UK Health Security Agency

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

Technical briefing 52

21 April 2023

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 SARS-CoV-2 variants. This specialist technical briefing contains early data and analysis on emerging variants and findings have a high level of uncertainty. Unless stated otherwise, this technical briefing uses a data cut-off of 17 April 2023 to allow time for analyses.

Due to changes in testing and availability of samples for sequencing, this is the last routine variant technical briefing in this format. The UK Health Security Agency (UKHSA) will continue to publish variant prevalence and growth rates regularly.

Interpreting variant data

Changes to coronavirus (COVID-19) testing came into effect on 1 April 2023 which scale back the use of polymerase chain reaction (PCR) testing and will therefore affect genomic surveillance. These changes include:

- all routine PCR testing outside NHS settings has ended
- in some cases, this is replaced with lateral flow device (LFD) tests, for example symptomatic testing in care homes, hospice, prisons, and other vulnerable settings, and people in the community who testing because they are eligible for therapeutics. Samples tested only by LFD are not available for sequencing.
- some hospital-based PCR testing will also be replaced with LFDs, for example testing individuals primarily for infection control purposes and for patients being discharged into care homes. Samples tested only by LFD are not available for sequencing.
- PCR testing continues to be used by the NHS for patients in hospital to guide clinically directed care.

In addition, at the end of March 2023, the Office for National Statistics COVID-19 Infection Survey (ONS CIS) was paused; the new community surveillance has not yet commenced.

In the absence of the ONS CIS, the samples available for sequencing are limited to hospital admissions and some research studies.

As a result, the profile of sequenced COVID-19 cases continues to be biased toward older people. Between 21 March 2023 and 17 April 2023, the median age of sequenced COVID-19 cases was 78 years old. The most recent data will also be biased towards more severe cases.

Situational assessment

Although surveillance has decreased, current epidemiology suggests a stabilisation in COVID-19 incidence and slow decline in hospitalisations. Sequencing data are currently not fully representative of viruses present in the population, since community surveillance has been paused for review and sequenced cases are older and likely to be more severe. Based on available data, a mix of XBB sublineages are in circulation.

Note is made of XBB.1.16, which shows marked growth in India in association with increasing reported cases, and some evidence of wider international growth. There are insufficient data to comment on severity. Based on the available epidemiological and laboratory data, it is unclear whether this growth will be replicated in the population immunity landscape of the UK. XBB.1.16 is currently at a low prevalence in the UK, showing some early evidence of growth advantage (low confidence due to low sample numbers), and will be monitored.

New data and analysis findings

Sequence variant prevalence (UKHSA designated variants)

From UK sequences collected from 3 April 2023 to 9 April 2023, 44% were classified as V-23JAN-01 (XBB.1.5), 8% V-22DEC-01 (CH.1.1), 4% V-22OCT-01 (BQ.1), 27% V-22OCT-02 (XBB). The remaining sequences (17%) were from lineages or variants representing less than 1% of the total samples, classed as other, or of insufficient quality to assign.

XBB.1.16 was designated as variant V-23APR-01 this week and is not yet present in the UKHSA definitions, however based on Pangolin (Ultrafast Sample placement on Existing tRee (UShER) analysis engine) lineage assignment, as of 14 April 2023 it accounts for 2.3% of UK sequences between 3 April 2023 and 9 April 2023, and falls within V-22OCT-02 in the variant definition designation.

Horizon scanning

XBB.1.16 is now a designated variant (V-23APR-01) as of 19 April 2023, due to increasing international growth. In addition to mutations common to the lineage XBB.1, XBB.1.16 contains 3 additional Spike mutations (E180V, K478R, and S486P). XBB.1.16 is found both in the UK and internationally. As of 14 April 2023, XBB.1.16 made up 2.3% of UK sequences between 3 April 2023 and 9 April 2023.

Since the last technical briefing, XBB.2 has been added as a signal in monitoring due to increasing global sequence numbers, although the total number of sequences available on the Global Initiative on Sharing All Influenza Data (GISAID) database is still small (less than 5,000). Some emerging XBB.2 sublineages such as XBB.2.3.1 have acquired additional mutations associated with previously successful lineages, such as SF486P. We will continue to monitor these newly emerging XBB.2 sublineages.

XBB.1.9.1 and XBB.1.9.2 continue to be monitored as described in the previous technical briefing.

Growth rates

XBB.1.9.2 and XBB.1.16 are the most competitive of the signals in monitoring or designated variants, across both logistic regression and generalised additive models (GAM). From English sequence data, both XBB.1.16 (36.37% GAM) and XBB.1.9.2 (40.62% GAM) have a growth advantage over XBB.1.5. However, XBB.1.16 sample numbers are very low, and results may change as further data becomes available.

XBB.1.16

As of 17 April 2023, 105 XBB.1.16 sequenced cases have been identified in England, with cases located in all regions apart from the North East. There were 5 deaths among these cases.

Global situation

Based on the presence of 3 mutations (T12730A, T28297C, A28447G) as a proxy for XBB.1.16, international counts of sequences uploaded to the GISAID database were identified. The global number of XBB.1.16 sequences started to grow in February 2023, with 3,715 total global sequences reported in 34 countries as of 17 April 2023. The 5 countries reporting the most XBB.1.16 sequences are: India (2,271), USA (446), Singapore (247), Australia (160) and Canada (94).

India, which accounts for 61% of global sequences of XBB.1.16, continues to see proportions rise nationally. Between 20 March 2023 and 3 April 2023, 1,181 of 1,730 (68%) of sequences uploaded to GISAID by India were XBB.1.16.

India has reported a simultaneous rise in COVID-19 cases since mid-February 2023, with new daily cases approximately doubling in each of the past 4 weeks, rising to a peak of 11,109 on 14 April 2023. Since March 2023, daily COVID-19 deaths have been rising.

Reports from Technical Group members

Preliminary analyses from the University of Oxford suggest there is little difference in the neutralisation titres of triple BNT162b2 (Pfizer-BioNTech) vaccinated sera between XBB, XBB.1, XBB.1.5 and XBB.1.16.

1. Surveillance overview

World Health Organization (WHO) nomenclature from 24 January 2022 is incorporated. Table 1 shows the current variants of concern (VOCs), variants (V-date-number), and signals in monitoring detected in the UK incorporating WHO designations with Phylogenetic Assignment of Named Global Outbreak Lineages (Pangolin lineages).

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

Variants of concern	Designated variants (Vs)	Signals in monitoring
VOC-21NOV-01 Omicron (B.1.1.529) sub-lineage BA.1 and descendant lineages	V-22JUL-01 Omicron BA.2.75	XBB.1.9.1
VOC-22JAN-01 Omicron (B.1.1.529) sub-lineage BA.2 and descendant lineages	V-22SEP-01 Omicron BA.4.6	XBB.1.9.2
VOC-22APR-03 Omicron (B.1.1.529) sub-lineage BA.4	V-22OCT-01 Omicron BQ.1	*XBB.2
VOC-22APR-04 Omicron (B.1.1.529) sub-lineage BA.5	V-22OCT-02 Omicron XBB Recombinant (BJ.1 x BM.1.1.1)	
	V-22DEC-01 Omicron CH.1.1	
	V-23JAN-01 Omicron XBB.1.5 Recombinant (XBB plus additional mutations)	
	*V-23APR-01 Omicron XBB.1.16	

* Newly escalated variants or signals in monitoring since the previous technical briefing.

