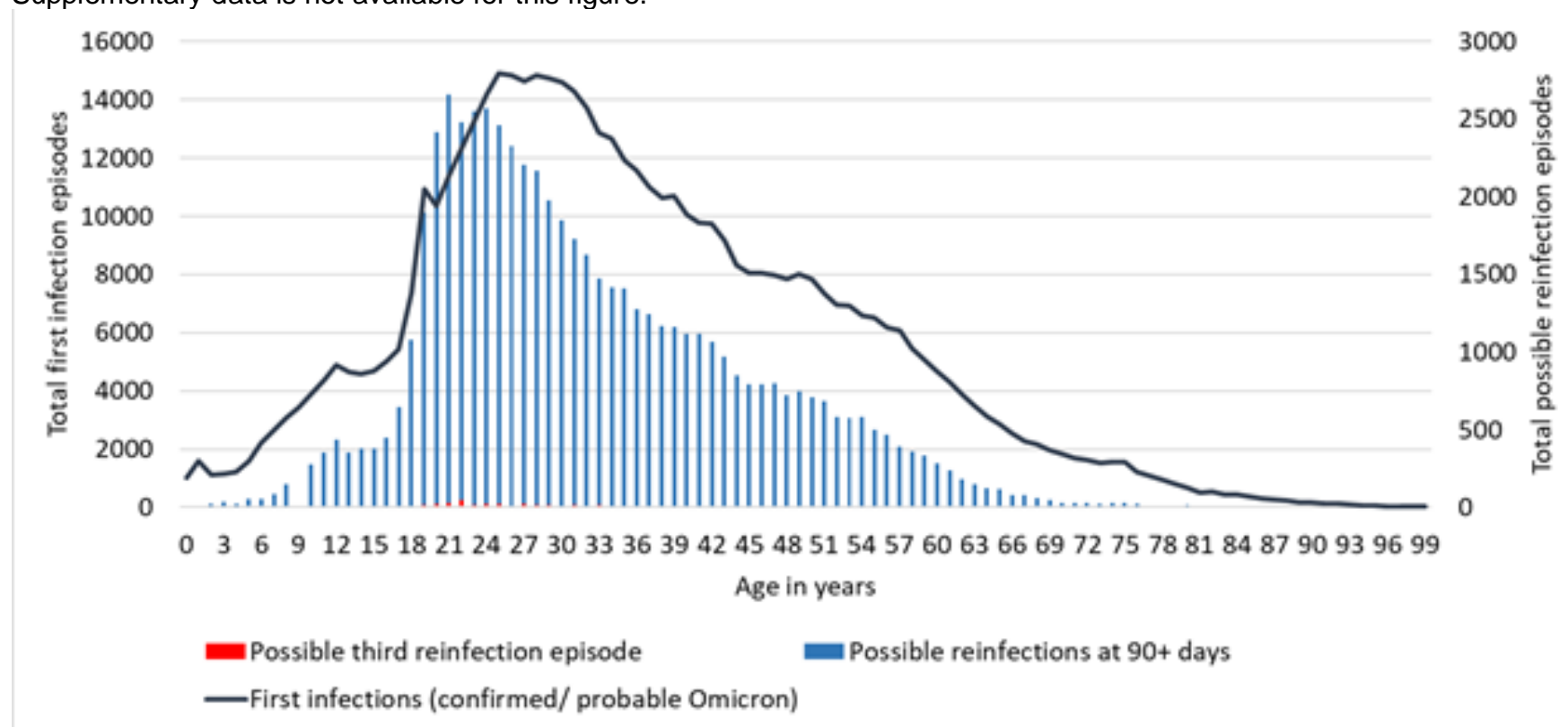
Cases of reinfection (at any interval) extracted on 8 January 2022 were identified amongst all SARS-CoV-2 positive cases in England. As Omicron now accounts for almost all SARS-CoV-2 infection, cases of possible reinfection (an interval between 2 sequential positive SARS-CoV-2 test results of ≥ 90 days) with the Omicron variant are no longer being distinguished. Details on overall reinfections are being published weekly in the [UKHSA National flu and COVID-19 surveillance reports](#) through January. Provisional data for week 2021-52 (beginning 27 December 2021) identified 106,297 possible reinfections accounting for 9.5% of all infections that week.

Reinfection rates are usually generated using the population of previous infections eligible to become a reinfection (that is with a previous positive test result at least 13 weeks (>90 days) earlier). Using this as a measure of current reinfection rates in the population there is now a marked increase in overall reinfection rates, this is disproportionate to the increase in first infections.