VOCs and other variants (V-date-number) 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. V-21APR-02 (Delta (B.1.617.2 and sub-lineages)) is currently the variant that has not been detected in the UK for the past 12 weeks but has been identified on GISAID internationally. If a VOC or variant 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. Variants and signals in monitoring may also be removed from the grid if they show consistently low growth rates.

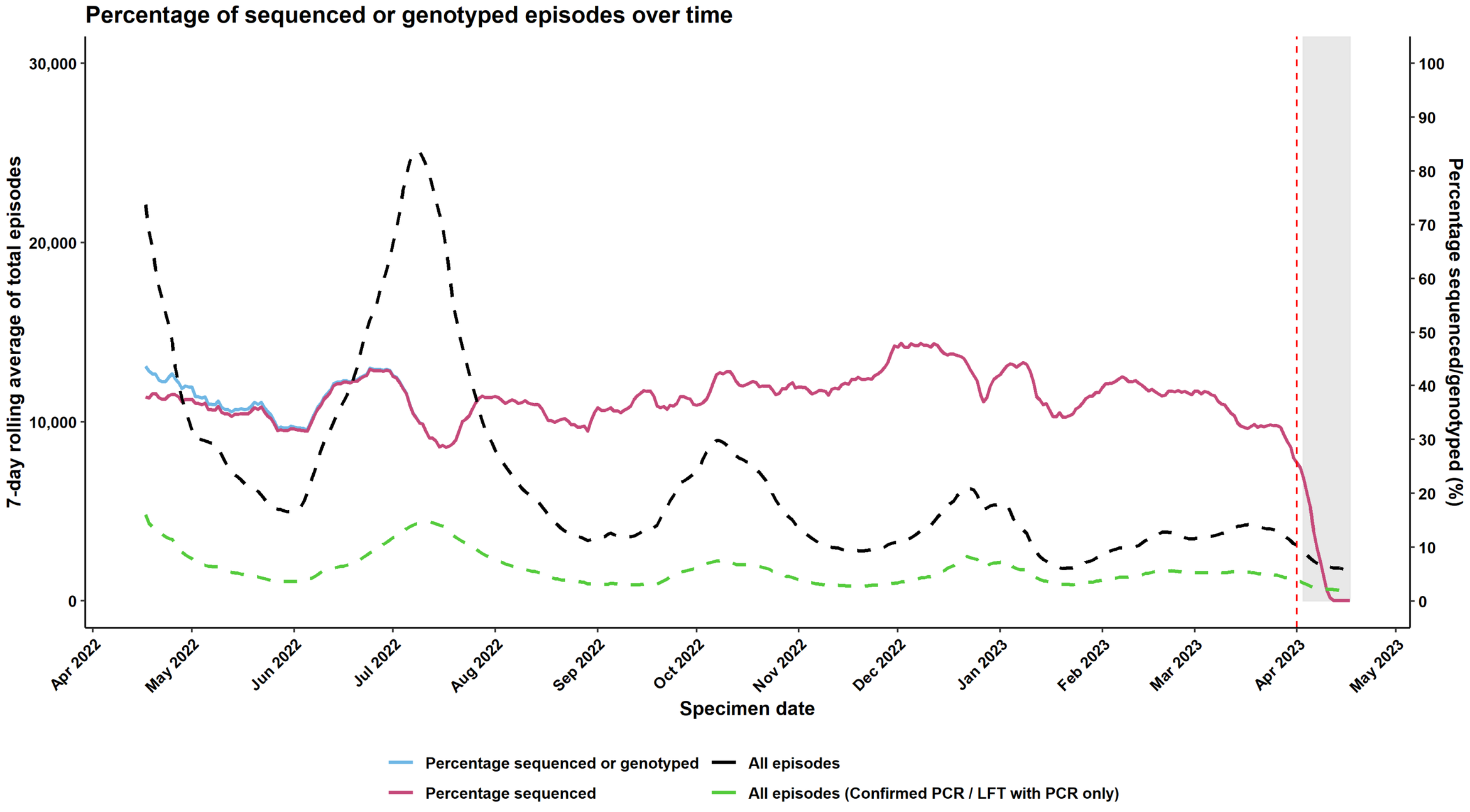
1.1 Sequencing coverage

Figure 1 shows the proportion of PCR-positive COVID-19 cases that have linked to a valid sequencing result (50% of the genome with sufficient read coverage) or genotyping PCR result over time. Figure 2 shows the proportion of cases sequenced and genotyped amongst individuals who tested positive whilst in hospital.

The data on people who tested positive whilst in hospital is derived from the Hospital-Onset COVID-19 data set (HO-COVID), which links confirmed COVID-19 episodes to admissions data from the Emergency Care Data Set (ECDS) and Secondary Uses Service (SUS) as provided by NHS Digital (Bhattacharya and others, 2021). The vertical dashed red line indicates the 1 April 2023 when PCR testing was scaled back and limited to patients in NHS hospitals and some research studies.

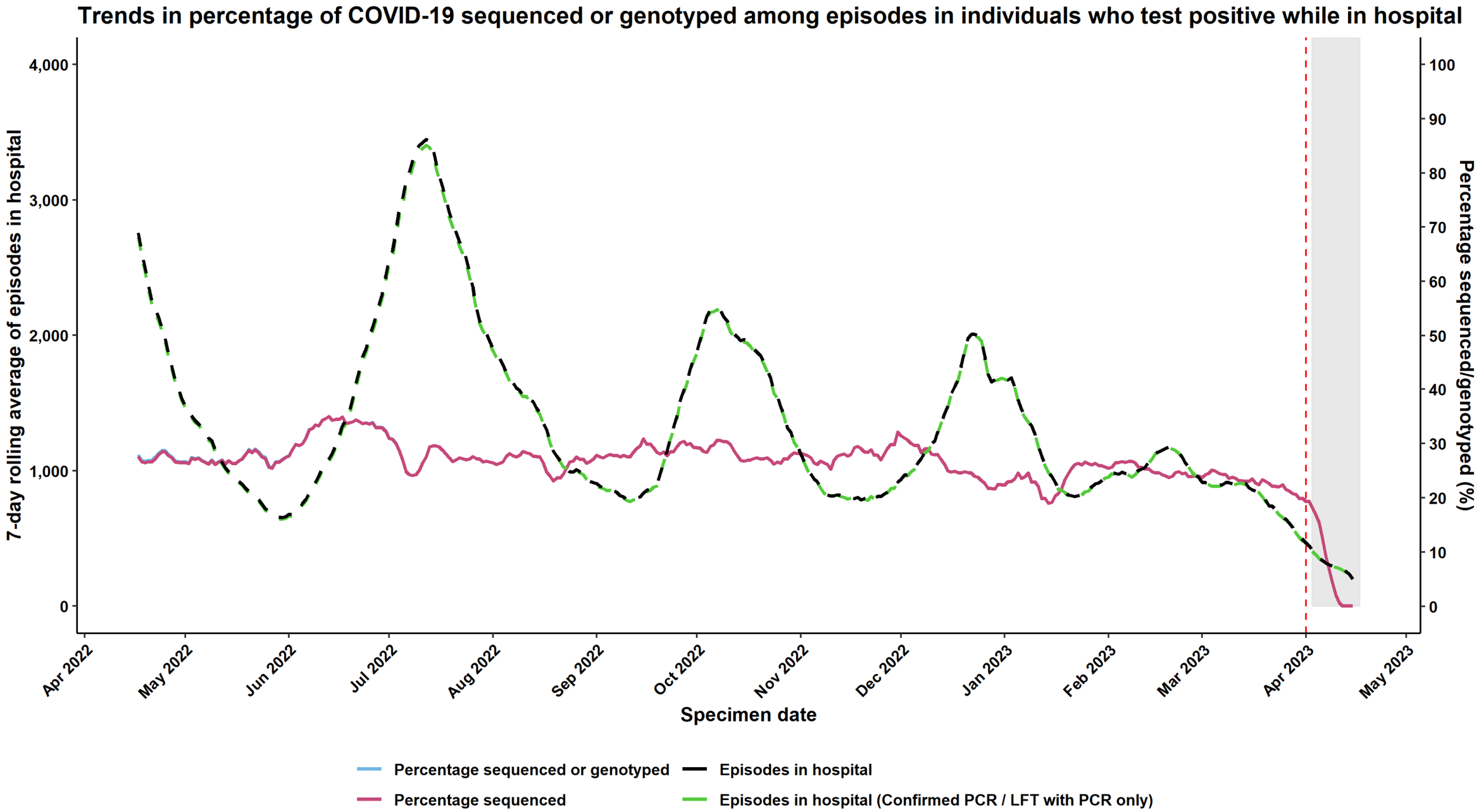
Currently, the sequencing strategy prioritises hospitalised cases, patients who are receiving specific antiviral therapy, and national core priority studies.

Figure 1. Coverage of sequenced cases with a valid result and genotyping over time (17 April 2022 to 17 April 2023)



Cases where the individual only tested using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. The dashed red vertical line denotes changes in PCR testing in April 2023. The data used in this graph can be found in the accompanying spreadsheet.

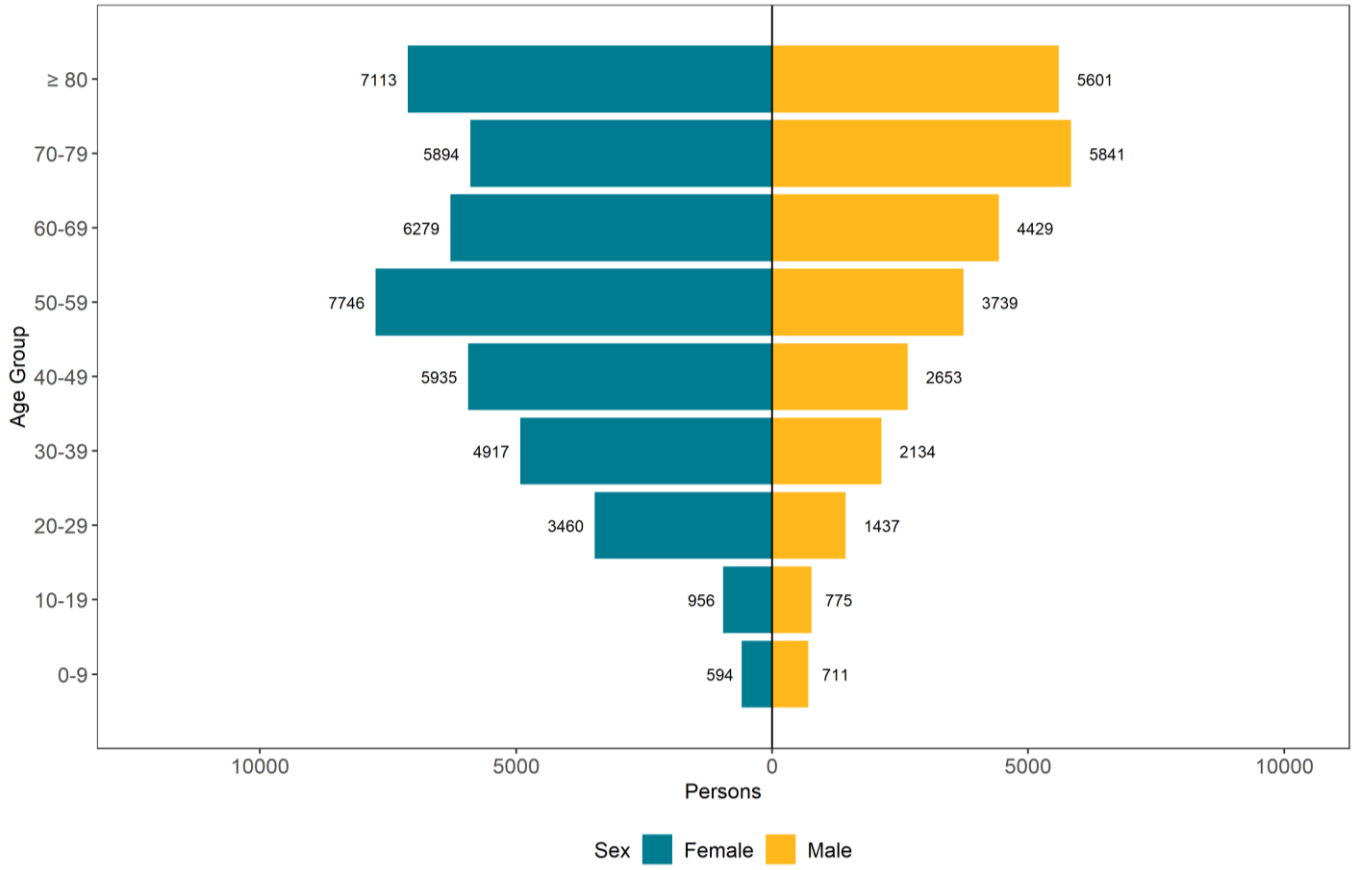
Figure 2. Coverage of sequencing with valid result and genotyping for cases who test positive in hospital (17 April 2022 to 17 April 2023)



Cases where the individual only tested positive using a lateral flow device are excluded. Grey shading was applied to the previous 14 days to account for reporting delays in sequencing data. The dashed red vertical line denotes changes in PCR testing in April 2023. The data used in this graph can be found in the accompanying spreadsheet.