The overall age distribution of possible Omicron reinfections with an interval of at least 90 days since the previous episode closely follows the overall distribution of first infections by Omicron through the same time period (confirmed or probable cases in England 1 November to 30 December 2021), Figure 14.

Figure 14. Age profile of first episodes of infection and possible reinfection (90+ day interval between sequential positive test results) with Omicron (1 November to 30 December 2021)

Supplementary data is not available for this figure.



For possible reinfections with a shorter interval between previous infection and confirmed/probable infection with Omicron at 60 to 89 days later, the highest possible reinfection case numbers have been seen in the secondary school age group. This closely follows the age distribution of first episodes in September/October (Figure 15) which means individuals in this age group are the most likely to fit possible reinfection criteria with a shorter interval. The age distribution of cases of possible reinfection with Omicron at 29 to 59 days after a previous infection also reflects the raised numbers of first positive tests in the school age groups through September/ October 2021 but is less well-defined in older ages (Figure 16), possibly as there is an increased likelihood of persistent detection of virus in this shorter interval.

Figure 15. Age profile of first episodes of infection (September to October 2021) and possible reinfections with Omicron (1 November to 30 December 2021) with a 60-to-89-day interval between Omicron positive test result and previous positive test

Supplementary data is not available for this figure.

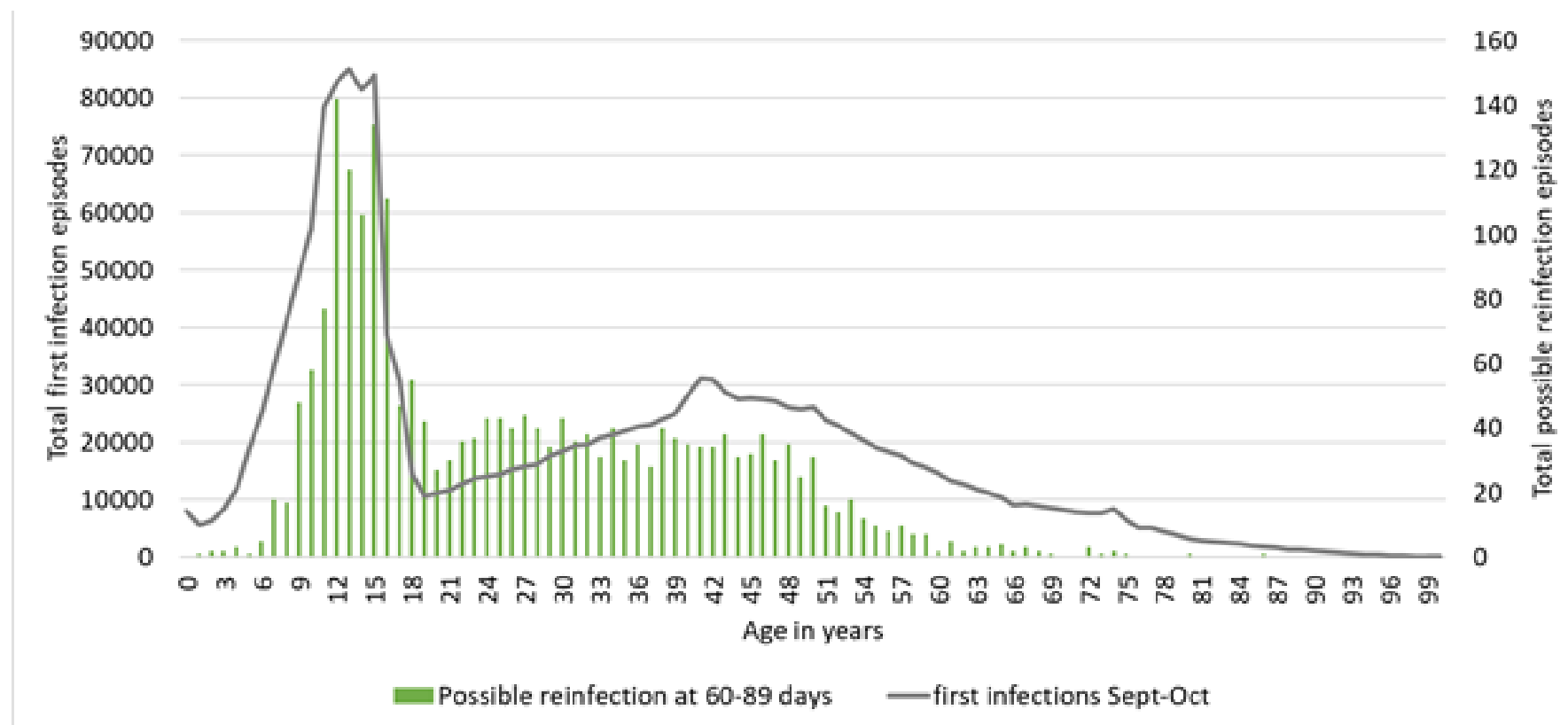
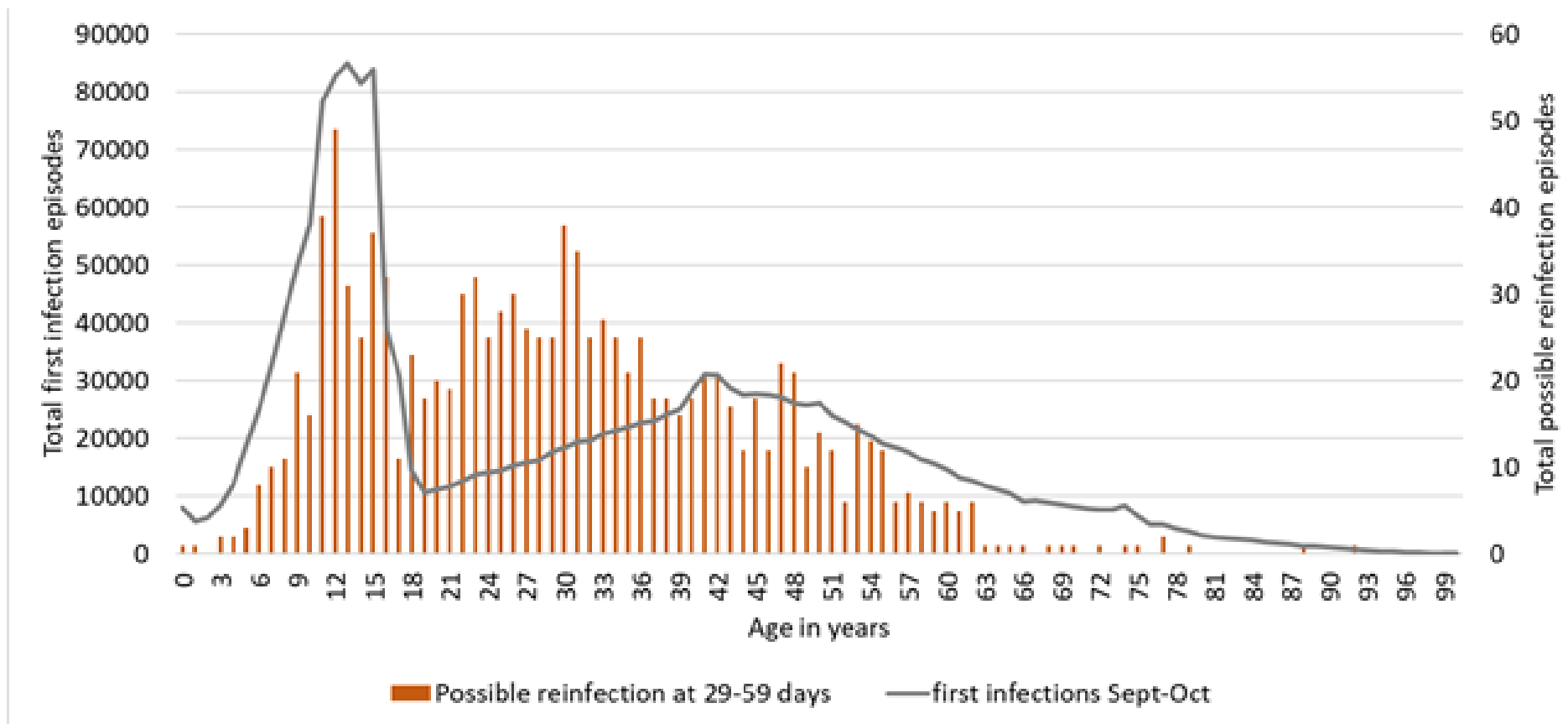


Figure 16. Age profile of first episodes of infection (September to October 2021) and possible reinfections with Omicron (1 November to 30 December 2021) with a 29-to-59-day interval between Omicron positive test result and previous positive test

Supplementary data is not available for this figure.



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 (SGSS), the Secondary Uses Service (SUS) data set, Emergency Care Data Set (ECDS), the UKHSA Case and Incident Management System (CIMS), and the SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) Study.

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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