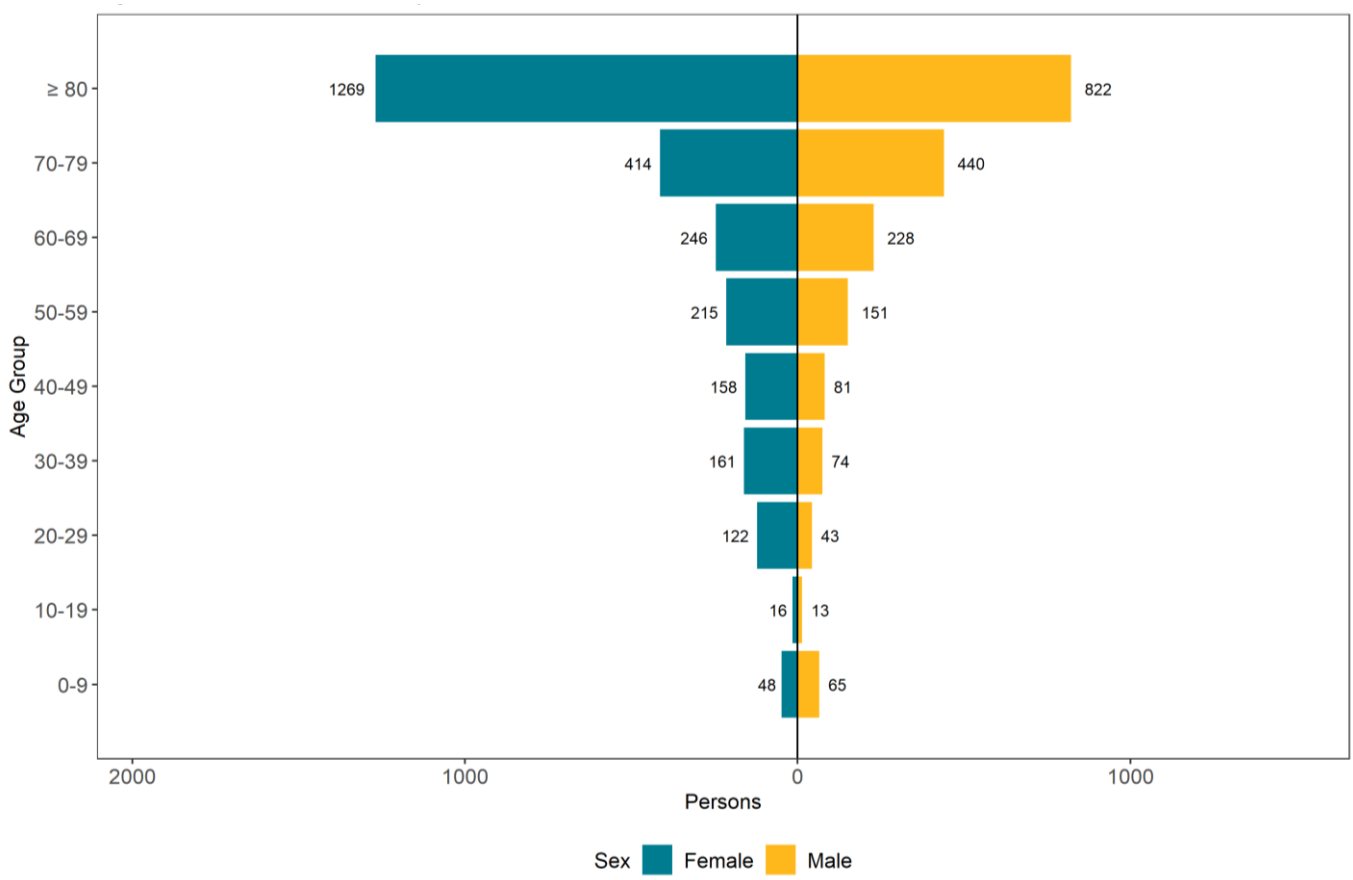
Due to prioritisation of samples for PCR testing and sequencing from hospitalised patients and care homes, sequenced cases in England are significantly older than reported cases. Between 21 March 2023 and 17 April 2023, the median age of reported COVID-19 cases was 60 years old. However, during the same period, the median age of sequenced COVID-19 cases was 78 years old (Figures 3a and 3b).

Figure 3a. Age-sex distribution of all COVID-19 cases for the past 4 weeks in England (21 March 2023 to 17 April 2023)*



* Excludes 290 cases with no age and/or sex information.

Figure 3b. Age-sex distribution of sequenced COVID-19 cases for the past 4 weeks in England (21 March 2023 to 17 April 2023)*



* Excludes 68 cases with no age and/or sex information.

The data used in this graph can be found in the accompanying spreadsheet.

1.2 Variant prevalence

The prevalence of different UK Health Security Agency (UKHSA)-designated variants amongst sequenced cases in England is presented in Figure 4. UKHSA designated variants are those assigned for more comprehensive epidemiological studies and may incorporate multiple sub-lineages. If a sub-lineage of an existing variant is also declared as a variant, it will be removed from the prevalence of the parent lineage (for example, V-22OCT-01 does not form part of the prevalence of V-22APR-04 in Figure 4).

A variant definition for V-23APR-01 (XBB.1.16) is in development, and will be available in due course, but is not currently identifiable in Figure 4. V-23APR-01 sequences are included under the V-22OCT-02 (XBB) classification in this data set.

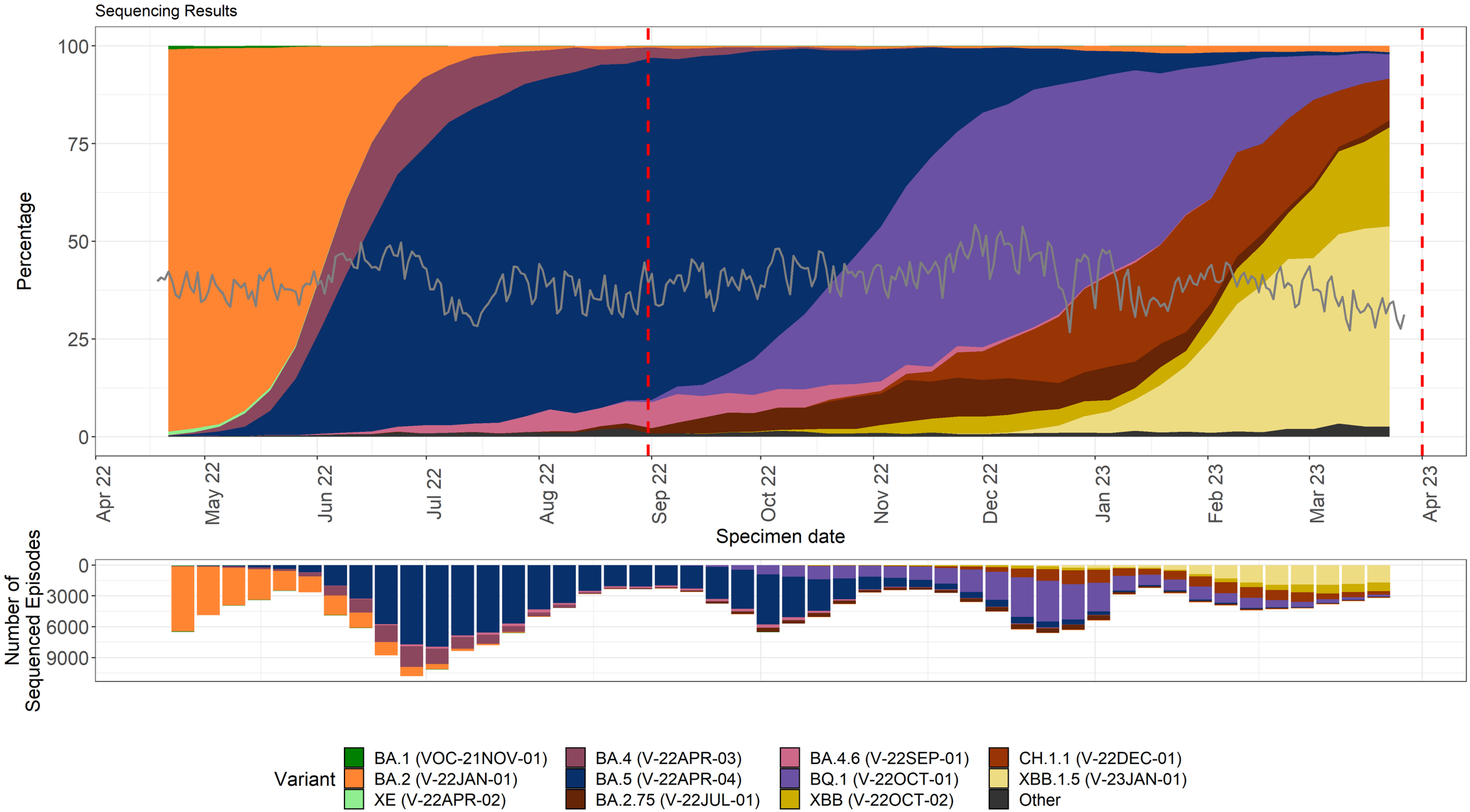
The number of sequenced cases has steadily declined from 600 per day in February 2023 to 400 per day at the end of March 2023.

To account for sequencing delays, we report the proportion of variants from sequenced episodes between 27 March 2023 and 2 April 2023. Of those sequenced in this period, 53.1% were classified as V-23JAN-01 (XBB.1.5), 25.2% as V-22OCT-02 (XBB), 10.3% as V-22DEC-01 (CH.1.1), 5.3% as V-22OCT-01 (BQ.1), 1.7% as V-22JUL-01 (BA.2.75), 1.7% as V-22JAN-01 (BA.2), 0.5% as V-22APR-04 (BA.5), and 2.4% as Other.

The prevalence of lineages amongst UK sequences by Pangolin designation is presented in Figure 5. This provides a greater resolution showing the breakdown of sub-lineages. Lineages are shown if there are more than or equal to 5,000 sequences since 7 November 2022 or if they are more than or equal to 1% of sequences within a single week over the last 6 weeks. Lineages that do not meet these criteria are combined with their parent lineage (for example, BA.2.4 is combined with BA.2).

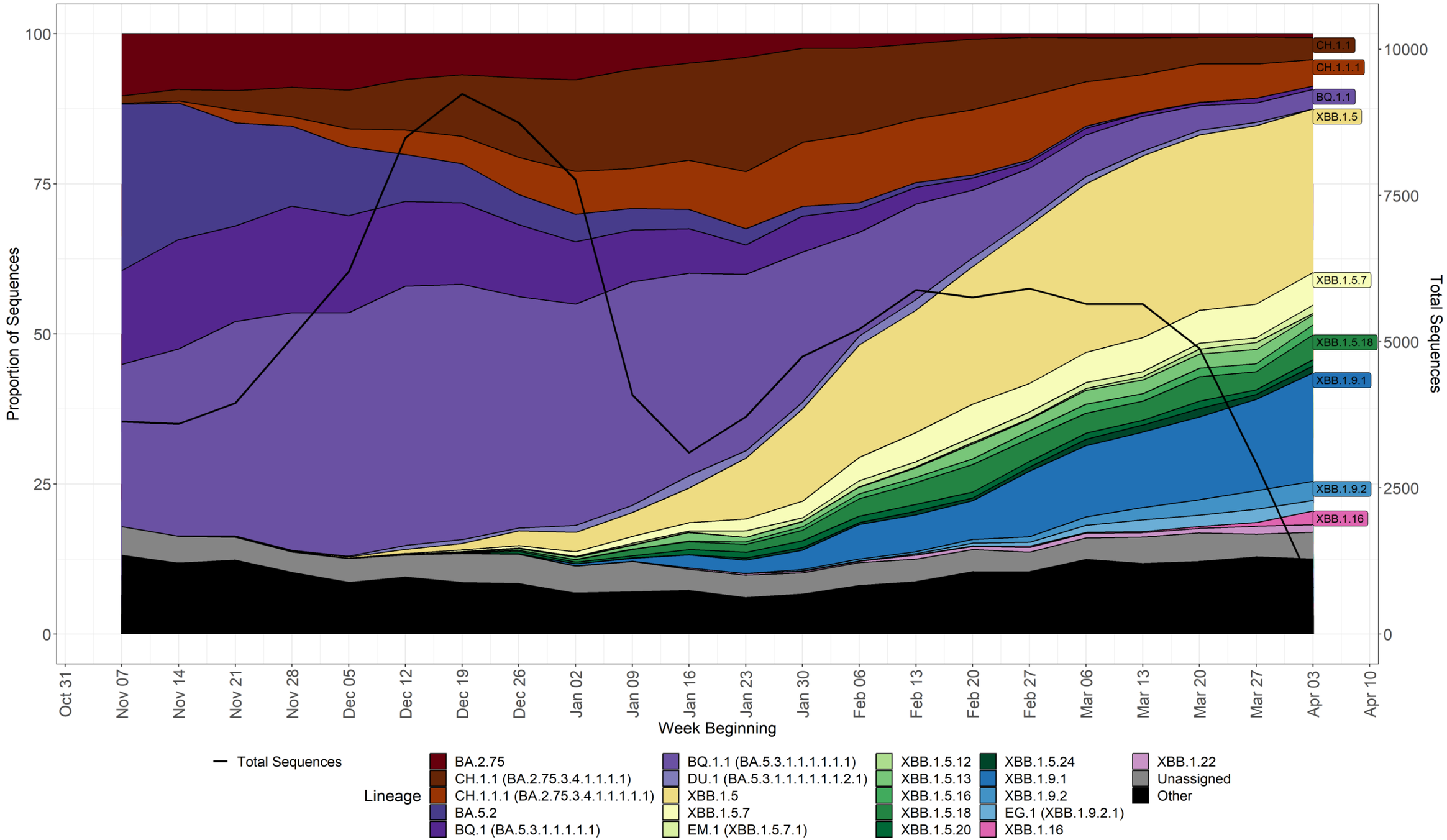
The lineages have been assigned using the accurate Ultrafast Sample placement on Existing tRee (UShER) mode and version 1.18.1.1 of the Pangolin data. The UShER mode identifies lineages based on their phylogenetic placement, rather than by specific mutation profiles. This allows sequences with reduced coverage to be assigned to lineages and easier separation of sub-lineages that are distinguished by a small number of mutations.

Figure 4. Variant prevalence (UKHSA designated variant definitions only) of available sequenced cases for England from 18 April 2022 to 2 April 2023



The grey line indicates proportion of cases sequenced. The first red dashed line denotes the start of England's 'Living with COVID' plan at the start of April 2022 and the second indicates the pause of asymptomatic testing for high-risk settings at the end of August 2022. The dashed red vertical line denotes changes in PCR testing in April 2023. The data used in this graph can be found in the accompanying spreadsheet.

Figure 5. Prevalence of Pangolin lineages in the UK with sequence data with a specimen date from week beginning 7 November 2022 to week beginning 3 April 2023, as of 18 April 2023



The total number of valid sequence results per week is shown by the black line. The ‘Other’ category in this plot contains all lineages that do not meet the relevant criteria after combining smaller sub-lineages. ‘Unassigned’ are sequences that could not be assigned a lineage by Pangolin. Lineages present in at least 2% of sequences in the most recent week are labelled to the right of the plot. The data used in this graph can be found in the accompanying spreadsheet.

2. Variant modelling

Multiple models are used to estimate the growth advantage of emerging lineages relative to currently circulating lineages. In previous versions of this report, samples from the ONS CIS were modelled. This survey was paused on 1 April 2023. Going forward, sequenced Pillar 1 cases (primarily positive tests conducted in hospital) are modelled as this is the best-defined cohort available for growth rate modelling. As before, only samples collected in England were used.

Previous issues of this briefing have included a multinomial model which relied on ONS samples. In the absence of the survey, this method has been paused. Two other models are still reported: logistic regression and generalised additive models, which are fitted with respect to a geographically matched data set reflecting growth with respect to the mixture of lineages co-circulating with a given variant.

Logistic regression and generalised additive models

The growth rate is estimated by logistic regression of a variant or lineage of each sample unit on time of sample selection, relative to all other variants. To characterise how growth rates change through time, a generalised additive model (GAM) is also fitted which allows the growth rate to vary over time. To adjust for geographic variation in case growth rates and differences in sampling intensity, lineage growth rates were estimated relative to a geographically matched sample of genomes. A logistic growth rate of zero would indicate no difference in growth rates between a given lineage and other variants. All reported growth rates are in logistic units and reflect growth in frequency of a given variant, not growth in cases or numbers of samples.

Growth rates were based on sequences sampled through Pillar 1 testing in England (Table 2). The sampling range for both logistic regression and generalised additive models is from 17 October 2022 to 3 April 2023. Both XBB.1.16 (36.37% GAM) and XBB.1.9.2 (40.62% GAM) have a growth advantage over XBB.1.5. However, XBB.1.16 sample numbers are low, and results may change as further data becomes available.

Table 2. Growth rate (GR) of variants and signals under monitoring as of 3 April 2023*

Lineage*	English Pillar 1 sequences used in logistic regression and GAM	GAM Estimated lineage prevalence in England	Generalised additive model most recent GR (1/week)	Logistic regression GR (1/week)
XBB.1.16	49	0.89% (95% CI: 0.46 to 1.72)	36.37% (95% CI: 27.31 to 45.43)	44.75% (95% CI: 8.12 to 81.38)
XBB.1.9.1	1,773	12.22% (95% CI: 8.69 to 16.93)	-11.09% (95% CI: -21.49 to -0.69)	7.09% (95% CI: -0.14 to 14.32)
XBB.1.9.2	265	7.88% (95% CI: 6.02 to 10.25)	40.62% (95% CI: 37.81 to 43.43)	41.68% (95% CI: 26.49 to 56.87)
XBB.1.5 (V-23JAN-01)	7,647	56.12% (95% CI: 50.16 to 61.92)	0.31% (95% CI -6.1 to 6.71)	5.13% (95% CI: -0.06 to 10.33)
CH.1.1 (V-22DEC-01)	4,974	10.12% (95% CI: 7 to 14.42)	1.16% (95% CI: -12.5 to 14.81)	-10.58% (95% CI: -18.62 to -2.53)
XBB (V-22OCT-02)	1,011	4.4% (95% CI: 2.79 to 6.87)	3.2% (95% CI: -8.66 to 15.06)	9.22% (95% CI: 7.12 to 11.31)
BQ.1 (V-22OCT-01)	14,121	3.32% (95% CI: 2.26 to 4.86)	-29.48% (95% CI: -41.66 to -17.3)	-34.27% (95% CI: -35.35 to -33.19)
BA.2.75 (V-22JUL-01)	1,963	1.4% (95% CI: 0.7 to 2.77)	10.74% (95% CI: -10.61 to 32.09)	-10.62% (95% CI: -35.59 to 14.34)

* Listed parent lineages include all sub-lineages, other than those explicitly modelled.

** Sampling range for both logistic regression and generalised additive models (GAM) is from 17 October 2022 to 3 April 2023.

CI = confidence intervals

3. Newly designated variant: V-23APR-01 (Omicron XBB.1.16)

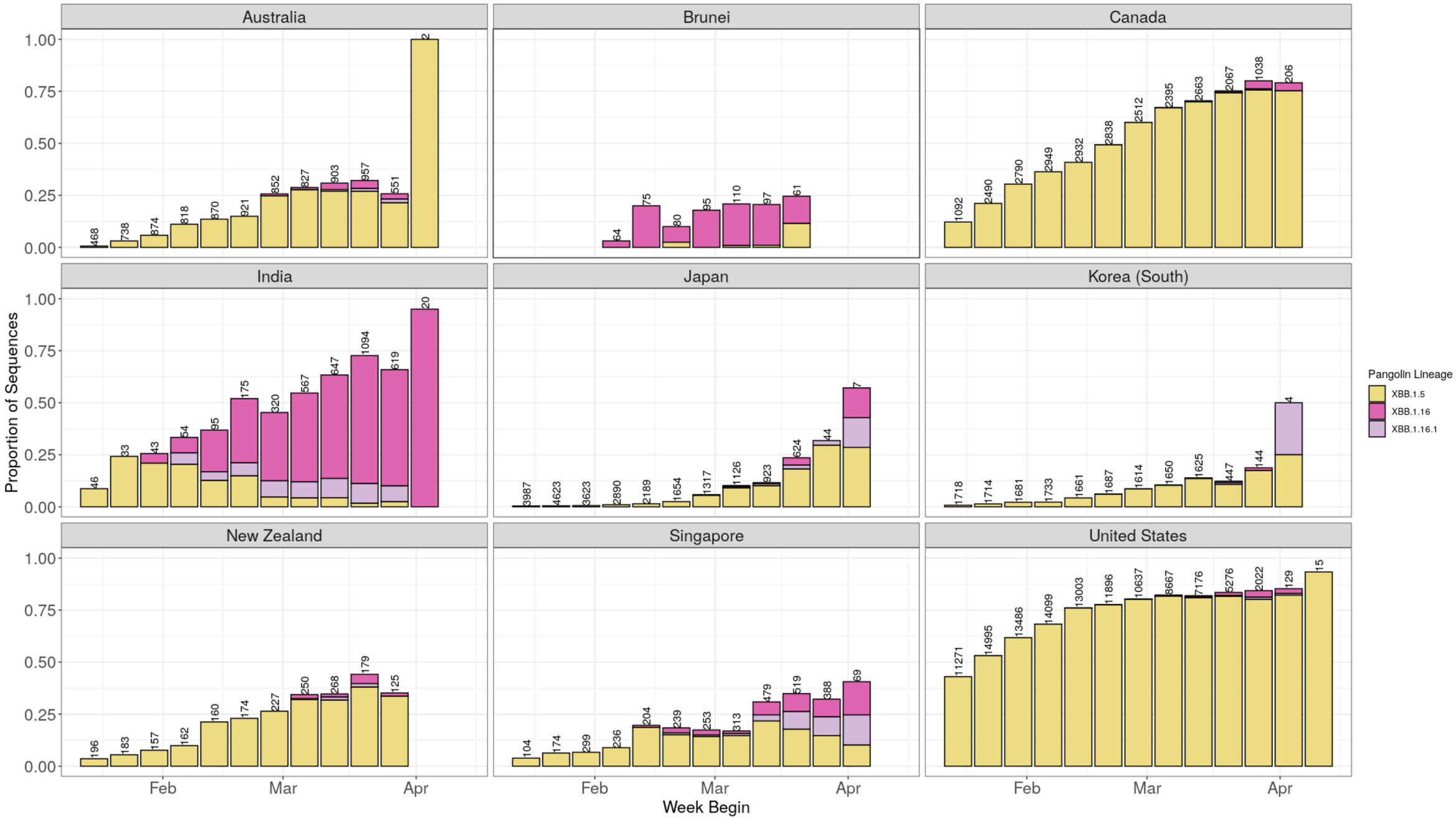
XBB.1.16 was first raised as a signal in monitoring on 6 March 2023 as part of horizon scanning due to its mutational profile. It was subsequently raised from a signal in monitoring to variant V-23APR-01 following a Variant Technical Group meeting on 19 April 2023. V-23APR-01 has been designated as a variant due to international case numbers. Relative to XBB.1 it has acquired Spike mutations E180V, K478R, and S486P as well as ORF9b:I5T, ORF9b:N55S, ORF1a:L3829F, ORF1b:D1746Y. Since then, there has been a rapid increase in sequences internationally, particularly from India which has uploaded 61% of the international sequences as of 14 April 2023. A full variant definition is in progress, and will be available on GitHub in due course.

As of 17 April 2023, there are 135 XBB.1.16 sequences in the UK (England (120), Wales (8), Scotland (5), and Northern Ireland (2)).

Analysis of international data from GISAID using Pangolin (UShER analysis engine) as of 14 April 2023 identified 3481 XBB.1.16 sequences from 28 countries, including the UK. The countries submitting the most XBB.1.16 sequences are India (2,115), the United States of America (USA) (357), Singapore (247), Australia (126) and Canada (94).

The proportion of sequences that have been uploaded to GISAID that are called as XBB.1.5 or XBB.1.16 (including sub-lineages) by Pangolin (UShER analysis engine) is shown in Figure 6 for the 9 countries with the highest total number of XBB.1.16 sequences. This data trend currently suggests that countries who have uploaded a higher proportion of XBB.1.5 sequences in previous weeks are uploading a smaller proportion of XBB.1.16 sequences (for example, the USA) compared to countries that have not previously uploaded a high proportion of XBB.1.5 sequences (for example, India).

Figure 6. Proportion of sequences from GISAID (where collection date complete) classified as XBB.1.5, XBB.1.16 and XBB.1.16.1 by country



Data from the 9 countries submitting the highest total XBB.1.16 sequences are shown. Sequence and date information collected from GISAID. Lineage data generated by Pangolin (UShER analysis engine). Data as of 14 April 2023. Supplementary data is not available for this figure.

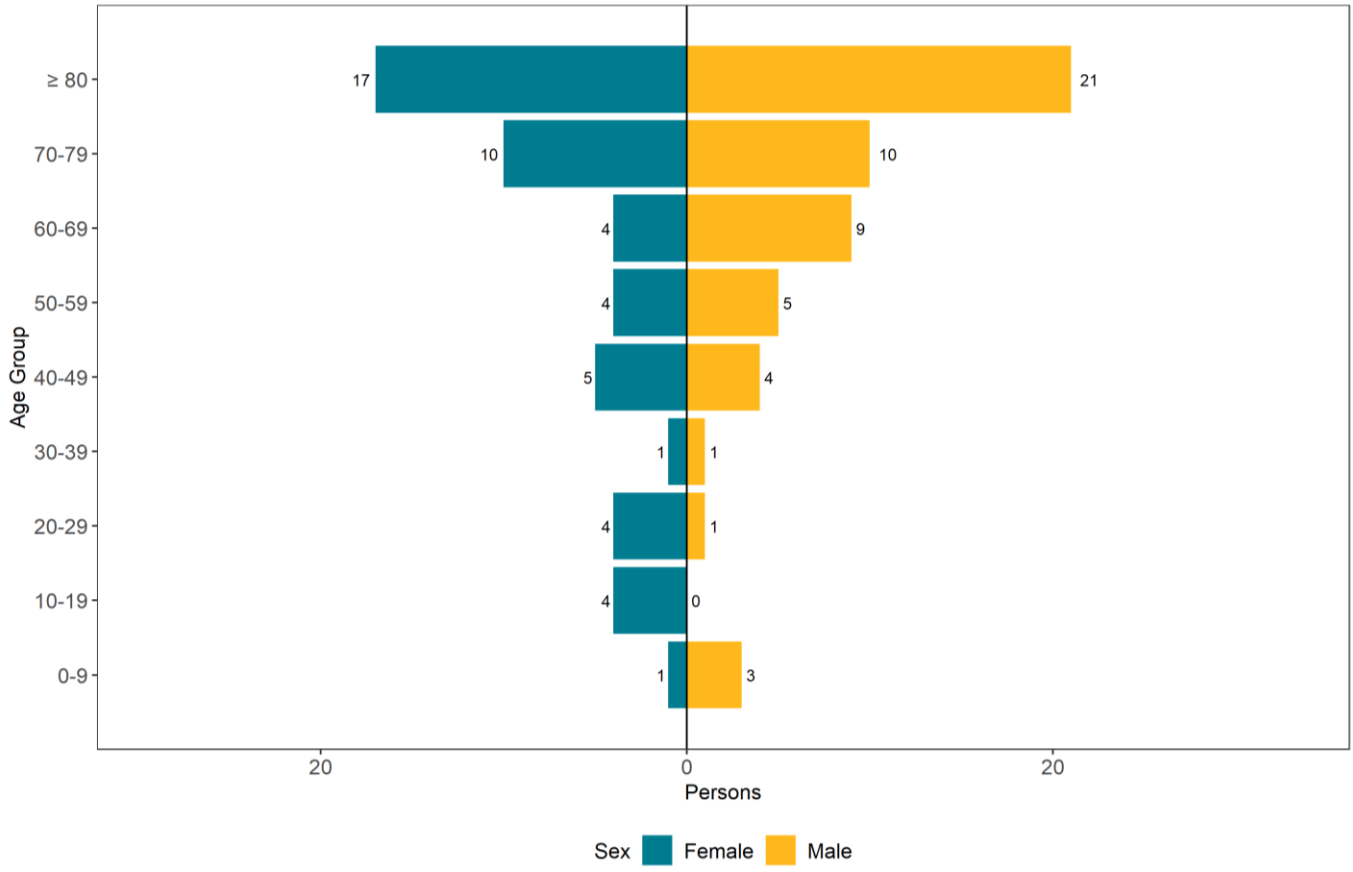
3.1 Epidemiology

As of 17 April 2023, 105 XBB.1.16 sequenced cases have been identified in England. There were 5 deaths among these cases.

The median age of cases was 74 years old. Fifty-four cases were male and 50 cases female (Figure 7). There have been cases in each region of England, with the exception of the North East, with the most cases being resident in London (30) and the North West (22) (Figure 8).

There is insufficient data to calculate severity or vaccine effectiveness compared to other variants circulating.

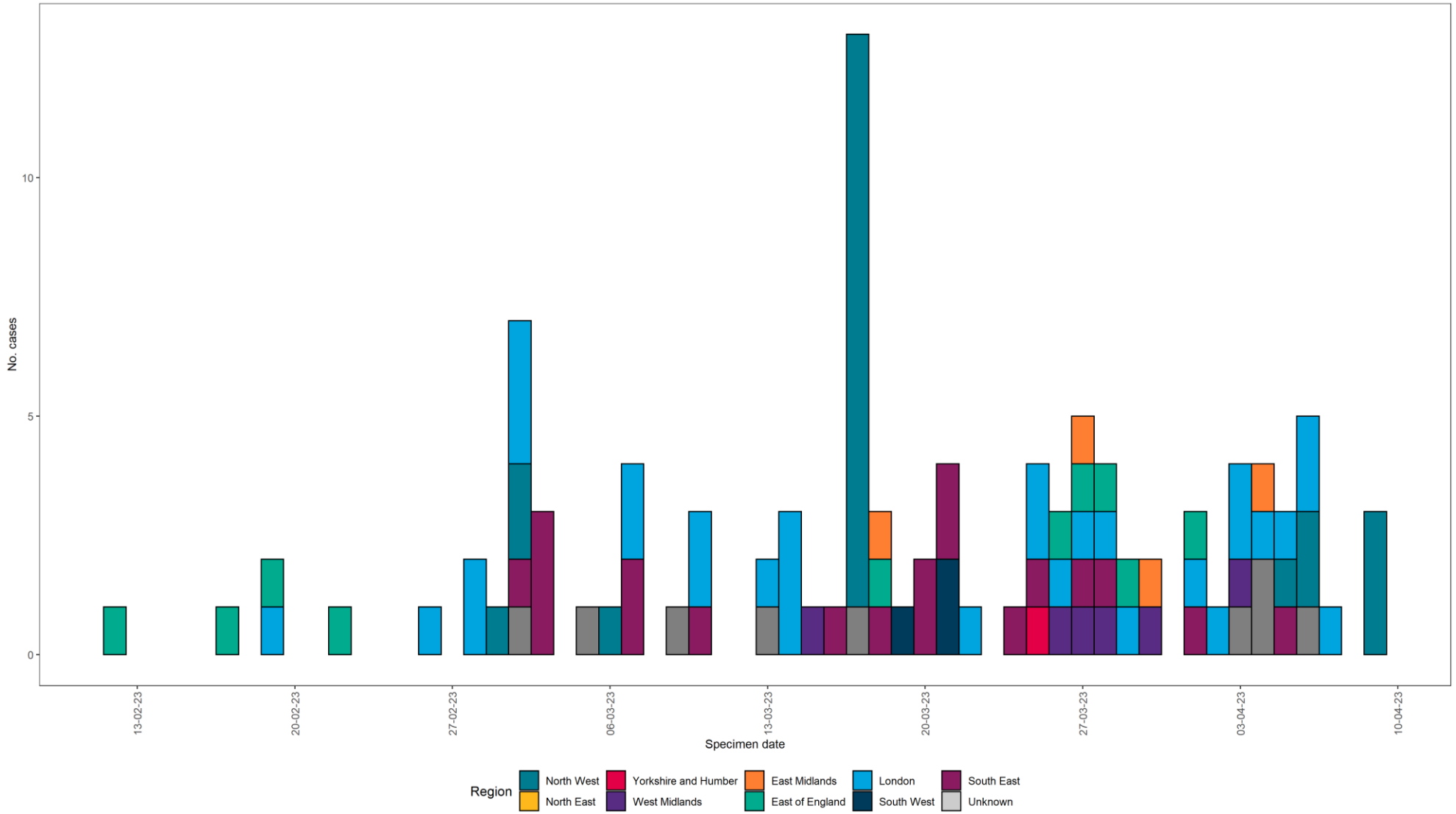
Figure 7. Age-sex breakdown of XBB.1.16 cases in England as of 17 April 2023*



* Excludes 1 case with no age and/or sex information.

The data used in this graph can be found in the accompanying spreadsheet.

Figure 8. Epicurve of XBB.1.16 cases by UKHSA region as of 17 April 2023*



* Excludes 9 cases with no region information. Supplementary data is not available for this figure.

Published information on variants

On 1 April 2022 UKHSA amended its variant classification system. Further details are available in technical briefing 39.

SARS-CoV-2 routine variant data update covers surveillance data and sequencing coverage data on all other variants of concern (VOCs) and variants under investigation (VUIs) up to 25 March 2022.

The collection page gives content on variants, including previous technical briefings. Technical briefings are published periodically.

The Public Health England (PHE) repository from 5 March 2021 contains the previous genomic definitions for VOCs and VUIs.

Sources and acknowledgments

Data sources

Data used in this investigation is derived from the Cloud Infrastructure for Microbial Informatics (CLIMB) and UKHSA genomic programme data set, ONS COVID-19 Infection Survey, the UKHSA Second Generation Surveillance System, the Secondary Uses Service data set, Emergency Care Data Set, the UKHSA Case and Incident Management System and the Global Initiative on Sharing All Influenza Data (GISAID).

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About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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